

# The Indian Journal of Tuberculosis

---

---

Vol. XXIII

New Delhi, July 1976

No. 3

---

---

## THE XXXTH NATIONAL CONFERENCE

The 30th National Conference on Tuberculosis and Chest Diseases was inaugurated by Shri S. Obul Reddy, Governor of Andhra Pradesh, in the Auditorium of the Institute of Medical Sciences, Osmania Medical College, Hyderabad, on November 8, 1975. Over a thousand persons who attended the inaugural session included 300 delegates from different parts of India. In his inaugural address, the Governor suggested the creation of a Ministry of National Insurance for purposes of rendering financial help not only to those who suffer from tuberculosis but from all diseases. Shri K. Rajamallu, Minister of Health, Andhra Pradesh, gave a bird's-eye view of the health facilities available in the State. Dr. S.N. Mathur accorded a warm welcome to the visitors and delegates. The Governor presented the T.A.I. Gold Medal to Dr. N.L. Bordia, the Wander-T.A.I. award to Dr. S.P. Pamra and the Benjamin Gold Medal instituted by the Andhra Pradesh TB Association to Dr. K.N. Rao.

In his Presidential Address, Dr. H.B. Dingley commented on the tuberculosis control programme, epidemiological assessment, BCG vaccination, case-finding, chemoprophylaxis, health education, notification of tuberculosis, TB in industry, treatment programme, role of surgery in tuberculosis, medical education, research, etc.

The Scientific sessions spread over five days included a Symposium on "National TB Control Programme" and sessions on "Primary Drug Resistance", "Follow-up of sputum negative X-ray positive cases in pulmonary tuberculosis", "Para-medical Services", "Pyogenic infections of the Lung", "Amoebic infections of the lung and pleura", "Chemotherapy" and some assorted papers. A session on TB Seal Sale Campaign provided a forum for representatives of State Associations to discuss this important central programme of TB Associations.

Delegates had the benefit of listening to four interesting talks during the conference days. Dr. K.N. Rao in his Benjamin Oration covered a wide range of interesting aspects of tuberculosis work supported by slides and diagrams. In his Wander-TAI Oration Dr. S.P. Pamra took the audience through different facets of chemotherapy, its rationale, current practices and shortfalls and the promise it holds for the future. Dr. C.W.L. Jeanes of Canada and Professor G. Daddi of Italy, the two distinguished guests, spoke in their inimitable way on "Medical Progress and anti-Progress" and "Primary Resistance to mycobacteria in TB patients" respectively.

Drs. P.R. Sen of Calcutta and Bhagat Singh Alag of Jabalpur were re-elected as representatives of the conference on the Central Committee of Tuberculosis Association of India.

Dr. D. Umapathy Rao, Honorary Secretary, TB Association of Andhra Pradesh, Drs. A.B. Ramachandra Reddy, C. Srinivasa Rao, O.A. Sarma and a Reception Committee made arrangements for the conference. A souvenir was brought out on the occasion. The Railway Board allowed concession for rail travel for the delegates to attend the conference. The Governor gave a reception to the delegates, who were also entertained to cultural shows on two evenings during the conference.

A notable feature of the conference was the enthusiasm shown in the deliberations by younger workers and the spirit of fellow-feeling extended by some of India's distinguished and senior most tuberculosis workers—like Drs. R. Viswanathan, B.K. Sikand, K.N. Rao, P.K. Sen and N.L. Bordia to mention a few whose participation in the deliberations provided a certain measure of “pep” to the conference. All the sessions were very well attended and delegates left Hyderabad for their respective places with the satisfaction that the conference provided for them extremely interesting fare well worth the time, energy and money they spent to attend the conference in Hyderabad. Some of the important papers presented at the conference and summaries of the other papers are given in the following pages.

## Dr. NANDLAL BORDIA

Born in Udaipur on 11.1.1910, Dr. N.L. Bordia passed his high school in 1926, L.C.P.S. (Bombay) in 1930, M.B.B.S. (Madras) in 1936 and M.D. (Madras) in 1941. He started his career as Sub-Assistant Surgeon in Indore



Dr. NANDLAL BORDIA

in 1930 and became an Assistant Surgeon in 1936 and Resident Medical Officer, TB Sanatorium at Rao. From 1939 to 44 he was District Medical Officer and during 1944-1959 he served as Medical Officer in-Charge of the TB Clinic, Rao Sanatorium, and as TB specialist in the M.R. TB Hospital. He was also incharge of BCG Vaccination, and Reader in TB, M.G.M. Medical College, Indore. In 1959 he was appointed as the Director of the National Tuberculosis Institute, Bangalore, which post he held till 1962. He was appointed as the Adviser in TB to the Government of India in 1962 and held this post till November 1969. During this period he also acted as the Technical Adviser to the Tuberculosis Association of India.

After retirement from Central Government service Dr. Bordia was appointed Emeritus Professor of Tuberculosis and nominated as Adviser-in-TB to the Government of Madhya Pradesh. He had two Fellowships, one in 1947-48 and the other in 1954-55, both to U.S.A. He was consultant in the W.H.O. H.Q. Office in Geneva from June to December 1955. He founded the TB Relief Society in 1949 and is the author of the Text-Book on TB in Hindi published in 1973.

In recognition of his meritorious services to the anti-TB cause, he was awarded "Padma Shri" by the Government of India in 1973 and the Tuberculosis Association of India awarded its Gold Medal to him in 1975.

Original articles on any aspect of tuberculosis and its control are invited for publication in the Journal. The Editorial Board will be happy to accommodate suitable contributions.

# SHORT-TERM CHEMOTHERAPY OF PULMONARY TUBERCULOSIS A CONTROLLED TRIAL

THE RESEARCH COMMITTEE OF THE TUBERCULOSIS ASSOCIATION OF INDIA\*

Studies carried out in different centres in India have shown conclusively that one of the main reasons for treatment failure is irregular and inadequate chemotherapy. With specific chemotherapy, characteristic symptoms disappear very quickly, giving a false sense of complacency to the patient who thinks that he is cured and that he no longer needs to take further treatment. It has also been found that the default rate markedly increases after 3 to 4 months. It was, therefore, felt that if the duration of treatment could be reduced from the usual 18 to 24 months as at present to about 4 months, the default rate could be considerably reduced and the number of successful results increased.

As early as 1968, the Technical Committee of the T.A.I., at the suggestion of its then Chairman, agreed to conduct a chemotherapy trial with a view to studying the immediate and late results (relapse rates) after 4 months of intensive chemotherapy with four drug combinations.

The trial is being conducted simultaneously in 3 institutions in Delhi, viz. L.R.S. TB hospital, Mehrauli, Rajen Babu TB Hospital and New Delhi TB Centre. In all, 225 patients will be randomly allocated to the following three groups:

Group A = INH + Streptomycin + Ethambutol + Pyrazinamide for 20 weeks, Placebo (Calcium Lactate) 21 to 80 weeks.

Group B INH + Streptomycin + Ethambutol + Rifampicin for 20 weeks; Placebo (Calcium Lactate) 21 to 80 weeks.

Group C = INH + Streptomycin for 8 weeks; INH and Thiacetazone from 9 to 80 weeks.

The dosage of the drugs was as follows:

Streptomycin	0.75 g daily
I.N.H.	300 mg. once daily
Ethambutol	25 mg/kg for first 6 weeks and 15mg/kg thereafter once daily.
Pyrazinamide	750 mg. B.D.
Rifampicin	600 mg. once daily.
Thiacetazone	150 mg once daily.

## Treatment allocation

Allocation was made at random by opening the next in a series of sealed envelopes after the patient had been accepted by the Research Committee of the TAI. The Committee was in overall charge of the trial.

## Selection of patients

All patients are residents of Delhi between 15 to 45 years of age, previously untreated, with positive sputum on at least 2 days. Pregnancy, extra-pulmonary tuberculosis, non-tuberculous coexisting diseases, poor general condition and involvement of more than four zones and weight below 36 kg. made patients ineligible for the trial.

## Routine Investigations

1. A conventional' sized chest x-ray was taken before the commencement of treatment and subsequently at 8, 20, 40, 52 and 80 weeks. All films were read by a central panel of readers who were not aware of the treatment group of any case.

2. The sputum specimens, one spot and the other overnight collection, from every patient were examined at the start of treatment and at 4, 8, 12, 16, 20, 24, 48, 52, 76 and 80 weeks. Direct smear was examined in the laboratories of the participating institutions as well as the New Delhi T.B. Centre, which functioned as a Central Laboratory in the present study. Culture and sensitivity studies were done at New Delhi T.B. Centre.

3. S.G.O.T. and S.G.P.T. estimation and routine blood and urine examination of the patient were done before treatment and at the end of 20 weeks.

The first 20 weeks' treatment in groups A and B and the first 8 weeks' treatment in group C was carried out in hospital. For the remaining period of treatment patients collected 4-weekly supplies of drugs from the domiciliary treatment service. After discharge from hospital, the patients were carefully followed up in their homes to ensure regularity.

---

The Research Committee consists of Dr. R. Viswanathan, (Chairman), Dr. S.P. Pamra, Dr. H.B. Dingley and Dr. M.M. Singh.

TABLE 1

*Initial Extent of Disease and Cavitation*

		Group	Group	Group	All Patients	
		A	B	C	No.	%
Zones involved	1	4	2	—	6	4.6
	2	25	19	17	61	46.6
	3	15	20	13	48	36.6
	4	6	4	6	16	12.2
Cavitation	None	5	9	4	18	13.7
	Single	27	19	14	60	45.8
	Multiple	18	17	18	53	40.5
All patients		50	45	36	131	100.0

Changes in chemotherapy were made permissible with the concurrence of the Research Committee and only in those patients who showed either major toxic reactions or definite clinical or radiological deterioration, or if the sputum continued to be positive up to 26 weeks.

The study started in March 1974 and intake is still continuing. Till 30th June 1975, 170 patients had been included in the study and of these 96 have completed 52 weeks, 114, 40 weeks and 131, 20 weeks. The present report, thus, is a preliminary communication based on interim analysis.

### Results

Nearly 80 % of the patients were males and half of them were between the ages of 15 and 25 years, nearly one-third between 26 and 35 years and the remaining between 36 and 45 years.

Table 1 shows the radiographic extent of disease and cavitation among 131 patients groupwise. Despite random allocation it would be noticed that certain important pre-treatment differences have crept in; notably there is a larger proportion with more extensive disease in group C. Some results therefore have had to be standardized to offset the possible effects of freak allocation.

Nineteen patients have been excluded from the main analysis since their pre-treatment cultures were found resistant to one or more drugs. Two patients migrated and another 7 gave up treatment against advice even before

completing 20 weeks of treatment, leaving 103 patients for the main analysis. There was no withdrawal from the trial because of major toxicity to any drug. Streptomycin had to be replaced by thiacetazone, as per protocol, in 6 patients because of intolerance. In one patient, thiacetazone had to be replaced by PAS. Minor reactions requiring temporary withdrawal of a drug for a few days were noticed in 11 patients in group A, 13 in group B, and 4 in group C. Major reactions were giddiness, rash and arthralgia in group A, giddiness, rash and anorexia in group B, and rash in group C. More than 80% of the patients did not miss a single day's treatment within 20 weeks. Ten patients missed the treatment because of minor toxic reaction for less than 7 days within 20 weeks. One patient missed the drugs for reasons other than intolerance for 25 days.

There was one death in group A in the 9th week of treatment, the cause being cor pulmonale in a patient with extensive disease. This death has been counted as adverse result in all subsequent tables.

Table 2 shows the results of bacteriological assessment in 103 patients at 20 weeks, and 66 of these who have completed 52 weeks. At 20 weeks nearly 97% of the patients in groups A and B had been converted whereas the corresponding figure for group C was 86.2 % The difference is not statistically significant. A patient was considered as converted if two consecutive sputum cultures were negative.

During the 20-52 weeks period, results in

TABLE 2

*Bacteriological results at 20 and 52 weeks*

	20 weeks		52 Total assessed	weeks
	Total assessed	Sputum converted		Sputum converted
Group A	39	38 97.4%	24	20 83.3%
Group B	35	34 97.1%	25	24 96.0%
Group C	29	25 86.2%	17	16 94.1%

group C improved further and were of the same order as in group B, whereas the results in group A worsened due to sputum reversion which will be referred to later.

The speed of sputum conversion too was a bit faster in groups A and B to begin with but group C caught up later on. There is very little difference in the comparative results of various groups whether one considered results of direct smear or culture.

