

The Indian Journal of Tuberculosis

Vol. XVII

New Delhi April 1970

No. 2

TUBERCULOSIS "CAMPS"

*"The old order changeth yielding place to new
And God fulfils himself in many ways
Lest one good custom should corrupt the world"*

—Tennyson

Institutional treatment which was the only solace to the tuberculous yielded place about two decades ago to domiciliary care and the core of tuberculosis control programmes adopted in India is the establishment of TB Control Units in the districts, usually in district headquarters. District Control Units can be fed by health centres at the lower levels also. Still, the gap between the urban, semi-urban and rural areas in regard to facilities for diagnosis, treatment and advice appears wide enough to defeat the basic purpose of a comprehensive anti-tuberculosis drive in the country unless we take the time by the forelock and forestall the inevitable danger.

Medical facilities are woefully lacking in our rural areas which account for over 80% of our population, while there are usually better facilities in the urban centres i e. in towns and cities. In a situation like this our thoughts should turn to finding out ways and means of redistributing or adding to the facilities or at least ensuring a continuous flow of help from the urban to the rural population. Unless such measures are taken prevention and control of tuberculosis will pose a big problem. The position will become worse because of increasing to-and-fro movement of rural population to the towns and big cities due to rapidly expanding industries and otherwise in search of jobs. Suggestions have been made for the introduction of mobile clinics with self-contained hospital facilities and stationing of specialised services in different localities in the districts for specified periods to serve the rural population. The location of future medical colleges in the rural areas is another suggestion for consideration. Long before this objective is achieved "adoption" of specific rural areas by a medical college in the region and regular visits by different specialists to medical centres like cottage hospitals, primary health centres and taluka dispensaries is worth considering.

Experience of holding 'camps' for medical relief in such areas has been encouraging though it may be said that anti-tuberculosis "shibirs" or TB "camps" were not feasible because of difficulties in diagnosis and treatment of a large number of patients within a short space of time. By Mobile miniature X-rays, radiological diagnosis could be made, but films had to be brought back to headquarters for processing and interpretation. Similarly, sputum examination

also takes time with the result that the psychological impact of diagnosis on the spot and prompt disposal may be lost. An easier approach would be to do fluoroscopic examination of the patients and sputum examination on the spot of the persons with suspicious shadows. The obvious advantage of this will be that the diagnosis can be made and drugs given before the patient returns to his village the same day. For follow up treatment a drug distribution centre can be established locally and regular supply of drugs from flu; headquarters arranged.

The Maharashtra State TB Association has been holding such camps on purely voluntary basis and the results has been encouraging. During, the past year that Association organised six camps. Of the 1,191 symptomatics in the rural areas of the State on whom fluoroscopic examination was done, 258 or 21.7% were found to have radiologically active disease, and of these 56 or 4.7% were sputum positive. But for these camps these patients would have remained undiagnosed and would have been a danger to themselves and to the community. In addition, it was possible to give B.C G. vaccination to 4,264 children. In a limited way these camps partly filled the gap between existing facilities and the measures to be provided in rural areas which are not adequately served by the District Control Programme. This project is well worth emulation by other State Associations to satisfy the crying need of the day even to a limited extent

AWARD OF TAI GOLD MEDAL

The Tuberculosis Association of India awards every year a Gold Medal too doctor who has done outstanding work in the tuberculosis field. The Association awarded the 1970 Cold Medal to Dr. B. K. Sikand, a distinguished colleague of all of us.

Dr. B.K. Sikand was born on 28th February, 1899 at Nabha in the State of Punjab. After basic education he joined KinuEdward Medical College, Lahore in 1916 and passed out with credit in 1921. He had a short spell of private practice at Nabha before joining in 1925 the Indian Medical Service as a short-term Commissioned Officer. On release from the Army in



Dr. B.K. Sikand

1934, he proceeded to U. K. for post-graduate qualification in Public Health. He spent time in U.K. in specialising in chest diseases in the Brompton Hospital. Returning from U.K., he worked for few months as Director of the Junior Red Cross and then took over in 1936 as Secretary of the King George's Thanksgiving Anti-Tuberculosis Fund. When the Tuberculosis Association of India was established in 1939, Dr. Sikand was appointed as its first Secretary. He worked in that capacity up to the end of 1940 when he was appointed Chief of the New Delhi TB Clinic which the Association established.

Soon after its inception, the Tuberculosis Association of India entrusted Dr. Sikand and other luminaries in the field with the task of formulating an anti-TB programme which could be made applicable all over the country in an organised way. Realising that the then traditional approach to the tuberculosis problem, viz. Sanatorium treatment, was beyond the means of our country with its gigantic tuberculous problem, domiciliary treatment or the organised home treatment as it was then baptized, was advocated as the only practical approach. Dr. Sikand was given the responsibility of trying out this scheme from the New Delhi TB Centre with a view to determine its acceptability, feasibility and utility. To Dr. Sikand, thus, goes the credit for initiating the domiciliary treatment scheme and showing its potentialities. The New Delhi TB

Centre which was started by the Association at the instance of the Government of India to serve as a model for the country and has made a name for itself at home and abroad with its scientific contributions, is a standing monument to Dr. Sikand's efforts and achievements. When the New Delhi TB Clinic was upgraded by Government of India in collaboration with the W.H.O., Dr. Sikand was made its Director.

Dr. Sikand's fight against the disease on the social front has been no less spectacular. The Care and After Care Committees that he started in Delhi, to work in collaboration with the New Delhi TB Centre with a view to ameliorating the social and economic difficulties of the poor tuberculous patients, serve as beacon light to the rest of the country.

Dr. Sikand embodies the rare combination of a born teacher, top class physician, keen research worker, organiser and administrator of a high order, and what is much more, he has been a path-finder *par excellence* ever ready to take up a challenge and blaze new trails. As an active member for several years of the Standing Technical Committee of the Tuberculosis Association of India and the Tuberculosis Expert Group of the Indian Council of Medical Research he has made significant contributions. He presided over the National Tuberculosis Workers' Conference in 1959. He retired as the Director of the New Delhi TB Centre in 1966. Thus, for nearly 30 years he has served the cause of tuberculosis with rare devotion, steadfastness and foresight. Dr. Sikand was recipient of Kaiser-i-Hind Gold Medal on two occasions before Independence in recognition of his services to the cause of tuberculosis.

It is in the fitness of things that the Tuberculosis Association of India honours this great son of the country who has rendered such yeoman service to the cause of tuberculosis in general and Tuberculosis Association of India in particular. The Tuberculosis Association of India have decided to award the 1970 Gold Medal to Dr. Sikand for his outstanding contributions. It is a happy co-incidence that this honour is being conferred on Dr. Sikand in the conference which is being held in his own State so near to his home town. On behalf of the Tuberculosis Association of India, Workers in the field and on my own behalf I congratulate Dr. Sikand.

DR. A.C. UKIL

We regret to record the death in the early hour of February 24 last of Dr, A.C. Ukil, one of the most prominent TB specialists and well known in India and outside.



Born on 14th November, 1888 Dr. Ukil graduated from the Calcutta Medical College. In 1922, he proceeded to Paris for post-graduate studies in Pathology and Bacteriology at the Pasteur Institute. On return from Paris after two years he started practice in Calcutta in Clinical Pathology, Bacteriology and Phthisiology. In 1927, he was appointed the Director of Tuberculosis Enquiry, Indian Research Fund Association. In 1928-29, he was awarded the Ghosh Travelling Fellowship of the Calcutta University and returned to the Pasteur Institute in Paris for further research work. He was appointed in 1931 the Physician-in charge of the Chest Department, Medical College Hospitals, Calcutta, which he developed into an important centre of teaching and research in Tuberculosis in the country. He also continued as the Director, Enquiry of the I.R.F.A at the All-India Institute of Hygiene and Public Health, Calcutta, till 1943, in which capacity he made outstanding contributions in the epidemiology of Tuberculosis. Dr. Ukil was appointed in 1948 the Consulting Physician to the Chest Department of the Medical Hospital and continued to serve as such till 1963, when his illness forced him suspend his activities.

Dr. Ukil was a member of the first Medical and Publicity Sub-Committee of the first Anti-Tuberculosis Organisation in India, the Tuberculosis Association of Bengal. He took over the Chairmanship of the Bengal TB Association from the late Dr. B.C. Roy in 1948 and relinquished it for reasons of health in 1963.

He was elected an Emeritus Fellow of the American College of Chest Physicians. He was Councillor Member of International Union Against Tuberculosis. He became a corresponding member of the French Pathological Society and a corresponding editor of the Danish Journal *Mycopathologiae Mycologia Applicata*.

Dr. Ukil was a member of the Standing Technical Committee of the Tuberculosis Association of India and also of its Central Committee. He was President of the All-India Tuberculosis Workers Conference in 1949- He was a founder member of the Indian Medical Association and was a Honorary Member of the Calcutta Branch of the Indian Medical Association and was elected President of the All-India body in 1955-56. He was President of the West Bengal State branch of I.M.A. He was an Honorary Member of the Indian Association for Chest Diseases and served as its President for the year 1960. He was President of the Medical College Re- Union in 1961.

Dr. Ukil was the Consulting Physician for Chest Diseases of the institute

of Post-graduate Medical Education and Research, Calcutta since its creation. He was appointed Principal, Medical College and Superintendent of the Medical College Hospitals Calcutta in 1947 but resigned after serving for a period of nearly one and half years.

He was elected President of the Calcutta Rotary Club in 1935 and became the District Governor of Rotary International in 1942-43. He was awarded the Kaiser-I-Hind Gold Medal in 1941. He had been for a long time associated with the Masonic Movement in India and held some of its highest offices. In 1955-56, he was nominated the Sheriff of Calcutta.

He served the National Institute of Science of India of which he became the President in 1955-56. He was President of the Section of History of Sciences of the Indian Science Congress. He also served as an editor of "Science and Culture" from 1938 to 1957. He was elected President of the Medical and Veterinary Section of the Indian Science Congress in 1941. He was Sir J.C. Bose Memorial lecturer in 1956. He was the President of the Indian Science News Association in 1961-62.

He was associated with the Asiatic Society for a long time. He was awarded the Barclay Memorial Medal of the Society in 1951 and in 1960-61 was elected its President. Dr. Ukil was senator of the Calcutta University for a number of years and for a period, the Dean of the Faculty of Medicine of the University. He was Honorary Fellow of the State Medical Faculty of Bengal, Consulting Physician for Chest Diseases, Medical College Hospitals, Calcutta and the Institute of Post-Graduate Medical Education and Research. He was awarded the Coates Memorial Medal of the Calcutta University in 1925 for researches in Medicine. He was appointed the Basanta Memorial Lecturer in Public Health of the University in 1954-55.

He was invited abroad on a number of occasions to participate in international conferences and seminars. In 1948 he travelled to Washington as a participant in the 4th International Congress on Tropical Medicine and Malaria. In 1951, he visited the U.S.S.R. as a member of a team of Indian scientists and academicians led by Prof. P.C. Mahalanobis. In April, 1955 he was invited by the World Health Organization to participate in a conference in Geneva and in September of the same year he visited Paris to take part in meetings of the International Union Against Tuberculosis. In 1962 he was invited by the Cornell University at Ithaca, U.S.A., to participate in the History of Medicine Symposium held there.

In the early part of his career, during the first World War, he was arrested and interned in his home town for a period by the British rulers because of his association with the revolutionaries in Bengal.

The Tuberculosis Association of India introduced in 1966 its senior award—a Gold Medal—to a distinguished TB worker in the country. In appreciation of his a remarkable and colourful career and substantial contribution to TB work the Association honoured Dr. Ukil by choosing him as the first recipient of this Award.

A TRIAL OF RELATIVELY INEXPENSIVE REGIMENS IN THE DOMICILIARY TREATMENT OF PULMONARY TUBERCULOSIS

S. P. PAMRA, R. NARASIMHAN, HEM RAJ & G. P. MATHUR
(From New Delhi Tuberculosis Centre)

A co-operative study to investigate the efficacy of some relatively inexpensive regimens of chemotherapy in the domiciliary treatment of pulmonary tuberculosis was conducted by the International Union against Tuberculosis from 1966 to 1968 in 9 centres in seven countries. The New Delhi TB Centre was one of the participating centres.

Interim results of treatment of the 59 patients included in the trial from this Centre have already been reported earlier (Pamra et al, 1968). The present report is based on the final results of the stipulated one year's treatment.

Methods and Material

Freshly diagnosed patients of pulmonary tuberculosis who attended the Centre from 1st July, 1966 to 30th June, 1967 and fulfilled the following criteria were included in the trial :—

- (a) Age 15 years or more.
- (b) Sputum positive by direct microscopy.
- (c) Residents of the domiciliary service area of the Centre for at least one year and likely to stay on for another year.
- (d) Should have had no previous treatment for tuberculosis.
- (e) It must appear possible to treat them with any of the drug regimens.

Since some patients had to be given injections for one year, only those patients could be included in the trial, who were either living near the Centre or an injection centre maintained by the Care & After Care Committee in their residential locality. All patients were treated as out-patients.

The patients were randomly allocated to one of the following three drug regimens by opening serially the envelopes provided by the International Union :—

TH : INH 300 mg. with thiacetazone 150 mg. in a single dose daily for 52 weeks.

STH/SH2 : Streptomycin 1 gm. with INH 300 mg. and thiacetazone 150 mg. daily (or for 6 days a week) in single doses for 4 weeks ; followed by streptomycin 1 gm. with INH 600 mg. in single doses twice weekly (at intervals of 3 or 4 days) upto 52 weeks. Pyridoxin was not prescribed.

STH/TH : Streptomycin 1 gm. with INH 300 mg. and thiacetazone 150 mg. daily (or for 6 days a week) in a single dose for 4 weeks; followed by INH 300 mg. with thiacetazone 150 mg. in a single daily dose up to 52 weeks.