Table 3 shows the radiological changes at 20 weeks. It would be recalled that there were considerable pre-treatment differences among patients allocated to the 3 groups. The table,

TABLE 3

*Radiological changes at 20 weeks*

(Percentages)

		+3	+2	+1	0	Worse	Dead
Group	Actual	15.4	66.7	12.8	2.6	—	2.6
A (39)	Standardised	9.4	68.7	14.5	3.7	—	3.7
Group B	Actual	2.8	68.6	25.7	2.8	—	—
(35)	Standardised	3.2	69.9	23.6	3.2	—	—
Group C	Actual	3.4	69.0	20.7	—	6.9	—
(29)	Standardised	3.0	69.9	19.1	—	7.9	—

therefore, includes besides the actual percentages, the percentages that would have been obtained on the basis of a standardised distribution. + 3 in this table means almost complete clearing; + 2 considerable clearing and + 1 some clearing '0' means more or less stationary results. The results appear to be slightly better in group A if one goes by percentage of patients achieving complete clearing at 20 weeks but the numbers are too small for a test of significance. Two patients worsened in group C.

Table 4 shows radiological results at 52 weeks. It will be seen that group B is well ahead and maintains its superiority. Group C is a little behind in a qualitative sense although the proportion of patients showing '+2' improvement or more is of the same order as in group B. Differences observed between the three regimens as regards proportion of '+3' are not statistically significant ( $P > 0.30$ ).

Back sliding is again seen between 20th and 52nd weeks in group A in radiological status as in bacteriological status referred to earlier.

Table 5 shows the rates of cavity closure. There is not much difference in the 3 groups at 20 weeks but at 52 weeks group A again lags behind groups B and C, although the difference does not attain statistical significance ( $.10 < P < .20$ ).

Finally we come to sputum reversion shown in Table 6. Of the 34 patients who were converted at 20 weeks in group B, 30 have completed 40

TABLE 4  
Radiological changes at 52 weeks  
(Percentages)

		-1-3	+2	+1	0	Worse	Dead
Group	Actual	29.2	54.2	4.2	—	8.3	4.2
A (24)	Standardised	24.1	55.2	6.9	—	6.9	6.9
Group B	Actual	40.0	56.0	4.0	—	—	—
(25)	Standardised	41.9	54.8	3.2	—	—	—
Group C	Actual	35.3	58.8	5.9	—	—	—
(17)	Standardised	34.7	59.2	6.1	—	—	—

TABLE 5  
Cavity closure at 20 and 52 weeks

	20 weeks		52 weeks	
	Initially cavitory cases	Cavities closed	Initially cavitory cases	Cavities closed
Group A	35	20 57.1%	23	16 69.6%
Group B	28	14 50.0%	20	17 85.0%
Group C	27	16 59.2%	15	14 93.3%

TABLE 6  
Sputum reversion after 20 weeks

	20-40 Weeks		20-52 Weeks	
	Total assessed	Reversions	Total assessed	Reversions
Group A	27	3	23	3
Group B	30	0	25	0
Group C	22	2	16	2

weeks' and 25 fifty two weeks' follow up. None of these has reverted so far. In group A, 3 patients have reverted and in group C, 2 only. Although numbers are small for valid conclusions, group B, i.e., Rifampicin group, appears to be superior here also. It may also be mentioned that bacilli were resistant to one or more drugs in all the 5 reversions. Only one of the 5 in group C had been somewhat irregular.

Nineteen patients have been excluded from the main analysis because their pre-treatment sputum culture was resistant to one or more drugs. Eight patients were resistant to INH, 4 to streptomycin, 3 to Pyrazinamide, 3 to Ethambutol and 5 to Rifampicin. At 20 weeks, 4 out of 6 in group A, all in group B and 4 out of 5 in group C were converted. At 52 weeks, however, 2 in group B reverted. No reversions in groups A and C have been seen in those who have completed 52 weeks so far.

To conclude (1) group B i.e. Rifampicin group appears to be as good as the control group on standard chemotherapy at 52 weeks though this conclusion is based only on an interim analysis. (2) Group A does not appear to give as good results as group B. In other words, Rifampicin is more suitable than Pyrazinamide for short-term chemotherapy in our type of patients, other 3 drugs being the same in the two groups. (3) Radiological clearing continues in groups A and B even after stopping the drugs at 20 weeks.

## MEDICAL PROGRESS AND ANTI PROGRESS

C.W.L. JEANES

(Special Adviser, Health and Population, Canadian International Development Agency, Ottawa, Canada)

Dr. Halfdan Mahler, Director-General of the World Health Organization, has stated:

“Traditionally, medicine has been viewed as the art of healing the sick. To this has been added in recent years the prevention of specific diseases. But a much broader concept is needed — that of improving the quality of life. In its early years WHO was fully occupied with relieving the burdens of disease. Although there is still a vital necessity for this to continue, WHO is now looking for ways to achieve a more stable equilibrium between man and his environment, in the hope that this will not only reduce man’s vulnerability to disease, but will also permit him to lead a more productive and satisfying life.”

In the world as a whole there is a wild irrelevancy of modern medicine — constantly seeking to raise standards and to achieve professional perfection, while getting farther away from the real problems of people. In the developed world the great and increasing problems are caused by man-made diseases — chronic bronchitis, emphysema, lung cancer, heart disease from stress and obesity, road accidents, alcohol and drugs. In the developing world the major problem is the high infant mortality rate, half the children dying before reaching the age of 5 years. Poverty and malnutrition are widespread and the biggest killers are diarrhoea, pneumonia, infectious and parasitic disease.

In both worlds medicine is not providing the medical care most needed. It provides much for the few and very little for most people. Half the world’s people live and die — and many of them die very young — without ever receiving medical care. The majority of people outside urban areas of developing countries, and those in some developed countries, are victims of the poverty-malnutrition-infection syndrome and live and die without these conditions being alleviated by modern scientific medicine. In this situation, cardiac surgery, neuro surgery and renal dialysis are irrelevant to the real needs of people.

The three vital factors in health services are budget, personnel and resources — and spreading these out equally among *all* people, with special emphasis on rural people — who represent 80% of the world’s population but who receive only 20% or less of the available resources.

The distribution of resources necessitates lowering standards for some, but raising it for many. All services have to be paid for and governments must set priorities within the Gross National Product of the country, from which must come the available health budget. No country can have unlimited health budget. It has to be related to the Gross National Product of the country.

The problems of health in both developed and developing countries can be listed under six headings:

- (1) The inability of the health care system to make available the services required to meet the demands of those most in need, who are usually too poor or too geographically or socially remote to benefit from such facilities.
- (2) Wide differences in the distribution of resources and services, and the multiplicity of institutions which are unrelated and not functioning as a system.
- (3) Emphasis has been given to *medical* rather than overall *health* care. Curative medicine is stressed with insufficient priority to promotive, preventive and rehabilitative care.
- (4) The training of health personnel is directed primarily towards medical and institutional care — and is largely irrelevant to the needs of people outside institutions.
- (5) A lack of recognition and rejection of useful traditional healing practices.
- (6) An inadequate assessment of community resources and interest. The people are rarely given the opportunity to decide on and participate in the services they receive.

In summary, in many countries, health services are not fulfilling their functions of providing services to *ALL* the population — and in fact *cannot do so using the present methods of delivery and resources*. The general health status of the majority of people is unlikely to reach an acceptable level - - consistent with Mahler’s “quality of life” without national action aimed at the poverty-malnutrition-infection syndrome and setting firm priorities relevant to the country and its resources.

What needs to be done to change this situation?

- (1) Primary health care must be shaped around the people it should serve and must meet the needs of the community.
- (2) Primary health care must be an integral part of a national health system and the system must be designed to meet the needs of the peripheral level. It must also be integrated with other community development, e.g. agriculture, water, housing, etc.
- (3) The local population must be actively involved in the formulation and implementation of health care activities so as to bring health care into line with local needs and priorities. What the community needs requires continuous dialogue between the people and the service.
- (4) The health care system must place maximum reliance on available community resources and must remain within the stringent cost limitations present in the country.
- (5) Primary health care must use an integrated approach, balanced according to community needs, for preventive, curative and rehabilitation services.
- (6) The majority of health actions should be taken at the most peripheral level practicable by workers most suitably trained for performing these activities.

Unfortunately in all societies there are obstacles to change. These are:

- (1) The political implications for a government to enter into a new and different health partnership with its people. China and Cuba have shown the way this can be done and it is a strange paradox that those totalitarian countries should be showing us how to deliver health care to all people.
- (2) *Opposition of the Health Professions:* A primary health care system may reduce the status, influence and income of some health workers, particularly in the cities. It will require redistribution of health workers (80% of doctors are now in the cities). The present system of medical education is based on the study of the sick patient in the hospital and not on the real needs of the community. There is also the argument of the reduction of quality, and providing second class service.

None of these fears can be substantiated, but this does not make their emotional impact any less persuasive.

#### **Conclusion**

Modern medicine does little for the health needs of the 80 % of the world's population who live in rural areas away from cities. These rural peoples bear an intolerable burden of disease, much of it related to their environment, and to infectious and parasitic disease.

The available health budget and resources must be distributed fairly to *ALL* people. A decrease in high technology, high cost health expenditures in the cities would have little effect on the health of the few and would increase the basic health needs for many.

## PRIMARY RESISTANCE TO MYCOBACTERIA IN TUBERCULOSIS PATIENTS

G. DADDI\* A. GIOBBI\*\* and M. LUCCHESI\*\*\*

This subject is not a new one. Very early, at the beginning of the antibiotic era, the phenomenon of primary resistance worried the therapist and the epidemiologist. We must point out how the true primary resistance is spontaneously present in extremely rare bacterial cells of wild strains: that is 1:100,000 to 1,000,000 for numerous drugs (INH, SM, EMB). For Rifampin the resistant mutants are even less numerous (1:2 and a half 500,000).

But you are all well acquainted with all these problems and it would be useless to continue to discuss them here now.

Anyway, we will speak of primary resistance according to common use of this term.

The multiple interests of the primary resistance decided even the IUAT to make 2 great surveys (Table 1). Similar research has been done in several countries of all continents. Here in India as far as I know, the problem has been repeatedly and carefully studied.

Table 1

*Primary resistance in Italy during the years 1957-1972*

		Year	%
Milano	Ganzetti e Coll	1957-60	14.05
Roma	Lucchesi e Zubiani	1961	14.05
Roma	Lucchesi e Coll	1962-64	10.15
Milano	Daddi e Coll	1961-64	7.07
Geneva	Giobbi e Coll	1965	16.94
Parma	Nitti	1966	10.08
Roma	Lucchesi e Mancini	1971	9.35
Napoli	Nitti	1971	14.35
Roma	Daddi e Coll	1972	10.58

Also in Italy we have been examining the problem for long years and it is my intention to report here briefly what we have found in our country.

As a general preliminary remark, in Italy as every where else the results have been different in connection with the epidemiology, with the

intensity of the specific contagion and with the socio-economic conditions of the population in the different areas.

From the view point of the infectiousness, the patients of tuberculosis can be divided in various categories:

(1) The patients not yet diagnosed but sputum positive; these are very dangerous, as they live unnoticed among the healthy people;

(2) the newly diagnosed and already treated patients; usually they are contagious for a short period: in the majority of the cases two or three months are sufficient to obtain the sputum conversion, but very often after a few weeks of treatment the Myc. tbe. disappear from the sputum or are too scarce to cause a morbigenous contagion;

(3) The chronic patients with resistant tubercle bacilli in the sputum; these patients spread the resistant mycobacteria, which, having been isolated from untreated patients, are called primary resistant strains.

The improvement of the methods of treatment and the greater number of effective drugs are extremely helpful in the associated therapies, which make the development of the resistance very difficult or even impossible because they rapidly produce the conversion of the patients. To prevent the infections resistant mycobacteria is the only way to bring about a reduction of the primary resistance.

As far as the socio-economic conditions are concerned, it is evident that poverty, malnutrition, bad housing etc., facilitate the contagion.

To ascertain if a newly diagnosed and untreated case is infected with resistant mycobacteria is an important matter for various reasons :

(1) because we should not adopt the anti-mycobacterial drugs in those cases in which they are no longer effective.

In practice we are obliged to start the treatment before having had the results of the anti-biogram: the treatment must begin immediately after having inquired about the therapy

\*Professor at the Faculty of Medicine, University of Rome.

\*\*General Director of the Dispensaries of Milan.

\*\*\*Director, 3rd Clinic of Pneumology of the University of Rome.

previously performed, obviously with the purpose not to go on using the drugs already administered.

But, in case following these criteria the patient should receive only so-called second line drugs, it is advisable to resume the administration of at least one of the more powerful drugs already used, according to the daily and global dosage reached before, the tolerance etc.

(2) Because this gives us a fairly good idea of the prevalence of the chronic sputum-positive patients present in the considered area.

In fact, the frequency of primary-resistance is directly proportional to the number of the chronic or hyperchronic patients, who are very often unsocial individuals, who do not respect any preventive measure.

(3) because it is an indirect indication of whether in the same area the specific therapy has been generally correct.