Pre-induction investigations consisted of 2 sputum examinations by direct microscopy and culture, a conventional sized chest x-ray, examination of urine and haemoglobin. RBC and total and differential white blood cell counts. Pre-treatment sensitivity of bacilli against streptomycin, INH and thiacetazone was also carried out. During the course of treatment, sputum, urine and blood examinations were repeated every 4 weeks and radiological examination of the chest every 3 months. The sensitivity tests were carried out in respect of all positive cultures.

Culture slopes of pre-treatment sputum specimen and 28 and 52 weeks' specimens (if positive by culture) were, in addition, sent to City Hospital Laboratory, Edinburgh, which was one of the Reference Laboratories designated for purposes of this study by the International Union.

There were in all 69 positive cultures during the entire study on which sensitivity tests were carried out in the Reference Laboratory and the Centre Laboratory. There was 91% agreement between the two laboratories in respect of streptomycin resistance and 87% agreement in respect of INH resistance. The analysis, however, is based on results from the Reference Laboratory.

A total of 59 patients were included in the trial. Their age and sex distribution, extent

TABLE 1
Type of cases included in the study

		TH	STH/SH2	STH/TH	Total
Total cases at start		18	21	20	59
Sex	Males	13	15	11	39
	Females	5	6	9	20
Age	15—35 years	11	14	17	42
	35 years and above	7	7	3	17
Extent of disease	Mod. advanced	3	3	7	13
	Far advanced	15	18	13	46
Cavitation	Not present	4	4	6	14
	Present	14	37	14	45
Drug resistant at start		4	2	2	8

of disease and cavitation is shown in Table 1. All cases were sputum positive by direct microscopy and culture. The results of pre-treatment sensitivity test are also included in Table 1.

All patients did not complete the stipulated treatment for 52 weeks. The number of patients withdrawn from the study with reasons thereof is shown in Table 2. There were 2 deaths during the entire study, one each

in regimen TH and STH/SH2. Both deaths occurred within the first month of treatment. Six patients, 2 in each regimen, left Delhi before the completion of treatment. Treatment as per protocol was unacceptable only to one patient in TH regimen who started taking streptomycin injections privately in addition to the drugs given from this Centre. He has been shown as non-cooperator in Table 2.

TABLE 2
Patients not completing 12 months' treatment and reason thereof

		TH	STH/SH2	STH/TH	Total
Total patients at start		18	21	20	59
Patients not completing 12 months' treatment	Major toxicity	2	5	2	9
	Pre-treatment resistance	2	1	1	4
	Non-cooperation or left area	3	2	2	7
	Unfavourable response (excluding death)	2		2	4
	Death	1	1	—	2
Patients completing 12 months		8	12	13	33
Patients whose results have been assessed		11	13	15	39

TABLE 3

Result of 12 months's treatment

	TH	STH/SH2	STH/TH	Total
Patients eligible for assessment	11	13	15	39
Sputum conversion	7/11 63.6%	12/13 92.3%	13/15 86.7%	33/39 82.2%
Cavity closure	5/8 62.5%	7/10 70.0%	7/10 70.0%	18/29 62.1%

Major toxic reactions accounted for 9 withdrawals from the study. It would be seen from Table 1 that the pre-treatment culture was resistant in 8 cases. Four of these were excluded from the final assessment because their pre-treatment culture was found resistant to streptomycin and INH in 2 cases, to INH in 1 case and to streptomycin in another. Of the remaining 4, 2 cases where the bacilli were resistant to a drug (streptomycin) which was not being given to the patient, were not withdrawn from the study. In one, the treatment regimen had already been changed because of major toxic reactions before sensitivity result became known and the 4th case had dropped out of the study (left the area) when the sensitivity result was received.

The protocol provided withdrawal of a case from the study because of 'unfavourable response' if the sputum was not converted by the 28th week or the sputum reverted at any time during the course of treatment after an earlier conversion. Three patients, two in TH and one in STH/TH regimen were withdrawn from the study because the sputum was not converted up to 28 weeks. One more patient in STH/TH regimen was converted in the 28th week but there was a reversion later, in the 48th week, along with radiological worsening. Thus, four patients in all were withdrawn from the study because of 'unfavourable response'.

In all, 26 patients did not complete the stipulated treatment and only 33 patients completed the treatment according to protocol. Assessment of results has, however, been based on 39 patients, counting 2 deaths and 4 'unfavourable response' as overall adverse results, even though the latter 6 did not complete one year's treatment.

Results

Table 3 shows the results of 12 months' treatment in respect of sputum conversion and cavity closure in the 3 regimens separately. The sputum conversion rate was 63.6%, 86.7%, and 92.3% in the TH, STH/TH and STH/SH2 regimens respectively. The number of cases in each of three regimens are too small for tests of significance to be applied. In the TH regimen, 4 patients are shown as unconverted. Excluding one death and 2 cases where treatment was changed because of 'unfavourable response' the fourth case is shown as unconverted in Table 3, since 48th & 52nd week cultures were reported as positive, having been converted earlier. Meanwhile the patient had completed 52 weeks' treatment.

All but two of the patients who completed 12 months' treatment had a regularity* of over 80% in the treatment. The two patients whose regularity was between 70 and 80 percent belonged one each to regimens ST^H,SH₂ and STH/TH. As both these patients had their sputum converted at the end of treatment, the results have been combined with those whose regularity was 80% or more.

Table 4 also shows the speed of sputum conversion in the three regimens. Most of the conversions in all regimens had taken place by the 28th week of treatment.

Table 4 also shows the emergence of resistant bacilli during the course of treatment among patients whose pre-treatment cultures were sensitive. Three patients in all

* Regularity has been defined as drugs actually consumed as 3 percentage of the amount that should have been consumed in any period.

TABLE 4

Speed of sputum conversion in the three regimens at various points in treatment

	TH	STH/SH2	STH/TH
4th wed.	2/13 (1)	4/18 (2)	6/18 (3)
12th week	*6/10 (1)	16/17	11/15
28th week	7/10 (2)	*15/17	13/14 (1)
48th week	7/8	13/14	13/13
52nd week	6/7 (1)	13/13	13/13

Figures in parenthesis show the number of cases with bacilli resistant to one or other drugs.

*One case, direct smear positive but culture negative, has been counted as unconverted.

showed evidence of resistant bacilli (to INH only in all three) in the TH regimen and out of these 3, one was converted during the course of treatment, one had to be withdrawn from the study because of unfavourable response and the third showed positive culture with resistant bacilli at 48 weeks and 52 weeks though he had been converted earlier in the 28th week and remained converted up to 44 weeks. One case with bacilli resistant to INH and the other to thiacetazone in STH/SH2 regimen were converted during the course of treatment. Out of 4 patients with resistant bacilli in STH/TH regimen, 2 with bacilli resistant to streptomycin and INH were converted during the course of treatment, one with bacilli resistant to streptomycin and INH was withdrawn because of unfavourable response and the fourth with bacilli resistant to thiacetazone had to be withdrawn because of major toxic reactions.

It has been mentioned earlier that the results of 4 cases have not been assessed because the pre-treatment culture was found to show resistant bacilli. By the time the results of the pre-treatment cultures were received, one of them in STH/SH2 regimen with bacilli resistant to streptomycin had been converted in the 12th week. The other 3 remained positive till they were withdrawn from the study. Of the 4 cases with pre-treatment resistant bacilli who have been included in the assessment for reasons already mentioned, one with bacilli resistant to streptomycin and INH was con-

verted in the 4th week of treatment in STH/SH2 regimen and one with bacilli resistant to streptomycin in TH regimen was converted in the 12th week. The remaining two (both with bacilli resistant to streptomycin only), one each in TH and STH/TH regimens remained unconverted.

The cavity closure rate is almost similar in all three regimens. Cavities closed in approximately two-thirds of patients in each regimen.

A significant feature of the 20 cases not included in the assessment in Table 3 (because of premature withdrawal from the study) was that whereas in all the 8 such cases in regimen STH/SH2, sputum had been converted, only one each out of 7 and 5 in regimen TH and STH/TH respectively were converted at the time of withdrawal.

Toxic reactions occurring during the course of one year's treatment are shown in Table 5. Reactions have been termed 'major' if the treatment had to be discontinued because of toxic reactions; 'moderate' if the reactions disappeared after a temporary withdrawal of drugs and did not recur when the drugs were restarted after a few days; and 'minor' if the reactions were mild and did not call for withdrawal of drugs even temporarily.

Nine patients had major reactions. One patient developed exfoliative dermatitis and

TABLE 5

Toxic reactions occurring during the course of treatment (12 months)

		TH	STH/SH2	STH/TH	Total
Total cases at start		18	21	20	59
Major toxic reactions	Exfoliative Dermatitis	1	—	—	1
	Stomatitis	1	—	—	1
	Giddiness	—	5	2	7
Moderate* toxic reactions	Giddiness	1	2	3	6
	Pruritus and skin rash	—	1	—	1
Minor toxic reactions	Giddiness	—	3	2	5
	Pruritus and skin rash	1	—	—	1
Total cases with toxic reactions		4	11	7	22
Cases with no toxic reactions		14	10	13	37
* Two cases of giddiness are included but in both of these streptomycin had to be discontinued in accordance with the protocol even if such toxicity had not occurred.					

one stomatitis in the first month in TH regimen. Five patients in STH/SH2 and 2 in SFH/TH regimen developed severe giddiness with or without vomiting.

Six patients developed moderate giddiness (2 in STH/SH2, 3 in STH/TH and 1 in TH regimen). One patient in this group developed skin rash and pruritus in STH/SH2 regimen. Minor toxic reactions were seen in 6 patients.

Six out of the nine 'major' reactions occurred during the first month of therapy (1 stomatitis and 1 exfoliative dermatitis in TH group, 3 giddiness in STH/SH2, 1 giddiness in STH/TH regimen). Three major reactions (giddiness) occurred after the first 6 months of treatment; (2 in STH/SH2 regimen in 32nd and 44th week and 1 in STH/TH regimen in 20th week). 'Moderate' giddiness appeared in one patient in TH group in the second month. All other 'moderate' reactions appeared in the first month. 'Minor' reactions continued to appear even upto the 10th month of treatment.

Giddiness developed in 2 cases in STH/TH

regimen just as they were completing first month of treatment and streptomycin was withdrawn not because of toxicity but because of the requirements of the protocol. These 2 cases are included in 'moderate' category in Table 5, since giddiness disappeared when streptomycin was withdrawn.

Thirty seven out of the total of 59 patients had no toxic reactions at all at any time during the treatment. Maximum toxic reactions of all degrees (11 out of 22) were seen in STH/SH2 regimen and minimum (4) in TH regimen. Regimen STH/SH2 also caused most of the 'major' reactions. Not a single case showed any evidence of INH toxicity in any regimen, even though pyridoxine was not administered. No abnormality in urine or blood examination was detected in any patient.

Discussion

The main objective of the study was to determine the relative superiority of one or other of the three regimens used in the trial. After one year's treatment, sputum conversion was obtained in 63.6 percent, 86.7 percent and

TABLE 6

Defaulter action (Home visits) for patients who completed 12 months' treatment

	TH	STH/SH2	STH/TH	Total
Number of patients	8	12	13	33
Total visits	32	45	56	133
Average visits per patient	4.0	3.7	4.3	4.0
Range of visits	0-9	0-5	0-12	0-12

92.3 percent in regimens TH, STH/TH and STH/SH2 respectively, No significance however can be attached to the differences in the conversion rate because :

- (i) The number of cases in each regimen was too small.
- (ii) In spite of randomisation, there were appreciable differences in respect of age and sex distribution, extent of disease and cavitation among the cases in the 3 regimens (because of small numbers).

Bignall (1969*) analysing the results of 454 patients who were eligible for assessment from all the nine participating centres, found sputum conversion after one year's treatment in 82 percent, 92 percent and 88 percent in regimens TH, STH/TH and STH/SH2 respectively. Further, the difference in the conversion rate in regimen TH and STH/TH was significant at 5 percent level but the difference between STH/TH and STH/SH2 was not significant. Bignall concludes that 'supervised intermittent regimen has no advantage over unsupervised oral regimen but addition of daily streptomycin during the first month in the unsupervised oral regimen significantly improves the conversion rate,

Superiority of a drug regimen however does not depend merely on its intrinsic efficiency and sputum conversion rates. In mass treatment, toxicity, acceptability, feasibility and cost of drug regimen have also to be reckoned with.

* Report on a controlled trial of three regimens of self administered and supervised chemotherapy for pulmonary tuberculosis presented at the International Tuberculosis Conference at New York, 1969.

Major toxic reactions in this study have been somewhat more in STH/SH2 regimen as compared to others but again the differences are not significant owing to small numbers. In Bignall's analysis based on the material from all the 9 participating centres referred to above, the frequency to toxic reactions of all types was practically similar in all the regimens. Therefore, from the toxicity point of view, none of the three regimens may be inferior to others.

When the intermittent regimen was tried in a few cases in this Centre in 1965, the results were rather discouraging. Consequently, there was some diffidence at the start of the trial. However, as the trial progressed it was obvious that all three regimens were almost equally acceptable to the patients. Almost all patients took treatment with a regularity of 80 percent. The visits to the patients' homes to bring about such a regularity are shown in Table 6, for patients who completed 12 months' treatment. It will be seen that there is no significant difference in the average number of visits per patient in the three regimens in respect of these patients. Nor did the pattern of regularity differ in the others who did not complete 52 weeks treatment, for one reason or other. It could, therefore, be inferred that if facilities for injections are provided within a reasonable distance from the patients' home, regularity and home visiting to obtain this, is no different in the purely oral regimen than in other requiring injections.

It may, however, be pointed out that considerable and elaborate arrangements had to be made for injections. Patients who were living nearby attended the Centre for injections. In some of the localities, the voluntary organisations (Care & After-Care Committees) have established injection centres where the

patients from the locality go at a fixed time and take an injection. Nearly half the domiciliary service area of the Centre was excluded from the trial because patients from those areas could not have been expected to come to the Centre regularly for injections because of long distance and there were no Care Committees in that area to establish subsidiary injection centres.