We know to day that the specific therapies, correctly performed with adequate drugs, in a short term are capable of bringing about the sputum conversion: that means also that the treatment to be efficient does not require of the tubercle bacilli such a prolonged contact with the drugs, as to allow them to become resistant.

(6) Because it makes it possible to establish which of the drugs may give the best results from the point of view of the rapidity of the antimicrobial activity and of the delay in stimulating the development of the resistance.

Evidently, the more effective a drug is, the less frequent is the resistance either primary or acquired to this drug.

The results of the research of several Italian authors have been reported in the table.

The percentages vary considerably from one author to the other and also in the same place from one year to the other. Globally, there has been a reduction of the primary resistance, but after an initial sometimes spectacular diminution, the incidence seem to be almost stabilised.

Even in the Forlanini Institute in Rome recently we have noticed that there is no clear trend towards the decrease of the primary resistance.

We must try to explain this fact that appears to be conflicting with all the treatment means we have at our disposal. As a matter of fact in our

country, as almost everywhere else, the TB mortality has had an enormous decrease, whereas the decrease of morbidity has not been as conspicuous. We believe that this can be attributed to the presence of many chronic patients, sorrowful inheritance of the past, who maintain the contagion.

Table 2  
*Tuberculosis mortality in the different Italian regions (1:1000)*

Regions	0/00 1950-52	0/00 1960-62	0/00 1970-72
North West : Total	0.43	0.28	0.09
North East : Total	0.44	0.20	0.10
Central Total	0.33	0.13	0.06
South Total	0.28	0.12	0.05
Islands Total	0.41	0.15	0.05
Italy	0.37	0.16	0.07

Table 3  
*Tuberculosis morbidity in the different Italian regions (1:1000)*

Regions	%o 1938-39	%o 1961-62	%o 1970-71
North West : Total	1.96	1.33	0.66
North East : Total	1.98	1.36	0.77
Central Total	1.62	0.92	7.46
South Total	1.54	0.97	0.51
Islands Total	1.42	1.15	0.83
Italy	1.74	1.05	0.58

It is confirmed by the age of the deceased in our country, almost all over 60 years, while on the contrary, almost all the new patients are young and recover rapidly.

Our research has been carried out testing 9 different drugs and we found that the resistant strains could be divided into 3 groups. The more numerous cases of resistance were to only 1 drug (SM or INH).

If we analyse the resistance towards the 9 drugs among the 331 strains isolated in the Forlanini Institute from untreated patients, it appears again that SM and INH are the drugs more frequently found with primary resistance; the less frequent is EMB.

The research work contemporaneously done in the dispensaries of Milan, carried out with the same technic on more than 2500 cases, has given analogous results.

Table 4

*Resistance to each drug among the 331 strains isolated from newly diagnosed patients (Sept. 1975)*

		%
SM	Resistan	15 (4.53)
INH	"	10 (3.02)
PAS	"	4 (1.20)
ET	"	6 (1.81)
CS	"	4 (1.20)
R/AMP	"	3 (0.90)
VM	"	1 (0.30)
KM	"	1 (0.30)
EB	"	1 (0.30)

R/AMP resistance is present in about 1 % of the cases (0.9 %) but shows a slight tendency to increase during the most recent years.

Table 5  
DISPENSARIES OF MILANO

*Pathogenicity for Guinea Pigs of the Myc TB isolated from the sputum after a long treatment with RJAMP*

Degree of Pathogenicity	Total of cases	Cases with R/AMP resistance	%
1° Degree +	80	48	60.0
2° Degree ++	43	27	62.8
3° Degree +++	49	12	24.5
	172	87	

No Lesions  
Lesions in the local lymphnodes  
Diffuse but Modest Lesions

This can be explained with the more widespread administration of the drug.

One of the characteristics of the Rifampin resistant strains is the *loss of virulence*, that we described years ago and that has been largely confirmed also in the large material collected and studied in Milan. On account of this loss of virulence the primary resistance to Rifampin does not seem to be an important factor of contagiousness.

Moreover the decisive influence of the adoption of Rifampin on tuberculosis is documented in the reduction of the period of hospitalisation in the Forlanini Institute since Rifampin began to be largely used (1968-1972).

From all our data we can deduce:

—the primary resistance, especially in some countries, may be a serious obstacle to a successful therapy;

—in our country there is a constant regression of the morbidity, but not so rapid as expected;

—the newly diagnosed patients are generally young and, if well treated, they heal quickly and well; moreover, they are usually not so richly bacillised as they used to be once and the severity of their disease, globally evaluated, appears also reduced. The cultural positivity on the first admission into hospital is also diminishing;

- but the number of primary resistances remains almost at the same level;

- this may probably be attributed to the fact that the number of chronic patients, spitting resistant tubercle bacilli, has remained almost the same, because these patients are eliminated little by little.

This explains why contagion decreases slowly, corresponding to the slow disappearance of the sources of contagion.

From all the above facts it is obvious that in order to eradicate tuberculosis it is necessary:

—*first*—to avoid creating chronic patients; in order to reach this goal the treatment must be the most effective possible from the very beginning;

—*second*— to try to cure the chronic patients and to render them abacillary or, at least to treat them intensively, with the purpose of inducing in the infecting flora a polyresistance

which renders the mycobacteria hypovirulent, especially if it includes a R/AMP resistance over 40-gamma;

- *third* — the role of the primary resistance in the epidemiology and the evolution of tuberculosis in the various countries and in the single patients, may be very different.

We feel justified to say, that the primary resistance certainly is one, though certainly not the main factor, of the persisting of the epidemics; but without any doubt it may be assumed as an index of the epidemiological situation and of the effectiveness of the therapeutical methods adopted on a large scale in a certain area.

# FIVE YEAR INCIDENCE OF TUBERCULOSIS AND CRUDE MORTALITY IN RELATION TO NON-SPECIFIC TUBERCULIN SENSITIVITY

G.D. GOTHI, S.S. NAIR, A.K. CHAKRABORTY and K.T. GANAPATHY

(From National Tuberculosis Institute, Bangalore)

## Introduction

Persons with small reactions to low dose of human type of tuberculin in whom strong reactions are elicited to a large dose are assumed to be infected with Mycobacteria other than Mycobacteria tuberculosis or other organisms. It is termed "non-specific sensitivity" or "low grade tuberculin sensitivity", and is believed to be a "cross reaction" due to heterologous antigen (Palmer *et al.*, 1953). Such skin sensitivity is commonly found in a high proportion of population in tropical areas (Edwards *et al.*, 1955. Chakraborty *et al.*, 1975) have also reported high prevalence of non-specific sensitivity in the age group of 0-24 in rural areas of Bangalore district.

The non-specific sensitivity is reported to afford certain degree of protection against tuberculosis in animal experiments (Palmer, 1966). Besides animal experiments, BMRC (1963) and Raj Narain *et al.*, (1972) have also observed lower incidence of tuberculosis among persons with "low grade tuberculin sensitivity". The report of Raj Narain *et al.*, is based on a 3 year follow-up of rural population of Bangalore district. The present report is a 5 year follow-up of the same population. The data are processed to find:

- (i) Incidence of disease among :
  - (a) tuberculin reactors to 1 TU, (b) reactors to high dose of tuberculin (20 TU) among non-reactors to 1 TU and (c) tuberculin non-reactors to high dose among non-reactors to 1 TU.
- (ii) Crude mortality in the above 3 population groups.

## Method

The study was undertaken in a sample of 103 villages out of 734 villages of 3 sub-divisions of Bangalore district, as a part of the 5-year study of epidemiology of tuberculosis (Nil, 1974). The entire population was surveyed four times. First survey was conducted between May 1961 and November 1962 and the last survey between May 1965 and November 1967. The intervals were 1.5 years between I and II surveys and between II and III surveys and 2.0 years between

III and IV surveys. The total interval between I and IV surveys was five years.

The entire population was registered on individual cards, examined for the presence of BCG scar and offered tuberculin test with 1 TU RT 23 with Tween 80. The tuberculin test reactions were read 72-96 hours after testing. Few days later, persons with the reactions of 0-13 mm to 1 TU were offered a second tuberculin test with 20 TU RT 23 with Tween. 80 at different sites. The reactions to this test were read 72-96 hours after testing. Though persons with induration of 0-13 mm to 1 TU were eligible for 20 TU test, the analysis of 20 TU test reactions were done only for the group with 0-9 mm reactions to 1 TU, since persons with indurations of 10 mm or more to 1 TU were classified as 1 TU reactors (see later).

All aged 5 years or more were offered 70 mm photofluorograms at each survey. These were interpreted by two independent readers and were classified in one of the following categories:

- (A) Normal; (B) Abnormal shadows judged as (i) non-tuberculous, (ii) tuberculous inactive and (iii) tuberculous active.

From each person whose photofluorogram was judged to be abnormal, two specimens of sputum/spot and one overnight, were collected. These were examined by direct microscopy and put up for culture. Identification and drug sensitivity tests were carried out on positive cultures.

Procedures of X-ray and sputum examination were uniform at each survey. Sputa were also collected from persons who had abnormal shadows at any of the previous surveys even though their photofluorograms were judged as normal during the current survey. Information was also collected about death and migration of the population registered at the first survey.

## Material

Out of 42,337 *de jure* population without BCG scar, results of 1 TU for 2,507 and of 20 TU for 5,284 were not available as they were not test read. Excluding these from analysis, 34,546 persons constituted the study population, 10,739 with reaction size of 10 mm or more and

23,807 with 0-9 mm reactions to 1 TU; the latter also had 20 TU test readings. X-ray and sputum examination coverages of the eligibles in the population considered for the analysis were of the order of 97%.

The population was divided into three groups on the basis of their tuberculin reactions (a) reactors to PPD RT 23 1 TU, O 10 mm) presumed to be infected with *Mycobacterium tuberculosis* (specific tuberculin sensitivity); (b) non-reactors to 1 TU (0-9 mm) but reactors to 20 TU (>8 mm), presumed to be infected with atypical *Mycobacteria* and (c) non-reactors to both 1 TU and 20 TU (0-7 mm to 20 TU), not infected with either *Mycobacterium tuberculosis* or other *Mycobacteria*.

For demarcating the population into groups with or without non-specific sensitivity (b) and (c) the distributions of reactions to 20 TU tests among non-reactors to 1 TU test (0-9 mm) in different age groups were studied by Chakraborty *et al.*, (1975). Persons with induration of 8 mm or more have been considered by them as reactors to 20 TU test (having low grade or non-specific sensitivity) and remaining persons with 0-7 mm reactions to 20 TU were classified as non-reactors to 1 TU and 20 TU. The proportions of population in the three groups (Table 1) were 31%, 44% and 25% respectively.

TABLE I

Total Population—Reactor and Non-Reactor to 1 TU and 20 TU PPD RT 23

Total Population	Non-Reactors to 1 TU (0-9 mm)		Reactors to 1 TU (10 mm or more)
	20 TU		
	Reactors 8 mm or more	Non-Reactors (0-7 mm)	
34546 (100.0)	15192 (44.0)	8615 (24.9)	10739 (31.1)

Figures in Brackets are Percentage of Total

In different age groups, sex-wise incidence rates of culture confirmed 'cases', culture negative 'suspects' (WHO 1964) and both together were calculated for the three tuberculin reaction groups. The differences in the incidence rates in the two sexes in different tuberculin sub-groups by age were generally not significant. Therefore, combined incidence for both sexes are presented. Excluding population in 0-4

years and those not X-rayed in higher age groups, as well as the prevalence cases, the incidence of tuberculosis has been studied among 28,571 persons, 10,093 -- reactors to 1 TU, 14,198 — reactors to 20 TU and 3,867 — non-reactors to 20 TU.

**Findings**

For computation of incidence, persons who developed fresh disease but were cured or died in between two subsequent surveys have not been included. The extent of this shortcoming in all three tuberculin groups is presumed to be similar. Thereby, the incidence rates in three groups may be imprecise; nevertheless they can be compared. Further, the groups were similar in respect of socio-economic and environmental conditions, age and sex, permitting comparison of incidence rates among the three groups.

The number of persons at risk and the incidence cases among groups with or without non-specific sensitivity except for the age group 5-14 years were inadequate for comparison of incidence of disease in other age groups. Therefore, the incidence of disease has been presented in only 3 broad age groups, and is not compared in higher age groups (15 years and more).

**Incidence of New Culture Positive Disease**

The five year incidence of culture positive disease was highest (10.8 per thousand) among reactors to 1 TU and least (1.4 per thousand) among 20 TU reactors (Table 2). Among reactors to 20 TU, the incidence rate was somewhat lower than that among 20 TU non-reactors, but significantly less than that among 1 TU reactors. The incidence of culture positive disease increased with age in all three tuberculin groups. It was lowest (0.7 per thousand) among 20 TU reactors of 5-14 years of age and highest among 1 TU reactors aged 55 years and more. The difference in incidence rates among 20 TU non-reactors as compared to that among 20 TU reactors in the age group of 5-14 years was statistically significant.