Lastly, the cost of treatment has also to be taken into consideration. Table 7 shows the

TABLE 7

Approximate cost of one year's treatment

TH	... Rs 27/-
STH/SH	... Rs 117/-
STH/TH	...Rs 49/-

average cost of one year's treatment per patient in each of the three regimens, including the cost of arranging injections. It would be seen that the cost of TH regimen is the lowest; the cost of STH/TH is nearly double of TH and the cost of STH/SH2 regimen more than 4 times that of TH. In a developing country where consideration of cost, both of the drugs

as well as of organisation (such as injection centres) cannot be ignored, regimen like STH/SH2 may not be feasible for mass application.

In conclusion, the supervised intermittent regimen does not seem to hold any appreciable advantage over the other two regimens, one partly and the other entirely unsupervised. since the results are not appreciably better inspite of organisational difficulties and the high cost, which would be almost prohibitive for treatment on a mass scale in poor developing countries. The cheapest unsupervised oral regimen (TH) does not appear to be much inferior to others, though if resources permit a little more expense, addition of daily streptomycin during the first month may further improve the results from this regimen.

ACKNOWLEDGEMENTS

Thiacetazone and INH tablets for this study were supplied free of cost by M/s. Smith and Nephew Pharmaceuticals Ltd. U.K.; cost of sending cultures to the Reference Laboratory in Edinburgh was met out of a grant from the Indian Council of Medical Research; the Care and After Care Committees of Wards No. 4 and 5, 8 and 9 financed injection centres in their areas. Help from all these is gratefully acknowledged. Thanks are also due to Dr. J.R. Bignall, Co-ordinator of the trial.

PAPER ELECTROPHORETIC STUDIES OF SERUM PROTEINS IN PULMONARY TUBERCULOSIS IN RAJASTHAN

C. R. VYAS, B. B. MAITRYA and T. C. APPANNA
(From Sardar Patel Medical College, Bikanar.)

Reversal of serum albumin-globulin ratio has been reported in a wide variety of diseases. Pilheu et al (1962) has quoted Adler who possibly for the first time in 1919 carried out serum protein studies in patients suffering from pulmonary tuberculosis, Luetscher (1941) was the first to conduct electrophoretic studies of serum proteins in pulmonary tuberculosis. Serum proteins in pulmonary tuberculosis have been studied electrophoretically in animals as well as in human beings but they lack unanimity regarding the percentage of their fractions during various stages of the disease, as reported by different workers. Total serum proteins have been reported to be increased (Gilliland et al 1956, Seibert et al 1947), normal (Leggat 1957, Schofield 1957) or decreased (Chievitz and Thiede 1960, Lawrence et al 1961) in tuberculosis. Alpha-1 globulins have been described as normal in minimal tuberculosis, but increased in the advanced disease (Chievitz and Thiede 1960, Schroeder 1960). A rise in the level of alpha-2 globulin in pulmonary tuberculosis has been mentioned by several workers (Luetscher 1941, Gaitonde et al 1958, Johnson et al 1967 and Agrawal et al 1969). Beta globulin has been found to be elevated in tuberculosis by some workers (Chievitz and Thiede 1960, Volk et al 1953, Gilliland et al 1956, Schroeder 1960 and Seibert et al 1947) while normal by others (Lawrence et al 1961, Schofield 1957 and McCuiston and Hudgins 1960). Johnson et al (1967) have observed an increase in the level of gamma globulin in pulmonary tuberculosis but Leggat (1957) and Schroeder (1960) have noted a low incidence of this abnormality.

There has been no diversity of opinions as far as the rise of alpha-2 globulin in pulmonary tuberculosis was concerned, but no such consistent findings pertaining to other fractions of serum proteins have been observed in this disease. So this problem to study the changes in total serum proteins and in their electrophoretic pattern during various stages of pulmonary tuberculosis in Rajasthan has been undertaken, which may be useful in assessing the severity of the disease and help in determining the prognosis, as in this part of the country the incidence of this disease is quite common.

Materials and Methods

This study was conducted on 56 male

subjects, out of them 11 were normal healthy adults devoid of any diseases and the rest (45) were patients admitted to G.G.J. Tuberculosis Hospitals, Bikaner. At the time of admission they were found to be suffering from pulmonary tuberculosis as evidenced by the raised E.S.R., positive radiographic findings and sputum.

These 45 patients were divided into the following groups;

1. *Tuberculous*—Patients suffering from well established pulmonary tuberculosis before starting any treatment—15.
2. *Treated*—Patients who were treated with streptomycin and PAS for three months and had responded to the treatment as was evident by diminished E.S.R., negative sputum and radiological findings—15.
3. *Resistant*—Those patients who failed to respond to streptomycin and PAS treatment given for three months—15.

All the patients belonged to poor class and had low nutritional status. The normal subjects also belonged to the same status and were treated as control.

5 ml of blood from antecubital vein was withdrawn and allowed to clot. Total serum proteins were estimated by the Micro-Kjeldahl method as had been described by Hawk et al (1965). The separation of various fractions of serum protein was performed by the standard technique of paper electrophoresis. The electrophoretogram (Fig. 1-4) was scanned by a photoelectric densitometer thereby obtaining a graph (Fig. 1-4) from which the percentage of protein fractions were calculated (Table I).

Results

The results have been shown in Table 1. The mean value of total serum protein in 11 normal subjects was 7.30 ± 0.15 which was found to be increased significantly in tuberculous (8.874 ± 0.12), treated (7.71 ± 0.11) and resistant (8.564 ± 0.15) cases. The total serum protein values in treated cases compared to tuberculous patients have been low, but were still higher than the normal subjects. The resistant cases showed quite a high value of serum proteins when compared to normal but was lower than the tuberculous cases.

TABLE I

Showing the total serum proteins (gm%) and their different percentage fractions in various groups of subjects.

Group	Total serum protein	Albumin	Globulin	Alpha-1	Alpha-2	Beta	Gamma
A-Normal 11*	7.30±0.15 (6.7-8.0)	54.78±0.37 (51.8-56.8)	45.22±0.47 (43.7-48.2)	4.34±0.15 (3.8-5.1)	8.83±0.52 (7.4-11.2)	14.25±0.34 (12.9-15.1)	17.80±0.19 (14.5-19.8)
B-Tuberculous 15*	8.87±0.12 (7.8-9.6)	39.60±0.47 (35.8-42.7)	60.40±0.53 (57.3-64.2)	8.15±0.19 (6.8-9.4)	14.96±0.26 (13.7-16.7)	14.62±0.31 (13.0-16.2)	22.67±0.55 (20.5-27.6)
C-Treated 15*	7.71±0.11 (7.1-8.2)	47.11±0.75 (38.8-49.4)	52.89±0.79 (50.6-61.2)	5.88±0.20 (4.9-6.8)	11.60±0.31 (9.4-13.1)	13.41±0.33 (11.6-15.9)	22.00±0.64 (20.7-26.5)
D-Resistant 15*	8.56±0.15 (7.2-9.5)	41.76±0.58 (38.5-45.9)	58.24±0.54 (54.1-61.5)	7.82±0.31 (5.6-9.1)	13.81±0.18 (12.2-15.4)	14.13±0.15 (12.2-15.4)	22.48±0.43 (18.1-26.3)
		‘t’ values					
Between A and B 24**	8.29 p<.001	25.20 p<.001	21.36 p<.001	5.17 p<.001	10.58 p<.001	0.81 NS	7.95 p<.001
Between B and C 28**	6.99 p<.001	8.43 p<.001	7.91 p<.001	8.38 p<.001	8.27 p<.001	2.67 P<.02	0.78 NS
Between B and D 28**	1.63 NS	2.87 p<.01	2.86 P<.01	0.90 NS	3.61 p<.01	1.41 NS	0.22 NS

Values are given as mean±S.E.; Figures in parentheses represent the range.

*Refer to the number of the subjects in each group.

**Show the degree of freedom in each group.

NS—Not Significant.

Albumin in normal cases was 54.78 ± 0.37 per cent which registered a fall in tuberculous (39.60 ± 0.47), treated (47.11 ± 0.75) and resistant (41.76 ± 0.58) cases. Globulin fraction in normal cases was 45.22 ± 0.47 per cent, which was raised to 60.40 ± 0.53 in tuberculous, 52.89 ± 0.79 in treated and 58.24 ± 0.54 in resistant cases.

Alpha-1 fraction was 4.34 ± 0.15 in normal and was raised to 8.15 ± 0.19 in tuberculous, 5.88 ± 0.20 in treated and 7.82 ± 0.31 in resistant cases. The alpha-2 fraction was 8.83 ± 0.52 in normal but was elevated in tuberculous (14.96 ± 0.26), treated (11.60 ± 0.31) and resistant (13.81 ± 0.18) patients. The beta globulin was 14.25 ± 0.34 per cent in normal and no significant variation was observed in tuberculous, treated and resistant group of patients. The gamma globulin in normal subject was 17.80 ± 0.19 which was raised to 22.67 ± 0.58 in tuberculous, 22.00 ± 0.64 in treated and 22.48 ± 0.43 in resistant patients.

Discussion

The mean total serum proteins were significantly increased (Table I) in tuberculous as compared to the normal cases ($p < 0.001$).

These observations are in close agreement with the findings of Gilliland et al (1956), Seibert et al (1947) and Antonini & Fava (1954) but disagree with that of Bobba et al (1948), Chievitz and Thiede (1960) and Lawrence et al (1961). The rise in total serum proteins has been solely due to increase in the globulin fractions as the albumin fraction has been decreased in pulmonary tuberculosis. It has been reported by Johnson et al (1967) that the most important factor affecting the protein abnormalities was fever which has dominant relationship with lower albumin, increased alpha-1 alpha-2 globulins. This increase in total serum proteins has been maintained in treated as well as in resistant cases. However, the total serum proteins in treated cases was lower than the tuberculous cases ($p < 0.001$), which has also been reported by Seibert et al (1947), Gilliland et al (1956) and Ratcliffe & Merricke (1957).

In tuberculous cases albumin fraction was increased ($p < 0.001$) and globulin fraction was decreased ($p < 0.001$) as compared to normal, possibly due to fever. When treated cases were compared to tuberculous cases they showed a significant rise in albumin ($p < 0.001$) and a fall in globulin ($p < 0.001$) fractions indicating a tendency towards normalcy when the pyrexia had subsided as a result of anti-tubercular treatment. The cases resistant to treatment, however, showed an intermediate level ($p < 0.01$), possibly due to the fact that though

they had been given anti-tubercular therapy but they had not responded to it.

There have been unanimous reports (Echelberger et al 1927, Molnar 1927 and Gilliland et al 1956) about the fall in the albumin and a rise in the globulin level of the serum proteins in pulmonary tuberculosis. Seibert et al (1942), working with rabbits had also reported that there was a progressive decrease in the amount and percentage of albumin which was in close corroboration with our studies.

Alpha-1, alpha-2 and gamma globulins were found to be elevated in tuberculous cases ($p < 0.001$). The increase in alpha-1 and alpha-2 fractions might be due to tissue destruction (Seibert et al 1947), severity of the lesion (Meyor et al 1955) and persistence of fever (Johnson et al 1967). The increase in gamma globulin seemed to be due to the immunological response of the host tissues for the production of anti-bodies (Seibert et al 1947, Everback 1950 and Knuchel and Kienle 1950) as well as might be due to liver impairment (Agarwal et al 1957 and Popper et al 1951). Increase of gamma globulin supposedly represented reactions in different phases of pulmonary tuberculosis like, activity (Volk et al 1953), chronicity (Maher et al 1957) or caseation (Virgilio and Anzano 1958). The bulk of the increment of gamma globulin, undoubtedly be not due to anti-body formation only but seemed to be due to nonspecific reactivity of the reticuloendothelial system (Baldwin and Hand 1953).

The fall of alpha-1 and alpha-2 globulin in treated cases as compared to tuberculous ($p < 0.001$) might be due to the caseation or diminution in tissue destruction, healing of the lesion and subsidence of fever as a result of anti tubercular therapy. However, no change could be detected in the level of gamma globulins in this group.

However, in resistant as compared to tuberculous cases all or some of these factors have not disappeared completely, thereby maintaining apparently low level of alpha-1 and alpha 2 ($p < 0.01$) globulins, while no change has been observed in gamma globulin. The persistently high level of gamma globulin in tuberculous, treated and resistant cases compared to normal might be due to the earliest to occur (Schofield 1957 and Pilheu et al 1962) and one of the last to disappear (Chievitz and Thiede 1960 and Maher et al 1957).

Beta globulin was unique as it continued to remain constant and did not show variations in any group, except a little fall as a result of treatment ($p < 0.02$) when compared to tuberculous cases. Our results were not in

agreement with those of Chievitz and Thiede (1960), Volk et al (1953), Gilliland et al (1956) and Schoroeder (1960), but were in close alignment with those of Lawrence et al (1961). Schofield (1957) and McCuiston and Hudgins (1960). Thus it seemed that beta globulin is least often abnormal. Johnson et al (1967) has also found a decreased albumin and increase of all the globulin fractions except the beta globulin.

Although these variations in serum proteins do not lead to a definite diagnosis of pulmonary tuberculosis but they do help in assessing the prognosis of disease.

Summary

Total serum proteins by micro-Kjeldahl method and its various fractions by electrophoresis were studied in 11 normal and 45 tuberculous patients who were divided into tuberculous, treated and resistant group of 15 each. A fall in albumin and a rise in the globulin fractions leading to an increase in the total serum proteins has been observed in tuberculous patients. Alpha-1, alpha-2 and gamma globulins were raised maximally while beta globulin did not show any variations in these patients. Anti-tubercular therapy tried to restore these values towards normalcy but resistant cases failed to do so. These results have been discussed in the light of the available literature.