**Incidence of Culture Positive and Suspect Disease**

The five year incidence of culture positive and negative tuberculosis by age and tuberculin status is presented in Table 3. The overall 5 year incidence of tuberculosis among tuberculin reactors to 1 TU was 20.1 per thousand; among 20 TU reactors it was 5.5 per thousand and among 20 TU non-reactors. 7.0 per thousand. The incidence in three tuberculin groups increased with age. The difference in incidence of disease between 20 TU reactors and non-

TABLE 2

*Five Year Incidence of Culture Positive Cases by Age and Tuberculin Status : Per Thousand of Population*

Age at 1st Survey	Reactors to 1 TU ( $\geq 10$ mm)			Non-Reactors to 1 TU (0-9 mm)					
				23 TU Reactors ( $> 8$ mm)			20 TU Non-Reactors (0-7 mm)		
	No. at Risk*	New Cases	Rate %	No. at Risk*	New Cases <sup>4</sup>	Rate %	No. at Risk* <sup>1</sup>	New Cases	Rate %
5-14	1281	5	3.9	5690		0.70	3234	9	2.8
15-54	7214	72	10.0	7544	11	1.5	490	1	—
55+	1598	32	20.0	964	5	5.2	143	—	—
Total	10093	109	10.8	14198	20	1.4	3867	10	2.6

\* Excludes not X-rayed and Sputum Positive Prevalence "Cases"

TABLE 3

*Five Year Incidence of Culture Positive and Suspect (Negative) Tuberculosis by Age and Tuberculin Status per Thousand of Population*

Age at 1st Survey	Reactors to 1 TU ( $> 10$ mm)			Non-Reactors to 1 TU (0-9 mm)					
				20 TU Reactors ( $> 8$ mm)			20 TU Non-Reactors (0-7 mm)		
	No. at Risk*	New Cases	Rate %	No. at Risk*	New Cases	Rate %	No. at Risk*	New Cases	Rate o/10
5-14	1265	13	10.?	5679	13	2.3	3229	19	5.9
15-54	7046	117	16.6	7509	43	5.7	484	4	
55+	1475	67	45.4	932	22	23.6	136	4	—
Total	9786	197	20.1	14120	78	5.5	3849	27	7.0

\* Excludes not X-rayed and TB Patients both Sputum Positive and Negative

reactors in the age group of 5-14 years was significant

The overall incidence rate of suspect disease among 20 TU reactors and non-reactors was more than the incidence of sputum positive disease, whereas among reactors to 1 TU, the incidence of sputum positive disease was more non-reactors. It was generally so, for almost all or less same as that of suspect disease.

### Crude Mortality by Tuberculin Reactions

Table 4 shows the annual crude mortality rates in the three tuberculin groups. The overall crude mortality rates were lower among 20 TU Reactors as compared to those among 20 TU non-reactors. It was generally so, far almost all the age group

TABLE 4

Annual Crude Mortality Among Reactors to 1 TU and Reactors and Non-Reactors to 20 TU by Age based on Five Year Follow-up

Age Group at First Survey	Reactors to 1 TU (> 10 mm)			Non-Reactors to 1 TU (0-9 mm)					
	Nos.	Deaths in 5 Years Numbers	Annual Death Rate %	20 TU Reactors (> 8 mm)			20 TU Non-Reactors (0-7 mm)		
				Nos.	Deaths in 5 Years Numbers	Annual Death Rate %	Nos.	Deaths in 5 Years Numbers	Annual Death Rate %
0-4	128	10	15.6	687	31	9.0	4537	222	9.8
5-14	1311	17	2.6	5777	59	2.0	3418	43	2.5
15-34	4321	116	5.4	5336	114	4.3	342	9	5.3
35-54	3278	148	9.0	2386	102	8.6	159	15	18.9
55+	1731	392	45.3	1006	195	38.8	159	56	70.4
Total	10739	683	12.7 N	15192	501	6.6	8615	345	8.0

Row-wise the differences between figures underlined are significant.

The difference in rates were not significant upto 34 years of age, but were significant in higher age groups (35+) as well as for overall. The crude mortality rates among persons in the age group 35 years or more without non-specific sensitivity are based on small numbers. Among females for all ages combined, crude mortality was significantly lower for groups with non-specific sensitivity. Among males, only in 55 years and above age group and in females in 5-14 years, 35 years and more, the crude mortality was significantly lower for persons with non-specific sensitivity as compared to those without.

**Discussion**

The study was undertaken in an area not covered by organised anti-tuberculosis services. This made it possible to get information on incidence of tuberculosis and crude mortality in relation to tuberculin sensitivity of the population under natural conditions. Chakraborty *et al.*, (1975) have reported that 46 % of the population in 0-24 year age group in the area were infected with the other Mycobacteria. In the entire population the overall prevalence of non-specific sensitivity was 47.4% (Table 5). It increased with age

and by the age of 15 years almost 96 % of the population was infected either with Mycobacterium tuberculosis or with other Mycobacteria. These findings identify the area to be one having high prevalence of non-specific tuberculin sensitivity and provided opportunity to study its influence on the incidence of tuberculosis. For this purpose, on the basis of tuberculin reactions, the study population has been divided into three broad groups. The first group is assumed to be infected with Mycobacterium tuberculosis (1 TU reactors), second with atypical or other Mycobacteria (20 TU reactors) and the third not infected with either of the two (20 TU non-reactors).

The overall incidence rate of tuberculosis among 20 TU reactors was the lowest as compared with the rates in the other two groups. In younger age group (5-14 years) the incidence of disease among reactors to 20 TU was significantly lower as compared with that among 20 TU non-reactors. The reduction of incidence in the former group over that in the latter was 75% for culture positive cases and 61 % for combined culture positive and negative disease. Persons at risk in the age group 15 years and more among

TABLE 5

*Prevalence Rates of Specific and Non-Specific Sensitivity by Age*

Age in Years	Total Population	Prevalence Rates		
		1 TU Reactor (> 10 mm) %	1 TU Non-Reactor (0-9 mm)	
			20 TU Reactor (> 8 mm) %	20 TU Non-Reactor (0-7 mm) %
0-4	6251	2.0	12.9	85.8
5-14	12107	10.0	56.1	33.9
15-34	11657	37.1	59.2	3.8
35-54	6529	49.7	47.2	3.1
55+	3287	52.7	40.9	6.9
Total	39830	27.0	47.4	25.6

Note : Estimated on the Basis of Observed Rates of Non-Specific Sensitivity Among 20 TU Test Read.

the 20 TU non-reactors, being very small, comparison of incidence between 20 TU reactors and non-reactors is not permissible. It could however be concluded that non-specific sensitivity, at least in the younger age group, provides some protection against tuberculosis. The finding of this study is in agreement with those of BMRC (1963) and Raj Narain *et al.*, (1972), even when the induration size of 10 mm was considered as the level of demarcation between reactors and non-reactors to 20 TU test by the latter. The analysis of the present material done at 10 mm level of demarcation showed that the incidence rates of the disease among reactors and non-reactors at this level were similar to those for reactors and non-reactors at 8 mm level.

As regards crude mortality, the overall rate was significantly lower among 20 TU reactors as compared to the non-reactors. It was highest among 1 TU reactors and lowest among 20 TU reactors. In younger age groups (0-34 years) the crude mortality rates between 20 TU reactors and non-reactors were not different. In this respect, the finding of Raj Narain *et al.*, (1972) for 0-14 year age group is at variance with this report, presumably because their observations

were based on the first three years of follow-up when mortality due to tuberculosis among the infected infants and children is believed to be higher soon after infection. The observed difference could also be attributed to their selection of a different level of demarcation (10 mm) between reactors and non-reactors to 20 TU. In the age group 35 years and more a significantly lower crude mortality was observed among 20 TU reactors as compared to that in the non-reactors. On the assumption that the groups were similar in all respects except for their 20 TU reaction status it may be suggested that the former enjoyed some degree of protection from tuberculosis. However, it could be argued that the environmental and biological conditions, which might be responsible for the initial differences in tuberculin sensitivity status in the first place, could also be responsible for other health hazards, leading to different crude mortality rates in relation to tuberculin sensitivity status of the population. For instance, the living condition of reactors to 1 TU test might be poorer, as compared to those of non-reactors, and be responsible for other health hazards as well, resulting in higher crude mortality among the 1 TU reactors. Similar factors may also be responsible for differences in crude mortality

between 20 TU reactors and non-reactors. In view of this, the differences in crude mortality rates among groups of population with different tuberculin status may not be attributed to tuberculosis alone. In fact, the contrary may be true because the lower crude mortality in 20 TU reactors was mainly confined to females aged 35 years or more, which has only 10% of the total prevalence (NTI, 1974). Apart from this, though the difference in the crude mortality rates between 20 TU reactors and non-reactors is significant, yet because of small number of persons without non-specific sensitivity studied in the material in age group 35 years or more, the significance of the finding is open to question.

The knowledge of the prevalence of non-specific sensitivity and its protective effect is necessary not only in determining the most suitable age group for BCG vaccination but also for planning large scale BCG efficacy trials.

In the age group 0-4 years, a large proportion of population (85 %) is not infected with any of the mycobacteria and therefore has little protection against tuberculosis compared to other age groups. Hence, in order to reduce the risk of disease and death, BCG vaccination programmes, in the areas where there is a high prevalence of non-specific sensitivity, should first aim at continuous high coverage in this age group.

As regards BCG trial, the ideal would be to carry it out in two different areas: (i) one with non-specific sensitivity and (ii) the other with very little non-specific sensitivity, so that information about the efficacy of BCG in different situations could be known. However, when the trials are conducted in areas with high prevalence of non-specific sensitivity, observed difference between control and experimental groups may not turn out to be significant because of the inclusion of persons with non-specific sensitivity, as seen in USPH Trials in Puerto Rico (Palmer *et al.*, 1958) and Alabama, Georgia (Comstock and Palmer 1966). In such areas, persons without non-specific sensitivity would be found only in

younger age groups and to have them in adequate numbers for a controlled trial, a very large study population would be required. The inclusion of only younger age group population into the study of BCG trials has another limitation of very low incidence rate of tuberculosis in them, requiring a long term observation (20-25 years) to get a sufficient number of new cases to enable one to draw valid conclusions. If sufficient resources for a prolonged study are not available, then it is better not to attempt BCG trials in such areas, but to undertake trials in areas having least non-specific sensitivity. The findings from areas without much non-specific sensitivity may be generally applicable to the younger population (0-4 years) only, who in either areas have very little non-specific sensitivity.

#### REFERENCES

1. Palmer C.E. (1953), *A.R. Tuberc.*, 68, 678.
2. Edwards L.B., Meijer J., Nyboe J., Benjamin P.V. (1955), 2, 66. *Indian Journal of Tuberculosis*.
3. Chakraborty, A.K., Ganapathy K.T., Nair S.S. and Kul Bhushan (1975)—Under publication.
4. Palmer C.E. and Long M.W., (1966), *A.R.R.D.*, 94, 553.
5. British Medical Research Council (1963), *B.M.J.*, 1, 973-978.
6. Raj Narain, Naganna K., Pyare Lai, (1972), *A.R.R.D.*, 105, 578.
7. NTI (1974), *WHO Bulletin*, 51, 473.
8. Palmer, C.E., Shaw L.W., and Comstock G.W. (1958), *A.R. Tuberc., Pul. Sisc.*, 77, 877-907.
9. Comstock G.W. and Palmer C.E. (1966), *A.R.R.D.*, 93, 171-183.
10. WHO, Expert Committee on Tuberculosis (1964), WHO Tech. Report Ser. 290.

## MYCOSES ASSOCIATED WITH PULMONARY TUBERCULOSIS

S.K. SHOME, H.B. UPRETI, M.M. SINGH and S.P. PAMRA  
(From National Institute of Communicable Diseases, Delhi).

The danger of mycoses threatening life either as complications in tuberculosis, uncontrolled diabetes etc. or arising as an independent clinical entity following prolonged administration of anti-biotics and/or corticosteroids or due to weak immunological defence mechanism is well established (Wilson 1961; Seeling 1966; Weinberg & Austen 1966 and Shome *et al.* 1969, 1973a&b, 1974). Complexities in medical practice have resulted in a large number of iatrogenic conditions of which mycotic infection is a prominent feature.

Pulmonary mycoses relatively by themselves are not grossly damaging but when superimposed in conditions like tuberculosis their impact on the morbidity and mortality pattern renders them vitally important. Recent past bears evidence to the fact that mycoses represent a greater health burden and challenge than is realised by people or their health officials.

The present study was undertaken with a view to get a better insight into the problem of pulmonary mycoses among pulmonary tuberculosis patients, their prevalence, variation in clinical picture, chemotherapy and epidemiology.