ACKNOWLEDGMENT

We are grateful to Dr. D.G. Ojha, Principal and Controller and Dr. J.N. Razdan, Reader in the Department of Tuberculosis. G.G.J. Tuberculosis Hospital, Bikaner for providing all the possible facilities.

REFERENCES

1. Agarwal, K.L., Kumar, A. Kumar, S. Mangalik, V.S. (1957) *7. Ind. Med. Assoc.*, 29 (10), 387.
2. Agarwal, K.L., Narasimha' Rao, S. and Agarwal, D.P. 1969j *Ind. J. Tub.*, 16 (2), 54,
3. Antonini, P.M. and Fava, Q. (1954) *Gior. Mat. Infett. e parassit.*, 6, 249.
4. Baldwin, R.W. and Lland, C.N. (1954) *Am. Rev. Tuberc.*, 68, 372.
5. Bobba, P., Wunderly, C. and Wuhrmann, F. (1945) *Minerva Med.*, 1, 432.
6. Chievitz, E. and Thiede, T. (1960) *Acta Tuberc. Scand.*, 399,270.
7. Echelberger, L. and McCluskey, K.L. (1927) *Arch. Int. Med.*, 40,831.
8. Everbeck, H. (1950) *Klin. Wchnschr.* 28, 638.
9. Gaitonde, B.B., Shinde, A.G. and Rao, G.S. (1958) *Ind. J. Tub.*, 6 (1), 12.
10. Gilliland, I.G., Johnson, R.N., Stradling, P. and Abdel-Waheb, EN. 1956 *Brit. Med. J.*, 1,1460 1460.
11. Hawk, P.B., Oser, B.L. and Summerson, W.H. (1965) *Practical Physiological Chemistry*, McGraw-Hill Book Co. Inc., New York, 14th Ed., 1081.
12. Johnson, J.R., Wakened, S.I. and Turk, T.L. (1967) *Dis. Chest*, 52 (6), 732.
13. Lnuchel, K. and Kienle, F. (1950) *Arzil Forsch.*, 4, 81.
14. Lawrence, S.H., Weimer, H.E. and Salkin, D. (1961) *J. Lab. Clin. Med.*, 57, 388.
15. Leggat, P.O. 1957 *Brit. J. Tuberc.*, 51, 139.
16. Luetscher, J.A. Jr. (1941) *J. Clin. Invest.*, 20, 99.
17. Maher, J.R., Miller, Fraser, R.S. and Lincoln, A.F. (1957) *Ame. Key. Tuberc.*, 75 999.
18. McCuiston, C.F. and Hudgins, P.C. (1960) *Am. Rev. Tuberc.*, 19,178.
19. Meyer, A., Kaufman, H., Gelin, J. (1955) *Rev Tuberc.*, 19,178.
20. Molnar, V. (1937) *Beiter. Klin. Terbeck*, 89, 83.
21. Pilheu, J.A., Lanello, J.A., Torrent, R.B. and Willson, J.A. (1962) *Dis. Chest*, 41,173.
22. Popper, H., Bean, W.B., De Lo Huerger, J., Franklin, M., Tsumagaris, Y., Routh, T.I. and Stiegmann, F. (1951) *Gastroenterology*, 17,138
23. Ratcliffe, H.L. and Merricke, J.V. (1957); *Am. J. Path.*, 33 1121.
24. Schofield, F.D. (1957) *W. Afr. J. Bio/ Chem.*, 1,44.
25. Sehroeder, K.J. (1960) *Ztschr Tuberk*, 116, 132.
26. Seibert, F.B., and Nelson, J.W. (1942) *J Biol. Chem.*, 143,29.
27. Seibert, F.B., Seibert, M.V., Atno, A.J. and Campbell, H.W. (1947). *Clin. Invest.*, 26,90.
28. Virgilio, R. and Anzano, O. (1958) *Arch Tissiolo.*, 13, 654.
29. Volk, B.W., Saifer, A., Johnson, L.E. and Oreskes, I (1953) *Am. Rev. Tuberc.*, 67, 299.

PRELIMINARY HOSPITALISATION IN THE DOMICILIARY MANAGEMENT OF PULMONARY TUBERCULOSIS

S. BRAHMANANDA RAO

(from Government Medical College, Kurnool)

Introduction

Domiciliary management is now an accepted method of treatment of pulmonary tuberculosis. It is shown by a well-known clinical trial that very good results can be obtained by domiciliary management provided the patients receive an adequate and regular anti-tuberculosis drug therapy (Madras tuberculosis Chemotherapy Centre (1955). But, in practice, this ideal situation is not obtained as many patients become defaulters and thus discontinue anti-tuberculosis drugs.

In this article an attempt is made to show whether or not a preliminary hospitalisation, lasting for two to three months, during which period, patients receive an intensive chemotherapy with daily Streptomycin, and I.N.H. will help in improving the results of a subsequent domiciliary management.

Material and Methods

This work is dependent on the assessment of radiological and sputum status of old patients of pulmonary tuberculosis who came for a check-up during the period of 1-3-67 to 31-12-67 at the T.B. Clinic, Government General Hospital, Kurnool. Only patients who are first diagnosed as suffering from adult type pulmonary tuberculosis during the year 1965 and 1966 were included in the survey. The following were excluded :—

1. Children 15 years and below.
2. Primary infections with their attendant complications like pleural effusions, miliary tuberculosis, mediastinal lymphadenitis with or without collapse etc.
3. Chronic fibroid type of disease.
4. Destroyed lung cine to atelectasis, bronchiectasis etc.
4. Bi-lateral extensive disease with lesions occupying four or more than four X-ray zones.
6. Patients whose period from the date of first diagnosis to the date of review is less than one year.

7. Patients whose original or present radiological and bacteriological data are not available for some reason or other,
8. Patients in whose case it is not known with definiteness whether he was previously hospitalized or not.

For each individual patient miniature X-ray photo of the chest was taken and his sputum was examined by direct smear for A.F.B. The X-ray pictures of the patients who came for review were read by the writer long after the patient came for review and at the time of reading the X-ray photo the reader was not aware whether the patient had preliminary hospitalization or not. Thus bias is avoided. The radiological status at the time of review is classified as follows:

- 1) Clear: If the chest X-ray was absolutely clear without any foci whatsoever.
- 2) Quiescent: If the chest X-ray showed foci calcified or fibrotic of which, there is no doubt regarding quiescence.
- 3) Active: If definitely active lesions are seen
- 4) Indefinite: Where foci are seen but there is doubt regarding activity or quiescence.

Information regarding whether the patient was previously hospitalized or not and the actual period of stay was obtained from the hospital and clinic records.

Total No. of patients analysed	229.
No. of patients who had the benefit of preliminary hospitalization	94
No. of patients who were from the beginning treated on domiciliary basis	135

Table I gives the sex-distribution of the patients. All the patients included are between the ages of 16 and 60. The patients were grouped into three stages according to the radiological extent of disease at the time of diagnosis.

First Stage: Extent of disease not more

TABLE I
Sex distribution of patients in the two groups

	M	F	Total
Hospital	52	42	94
Home	89	46	135

than one zone. If bilateral total extent of disease should not be more than one zone.

Second Stage : Total extent not more than 2 zones. If bilateral total extent should not be more than one zone on each side.

Third Stage : Total disease not more than three zones.

All patients who showed lesions more extensive than the above were excluded from the survey, as in such cases it is thought, it will be difficult to determine the radiological activity at the time of review. Thus 2 from hospital group and 12 from home group were excluded.

Table II gives Stage distribution in the 2 groups

It can be observed that I stage disease is more common in the home group, where as II stage disease is more common in hospital group. III stage disease has equal proportion in both groups.

TABLE II
Distribution of stages in the two groups

	Total	I	II	III
Hospital	94	10(10.6%)	55(58.5%)	29(30.9%)

Among the 94 hospital patients, their period of stay is as follows :

19 Patients stayed in the Hospital for about			
			2 months.
22	—do—	—do—	3 months.
36	—do—	—do—	4 months.
9	—do—	—do—	5 months.
8	—do—	—do—	6 months.

Observations

A) Hospital Group :—Of the 94 patients, 31 patients (33%) had complete radiological clearance. 45 patients (47.9%) had quiescent foci. 15 patients (15.9%) had active lesions of whom 8 (8.5%) were sputum positive. 3 (3.2%) were having X-ray shadows which were classified as indefinite.

B) Home Group :—Of the 135 patients 24 patients (17.8%) had complete radiological clearance. 46 (34.1%) had quiescent foci. 58 (43%) had active lesions of whom 21 (15.6%) are sputum positive. 7 had indefinite lesions. The results are summarised in Table III.

From Table III, it can be observed that a favourable result (radiological quiescence and complete clearance) is obtained more often in the hospital Group than home Group, 80.9% compared to 51.9%. The difference of about 29% is quite significant.

Table IV gives the result of hospital and home groups stage wise. It can be observed that in all stages, the hospital Group fared better than home group. But in Stage I disease, even home group gave a very satisfactory result, 85% having obtained radiological clearance or quiescence. In stage III disease the hospital patients fared far better than home patients. (64.5% compared to 23.8%).

Table V gives the details regarding sputum

TABLE III

Radiological and sputum status at the time of review

	Clear	quiescent	Active	Indefinite	Sputum positive
Hospital 94	31(33%)	45(47.9%)	15(15.9%)	3(3.2%)	8(8.5%)
Home 135	24(17.8%)	46(34.1%)	58(43%)	7(5.18%)	21(15.6%)

DOMICILIARY MANAGEMENT OF PULMONARY TUBERCULOSIS

TABLE IV

Radiological status stage-wise at the time of review

	Stage I		Stage II			Stage III					
	Clear cent	Quies	Active Clear		Quies-cent.	Doubtful Active		C	Q	A	Dbt.
Hospital	4	6	—	20	26	6	3	7	13	9	—
Home	14	12	5	8	26	25	3	2	8	28	4

TABLE V

Details regarding sputum conversion by direct smear

	Hospital	Home
Originally sputum positive	49	79
Became sputum negative	43	61
Still sputum positive	6(12.2%)	18(22.8%)
Originally sputum negative	45	56
Remained sputum negative	43	53
Became sputum positive	2	3

conversion by direct smear. It can be observed that out of 79 home patients who are sputum positive at the outset. 18 (22.8%) remained sputum positive at the time of review, whereas in the hospital group out of 49 sputum positive patients, only 6 (12.2%) remained sputum positive.

Table VI gives the radiological quiescence, when related to the duration of hospital stay

TABLE VI

Radiological quiescence related to duration of stay in hospital

Duration of stay	Total No. of patients	Radiological quiescence
2 months	19	14(73.7%)
3	22	18(81.8%)
4	36	28(77.7%)
5	9	9
6	8	8

in respect of the hospital group. Taking all the patients whose stay in the Hospital is 4 months or less, 73.7%, 81.8% and 77.7% became quiescent for 2, 3, 4 months stay respectively. This compares very favourably with the home group, whose over-all quiescent lesions are about 51.9% only.

In addition, an attempt is also made to study the regularity or otherwise in treatment of the patients under review. This information is obtained from the treatment cards of these patients. Those patients who received 80% or more of treatment during the first one year after diagnosis are considered as regulars. The rest are considered as defaulters. Table VII

TABLE VII

Regulars and defaulters in both groups

	Total	Regular	Defaulters
Hospital	63	41(64.2%)	22(35.8%)
Home	96	44(45.8%)	52(54.2%)

gives the number of regulars and defaulters in both groups. Only 63 patients of the hospital group and 96 patients of the home group could be studied. It can be observed that 64.2% of the hospital group were regular, whereas only 45.8% of home group were regular. The difference of 18.4% is significant.

Table VIII gives the radiological status of the regulars and defaulters of both groups. It can be observed that the regulars in both hospital and home groups have done very well, 93% and 75% showing radiological quiescence. Even here the hospital group showed better result. As far as sputum conversion by direct smear is concerned, the results are extremely satisfactory in both groups. Among the defaulters, 68.1% of hospital group showed radiological

quiescence compared to 28.8% in home group. The differences are very high. But, regarding sputum conversion by direct smear, the differences are not impressive, 22.7% of hospital group compared to the 28.8% in home group are still sputum positive at the time of review.

TABLE VII

Radiological and sputum status related to regularity

	HOSPITAL		HOME	
	Regular	Defaulter	Regular	Defaulter.
Total	41	22	44	52
Quiescent & Clear.	39	15	33	15
Active	2	7	8	36
Indefinite	-	—	3	1
Sputum Positive	Ni!	5	1	15

Discussion

At the outset it is to be remembered that this is not a comparison between hospital patients and home patients. All the patients are mainly treated on a domiciliary basis except that some of them have stayed in the hospital for varying periods during the initial stages of their management. The findings in this study are mainly dependent upon a radiological assessment of patients at the time of review. Radiological assessment, as is well known, is somewhat subjective, and mistakes are likely to creep in in determining whether a lesion is active or quiescent. However, an attempt is made to make the findings as objective as possible. Absolute radiological clearance and absolute radiological quiescence indicated by fibrotic scars and calcified shadows only are included as quiescent. It is therefore possible, that some of the lesions termed as active may be quiescent lesions, especially in view of the fact, majority of them are sputum negative by direct smear. Bias is avoided by reading the X-ray films first, without knowing whether they belong to hospital or home group.

Domiciliary management is our mainstay in the attack against tuberculosis. Under ideal circumstances it is very efficacious, but in practice, it encounters many difficulties, of which the defaulter problem has become a real menace. No satisfactory solution has yet been found to answer this problem.