### Material and Methods

Specimens of sputum, bronchial aspirate and bronchoscopy material were collected from pulmonary tuberculosis patients, chronic, acute or those with a prolonged history of therapy with antibiotics and corticosteroids.

Early morning sputum, bronchial aspirate or bronchoscopy material were collected aseptically and subjected to routine processes (Shome *et al.*, 1969) for mycological investigations comprising of (i) direct microscopic examination, (ii) inoculation on nutrient media fortified with chloramphenicol and/or actidione and (iii) intraperitoneal inoculation in Swiss albino mice with antibiotic treated clinical material. Along with this, each specimen prior to treatment with antibiotics was inoculated into three tubes of McClung's broth with a paraffin coated glass rod (McClung, 1960).

The inoculated specimens in Sabouraud's dextrose agar media were incubated at 27° C and those in McClung's broth at 37° C and observed at regular interval upto four weeks. The yeast like colonies and filamentous growth appearing on nutrient media were subsequently

processed for specific identification (Shome, *et al.*, *loc. cit.*) whereas the suspected colonies on paraffin coated glass rods were processed for identification of *Nocardia* (Shome *et al.*, *loc. cit.*). For rapid identification of the isolated *Nocardia* strains the modified technique of Shome and Raghavan (1970) was used which was later complimented by the detailed physiochemical tests (Shome *et al.*, *loc. cit.*)

The inoculated mice were put under observation for 4 weeks and thereafter sacrificed in the absence of spontaneous death. All were checked for lesions on lung, liver, spleen and kidney. Portions of macerated tissue from these organs were inoculated on Sabouraud's dextrose agar media fortified with chloramphenicol and/or actidione and another set in McClung's broth.

Case histories of all the patients were maintained including the lines of previous general treatment and specific antifungal treatment, if any.

### Results

Pulmonary mycoses confirmed by direct sputum culture and/or mouse passage cultures were one hundred and fifty five (155). A total of 18.02% cases of pulmonary tuberculosis showed the presence of concomitant or secondary mycotic involvement whereas the remaining 81.98% were negative (Table I).

From among 860 cases screened, 245 were positive for fungal elements on direct microscopic examination whereas only 18.02% were positive by direct culture and 7.3% by mouse passage technique for mycotic infections (Table II). The results show an overwhelming majority of males (147) in relation to females (8) showing a ratio of approximately 18M:1F among the positive cases.

Of the 155 positive cases, 79 were of candidiasis, 38 of cryptococcosis, 32 of nocardiosis and 6 of aspergillosis, the remaining 705 being negative for any mycotic involvement (Fig. I). Detailed analysis of the positive cases shows that about 67 % were under antibiotic therapy and another 6 % under antibiotics with corticosteroids, the remaining 27 % without any proper history of previous regimen of treatment (Table III). The age analysis of the cases shows that the pulmonary mycoses were most prevalent in the age

Table I

Numbers of cases of pulmonary mycoses as per the isolation of pathogenic fungi

Sr. No.	Diagnosed cases	No.	With isolation of established fungal pathogen. Percentage of suspected cases
	Pulmonary Tuberculosis -f- Mycoses -f-	155	705 18.02
	Pulmonary Tuberculosis + Mycoses —	860	81.98
	Total		<b>100.00</b>

Table II

Direct examination, direct culture and mouse passage culture evidence of fungal isolations

Specimens screened	Direct examination		% positive	Culture on nutrient media		% positive	Mouse passage culture		% positive
	Positive	Negative		Positive	Negative		Positive	Negative	
860	245	615	28.3	155	705	18.02	63	797	7.3

group 20-50 years with a peak between 21-30 years (Fig. II). The fungal strains isolated and of importance for human mycopathology were *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Nocardia asteroides*, *N. brasiliensis* and *Nocardia spp.*

Seventy nine (79) cases positive for *Candida albicans* were encountered in the study. The criteria used for labelling the cases positive for candidiasis were (1) the repeated 'heavy' primary isolation of the same strain from the clinical material (sputum, bronchoscopy or bronchial aspirate) within a period of 2-3 weeks, (2) presence of blastospores and pseudomycelium in the fresh clinical material and/or (3) positive response of the patient to specific antifungal antibiotics.

All the cases were among males with a preponderance in the age groups 21-50 years showing a peak between 21-30 years. Case histories showed that about 66% had previous continued administration of antibiotics, 33% giving no definite history of treatment and only about 1 % with both antibiotics and corticosteroids as therapy. Chemotherapeutic studies with 'Nyastatin' yielded good results. In certain instances where 'Hamycin' was tried (oral) the results were similar to 'Nyastatin'.

Pulmonary cryptococcosis was the second

highest involvement of the tubercular lung with 38 cases. Diagnosis was mainly based on the repeated isolation of *Cryptococcus neoformans* and its pathogenicity on swiss albino mice via intracerebral route. There was an over-whelming majority of males with a ratio of 34M :4F. Although the disease was spread over the age group 11-80 years the peak was in the age groups 21-40 years with majority of them (71%) giving a history of prolonged antibiotic administration. Almost all the cases had complaints of cough with expectoration, fever, chest pain, loss of weight, haemoptysis and dyspnoea. Therapy with amphotericin-B (tried in 4 cases) gave very good results with the sputum becoming negative after treatment.

Nocardiosis was encountered in 32 cases initially diagnosed as tuberculous and put up on the normal anti-tubercular treatment. The pathogen *Nocardia* was represented by *asteroides* and *brasiliensis* species on 15 and 3 occasions respectively, the remaining 14 strains being untypable. Disease was predominant among males (28M:4F) with the highest incidence in the age groups 21-40 years with 75% under continued treatment with antibiotics and/or corticosteroids. Remarkable results were obtained with sulphadiazine for chemotherapy.

Six (6) cases resulted in the isolation of

Table III

Details of mycoses associated with pulmonary tuberculosis

Disease	No. of cases	Age Groups in Years*							Sex**			Therapy			Pathogen Isolated
		A	B	C	D	E	F	G	H	M	F	None	Anti-biotics	Antibiotics with corti-costeroids	
Candi-diasis	79	7	24	16	18	7	3	1	79			26	52	1	<i>Candida albicans</i>
Crypto-coccosis	38	4	10	12	9	3			34	4		8		3	<i>Cryptococcus neoformans</i>
Asper-Gillosis	6	2	1	2	1					6			6		<i>Aspergillus fumigatus</i>
Nocar-diosis	32	4	11	8	4	4	1		28	4		8	19	5	<i>N. brasiliensis</i> -3 <i>N. asteroides</i> -15 <i>N. spp.</i> 14

\*A 0-10

B 11-20

C 21-30

D 31-40

E 41-50

F 51-60

G 61-70

H 71-80

\*\*M Male F

Female

*Aspergillus fumigatus*, a well established human pathogen. All were male and between the ages of 11 and 50 years. None of the cases showed any sign of aspergilloma. The case histories gave an indication of majority of them (83%) being 'allergic aspergillosis'.

### Discussion

As a necessary corollary to the epoch-making discoveries in the fields of medicine and therapy, the recent past has witnessed the gradual emergence of less cognisable diseases like mycoses as potential public health problems. Aggravating predisposing conditions, like tuberculosis, Hodgkins disease, carcinoma of the lung etc., leading to an irreparable pathology is perhaps more important in the development of mycoses than primary infection. Chronic nature of tubercular infection with concurrent prolonged administration of heavy doses of antibiotics not only leaves the patients with an impaired or weak immunological status but also predisposes them to mycotic infection.

High incidence of mycotic involvement among pulmonary tubercular cases is a well documented feature (Beatty and Saliba 1963, Shome *et al.*, 1969, 1969a, 1969b, 1972, 1973, 1974 and 1975, Sandhu *et al.*, 1964, 1966, Chakravartty *et al.*, 1962, 1963, 1964, 1967). The complete absence/

lack of any characteristic syndrome, radiological picture and in certain cases very close resemblance *Mycobacterium tuberculosis* renders the diagnosis of pulmonary mycoses problematic. In fact not a single case among the positively diagnosed (155) had any specific feature in the symptoms or radiological picture which would suggest or help in the diagnosis of pulmonary mycoses. In spite of this an interesting point to note was the association of cough with expectoration, low grade fever, loss of weight accompanied with chest pain, haemoptysis and dyspnoea in one or the other form with all the cases of pulmonary mycoses in the current study.

Direct examination of clinical material showed the presence of fungal element in 245 instances whereas only 18.02% were positive by direct culture and 7.3% by mouse passage technique emphasising the need for a proper laboratory exercise for specific diagnosis.

Spread over the age groups to 11-90 years the mycoses in general show a peak around the most active period of life i.e. between 21 and 40 years (Fig. II). The predominance of men is self evident although it is backed up by the fact that the population screened had an overwhelming majority of men.

The 38 cases of cryptococcosis re-emphasizes

that in contrast to the earlier reports, cryptococcosis in India is on the increase with a positive shift towards pulmonary involvement (Shome *loc. cit*) in contrast to meningeal infection (Aikat, *et al*, 1967, Basu Malik, *et. al*, 1967). Pulmonary involvement continues to pose a potential danger for meningitis (Wilson 1957) apart from its initial damage which quite often happens to be the terminal factor in far advanced cases of tuberculosis.

The probability of about 5 % of the patients in tuberculosis hospitals in U.S. A. suffering from nocardiosis has been mentioned by McQuown (1955) although not supported by any data. Pulmonary nocardia due to its close resemblance to tuberculosis or acute penumonic condition is extremely difficult for clinical diagnosis. Louria & Armstrong (1970) suggest that every pulmonary lesion should be considered for *Nocardia* if routine cultures and smears show no pathogen. All the 32 cases of pulmonary nocardiosis in the current study were diagnosed as tubercular cases and subjected to routine antitubercular therapy. The incriminating pathogens were mainly represented by *N. brasiliensis* and *N. asteroides* which becomes still more important because of their common occurrence in Indian soil (Kurup *et. al.*, 1964, Kumar and Mohapatra, 1968).

*Candida* very often considered as commensals in man (Rosebury, 1962) has been frequently responsible for bronchopulmonary diseases (Contant *et al.*, 1971) or even fatal cases of fungemia with endocarditis (Ellis and Spirak 1967). The relatively high incidence of Candidiasis among tuberculous cases is quite in line with the earlier records (Chakravarty *et. al.*, 1959; Pandalai & Kurup 1962; Shome *et. al.*, 1969, Barun 1960 and Batista *et. al.*, 1961). The occurrence of candidiasis concomitantly with tuberculosis is of paramount interest in the treatment and management of tuberculous patients as *C. albicans* is supposed to enhance the virulence of *M. tuberculosis*. It is considered worthwhile by the authors to emphasise here that patients under prolonged therapy with antibiotics may also be given a protective covering dose of anti-fungal antibiotics *e.g.* Nystatin, Hamycin and Fungizone.

The association of *A. fumigatus* in six cases with a history of tuberculosis of long duration and associated symptoms is suggestive of allergic aspergillosis as has been recorded earlier by Mishra (1971) and Shome (1974). The most alarming feature was the complete absence of aspergilloma even in cases with cavities because of tuberculosis.

India today has the largest number of

recorded tuberculosis cases, which in itself is a monumental public health problem. The current study shows that far more damaging and dangerous dimensions are added to it with the complication of this condition with mycoses. The lack of proper laboratory and diagnostic facilities not only lets pulmonary mycoses go undiagnosed but quite frequently untreated as well. The complete lack of any specific clinical or radiological symptoms in case of mycoses is confusing leading to complication in treatment as in the case of Candidiasis or Nocardiosis of the bronchus. In spite of the absence of proper reporting system of pulmonary mycoses in India it is evident that the importance of mycoses of the human bronchopulmonary system far surpasses our current estimation and is a positive hazard to the health of the people.

#### Acknowledgements

The authors wish to thank Dr. M.I.D. Sharma, Director, National Institute of Communicable Diseases, Delhi for permission and providing facilities to work and Dr. S.N. Ray, Deputy Director, Microbiology Division, N.I.C.D. for his constant encouragement. Thanks are also due to I.C.M.R. for financial support during part of the work.

#### REFERENCES

1. Aikat, B.K., Chatterjee, B.D. and Banerjee, P.L. 1967. *Ind. J. Med. Res.* 55, 43.
2. Basu Malik, K.C., Chatterjee, B.D., Banerjee, P.L. and Manjula Dutta, 1967. *ibid.*, 55, 529.
3. Batista, A.C., Fischman, O. and Vasconcelos, C.T. 1961. *Publ. I.M.U.R.* 324.
4. Barun, G.L., 1960, *New Engl. Med.*, J. 263, 70.
5. Beatty, O.A. and Saliba, A. 1963. *Kentucky Med. J.* 61, 502.
6. Chakravarty, S.C. and Sandhu, R.S., 1962, *Acta. Tuberc. Pneum. Scand.*, 42, 198.
7. — 1963. *Ind. J. Chest Dis.* 5, 40.
8. — 1964. *Acta. Tuberc. Pneum. Scand.*, 44, 52.
9. — 1967. *dis. Chest.* 51, 608
10. Randhawa, H.S., Roy, B. and Viswanathan, R., 1959. *Bull. Cal. Sch. Trap. Med.*, 7, 36.
11. Conant, N.F., Smith, D.T., Baker, R.D., Collaway, J.L. and Martin, D.S., 1971. W.B. Saunders & Company, Philadelphia.

12. Ellis, C.A. and Spirak, M.L., 1967. *Ann. Intern. Med.* 67, 511.
13. Kumar, R. and Mohapatra, L.N., 1968. *Sabouraudia*, 6, 140 & 192.
14. Kurup, P.V., Sandhu, R.S. and Damodarn, V.N. 1964. *Ind. J. Med. Res.* 50, 1057.
15. Louria, D.B. and Armstrong, D., 1970. *Med. Treat.* 7, 511.
16. Mankiewlitz, E. and Liivak, M. 1960, *Nature*, 187, 250.
17. McClung, N.M. 1960. *Mycologia*, 52, 154.
18. McQuown, A.L., 1955. *Amer. J. Clin. Path.* 25, 2-13.
19. Mishra, S.K. 1971, Ph. D. Thesis, Delhi University.
20. Pandalai, N.G. and Kurup, P.V., 1962. *Ind. J. Path. Bact.* 5, 75.
21. Rosebury, T., 1962. McGraw Hill Book Co. Ind. N.Y.
22. Sandhu, R.S., Jaggi, O.P., Randhawa, H.S., Sandhu, D.K. and Gupta, I.M., 1964. *Ind. J. Chest. Dis.*, 2, 93.
23. Sandhu, R.K., Sharma, N.V., Sandhu, R.S., Damodaran, V.N. and Randhawa, H.S., 1966. *Ind. J. Chest. Dis.*, 7, 198.
24. Saliba, A., Beatty, O.A. and Pacini, L., 1962, *South Med. J.* 55, 249.
25. Seelig, S., 1966. *Amer. J. Med.*, 40, 887.
26. Shome, S.K., Gugnani, H.C., Sirkar, O.K., Murty, O.K., Raghavan, N.G.S. and Rao, P.U., 1969. *Ind. J. Chest Dis.*, 11, 45.
27. Shome, S.K. and Raghavan, N.G.S. 1969a, *J. Comm. Dis.*, 1, 1.
28. Shome, S.K., Sirkar, O.K., Raghavan, N.G.S., Rao, P.U., 1969b, *ibid.*, 1, 13.
29. Shome, S.K. and Raghavan, N.G.S., 1970. *Curr. Sci.* 30, 135.
30. Shome, S.K., Sirkar, D.K. and Gugnani, H.C. 1973a, *Ind. J. Med. Res.*, 61, 23.
31. Shome, S.K., Sirkar, D.K., Majumdar, P.R., Baktu, S.V. and Singh, M.M. 1973b, *ibid.*, 61, 30.
32. Shome S.K., 1974, *Curr. Trends in Fit. Path.*, Lucknow University, 312.
33. Shome, S.K., 1974-IX I.U.A.T. & 29th TB & Chest Diseases' Workers' Conference New Delhi.
34. Shome, S.K. & Upreti, H.B. 1975, *Sym. Human Mycoses & Miconazol*, Ethnor Ltd., New Delhi.
35. Weinberg, A.N. & Austein, F. 1966, *Med. Treat.* 3, 1147.
36. Wilson, J.W. 1957, *J. Chrome, Dis.* 5, 445.
37. Wilson, J.W. 1961, *Arch. Int. Med.*, 108, 292.

# **Summaries of Papers Presented *at* The Thirtieth National Conference on Tuberculosis and Chest Diseases**

## **NATIONAL TUBERCULOSIS PROGRAMME**

B.N.M. BARUA

After referring briefly to the premises on which the district tuberculosis control programme is based, Dr. Barua referred to the extent of the tuberculosis problem, number of sputum positive cases to be found in the urban and rural areas respectively in an average district and hitherto unsatisfactory output of work specially in the peripheral health institutions. He pin-pointed the reasons for short-fall e.g. lack of appreciation of the problem, co-operation at all levels and supervision; non-utilization of trained personnel fully and ignorance about the available facilities on the part of the public. He suggested a number of corrective actions to improve the output and also stressed the role of voluntary organisations in ensuring better participation of people and their education in curative and preventive aspects of tuberculosis.

## **AN APPROACH TO ASSESSMENT OF NATIONAL TUBERCULOSIS PROGRAMME**

D.R. NAGPAUL

While emphasising the desirability of assessment of the DTP and NTP, the need for evolving a standard methodology for assessment, which is not easy, was brought out. The problems involved in the methodology e.g. procedure, sampling, criteria of assessment etc. have to be resolved. Methodology will also depend on time and money available for assessment. Expectations in respect of any of the standard activities of the DTP should take into consideration the circumstances under which the DTP is working. Assessment should be fact-finding and not merely fault finding; not only short-comings but achievements should also be taken into consideration.

## **CONTRIBUTION OF BCG VACCINATION & TREATMENT PROGRAMMES TOWARDS TUBERCULOSIS CONTROL**

S.S. NAIR

Simple models based on the usual programme parameters for calculating the impact of different types of BCG vaccination and treatment programmes on the epidemiological indices were shown. He brought out the urgent need to improve case-finding activity under the district control programme and to improve the coverage of vulnerable population with BCG vaccination. One of the models showed that efforts to improve regularity of treatment or to use more effective drug regimens is comparatively not so rewarding as efforts to improve case-finding.

## **COST OF CASE-FINDING -- AN APPROXIMATE DERIVATION**

K.V. KRISHNASWAMI and R. PARTHASARATHY

The paper was based on an attempt to calculate the per capita cost of case-finding under procedures prevailing in the Government Chest Institute, Madras. The word case has been used in its broad sense to include both sputum positive as well as sputum negative (x-ray positive) cases needing treatment. The cost of finding such a case by x-ray examination worked out to Rs. 5.30 per case whereas the cost of finding a case by sputum examination was Rs. 8.80.

**Ind. J. Tub., Vol. XXIII, No. 2**

## **PROBLEMS OF DISTRICT TB OFFICER RELATING PARTICULARLY TO KERALA STATE AND SUGGESTIONS TO SOLVE THEM**

C.T. OUSEPH

The problems were identified as: full compliment of staff not being in position; DTC staff being transferred without the knowledge of DTO and without the provision of substitute; irregular and inadequate supply of drugs, cards, forms, chemicals etc; lack of rate contract for miniature x-ray films; inadequate provision of P.O.L. and withdrawal of vehicles. The staff of the peripheral health institutions think that sputum examination is not their responsibility and demand compensatory allowance for tuberculosis work. He suggested that the DTC staff who were trained at the NTI more than 10 years ago should be given a short refresher course on health education and health education programme should be stepped up to make people aware of the facilities available at the DTC and the peripheral health institutions. He also suggested that the DTO should be responsible only for work in the DTC and the duties of the DTO in relation to work at the PHIs should be entrusted to another NTI trained doctor posted in the Civil Surgeon's office with the salary of a second grade Civil Surgeon.

## **DISTRICT TUBERCULOSIS CONTROL PROGRAMME IN ANDHRA PRADESH**

G. SATYANARAYANA

The deficiencies in the working of the DTP were attributable to the lower status of the DTO and lack of cooperation from the PHI staff. Some of the staff is on year to year basis and they do not get their salaries in time. Staff engaged in tuberculosis work in some states is being paid risk allowance whereas such an allowance is not being paid in Andhra Pradesh. Good workers avoid being posted as DTOs since there was no incentive, no job satisfaction, no chance of promotion and even non-practising allowance was not being given.

## **NATIONAL TB CONTROL PROGRAMME IN GUJARAT**

A.G. PATEL

The details of the work carried out by the DTCs in 17 districts of Gujarat where the DTP has been implemented were given. The output was unsatisfactory up to 1974 in all the districts. In 1975 exclusive health workers were provided in Baroda district and each one of these workers was set a target of at least 100 sputum examinations per month. As a result the output in 1975 was 4 times that of 1974 and 9 times that of 1965. Of the total sputum examinations, 12.7% were found positive. Out of 1,090 new bacillary cases, 50% belonged to the rural area, 25% to Baroda city and the remaining 25% to adjoining districts.

## **CASE-FINDING AND HEALTH EDUCATION SHIBIRS**

H.P. RAMESH

Role of shibirs arranged in addition to the routine activities of PHIs was highlighted in respect of promoting health education, BCG vaccination and case-finding in the rural areas. Such camps organized with the co-operation of community leaders and the official agencies like school teachers, B.D.O., block workers etc. are found very successful. The author recommends that every DTO should arrange one such camp every month.

## **PHYSICAL DIAGNOSIS OF PULMONARY TUBERCULOSIS**

S. BRAHMANANDA RAO

Out of 270 patients who were finally diagnosed as cases of pulmonary tuberculosis, 173 had definite physical signs on the basis of which diagnosis of pulmonary tuberculosis could be made without x-ray and sputum examination. Over diagnosis was only 4%. The author is of the opinion that physical examination is a reliable method of detecting cases of pulmonary tuberculosis in a case-finding programme under the DTP.

## STUDY OF PREVALENCE OF TUBERCULOSIS AMONGST VAGRANTS

A.K. KOLEH

Seven hundred and eighty three inmates of 2 vagrant homes in Calcutta were examined by miniature radiography. No bacteriological examination was carried out. Prevalence of disease judged as active and tuberculous on radiological evidence alone was found to be 8.7%. The prevalence rate increased with age. The rate in physically and mentally disabled vagrants was double of that in the active vagrants.

## PREVALENCE OF TUBERCULOSIS AMONGST BIDI WORKERS

G.P. SAXENA

Out of 1,257 bidi workers included in the survey, 375 had chest symptoms and were x-rayed. One hundred and twelve of these 375 had radiological evidence of disease and of these 86 were sputum positive.

## PREVALENCE OF DIABETES MELLITUS IN PULMONARY TUBERCULOSIS

H.Y. BAHULAR *et. al.*

4.48 % of 470 pulmonary tuberculosis patients had diabetes mellitus as detected by screening test or by oral glucose tolerance test. In 25 patients subjected to cortisone primed glucose tolerance test, 21.8% were found to have latent or stress diabetes. There was no difference in the extent of disease between diabetics and non-diabetics. Diagnosis and management of pulmonary tuberculosis in conjunction with diabetes was discussed. 80 % required insulin for control of diabetes. The remaining 20% had only mild diabetes and could be controlled with diet or oral hypo-glycaemic drugs.

## PULMONARY TUBERCULOSIS & DIABETES MELLITUS

J.L. BHATIA *et. al.*

One hundred and fifty cases of active pulmonary tuberculosis were investigated for presence of diabetes. Ten patients were known diabetics before pulmonary tuberculosis was diagnosed. Screening test for diabetes was abnormal in 50% of the remaining 140. There were 12 cases of frank diabetes. Pulmonary disease in diabetics was predominantly exudative, involving middle or lower zones in 50% of the cases. Fasting blood sugar estimation and routine urine examination are enough to detect frank diabetes in cases of active pulmonary tuberculosis.

## PREVALENCE OF INITIAL DRUG RESISTANCE IN PATIENTS ATTENDING THE TUBERCULOSIS CHEMOTHERAPY CENTRE

S. SUBBAMMAL

The prevalence of initial drug resistance in patients admitted to various studies carried out at the Tuberculosis Chemotherapy Centre between 1956 and 1974 was reviewed. All patients were aged 12 years or more and were newly diagnosed. Sensitivity tests to streptomycin and INH were set up on 2 pretreatment cultures. Methodology was uniform throughout this period. An increase in the level of initial resistance was noticed both for INH and streptomycin during the last 18 years. The author believes that it is due to a proportion of patients withholding the history of prior chemotherapy and, therefore, a part of the drug resistance considered initial is probably acquired.

## INITIAL DRUG RESISTANCE IN DELHI

V.K. PERUMAL

The initial drug resistance noticed in newly diagnosed cases of pulmonary tuberculosis attending New Delhi TB Centre in 1968, 1971 and 1974 was compared. There was no significant difference in the initial resistance to INH and streptomycin during this period. Proportion of patients with bacilli resistant to one or more drugs has consistently remained about 20%.

**INITIAL DRUG RESISTANCE AMONGST TUBERCULOSIS PATIENTS ADMITTED IN  
TB DEMONSTRATION AND TRAINING CENTRE, AGRA**

M.L. MEHROTRA *et al.*

Sensitivity tests were carried out on 354 newly diagnosed adult cases of pulmonary tuberculosis. Seventy tests were carried out in 1967-68, 74 in 1970-72 and 210 in 1972-75. 9.8% of the total patients were resistant to one or more drug, the rates in 3 successive periods being 7 %, 7 % and 12% respectively.