In addition, it is to be emphasised that we have yet to find a suitable drug combination for domiciliary regimes, especially for the initial management of pulmonary tuberculosis. Any combination containing streptomycin is administratively not easy. It puts heavy burden on the clinic Staff. It has been shown in a recent clinical trial, that intermittent chemotherapy with S.M. 1 gram B.W. & I.N.H. 650 M.G. B.W. (J.L. Bhatia & Baldev Raj. 1968) is associated with high defaulter rate. 56.7% did not collect full 12 months drugs supply. Besides it involves additional expenditure to the patients who have to make frequent visits to the clinic. It is clearly unsuitable for a patient who is coming from a long distance. The authors also felt that the radiological healing was less dramatic was accompanied with more fibrosis than is and seen with vigorous streptomycin and I.N.H.

Thiacetazone and I.N.H. combination promises to be a good regime, as it is cheap and efficacious. But its main drawback is its intolerance and some times serious toxicity. In a series reported by G.D. Gothi, et al, when the drugs were given in a single daily dose, 4% had major side effects and 18 out of the 127, put on treatment developed minor side effects, mainly giddiness and vomiting. Only 41%, completed 10 months to one year treatment. According to the authors, serious toxicity in some patients might contribute to enhance irregularity and even permanent drug default in other patients.

PAS & I.N.H. combination is too costly and PAS has similar difficulties like thiacetazone though on a lesser scale.

In the T.B. Clinic, at Government General Hospital, Kurnool, it was the practice at the time of this study to put local patients on S.M. one gram B.W. and I.N.H. 650 M.G. B.W. and for patients coming from a long distance Thiace-tazone 150 M.G. and I.N.H. 300 M.G. daily. (One month's quota being given in each attendance). Both regimes were given for a period of 1 year. During the period of hospital stay, Streptomycin 1 gram daily with I.N.H. 300 m.g. daily was given for a period of 3 months.

From the analysis of the results mentioned already, it is observed that 80.9% of patients who had preliminary hospitalization showed radiological stabilization (33% had complete clearance) whereas only 51.9% of the home patients showed radiological stabilization (17.8% had complete clearance). The difference of 29% is of reasonable magnitude. In the hospital group 12.2% of the originally sputum positive cases are still positive at the time of

review. While in home group 22.8% are sputum positive, here also results are better with hospital group. Correlating the duration of stay with radiological stabilization, it may be observed that the radiological stabilization of patients with 2, 3, or 4 months stay are 73.7%, 81.8% and 77.7% respectively. This compares favourably with the home group whose over-all quiescent lesions are about 51.9%. Hence it is felt that a preliminary stay in the hospital of 2 to 3 months duration is likely to give optimum results with a good turnover. An attempt is also made to find out the factors which may be responsible for better result in the hospital group.

(1) From Table VII, it is observed that 64.2% of hospital group patients have received 80% or more of 1 year's treatment compared to 45.8% of home group. The patients who had the benefit of preliminary hospitalization appear to be more regular in drug taking. This itself can be due to a strong motivation and education generally given in wards. In addition the patient may become somewhat disciplined and is more likely to realise the importance of regular drug taking as well as the dangers of untreated disease.

(2) Even among the regulars in both groups, though the results are quite good in the home group (33 out of 44, "75%" had radiological stability) they are further improved by a preliminary hospitalization (39 out of 41 had radiological stability.) This may be due to the intensive chemotherapy with daily streptomycin and I.N.H., that is given during the period of hospital stay.

(3) Among defaulters, 68% of hospital group showed radiological stabilization compared to 28.8% in home group. It is possible that if a strong anti-tuberculous combination is given at the outset, relapses may not occur subsequently, even if a patient becomes a defaulter. However as the difference in sputum conversion (22.7% in hospital group and 28.8% in home group are sputum positive at the time of review as seen in Table VIII) are not so impressive, conclusions on this aspect cannot be drawn.

From Table IV, it can be observed that patients who have I stage disease at the time of diagnosis fared well in both groups. Therefore, patients with early disease may be put on domiciliary treatment without any preliminary hospital stay.

For the rest of the patients, preliminary hospitalization for a short period of 2 to 3 months, during which period an intensive chemotherapy is given, appears to be a very important and necessary step in a successful domiciliary programme.

REFERENCES

- (1) Madras Chemotherapy Centre; (1959; *Bull Wld Hlth Org* ;21, 51.
- (2) Bliatia J.L. and Baldev Raj ; *Indian Journal of Tuberculosis*, 67.
- (3) GothiG.D. O' Rourke, Raily C-V.J : N.T. *News Letter* ; 1

A STUDY OF AMYLOIDOSIS IN PULMONARY TUBERCULOSIS

C.R.R.M. REDDY, G. SULOCHANA, T. RAMA RAO AND C. SITA DEVI
(From Kurnool Medical College, Kurnool.)

Though once amyloidosis was regarded as rare in this country (Gharpure 1951, Reddy 1951) recent reports suggest that amyloidosis is not so uncommon (Mathur and Jhala 1964, Chitkara et al 1965, Reddy and Parvathi, 1968). The type, where a chronic destructive lesion like tuberculosis or pulmonary suppuration led to amyloidosis, was more common. Among the diseases which give rise to amyloidosis, tuberculosis was the commonest recorded. Thus Chitkara et al 1965 recorded tuberculosis as the cause in 35 out of 56 cases of secondary amyloidosis seen at autopsy. In the 22 cases of secondary amyloidosis recorded by Reddy and Parvathi (1968) 17 were due to tuberculosis. Prospective studies to find out the actual incidence of amyloidosis in tuberculosis are not many in this country. It has been done extensively in other countries and even changing patterns have been recorded. Thus Cohen 1943 recorded that 39 percent of 143 autopsies on tuberculosis cases showed amyloidosis and also that in 26 out of 79 patients suffering from tuberculosis amyloidosis was present. Kozello (1963) recorded an increase of incidence of amyloidosis over the years. Yoshizumi (1962) also recorded a changing pattern. Chugh et al (1960) did a general prospective study in this country. We felt it will be worth while to know the incidence of amyloidosis in cases of pulmonary tuberculosis in this part of the country and the following study was undertaken. Material and Methods

All the cases of amyloidosis seen in our autopsy series were analysed. In one year autopsy was done on all cases dying of pulmonary tuberculosis which came to the mortuary.

A prospective study was undertaken in 60 patients with proved bilateral pulmonary tuberculosis of long duration. The cases were fresh ones and not treated ones.

All the 60 cases had bilateral pulmonary tuberculosis by X-ray. 38 of them showed extensive bilateral pulmonary tuberculosis. 11 had more lesions in the right lung and the other 11 had more lesion in the left lung. 11 had extensive cavities and the others had infiltration. 21 gave a history of less than 6 months duration, 19 between 6 months and one year, 10 between 1 year and 2 years, 4 between 2 and 3 years and 6 above 3 years history. The history usually consisted of fever and cough with expectoration. The following examinations were carried out:—

- (1) Urinalysis for proteins and casts was done in all the patients to know how many of them had albuminuria.
- (2) Classical congo-red test was done in 40 out of 60 cases. If there was 0—20 percent retention of the dye in serum the test was taken to be positive, 21 percent—40 percent serum retention was taken as suggestive and 41 percent—100 percent serum retention was taken as negative.
- (3) Gum biopsy was done in 57 cases. In 37 cases both gum biopsies and congo-red tests were done. In all the 60 cases either a gum biopsy or congo-red test was done.

The gum biopsies and the autopsy material was stained by haematoxylin-eosin, congo-red and crystal violet. Congo-red sections were seen between crossed polars for green birefringence for amyloid (Cohen 1967).

Results

Between September 1960 to June 1969, 1988 (excluding still births) autopsies were done and in them 32 had amyloidosis, 4 of them of the primary type and the other 28 of the secondary type. Out of these 28, in 22 there was extensive tuberculosis.

During one year in 1967, 57 people died of tuberculosis and came for autopsy and in 11 of them there was amyloidosis thus forming 19.3 percent.

The 60 patients on whom a prospective study to find the incidence of amyloidosis was done, consisted of 52 males and 8 females — 4 belonged to 2nd decade, 18 to 3rd, 25 to 4th, 6 to 5th, 6 to 6th decade and one was above 60 years.

Out of the 57 gum biopsies done 14 were positive for amyloid. In the 40 congo-red tests done, in only one case there was 38 percent serum retention of dye but in all the other cases the serum retention of congo-red was above 40 percent showing that it was negative. Albuminuria was present in 14 cases ranging from traces to three plus but in only 5 cases albuminuria was associated with a positive gum biopsy for amyloid. In the case where there was 39 percent congo-red retention in serum the gum biopsy was positive and also albuminuria was present. Thus 14 out of 60 cases were positive for amyloid forming 23.34 percent of cases. These 14 cases consisted of one female of 16 years and 13 males, all being above 30 years of age.

14 cases which showed amyloid had bilateral lesion in 9, more right sided in 3 and left sided lesion in 2. 5 of them gave less than 6 months history, 2 between 6 months to 1 year, 3 between 1 year and 2 years, 2 between 2 and 3 year; and 2 above 3 years.

Comment

We did not come across any report of a study to determine particularly the incidence of amyloidosis in tuberculosis prospectively in this country. Chugh et al (1960) tried to find out the incidence of amyloidosis in a variety of diseases and also studied 24 cases of pulmonary tuberculosis in 4 of whom there was amyloidosis thus forming 16.7 percent. All 4 of their cases had albuminuria also 2 out of the 3 congo-red tests done by them were suggestive for amyloid and one was negative. In Cohen's (1943) studies, 26 (33 percent) out of 79 patients had amyloidosis, some of them even confirmed at autopsy later. In the same series 75 percent had albuminuria and casts and Cohen remarked that albuminuria should make one suspect of amyloidosis. In the same series, congo-red test showed in a number of cases (33 percent) no serum retention of the dye indicating not only a large number of positive cases but also complete absorption of the dye by the amyloid tissue. In the present series of 60 cases, 14 (23.3 percent) showed amyloidosis by gum biopsy. One congo-red test only was suggestive and five out of the 14 with amyloidosis had albuminuria. These findings show that amyloidosis is less in cases of tuberculosis in this country, when compared to the West. Congo-red test is not of much use in these parts because only in one case out of 40 the test was of some value and even in that it was only suggestive. This probably may be due to the fact that amount of amyloid formed in cases in this country may not be extensive.

Calkins et al (1960) are of the opinion that gum biopsy is very helpful in diagnosis of amyloidosis and with the added method of seeing the sections between crossed polars the use of the procedure is enhanced. Gum biopsy in our hands was also quite helpful.

Autopsy evidence also proves that amyloidosis though present is not as much as is present in the West in cases of tuberculosis. 19.3 percent of our cases of pulmonary tuberculosis showed amyloidosis at autopsy. Whereas 39 percent of cases showed amyloidosis in Cohen's (1943) series. Kozello (1963) recorded an incidence of 20.2 percent in 1946 and 41.3 percent in 1956 thus showing an increase in Moscow. Yoshizumi (1962) recorded a sharp drop of incidence of amyloidosis after the advent of chemotherapy and recorded an

over all percentage of 19 percent in 1109 cases of tuberculosis. These figures again show that the percentage incidence of amyloidosis in tuberculosis patients in West is higher when compared to ours.

The figures in the present series are in sharp contrast to those of Muir and Thomas (1963) from Singapore. He recorded only 2 cases of amyloidosis in over 10,000 autopsies. We have no explanation to offer for this sharp difference.

Similar studies in leprosy have shown that amyloidosis in leprosy is high in the U.S.A. whereas in Mexico it is very low (Williams et al 1965).

Summary

The incidence of amyloidosis in pulmonary tuberculosis in South India is about 19 percent in autopsies and about 23 percent in a prospective study of patients. This is in sharp contrast to Western figures where the incidence is much higher both in autopsy and living population.

REFERENCES

1. Calkins, E., Cohen, A.S., and Larsen, B. (1960). Amyloidosis. *Ann. New York Acad. Sci.* 86 : 1033-1042, 1960.
2. Chitkara, N.L., Chugh, T.D., Chhuttani, P.N., and Chugh, K.S. : Secondary amyloidosis. *Ind. J. Path. Bad.* 8 : 285-293, 1965.
3. Chugh, K.S., Singh, S., Balasubramanyam, M., and Chhuttani, P.N. : Secondary amyloidosis. *Jour. Asso. Phy. of India*, 8 : 583-594, 1960.
4. Cohen, A.S. : Amyloidosis, *New Eng. Jour. of Med.* 277 : 522-530, 574-583, 528-638, 1967.
5. Cohen, S. : Amyloidosis complicating tuberculosis, diagnosis, prognosis and treatment. *Ann. Int. Med.* 19 : 990-1002, 1943.
6. Gharpure, V.V. : Amyloidosis—A report of 7 cases. *Ind Med. Gaz.* 86 : 545-548, 1951.
7. Kozello, N.A. : Serum protein changes in Amyloidosis. *Klin. Med. Mosk.* 41 : 79-85, 1963.
8. Mathur, B.B.L., and Jhala, C.I. : Amyloidosis—An emphasis on increasing incidence in India. *Ind. J. Path. Bad.* 7 : 133-145, 1964.
9. Muir, C.S., and Thomas, M.A. : Geographical pathology of Amyloidosis in Singapore. *Path Microbiol.* 27:848-849, 1964.
10. Reddy, D.J. : Amyloidosis. *Intl. Med. Gaz.* 86 : 548-55J, 195J.
11. Reddy, C.R.R.M., and Parvathi, G. : Amyloidosis. *Ind. Jour. Med. Sci.* 22 : 770-774, 1968.
12. Williams, R.C., Cathcart, E.S., Calkins, E., Fite, G.L., Rubio, J.B., and Cohen, A.S. : Secondary amyloidosis in lepromatous leprosy. *Ann. Int. Med.* 62 : 1000-1007, 1965.
13. Yoshizumi, M., and Li, T.G. : Incidence of amyloidosis in tuberculosis. *Amur. Rev. Resp. Dis.* 85 : 432-435, 1962.

CONJUNCTIVAL TUBERCULOSIS REVIEW AND A CASE REPORT

MRS. SUNDERI MIRCHANDANI, Miss T. J. PATEL, P. A. DIKSHIT AND M. R. LOKESWAR
(From TopiwaJa National Medical College, Bombay)

and

(B. Y. L. Nair Charitable Hospital, Bombay)

Review

The credit for first description of ocular tuberculosis goes to Maitrejan in 1740. Langenbeck in 1835 gave a clear description of the case of uveal tuberculosis at necropsy and Jager in 1855 gave description of clinical ocular tuberculosis. Arit described tuberculous conjunctivitis and demonstrated the spread of lupus from cheek into conjunctival sac. Roaster reported (1873) tuberculous nodule in Conjunctiva and Shattler (1874) demonstrated ulcerative tuberculous conjunctivitis, who also formulated a clinical classification of conjunctival lesion or morphology of the lesion.

Even though tuberculosis is a major cause of morbidity and mortality in our country ocular tuberculosis is uncommon and conjunctival tuberculosis is a rarity. Very few reports are available on Indian literature so it is difficult to give exact incidence. Brodely had found no case among 41730 patients treated at Baltimore, Eye, Ear, Nose and Throat Charitable Hospital and also at Institute of Ophthalmology at Presbyterian Medical Centre. Reports from Tuberculosis sanatorium showed incidence of ocular lesion less than 0.1% among 10400 patients and was turned out 1.5% when examined by an Ophthalmologist. Amster (1957) placed ocular tuberculosis in tuberculous sanatorium as less than one percent. Incidence has decreased markedly recently because of decline in the incidence of systemic tuberculosis. Majority of cases are seen in younger group under 20 years and it is twice as common in females than males.

Mode of infection of ocular tuberculosis is mainly by two ways :—

I-Infection of ocular tissue by organisms. *Clinical picture*

II—Allergic manifestation to the tuberculous protein.

(a) *Direct extension* - from surrounding lesion such as lupus.

(b) *Direct Inoculation of the Eye*: The source may be : Contact with actively infected individual, contaminated

articles of clothing, fingers infected with infected sputum or milk, dried particles of infected material in the air. Majority of the cases get infected by this way as suggested by Eyer.

(c) *Endogenous source* :—From active or apparently inactive focus in some part of body, milliary or disseminated spread may occur and metastatic focus may be seen in conjunctiva or other ocular tissue. Eyer was unable to produce this experimentally in rabbits and concluded this type of infection rare. The primary focus is usually considered in mediastinal glands with or without active pulmonary tuberculosis. Wardenbey reported 500 cases of ocular tuberculosis of which 60% showed hilar lymphadenopathy 30% showed old inactive lung lesion and 10% showed active systemic lesion.

Clinical picture

It is characterised by protien symptomatology and pleomorphic appearance. Symptoms may be trivial or severe and so ranging from discomfort and redness of eye to mucopurulent discharge lamination with inflammed oedematous eyelids with or without involvement of preauricular and submaxillary lymph nodes. Palpabral conjunctivitis is more common than bulbar and follicles may form on conjunctiva which may break down to form ulcer. Primary conjunctivitis is unilateral while secondary conjunctivitis is usually bilateral.

(A) According to mode of infection :

Primary—Exogenous infection in an individual who has not previously suffered from tuberculosis, infection may be air borne by contaminated dust particles or by direct contact with infected particles or by direct contact with infected person contaminated particles, clothes, etc.

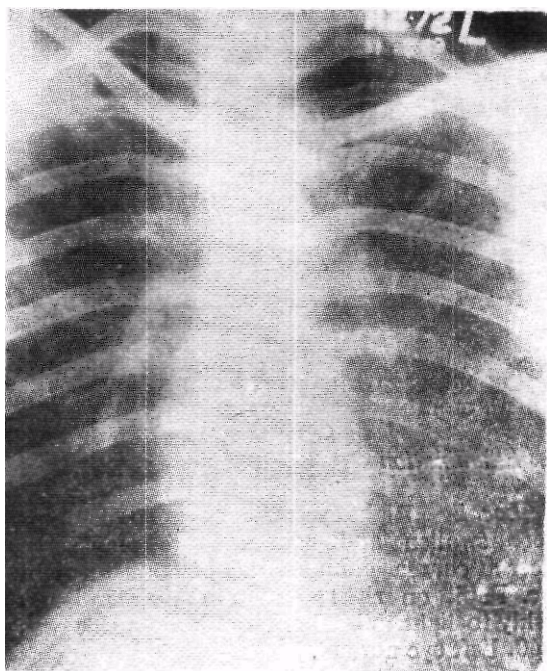


FIG. 1

X-ray of chest having miliary type of lesion both the sides., and apical infiltration.



FIG. 2

Shows right eye with lacrimation & inflamed oedematous eye lids.

Secondary—Patient has got clinical or sub-clinical tuberculosis. It may be exogenous by contaminated fingers, handkerchief etc., or endogenous through blood streams.

(B) According to morphological appearances:

- Ulcerative tuberculosis.
- Milliary tuberculosis.
- Hypertrophic granulation.

Pedunculated polypodal tumour.
Conjunctival tuberculoma. Lupus.

(C) According to anatomical situation:

Palpabral	70%
Bulbar	20%
Fornix	8%

Diagnosis

Diagnosis of ocular tuberculosis is based positively on histological study of biopsy

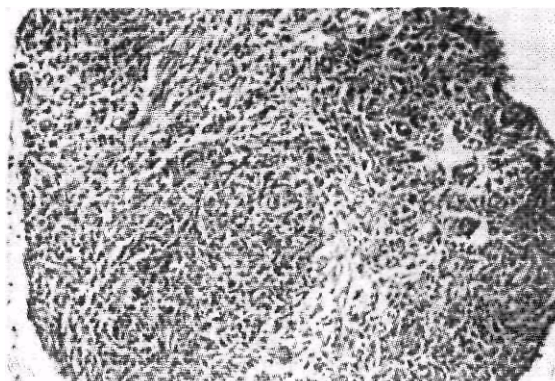


FIG 3

(Before treatment)

The section shows ulceration of the lining epithelium and inflammatory exudate rich in epithelioid cells,, lymphocytes, one or two giant cells. Suggestive of tuberculous lesion.

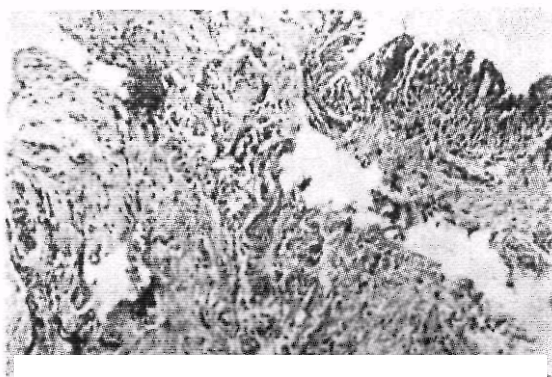


FIG. 4

(After treatment)

Section shows irregular hyperplastic squamous epithelium and dense fibrosis with dense mononuclear cells scattered irregularly. There is no evidence of active tuberculous inflammation in this section.

specimen or by isolation of tubercle bacilli. Only 25% of cases of ocular tuberculosis showed tuberculous bacilli on microscopic examination of secretion or excised tissue. Dignosis may be suspected by considering following points :—

- History of tuberculosis in past or history of contact.
- Symptomatology and clinical appearance of lesion.
- Culture and isolation of tuberculous bacilli from secretion of excised tissue.
- Guinea pig inoculation and subsequent isolation of organisms.
- Biopsy of conjunctival tissue and histological study of specimen.
- Response to anti Koch's treatment.
- Immunological study—like mantoux which is not of much value.

Differential diagnosis

- Parinaud's ocular glandular syndrome caused by tularemia.
- Phlyctinular Conjunctivitis.
- Episcleritis.
- Trachoma.
- Simple follicular conjunctivitis.
- Syphilis and venereal catarrh
- Epithelioma and rodent ulcer.
- Benign lipoma and adenoma.
- Parasitic and dermoid cyst.
- Pustule of anthrax and vaccinia,

Treatment

Prior to advent of antibiotics treatment of this disease was a problem. Radical excision of the lesion, local ultra-violet light, X-ray therapy, local insufflation of iodoform powder, irrigation with potassium iodide solution was attempted. Desensitization with tuberculin did not give good result.

The present preferred treatment is the combination of following drugs because of their synergistic action on tubercle bacilli to be given systematically.

Streptomycin or Dihydrostreptomycin

PAS

Isoniazid and Streptomycin can also be given locally.

Wood recommended a combination of all three drugs to be given at least for 42 days. Kralre suggested that two to three months therapy as necessary for satisfactory clinical result.

Ind. J. Tub., Vol. XVII, No. 2

Case Report

25 years old male patient was admitted on 23.7.69 in Ophthalmology Ward. Patient was admitted with following complaints: —

Swelling of right sided eye lids. Mucopurulent discharge and blurring of the vision—since five months.

He also gave history of evening rise of temperature and dry cough off and on— one month.

Patient was treated by a private doctor for five months but did not improve.

On Examination

Locally—Right eye was congested. Eyelids were swollen and congested. There was an ulcer at cornea conjunctival junction on right eye. Pupil on right side were reacting sluggishly to light. Visual acuity on right side was 6/60. Left eye normal.

Systemic Examination

Showed nothing abnormal except in respiratory system. Bilateral moist sounds were heard on auscultation.

In view of auscultation findings and radiological findings which showed milliary type of lesion, patient was transferred to tuberculosis Ward.

Course and Treatment given

Patient was on antibiotics, vitamins and sulphacetamids atropine locally till 6.8.1969. Later on switched on to anti-koch's line of treatment with streptomycin isonex and Pas along with corticosteroids in tapering doses. Locally streptomycin hydrocortisone and atropine were given. The patient improved with anti-koch's treatment. Lung lesion responded tremendously but eye improvement remained stationary. Later on subconjunctival injection of 1/8 gm. streptomycin with hydrocortisone given from 6.10-69. Lung lesion improved markedly at the end of three months but eye lesion did not improve much after initial improvement. Also it did not deteriorate.

Investigations done

Hb—12.5 gms%-10,000/cmm DC— P.
60%L.40%

ESR—85mm of Hg. Sputum for AFB—Ve.

Conjunctival swab—No AFB detected

Streptococci haemolyticus and other gram+Ve cocci gram sensitive to Sulpha and pencillin.

Peritoneoscopy—shewed no evidence of milliary tuberculosis.

Fundoscopy—No evidence of milliary tuberculosis.

X-Ray chest—showed milliary tuberculosis with left apical dense infiltration.

Conjunctival biopsy—Histopathological examination—Tuberculous lesion without caseation. AFB+Ve.

Biopsy was repeated after antituberculous treatment with approximately two months. It showed subepithelial fibrosis with no evidence of active tuberculosis, AFB-Ve.

Discussion

Tuberculosis conjunctivitis is a rare condition now a days. Patient may present with acute ulcerative or chronic progressive type of lesion. The relationship between clinical picture and state of immunity or allergy due to exposure to tuberculous infection is still a controversial point. In present case patient does not give any history of tuberculosis in past or history of contact with tuberculous patient, but there is definite history of low grade pyrexia with dry cough for one month. The lesion is secondary type but mode of infection may not be milliary spread through blood stream as unilateral lesion and absence of tubercles on funduscopy and peritoneoscopy are points against the blood stream spread, Infection might be due to direct inoculation of right eye with infected fingers or dust particles or infected articles, clothes etc. Acute ulcerative type of lesion suggest previous exposure to tuberculous infection but patient does not give relevant history. Tuberculosis might be in form of subclinical infection initially with left apical lesion and later might have spread. Marked improvement in lung lesion and initial eye lesion which was not responding to five months treatment with sulphas and antibiotics suggest lesion was conjunctival tuberculosis. This was confirmed definitely by conjunctival biopsy report which also after two months treatment showed fibrotic lesion.

ACKNOWLEDGEMENT

We are very thankful to Dr. E.J.D'Souza, the Dean, B.Y.L. Nair Charitable Hospital for kind permission to utilise the hospital records and various help. We are also very grateful to Dr. C.K. Deshpande, Professor of Pathology, Dr. A.M. Gokhale, Honorary Ophthalmologist, B.Y.L. Nair Charitable Hospital, for their kind help.

REFERENCES

1. Amster M. 1905 In A. Sorbys "Modern trend in Ophthalmology" *Third serial Baltenworth*, London P. 1-37.
2. Amster M. *Acta Tubere Bely* 48-89, 1957. Quoted by P.N. Shrinivasrao, K. Shankar Bhat.
3. Bruce G.M. and Locatcher, Khoraso D. Primary tuberculosis of Conjunctiva. *A.M.J. Arch. Oph.* 37,375, 1947.
4. Dohegan J.M.—Primary tuberculosis of conjunctiva. *A.M.J. Oph.* 33, 1117. 1950.
5. Duke Elder W.S.—System of Ophthalmology Vol. VIII Part 2. *Henry Kington*. London. P. 833,1028,1965.
6. Eadie S. Primary tuberculosis of conjunctiva treated with Streptomycin and PAS. *B.J. Oph.* 38,568, 1954.
7. Edwards Anhalf, M.D., Saul Zavell M.D., Gilbert Chain PHD. *B.J. Oph.* Vol. 50,265, 1960.
8. Tritz M.H., Thygesoh P. & Durhan D.G. *Amer J. Oph.* 34, 177, 1951.
9. Gold Farb A.A., Shattler I. Primary tuberculosis of conjunctivitis. *Am. J. Dix. Chest* 12, 211 : 1956,
10. Juler F.N.—T.B. of conjunctivitis treated with Streptomycin, *J. Oph. Sue.* 4. Kingdom 69,297, 195d.
11. Woods A.C. (1956) Endogenous inflammation of uveal tract. *Williams and Vilkin's Baltimore*. P. 34TM18.
12. Woods A.C.—Pathogenesis and treatment of ocular tuberculosis. *AM A Arch. Oph.* 52,174, 1954.
13. P.N. Shrivasanrao, K. Shanker Bhat.-Active systemic lesion in case of suspected ocular tuberculosis. *J. All India Oph. Society* 1967. 173, 180.
14. P.N. Shrivasanrao and K. Shanker Bhat 1967. *J. Indian Medical Association* 48, 502, 1967.