**PREVALENCE OF PRIMARY DRUG RESISTANCE AMONGST PATIENTS SUFFERING  
FROM TUBERCULOSIS ATTENDING THE CHEST INSTITUTE, MADRAS, FOR THE  
FIRST TIME**

K.V. KRISHNASWAMY AND ABDUL RAHIM

Testing for initial drug resistance to streptomycin and INH was carried out in 186 patients. 9% were resistant to streptomycin and 14% were resistant to INH. 6% were resistant to both streptomycin and INH.

**PREVALENCE OF INITIAL DRUG RESISTANCE IN RURAL MAHARASHTRA**

M.D. DESHMUKH *et al.*

Of the 66 patients who had no anti-tuberculous treatment before sensitivity testing and were detected in the anti-TB shibirs, 10% were resistant to streptomycin, 6% to INH and 8% to both streptomycin and INH. There was no difference in respect of age, sex, extent of disease and degree of sputum positivity.

**PRIMARY RESISTANCE TO MYCOBACTERIA IN TUBERCULOSIS PATIENTS**

G. DADDI *et al.*

(The paper is published in full in this issue)

**PROBLEM OF SPUTUM NEGATIVE CASES**

S.P. PAMRA *et al.*

Two hundred and seventeen pulmonary cases considered as active and tuberculous on clinical and radiological evidence (sputum being negative by direct smear and culture) were reviewed. One hundred and seventy eight of these were available for assessment 3 years later. Nearly 1/4th became sputum positive after the initial diagnosis. In another two-thirds subsequent behaviour of the cases left no doubt about the initial assessment. Only 10% of the cases were subsequently proved to be either non-tuberculous or with inactive tuberculous lesions.

**FOLLOW UP OF SPUTUM NEGATIVE X-RAY POSITIVE PULMONARY TUBERCULOSIS  
CASES**

K.V. KRISHNASWAMY

Two hundred and fifty three out of 1026 such cases diagnosed in a 3 year period were followed up. 11% of the 253 had subsequently become bacillary. 9% were proved to be non-tuberculous. One hundred and fifteen out of the original 1,026 (11 %) were known to have died. Follow up suggests that majority of the cases originally judged as active radiologically were in fact tuberculous and active.

### **FOLLOW UP OF SPUTUM NEGATIVE RADIOLOGICALLY JUDGED CASES OF PULMONARY TUBERCULOSIS UNDER PROGRAMME CONDITIONS**

R.K. PACHOLI

Three hundred and two clinically and radiologically judged sputum negative patients were assessed after treatment under programme conditions. One hundred and sixty one were cavitory. Forty three cases were subsequently proved to be inactive and 9 were proved to be non-tuberculous.

### **FOLLOW UP OF SPUTUM NEGATIVE PULMONARY TUBERCULOSIS CASES**

S.N. TRIPATHY

Treatment results of 974 cases of pulmonary tuberculosis were reviewed. Three hundred and sixty one of these were sputum positive and 613 sputum negative. Most of the sputum positive cases were far advanced, cavitory and symptomatic. Positive cases were more co-operative in treatment than the sputum negative cases. In 19% of the negative cases, 12 months' treatment was enough but in sputum positive cases, 18 months' treatment was necessary to achieve the same results.

### **THREE YEAR FOLLOW UP OF SPUTUM NEGATIVE X-RAY POSITIVE CASES OF PULMONARY TUBERCULOSIS IN EASTERN RAILWAY HOSPITAL**

N.K. KUNDU

Three hundred and one cases were treated in 3 years (1972 to 1974). Twenty patients stopped treatment against advice, 19 died and the treatment was successful in the remaining 262.

### **TRAINING OF NURSES AND PARA-MEDICAL PERSONNEL IN TUBERCULOSIS**

M. PAUL

Present day duties of nurses and para-medical personnel make it necessary that they must have a sufficient basic knowledge about causation and spread of disease to be able to reduce ignorance and superstition in the community and to promote health education about prevention. They should also be able to prepare and stain sputum smears, organise drug distribution and take prompt defaulter action. They should also be able to take over certain routine activities which are at present discharged by doctors.

### **ROLE OF HEALTH VISITORS & SOCIAL WORKERS IN DOMICILIARY TREATMENT PROGRAMME OF TUBERCULOSIS**

J.L. MONGA

Lack of education and motivation are unsatisfactory in rural population leading to high default rate. Periodical supervision of the work of health visitors posted in rural areas is essential. Efforts must also be made to improve the working conditions and eliminate personal grievances of the health visitors as far as possible.

### **PARA-MEDICAL SERVICES**

M. SAMUEL

Para-medical services are the back-bone of health schemes and have an important role in the prevention and treatment of disease and rehabilitation.

## **CHANGES IN THE ROLE OF PARA-MEDICAL WORKERS IN THE FIGHT AGAINST TUBERCULOSIS**

M.A. SEETHA

Changes in the functions of para-medical workers from the days of sanatorium treatment to the present multi-purpose workers' era were briefly referred to. Success of the DTP depends as much on the performance of medical officers as the para-medical personnel. Adequately trained and properly motivated multi-purpose workers would enhance their utility as they will be better accepted in the community. Further integrated approach towards all health problems of the community will also improve the efficiency of tuberculosis services.

## **DIFFICULTIES OF PARA-MEDICAL PERSONNEL IN DISTRICT TB CONTROL PROGRAMME**

R.R. SHARMA

Administrative, organisational and operational difficulties of the health visitors posted in DTCs, irregularity and inadequacy of supplies and indifference of the staff of the peripheral health institutions towards tuberculosis work were highlighted. Though most of the PHIs have sufficient staff, hardly any one cares to carry out tuberculosis work.

## **DOMICILIARY ANTI-TUBERCULOSIS CHEMOTHERAPY—EVALUATION OF THE INFLUENCE OF HOME SUPERVISION IN A RURAL AREA**

R. GARAI and P.K. SEN

Three hundred and sixty three cases of pulmonary tuberculosis in 3 health centres in a rural area were followed for 18 months to assess the efficiency of home supervision through uni-purpose and multi-purpose workers. Controls had no home supervision. No significant difference in the extent and pattern of irregularity in domiciliary chemotherapy could be detected under different systems of home supervision. Retrieval of cases however was slightly more effective with uni-purpose workers.

## **A SOCIO MEDICAL STUDY OF THE BEHAVIOUR AND SYMPTOMS OF TB PATIENTS PRIOR TO REPORTING AT THE SPECIALIZED AGENCY**

JASWANT SINGH

Three thousand two hundred and seventy one patients attending the TB Centre, Patiala, from May 1972 to August, 1975 were reviewed with a view to study the factors responsible for late diagnosis. Nearly 40 % of the patients were treated as non-tuberculous before reporting and this treatment had lasted for more than 6 months usually from unqualified doctors or practitioners of indigenous medicine. Nearly 50% of the symptomatics had approached some medical facility within one month of the onset of symptoms. Only 10 % of the patients were referred by private practitioners. The author concludes that there is a dire need of concerted efforts to motivate not only the general public but also the general practitioners of all systems of medicine to suspect early and take requisite steps for diagnosis.

## **ANALYSIS OF RESPONSE TO SECOND DEFAULTER ACTION BY LETTER COMPARED TO HOME VISITS**

B. KRISHNACHARYA AND B.S. NAGARAJA RAO

Second defaulter action was through letter in 249 patients and through health visitor in an equal number, the first action having been through letter in both the groups. The response through home visiting was 23% better than by letter writing. The response however was temporary as only 9% more completed the treatment successfully. This achievement has to be judged against the cost involved viz. Rs. 6.77 per visit to the home and Rs. 0.48 for each letter written.

## PYOGENIC INFECTIONS OF THE LUNG IN CHILDREN

H.B. DINGLEY

Pyogenic pulmonary infections in children are not uncommon. Commonest of these is bronchiectasis followed by staphylococcal pneumonia with or without empyema and infected cysts of the lung. The clinical features, pathogenesis, pathological changes and management of these manifestations were discussed. The role of surgery in the management of bronchiectasis and pyogenic infections was highlighted.

## PULMONARY ABSCESS — A 10 YEAR CLINICAL STUDY

V.K. JHA *et al.*

Eighty cases of pulmonary abscess were reported. Majority of the patients were in the 20 to 50 year age group and males were nearly 3 times more than females. Right lung was involved more than the left, lower lobe more than the other lobes. Causative micro-organisms were mostly staphylococcus, haemophilus, klebsiella and streptococcus. Eleven cases died. Age over 40 years, symptoms for more than 2 months prior to diagnosis, lower lobe involvement and klebsiella, echerichia coli, staphylococcal and pseudomonas were more often associated with mortality.

## PLEURO-PULMONARY AMOEBIASIS

O.P. MITAL & S.K. KATIYAR

Forty six cases of pleuro-pulmonary amoebiasis were reported. Maximum number of cases were seen in the 3rd and 4th decades of life, males nearly 3 times more than females. Onset was acute in 15 cases and insidious in the remaining 31 cases. 15% were alcoholics. Sixteen cases had un-productive cough. Sputum was typical anchovy sauce like in 12 cases. Entamoeba histolytica was isolated from sputum in 4 cases, pleural fluid in 6 and stool in 21. Pleural biopsy was done in 16 cases and it only revealed non-specific lesions. In 4 cases lung abscess was complicated by empyema. Therapeutic response was very good in 65% and moderate in 35%. Two patients died. In the authors' opinion, no major surgical procedure is normally required if cases are diagnosed early and treated promptly, and amoebiasis should always be considered in the differential diagnosis of right-sided pleural effusion.

## PLEURO-PULMONARY COMPLICATIONS IN AMOEBIC LIVER ABSCESS — A 5 YEAR FOLLOW-UP

P. RAVINDRAN *et al*

Seven hundred and forty one cases of amoebic liver abscess were diagnosed in Medical College Hospital, Trivandrum, between 1970 and 1974. Right lobe of the liver was the seat of abscess in 95 % of the cases. Majority of the cases were between 30 and 50 years in age and the ratio of males to females was 16:1. Pleuro-pulmonary complications were present in 196 out of 741 (26.5%). 33% were alcoholics. Haemoptysis and/or chocolate-coloured sputum were present in 26.5% and pleuritic pain in 25%. History of past or present dysentery was elicited in 38%. Jaundice was present in 16 %. Pleural effusion was present in 62.7 % and consolidation of right lower lobe in 25%. Three patients had inter-lobar effusion also. Liver scanning was carried out in 219 cases and all were positive. Early diagnosis and prompt treatment gives complete cure. Recurrence was seen in 5% of the cases.

## PULMONARY AMOEBIASIS

A.L. ANAND

Thirteen cases of pulmonary amoebiasis were treated in Amargadh TB Hospital from 1958 to 1972. In 11 cases hepatitis was also present while the remaining 2 had no clinical evidence of involvement of the liver. E. histolytica was demonstrated in the sputum in one case. Two cases had empyema; haemoptysis was present in seven cases and the sputum was muco-purulent in 4 cases.

## PLEURO-PULMONARY COMPLICATIONS OF AMOEBIASIS

A. CHAKRAPANI RAO

Twenty two cases of pleuro-pulmonary amoebiasis were reported. Twenty were males, majority between 30 and 40 years. Pleural effusion was present in 11 cases. Anchovy sauce sputum was present in one case. Anchovy sauce like pus was aspirated from pleural space in 2 cases. Amoebae were not isolated from sputum in any case. Three patients had cysts in the stools. Liver was enlarged in 8 cases. Therapeutic response to drugs was satisfactory in 20 patients.

Lecture by  
C.W.L. JEANES

on  
**'MEDICAL PROGRESS AND ANTI-PROGRESS'**  
and  
paper on

### FIVE YEAR INCIDENCE OF TUBERCULOSIS AND CRUDE MORTALITY IN RELATION TO NON-SPECIFIC TUBERCULIN SENSITIVITY

G.D. GOTHI, *et al.*

are published in full in this  
issue.

### CASES OF PULMONARY DISEASE DUE TO UNCLASSIFIED MYCOBACTERIA DETECTED AT THE TUBERCULOSIS CHEMOTHERAPY CENTRE, MADRAS

By  
C.V. RAMAKRISHNAN

Unclassified (atypical) mycobacteria (UMB) were isolated from the sputum of 17 cases during the last 17 years. Eight of these patients excreted UMB from the start and the remaining 9 excreted these after a time interval following quiescent pulmonary lesions. In 5 patients the time interval was less than 4 years and in 4 more than 4 years. Of the 17 patients, 10 were males and most of them 30 years or more in age. Eight patients were engaged in dusty occupations. All except one denied any history of bronchial asthma or chronic bronchitis. UMB in 9 patients belonged to Runyon's group I (Photochromogens) and 8 to group III (non-chromogens). The number of positive UMB cultures ranged from 2 to 51 with a mean value of 16.4 cultures per patient. The organisms were resistant to 5 u/ml concentration of INH. Pulmonary radiographic shadows were similar in appearance to those observed in tuberculous patients. The bacteriological conversion rate with anti-tuberculous drugs was unsatisfactory.