HYPOGLYCEMIA IN A CASE TREATED WITH ETHIONAMIDE

R. K. NARANG, O. P. MITAL AND S. K. JAIN
(From G., S. V. M. Medical College, Kanpur)

It has been observed that a diabetic on ethionamide treatment may have difficulty in the control of his diabetes. However, in a non diabetic the drug has no obvious effect on carbohydrate metabolism. Hence, our interest in reporting a case of pulmonary tuberculosis who developed hypoglycemia while on ethionamide therapy.

Case Report

H.L., a 40-year old school teacher, was diagnosed a case of pulmonary tuberculosis on October 1, 1968. He had chest symptoms for one year and was treated with a few injections of penicillin and streptomycin giving him temporary relief. He denied any history of smoking or alcohol consumption.

Mantoux test was positive (induration 22 mm.). Sputum was positive for A.F.B. A skiagram chest showed extensive disease in both the lungs with cavitation and fibrosis in the left upper zone.

Treatment with streptomycin 1 Gm. O.D., PAS 4 Gm. b.i.d. and isoniazid 150 mg. twice a day was started on 1.10.1968. The patient developed generalised itching and urticaria. As PAS was thought to be responsible for the symptoms it was stopped and ethionamide 250 mg t.i.d. substituted on 4.10.68. The patient reported on 17.10.68 complaining of extreme general weakness, drowsiness in the morning, giddiness and feeling of intoxication. Hypoglycemia was thought as a possibility. However, the size of the pupils, tone of the muscles and the reflexes were normal.

Blood Sugar estimation one hour after the morning dose of 250 mg. of ethionamide was 28 mg. percent. At 2 hours the level was 38 mg. percent. This confirmed the diagnosis of hypoglycemia. The patient was asked to stop ethionamide and continue treatment with streptomycin and isoniazid only. The symptoms of general weakness, drowsiness and intoxication completely disappeared on withdrawal of ethionamide. A glucose tolerance test done on 29.10.68 (fig. 1) was normal except for slightly low fasting sugar level.

Discussion

Hypoglycemia, in our case, was definitely

due to ethionamide as the symptoms and low blood sugar were present only when the patient was getting ethionamide. Blood sugar levels returned to near normal 12 days after withdrawal of the drug. The "hypoglycemic" symptoms also disappeared.

It has been observed (Somner and Brace, 1962) that patients of diabetes mellitus when treated with ethionamide for pulmonary tuberculosis are difficult to control. Such patients are liable to severe hypoglycemic attacks.

Recently Cameron and Crompton (1967) reported fatal hypoglycemia in a case who was being treated with streptomycin, isoniazid and ethionamide. He was an alcoholic and there was a past history of partial gastrectomy. He had no evidence of diabetes mellitus. This case was the first on record of hypoglycemia developing in a non-diabetic. Our case is the second.

It is possible that ethionamide may have an action similar to that of phenformin, which lowers blood sugar in the diabetics but not in the normal subject. But in a non-diabetic patient, like the one we have reported, obviously some other mechanism is operative. Pfaffenberg (1964) was unable to demonstrate

an insulin sparing action of ethionamide either in the diabetic or non-diabetic subjects. However, as suggested by Conn et al (1964) ethionamide may cause disturbance in carbohydrate metabolism due to anicteric hepatic damage. Routine liver function tests show hepatic dysfunction in a high percentage of cases on ethionamide treatment (Bhatia and Lai, 1966, British Tuberculosis Association, 1968).

Hypoglycemia is probably rare with ethionamide treatment. But it is important to keep the possibility in mind in any patient who develops bizarre symptoms.

Summary

A case of pulmonary tuberculosis treated with streptomycin, ethionamide and isoniazid developed hypoglycemia which was shown to

be due to ethionamide. Hypoglycemia was reversible. This is the second report of this complication occurring in a non-diabetic patient.

REFERENCES

1. Bhatia, J.L. and Lal, H. (1966): *Indian J. Tuberc.* **13**: 57.
2. British Tuberculosis Association (1968) *Tubercle, Lond.* **49**, 125.
3. Cameron, S.L. and Crompton, G.K. (1967): *ibid*, **48**, 307.
4. Conn, H.O., Binder, H.J. and Orr, H.D. (1964): *Amer. Rev. Tuberc.*, **90**, 542.
5. Pfaffenberg, R. (1964): *Prax Pneumol*, **18**, 430.
6. Somner, A. R. and Brace, A. A. (1962): *Tubercle. Lond* **48**, 137.

SUSPECTED LUNG TUBERCULOSIS

R. S. RAMACHANDRAN, AND K. RAMANATHAN,
(From Thanjavur Medical College, Thanjavur)

Congenital tuberculosis is rare. The incidence of tuberculous infection in the infants in relation to the number of women who become pregnant when they have active tuberculous lesions seems very small. Debre' (5) found no signs of congenital tuberculosis in the infants of 1369 tuberculous mothers. Miller et al (12) saw only four patients in their large series of 2500 patients with tuberculosis. In our own material which consists of 2950 cases of childhood tuberculosis seen in a six year period (1963-69) only two patients less than six weeks of age were diagnosed to have tuberculosis. The rarity of this entity has prompted us to present these two cases.

Case 1 : 28 days old male infant was admitted for fever and breathing difficulty of 10 days duration. Mother was diagnosed to have pulmonary tuberculosis two weeks after delivery and was started on anti-tuberculous therapy. Her sputum for AFB was positive. On admission to the hospital the infant appeared thin and weighed only 5 lbs., whereas the birth weight was 6.4 lbs. He was not feeding well. The nostrils were filled with purulent discharge. The abdomen was distended and liver was palpable for 3 cm. below the right costal margin. X-ray chest revealed multiple infiltrates in the right upper lobe. 10 mm. induration was obtained to the intradermal injection of 1 T.U., P.P.D. Hb 9.2 gms; WBC 1100 per cmm. Liver biopsy showed isolated foci of histiocytes and round cell infiltration. (Grade I). (15). Treatment was started with streptomycin, INH and steroid within 72 hours after admission. The infant showed progressive improvement, gained 1½ lbs and was discharged from the hospital three weeks after admission. This unfortunate child who was attending the out-patient clinic regularly died of cholemia secondary to Indian childhood cirrhosis at the age of 1½ years.

Case 2 : 41 days male infant was hospitalised for irregular fever. Mother died of pulmonary tuberculosis 15 days after delivery. While in the hospital the infant was found to feed poorly and had loose bowel movements. The infant looked emaciated and weighed 5.6 lbs. Abdomen was distended and liver was enlarged 4 cm. below the right coastal margin. Hb. 8 Gm; WBC 21000 per cram. X-ray chest was negative. There was 10 mm. induration to 1 T.U., P.P.D. Liver biopsy showed Grade II granulomatous changes (15). The infant was started on streptomycin, INH and steroid. The

temperature abated in a few days, the infant started to feed well and was discharged two weeks after admission. The infant gained 1.8 lbs. during the hospital stay. The child is still attending the out-patient clinic and is on INH and multivitamins for about a year now,

Discussion

Beitzke's Criteria

Beitzke (2) has laid down certain criteria to indicate that tuberculous infection is truly congenital. The criteria are a) tubercle bacilli must be grown from the infant's tissues b) a primary complex must be demonstrated in the infant's liver since the bacilli must have been carried to the liver by the umbilical vein and c) tuberculous lesion must be discovered either at birth or within a few days thereafter. Using these criteria, Beitzke (2) in 1935 collected 101 cases of congenital tuberculosis from the literature. Corner and Brown (4) in 1955 reviewed the literature and found 133 cases of congenital tuberculosis. Grady and Zuelzer (7) recorded five fatal cases of congenital tuberculosis, four premature and one full-term. Hudson (10) reported a successfully treated infant born of a mother with pleural effusion who subsequently developed miliary tuberculosis. Todd (17) reported an infant with congenital tuberculosis who had generalised lymphadenopathy which he thought represented blood stream spread before delivery. O' Donohoe reported an infant who died at the age of eight weeks from tuberculous disease. The infant's mother, having had sarcoidosis in the past, was treated with INH, PAS and steroid for a year ending when she was one month pregnant. One month after delivery the mother developed tuberculosis arthritis. (14). Avram et al (1) saw an infant born of a mother with tuberculous endometritis. The infant was found to have bilateral caseating pulmonary tuberculosis who responded to therapy well. Miller et al (12) came across four infants suffering from tuberculosis admitted in the hospital before the eighth week of life. Voyce and Hunt (18) reported an infant who died at the age of 10 weeks in whom they suspected the infection as transplacental since there was severe involvement of liver and spleen with less extensive lesions in the lung. The mother had received a two year course of anti-tuberculous therapy which was discontinued during pregnancy.

Beitzke's (2) criteria have certain pitfalls. It

is easy to be sure of the nature of infection if one finds a primary focus in the liver with nodes at the porta hepatis. But it is difficult to be sure if an infant who develops tuberculosis in the first few weeks of life, has been infected in utero before birth, by aspiration of infected amniotic fluid during delivery or by inhalation.

Miller's Classification

Miller et al (12) noting the disadvantages of Beitzke's (2) criteria attempted a pathological classification. They divided cases of congenital tuberculosis into two groups. The first group comprises infants with a primary focus in the liver and a mass of glands at the porta hepatis. The picture is compatible with transplacental transmission via umbilical vein. The second group does not have a primary complex in the liver but have large number of tuberculous foci apparently of same age, scattered over both lung fields and cassation of mediastinal lymph nodes. Here, obviously the source of infection is either a) aspiration of infected amniotic fluid, as seen in infants born of mothers with tuberculous endometritis (1 and 16), material from the genital tract during delivery or b) exposure to tubercle bacilli after delivery.

Cases belonging to the first group of Miller et al (12) must be exceedingly rare. Debre' and LeLong (5) demonstrated convincingly that the disease in most instances was acquired by contact after delivery. They separated new horns from their tuberculous mothers immediately and in a large series found that none of the offspring had been infected. In only one out of Miller et al's (12) four cases, the infection was thought to be transplacental. Voyce and Hunt (18) reported an infant in whom they believed that the infection was transplacental. *Our two cases too most probably must have been infected by their mothers after delivery.* Cases belonging to the second group of Miller et al (12) are common. In this group, the mothers of infants with congenital tuberculosis usually have advanced tuberculosis in themselves (4 and 11) as also seen in both the mothers in this presentation

The mortality rate of congenital tuberculosis is quite high in spite of the advances in chemotherapy (13). Only five cases of survival from congenital tuberculosis have been recorded in the literature before 1959 (9 and 10). Since that time, Miller et al (12) successfully treated two infants and Avram et al (1) one. The high mortality rate is due to the difficulty in diagnosing the entity early. Sometimes, the presence of tuberculous infection in the neonate is

not at all suspected until after death as seen in the case of Horley (9). Death occurred in this case after a sudden cyanotic spell. The differentiation between congenital intranatal and early postnatal infection does not serve the purpose. What is more important is the awareness as to when to suspect tuberculosis in a new born or an infant of a few weeks of age. The physician should be very alert to the possibility of congenital tuberculosis in an infant especially if the mother is known to have tuberculosis, present or past. If the infection is transplacental (Group I—Miller et al), the infant will usually present as obstructive jaundice. But if the infection is transmitted by aspiration of infected material during delivery or by inhalation thereafter (Group II—Miller et al), the clinical picture resembles pneumonitis. The clinical features include pyrexia, dyspnoea, cough, nasal discharge, rales on auscultation, hepatomegaly and radiographic evidence of tuberculous disease. The tuberculin reaction is usually positive. Tubercle bacilli can be recovered from the gastric contents. Successfully salvaging these infants will depend upon early institution of anti-tuberculous therapy,

Summary

Congenital tuberculosis is exceedingly rare. A review of the literature revealed only 147 cases. Two cases presented in this report were seen in a teaching hospital in a six year period. Both the infants were seen before six weeks of age. Both presented with prolonged pyrexia. Mothers were known to have pulmonary tuberculosis in both the instances. Tuberculin tests were positive. Radiographic evidence of tuberculosis was present in one case only while histological evidence was present in the other. Both responded to the therapy well. The need for early diagnosis in successful salvaging these infants is emphasized.

REFERENCES

- (1) Avram, C., Corpude, V. and Aricescu, B.: Congenital tuberculosis caused by aspirations of amniotic fluid. *Ftiziologia*, 6:545, 1963.
- (2) Beitzke, H.: 'Uber die angeborene tuberkulose infection'. *Ergebn, ges. tuberk-Forsch.*, 7:1, 1935.
- (3) Cashman, J.M.: Congenital tuberculosis. *Proc. Roy. Soc. Med.*, 52:297, 1959.
- 1,4.) Corner, B.D. and Brown, N.J.: Congenital tuberculosis. Report of a case with necropsy finding in mother and child. *Thorax* 1099 1955.