### MYCOSES ASSOCIATED WITH PULMONARY TUBERCULOSIS

S.K. SHOME *et al.*

(The paper is published in full in this issue).

### STUDY OF IMMUNOGLOBULINS IN PULMONARY TUBERCULOSIS

K.L. SOBTI and R.S. HOON

A study was undertaken to determine any alteration, in serum immunoglobulins IgA, IgD, IgG, IgM & IgE in 20 sputum positive patients of pulmonary tuberculosis and 20 controls. Serum immunoglobulins IgA, IgD, IgG & IgM were measured by radia immunodiffusion and IgE by radio-immunoassay (Phadebas IgE test). IgA was raised in 5 patients and IgM in 7 patients. There was no alteration in IgD & IgE. IgG was raised in all cases. The normal values for IgA were 42-280 mgs %, IgD 0-6 mgs% IgG 580-1400 mgs %, IgM 45-270 mgs % and IgE 250 u/ml. The significance of raised IgA and IgM is not known. The rise in IgG is related to activity and severity of disease.

## PLEURAL BIOPSY WITH COPE'S NEEDLE

S. R. RAO *et al.*

Pleural biopsy was performed by cope's needle in 50 cases of pleural effusion. The procedure is completely painless. No complications were seen. The biopsy yielded sufficient material for diagnosis in 90 % of the cases. The diagnosis was tuberculosis in 28, congestive heart failure in 4, nephrotic syndrome in 2 and malignancy in 9.

## SPROSITIS IN TUBERCULOSIS

O.A. SARMA

Twenty five cases of a combination of involvement of broad serous sacs in the body were seen in 10 years. The age range was 20 to 68 years and 20 were males. In 15 cases pleura on both sides were involved, in 4 pericardium and one pleural sac, in 5 peritoneal and one pleural sac and in one pleura with synovial membrane of the knee were involved. No case had miliary tuberculosis. Pulmonary parenchymal lesions were present in 20 cases. Sputum was positive in 8 cases.

## SEASONAL VARIATIONS IN INCIDENCE OF TROPICAL EOSINOPHILIA

S.K. PATHAK *et al.*

More than 140,000 total and differential WBC counts were carried out in Nagpur between 1963 and 1974. An absolute eosinophil count of 1500 or more was taken as evidence of eosinophilia. Eosinophilia was found to be maximum in summer months namely April, May and June after which there was a gradual decline. Incidence showed a second peak in October and thereafter there was decline again and incidence was lowest in December and January.

## SOME OBSERVATIONS ON TB SEAL CAMPAIGN

M.M. SINGH

The history of TB seal campaign starting in Denmark in 1904 up to the last campaign in India was traced. The anti-tuberculosis activities for which the TB seal collection is utilized e.g. financial assistance to poor patients, health education, promotion of domiciliary treatment, research, training etc. were highlighted. Some of the difficulties in the organisation of the campaign with particular reference to the situation in Delhi were brought out and suggestions were made for stepping up of the seal sale campaign such as publicity, incentives etc.

## SHORT-TERM CHEMOTHERAPY OF PULMONARY TUBERCULOSIS

RESEARCH COMMITTEE OF THE TUBERCULOSIS ASSOCIATION OF INDIA

(This paper is published in full in this issue)

## CLINICAL TRIAL OF SHORT COURSE (6 MONTHS) CHEMOTHERAPY IN PULMONARY TUBERCULOSIS—ONE YEAR FOLLOW UP

M.L. MEHROTRA *et al.*

Three hundred and twenty four previously untreated sputum positive cases were included in the study. Controls were given streptomycin, INH and thiacetazone for 4 weeks followed by INH and thiacetazone for the next 48 weeks. Study group I was given streptomycin, INH, pyrazinamide and ethambutol for 4 weeks, followed by pyrazinamide, ethambutol and INH for the next 20 weeks and then streptomycin, INH, pyrazinamide and ethambutol again for 2 weeks. In study group 2, the treatment for first 4 weeks was the same as for study group I and thereafter they were given INH and thiacetazone for 32 weeks followed by 2 weeks of initial 4 drugs again. Study group I was given placebo for the subsequent 26 weeks and study group 2 for 14 weeks. Sixty-seven patients had to be excluded from the trial for various reasons, majority because of initial culture being resistant to INH and/or streptomycin. There were 9 deaths in all. The sputum conversion was 87 % in the control group and 100 % in the study group at 6 months. At 12 months the sputum

conversion rates were 85 % and 82% respectively. Relapse occurred in 7 patients in the study group and none in the controls.

### **SLOW RELEASE PREPARATION OF ISONIAZID-THERAPEUTIC EFFICACY AND ADVERSE SIDE-EFFECTS**

S.P. TRIPATHY

Matrix INH in a dose of 40 mg/kg appears to be marginally more effective than ordinary INH in once weekly chemotherapy in the rapid inactivators in Madras. The best results so far achieved were with a combination of ordinary INH plus matrix INH given to rapid inactivators. It is however not certain whether the results were as good as those with ordinary INH in slow inactivators. The regimens of matrix INH 40 mg/kg and of matrix plus ordinary INH were both of fairly low toxicity and could be given to 96 % of the patients for the full course of 12 months in full dosage.

### **RELATIVE VALUE OF STREPTOMYCIN AND PYRAZINAMIDE WHEN GIVEN IN COMBINATION WITH ISONIAZID AND PAS IN THE TREATMENT OF PULMONARY TUBERCULOSIS**

T.B. MASTER *et al.*

Thirty one patients were put on streptomycin, INH and PAS and 29 on pyrazinamide, INH and PAS. The duration of treatment was one year. Five patients were excluded from the streptomycin group and 3 from the pyrazinamide group. Sputum conversion was obtained in 96 % in the pyrazinamide group and 83 % in the streptomycin group. Radiological improvement was 100 % and 84% respectively. Toxic effects were seen in 2 cases in the streptomycin group and none in the pyrazinamide group. The authors recommend pyrazinamide with INH and PAS for the first 3 months followed by INH and PAS subsequently as standard treatment.

### **EXPERIENCES IN PULMONARY TUBERCULOSIS IN THE ARMED FORCES**

D.S. RASTOGI

A profile of pulmonary tuberculosis in Armed Forces and its treatment with first-line and reserve drugs was presented. Average age of the patients was 31 years. 3 % had diabetes as a complication. Extra-pulmonary disease was present in 3%. 60% of the pulmonary patients had positive sputum. The disease was minimal in 17%, moderately advanced in 34% and far advanced in 49%. 40% of the patients had had BCG in childhood. Treatment was completely supervised; intensive therapy with 3 drugs was given in first 3 months followed by intermittent biweekly treatment for the subsequent 15 months. Ethionamide was used as third drug in doses of 500 mg twice a day (for patients weighing above 50 kg.) in the 3 months intensive phase. It had to be withdrawn because of intolerance in 6% of the patients only. Ethionamide was not given to pregnant women. Its unpleasant toxic reactions were neuropathy, hypoglycaemia. Sputum conversion was obtained in 100% and cavity closure in 93 %. In 12 % of the patients resection was carried out in addition to the drugs. 70% of the patients were fit for military service. Fifty eight patients whose earlier treatment with streptomycin, INH and PAS had failed were given reserve drugs, viz. rifampicin, themibutol, capreomycin, cycloserin, pyrazinamide in various combinations. Sputum conversion was obtained in 54 out of 58. Cavity closure was obtained in 51 patients, in 7 after resection.

### **DERMATITIS MEDICAMENTOSA DUE TO ANTI-TB DRUGS**

A.B. DESHPANDE & V.S. BHATE

PAS is the most and INH is the least offending agent in the causation of dermatitis. PAS and thiacetazone can both cause severe and life threatening complications like exfoliative dermatitis and Stevens-Johnson Syndrome. Reserve drugs do not usually give allergic reactions though their toxic reactions are more than with primary drugs. The time and onset of dermatitis varies in different patients. .

## NEWS & NOTES

### NEW CHAIRMAN

Dr. Padma Prakash Goel who took over as Director General of Health Services, on 2nd March, 1976, succeeds Dr. J.B. Shrivastav, as the Chairman of the Tuberculosis Association of India.

### ANNUAL MEETINGS

The 37th Annual General Meeting of the Association will be held on Thursday, 22nd April, 1976, in the Conference Hall of the Association, 3, Red Cross Road, New Delhi. This will be followed by a meeting of the Central Committee of the Association on the same day.

A meeting of the Technical Committee of the Association will be held on the 21st April, '76. The Conference of Secretaries of State TB Associations will be held in the afternoon on 22nd April, 1976.

### KHUSHI RAM SHIELD

The Association has decided to award the RAI SAHEB KHUSHI RAM SHIELD for 1975 to the Bengal Tuberculosis Association for the best work done during 1975. The Bengal Association wins this Shield for the third year in succession. The Association has also decided to award a Certificate of Merit for good performance to the Kerala TB Association.

### SEAL SALE AWARDS

The Association has decided to award the Shield for the highest collections made in the 25th Seal Sale Campaign to the Tamil Nadu TB Association. As against Rs. 6,74,278.50 collected in the 24th Campaign, the Tamil Nadu Association collected in the 25th Campaign Rs. 6,99,875. The Tamil Nadu Association is winning this Shield for the ninth time in succession.

The Association decided to award the Runner-up-Cup for the collections in the 25th Campaign to the Kerala TB Association which is winning this distinction for the fourth time in succession. They have improved their collections from Rs. 2,85,930.38 in the 24th Campaign to Rs. 3,27,402.55 in the 25th Campaign. Certificates of Merits will be awarded to Andhra Pradesh and Madhya Pradesh TB Associations.

The Cup for the best performance made by smaller States and Union Territories has been

won for the third time by the Goa TB Association. A Certificate of Merit will be awarded to the Tripura TB Association.

### NATIONAL CONFERENCE

The Thirtyfirst National Conference on Tuberculosis and Chest Diseases will be held in Lucknow (Uttar Pradesh) sometime in October/November 1976. The exact dates will be announced in due course. Subjects selected by the Programme Committee for discussion at the Conference include (1) Surgery; (2) Air Pollution; (3) Symposium on 'Smoking Hazard'; (4) National TB Control Programme with special reference to the working of peripheral health institutions; (5) TB Seal Sale Campaign; (6) Childhood Tuberculosis; (7) Chemotherapy including management of resistant cases; (8) Problem of Drug Default — its reasons and management; (9) Fungal infections and (10) Extra-pulmonary Tuberculosis.

Those who wish to present papers at the Conference may send in the titles of their papers along with an abstract immediately to the Secretary-General, TB Association of India, 3, Red Cross Road, New Delhi-1,

### CHANCHAL SINGH MEMORIAL AWARD —1976

The Tuberculosis Association of India will award a cash prize of Rs. 500/- to a TB worker preferably 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 Tuberculosis Association of India office latest by 31st August, 1976.

### CONFERENCE/SEMINARS

The Maharashtra State Anti-TB Association held its XVth TB and Chest Diseases Conference in Sholapur on 29th February and 1st March, 1976. The inaugural function was followed by a panel discussion on "Recent advances in chest diseases". An orientation course for TB workers was held on 1st March followed by a panel discussion in Marathi.

The Goa TB Association and Indian Medical Association, Panjim branch jointly organised a symposium on Tuberculosis on 7th March and the same was inaugurated by the Lt.-Governor of Goa, Shri S.K. Banerjee.

**ESSAY COMPETITION**

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, adjudged best by a special committee of this Association. The subject selected for the 1976 competition is Domiciliary Treatment of Pulmonary Tuberculosis and causes of its Failure. The essay should be written in English, typed in foolscap size, double-spaced and should not exceed 15 pages (approximately 3,000 words excluding tables, diagrams, etc.). Four copies of the manuscript should reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001, not later than 31st August, 1976 and should be forwarded through

the Dean or Principal of the College/University.

**INDIAN ASSOCIATION FOR CHEST DISEASES**

The Indian Association for Chest Diseases has instituted a cash prize of Rs. 200/- to be given to the author of the best article published during the previous year either in Indian or Foreign Journal and/or read at the annual conference of the Association on any subject in the speciality of Chest Diseases. The prize is open only to those under 40 years of age. The work on which the article is based must have been conducted in India. Please send six copies to the Secretary, Indian Association for Chest Diseases, 177, Satya Marg, New Delhi-110021 to reach not later than 31st July, 1976.