- (51) Debre¹, M.: Personal Communication Quoted by Rich, AR; (1944). The Pathogenesis Tuberculosis, *Springfield*, Thomas
- (6) Debre', R. and LeLong, M.: The infant born of tuberculous parents, separated before contamination; its growth and resistance to disease. *Am. Meet.* 18:317, 1925.
- (7) Grady, R. C. and Zuelzer, W.W.: Neonatal tuberculosis, *Am. J. Dis, Childhood* 90:381. 1955.
- (81) Hertzog, A.J., Chapman, S. and Herring, J.: Congenital pulmonary aspiration tuberculosis *Am. J, Clin. Path.* 19 1139. 1945.
- (9) Horley, J.F.: Congenital tuberculosis *Arch. Dis, Childhood.* 27:167, 1952.
- (10) Hudson, P.P.: Clinical aspects of congenital, *Arch. Dis. Childhood*, 31:136, 1956.
- (11) Hughesdon, M.R.: Congenital tuberculosis. *Arch. Dis. Childhood*, 21:121, 1946.
- (12) Miller, F.J.W., Seal, R.M.E. and Taylor, M.D.: Tuberculosis in children. *J&A Churchill Ltd.* London. 1963.
- (13) Morrison, J.E.: Foetal and neonatal pathology, 2nd Edition. *Butterwonh. London.* 1963.
- (14) O'Donohoe N.V.: Congenital tuberculosis and maternal sarcoidosis. *Arch. Dis. Childhood.* 38:83. 1963.
- (15) Ramachandran, R.S. Shetty, B.M.V. and Kamala, K.G.: Hepatic lesions in Childhood tuberculosis *Ind. Fed.* 3:212, 1966.
- (16) Riechle., H.S. and Wneelock, M C.: Aspiration type of congenital tuberculosis. *Arch. Din. Childhood*, 28:799, 1939.
- (17) Todd, R. McL-: Congenital tuberculosis: report of a case with unusual features *Tubercl. (Lond).*, 41:71, 1960.
- (18) Voyce, M.A. and Hunt, A.C.: Congenital tuberculosis. *Arch. Dis. Childhood*, 41:299, 1966.

25th NATIONAL CONFERENCE, PATIALA

The Twenty fifth National Conference on Tuberculosis and Chest Diseases was held at Patiala from the 28th to 30th of January, 1970. The conference was inaugurated by Shri D.C. Pavate, Governor of Punjab. Dr. B K. Sikand was awarded the "T.A.I. Gold Medal" by the Governor for his outstanding services for the cause of tuberculosis and Dr. Govind Prasad was presented the cash prize for his article on tuberculosis. Dr. Chandrasekhar, President of the Tuberculosis Association of India, in his message highlighted the importance of District TB Control Programme, Role of General Practitioners, Health Education, Control of air pollution and community participation in the control of tuberculosis. The Governor in his address referred to the seriousness of the tuberculosis problem and stressed the need for sufficient number of tuberculosis clinics and adequate facilities for domiciliary treatment.

In the Presidential Address Dr M. Umesh Rao specially suggested institution of insurance scheme to cover tuberculosis, homes for incurable patients, indigenous methods of treatment, integration of BCG vaccination with other health services and supply of drugs and X-ray equipment to tuberculosis institutions.

Dr. N.L. Bordia, Hony. Technical Adviser, Tuberculosis Association of India, discussed in his address the progress of tuberculosis control programme during the last year.

The programme of the conference was prepared by the Technical Committee of the Tuberculosis Association of India. The conference included two panel discussions on "Integration of Tuberculosis Services"¹ and "Urban TB Programme" five sessions on "Tuberculosis of Bones and Joints", "Prevalence and incidence of Tuberculosis amongst Contacts", "Chemotherapy", "Pyogenic Diseases of the Chest" and "Family Planning" and other important papers on Tuberculosis.

A very attractive and informative souvenir was published by the Tuberculosis Association of Punjab and Haryana on the occasion of the conference. They also organised an Exhibition on Tuberculosis and this was inaugurated by Dr. P.K. Duraiswami, Chairman, Tuberculosis Association of India.

The conference was attended by about 400 delegates and included two foreign delegates, Dr. J.H. Harley Williams, Director General, Chest and Heart Association, London, and Prof. G. Daddi, Director, Carlo Forc-mini Institute of Rome.

The success of the conference in all respects was due to the local organisers and the Governments of Punjab and Haryana. Dr. Khushdeva Singh and Dr. Jaswant Singh were in overall charge of the arrangements connected with the conference.

NEWS & NOTES

ANNUAL MEETINGS

The thirty-first Annual General Meeting of the Tuberculosis Association of India was held on 16th April in the Conference Hall of the Association. Dr. P. K. Duraiswami, Chairman of the Association, presided. The Report on the working of the Association and its Accounts during 1969 was presented by Chairman and Honorary Treasurer respectively. The meeting elected members to the Central Committee as provided for in the rules.

The Conference of the Secretaries of the State TB Associations and Seal Sale Organisations in India was held in the Conference hall of the Association on 16th April and the Technical Committee of the Association will meet on 17th April.

SEAL SALE AWARD 1970

The 1970 Trophy for the highest Seal Sale collections was awarded to the Tamil Nadu TB Association at the General Meeting of the Association on 16th April, 1970.

NEW DELHI TUBERCULOSIS CENTRE

The New Delhi TB Centre held a short re-orientation course in Tuberculosis for Sister Tutors of the various hospitals in Delhi where nurses are being trained. Since the national tuberculosis control programme envisages integration of tuberculosis with the general health services of the country, a refresher course for Sister Tutors is necessary to make the nursing students conversant with recent concept about control of tuberculosis. The course which was inaugurated by Dr. P. K. Duraiswamy, Director General, Health Services and Chairman, Tuberculosis Association of India, was attended by 13 Sister Tutors from the various hospitals in Delhi from 31st March to 6th April 1970.

JUNIOR AWARD 1969-70

Dr. Govind Prasad, Medical Officer, New Delhi TB Centre, was awarded the 1969 cash prize award of Rs. 300/- for the best article on Tuberculosis entitled, "Changes in the pattern and behaviour of pulmonary Tuberculosis 1955-66". The prize was given away by the Governor of Punjab at the inaugural session of 25th National Conference on TB and Chest Diseases at Patiala.

From this year the cash prize award has been raised from Rs. 300/- to Rs. 500/-. Any Tuberculosis worker, 45 years of age, is eligible for the award, which will be on the basis of an original article not exceeding 30 double spaced full scape typed pages (approximately 6,000 words) excluding charts and diagrams, on a subject relating to tuberculosis in which he or she is specialising or has worked and adjudged best by a special Committee of this Association.

A summary of the article selected for the prize will be presented by the author at the time of the next National Conference on TB and Chest Diseases to be held early in 1971. An article or paper already published will not be considered for this award. Papers may be sent in *quadruplicate* to reach the office of the TA1, 3 Red Cross Road, New Delhi on or before the *31st October 1970*.

7TH ANTI-TB SHIBIR CAMP. MAHARASHTRA

The seventh anti-TB Shibir camp was organised at Ashta in district Sangli by the Maharashtra State anti-TB Association. The Mata Bal Welfare Unit, Bhilwadi, of the Bombay Mothers and Children Welfare Society, rendered considerable assistance in organising the camp along with Dr. M.M. Wagle who has recently taken over the post of Joint Secretary of the Society.

The site was chosen because the Society have 3 peripheral centres at Bhilwadi, Ashta and Waive which are efficiently run by Dr. (Mrs.) N. Kuddayady, the Medical Officer. A new item introduced during this camp was 'Nutrition Clinic'. A large number of children examined at Ashta had different forms of malnutrition i.e. protein calorie deficiency, kwashiorka, rickets, vitamin A & B deficiency etc. There were also 10-12 suspected cases of Leprosy. About 200 school children were given B.C.G., oral polio and triple vaccination. During the camp 132 patients were screened, 200 children administered oral polio and the same number received triple vaccination. 1,387 were given B.C.G. vaccination.

The Shibir party consisted of Dr. M.D. Deshmukh, Honorary Secretary, Maharashtra State Anti-TB Association, Dr. M.M. Wagle, Pediatrician, Sir J.J. Group of Hospitals and Dr. TB Master, TB Specialist, Sir J.J. Group of Hospitals besides a number of physicians, laboratory technician, B.C.G. technician and Nutrition Specialists from Haffkin Institute.

HEALTH VISITORS' COURSE

The Tuberculosis Health Visitors' Course will commence in New Delhi from July this year and will be conducted at New Delhi TB Centre, College of Nursing, Lady Reading Hospital and Lala Ram Sarup TB Hospital. Applications for the course will be received by the T.A.I., 3 Red Cross Road, New Delhi.

TEXT BOOK ON TUBERCULOSIS

M/S Kothari Book Depot, Bombay, has undertaken to publish the text book on Tuberculosis which is being published by this Association. The book is expected to be out in the market sometime in August this year.

OBITUARY

The Association regrets to record the death of Shri O.V. Ramadoni, who has been Financial Adviser to the New Delhi TB Centre and a member of our Executive Committee. He was 62. His advice was available to us on administrative and financial matters.

WARNING ON SAFETY OF DRUGS

Director General of Health Services, Government of India, has brought to the notice of the medical practitioners the warning issued by the Committee on Safety of Drugs in the U.K. The Note is in respect of oral contraceptives containing oestrogens and suggests that reports of suspected adverse reactions received by the Committee on Safety of Drugs now provides evidence that the incidence of thromboembolism is higher among women taking preparations containing oestrogen in smaller dose. The committee recommends that oral contraceptives containing smaller dose of oestrogens may be prescribed since oral contraceptives containing 50 micro-

grammes of oestrogen have not been found less effective as a contraceptive.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE

The XIth International Congress of Internal Medicine will be held in New Delhi from 25th to 30th October, 1970. The conference is being organised by the Vallabhbhai Patel Chest Institute, University of Delhi. Eminent medical scientists from different parts of the world have been invited to act as Chairmen of various scientific sessions. For further information please write to Dr. R. Viswanathan, Emeritus Scientist, Vallabhbhai Patel Chest Institute, Delhi University, Delhi-7.

NATIONAL AWARD FOR FAMILY PLANNING

The Indian Council of Medical Research has invited applications or nominations for the National Award of the value of Rs. 5,000/- to an Indian national for outstanding research work in Biomedicine in the field of Family Planning done in an Indian Institution and published in Indian/Foreign Journals during 1969-70. For full details please write to Director General, Indian Council of Medical Research, P.O. Box-4508, New Delhi-16.

SHRI AMRUT MODY RESEARCH FOUNDATION

The Uni Trust have announced their first annual award of the value of Rs. 10,000/- to be given in recognition of an outstanding and notable research work done not earlier than 1st January, 1963 in Medicine and its special branches and Pharmacy and Pharmaceutics. Nomination forms are to be submitted by 31st May, 1970. For full details please write to Amrut Mody Research Foundation, c/o Unichem Laboratories Limited, 4,5,6 Prabhat Estate, S.V. Road, Jogeswari, Bombay 60(NB).

The Indian Journal of Tuberculosis

ABSTRACTS

Vol. XVII

April 1970

Abst. No. 2

Isoniazid Inactivation Status and the Development of Chronic Tuberculosis.

Hilkka Tiitinen. Scand. J. Resp. Dis.; 1969, 50, 221.

The isoniazid (INH) inactivation status was investigated in 116 Finnish tuberculosis patients; 45 fresh, 45 chronic and 26 relapse cases. Serum INH concentrations were measured chemically 30, 90 and 180 minutes after an intravenous injection of 5 mg/kg of INH, and free INH and total hydrazides were measured from the three-hour urine sample. Of the subjects, 47 (41 percent) were rapid and 69 (59 per cent) were slow inactivators of INH. No difference could be found in the occurrence of the two phenotypes among fresh cases, chronics and relapses. Forty-one chronics exhibited INH-resistant bacilli in sputum; this resistance to INH was found in 95 per cent of rapid and 89 per cent of slow inactivators. The author concludes that the rate of inactivation of INH does not seem to influence the sputum conversion rate or the emergence of drug resistant bacilli, these are more due to irregularity or inadequacy of the treatment.

S.P.P.

Cancer Death Rate in Patients Receiving Prolonged Isoniazid Therapy.

Gerald R. Kerby, Alfred A. Rimm, Arthur A. Zolecki and William W. Stead. Transactions of the 28th V.A.-Armed Forces Pulmonary Diseases Research Conference; 1969, 12.

Causes of death of 1,196 white males aged 40 or more who were treated for active tuberculosis with INH were reviewed. The mean duration of INH therapy was 41 months and the mean duration of follow-up after completion of INH treatment was 57 months. Age, sex, race, specific expected death rates from cancer were calculated from the reported mortality statistics of the country for the years 1960 to 1965. The ratio of observed/expected deaths from cancer decreased with increasing duration of INH therapy. The data do not

support the hypothesis that INH is carcinogenic in man.

SP.P.

Hepatocellular Damage Due to INH.

Richard D. Perera and Ray G. Cowley, Transactions of the 28th V.A.-Armed Forces Pulmonary Disease Research Conference; 1969, 12.

In 1968, two persons out of 238 placed on INH chemoprophylaxis in Fitzsimons Hospital developed clinical jaundice. Jaundice disappeared on withdrawal of INH but re-appeared when the drug was re-started. Although no specific diagnostic test is available to differentiate viral from drug-induced hepatitis, the evidence is in favour of INH being responsible for hepatitis in these two persons. Among 9,500 tuberculous persons on treatment for tuberculosis in 16 years in that hospital, 0.5 per cent developed hepatitis. Although in a multiple drug regime, it is difficult to determine the incriminating drug, INH as a possible cause has also to be kept in mind.

S.P.P.

Isoniazid and the Survival of Tubercle Bacilli in Airborne Droplet Nuclei.

Robert G. London, Linda R. Birgarner & Gary K. Coffman, Amer. Rev. Resp. Dis.; 1969, 100, 172.

It has been suggested that increased concentration of anti-tuberculous drugs, particularly INH, in secretions in which tubercle bacilli are expelled that results from evaporation of droplets to droplet nuclei might kill the organisms in aerial suspension. No such effect was seen in the experiment carried out by the authors. The biological decay rate of tubercle bacilli in aerial suspension, was not affected by incorporation of INH in the suspending medium.

S.P.P.

ABSTRACTS

Tuberculosis, Corticosteroid Therapy and Pulmonary Function.

Suresh K. Malik and C. J. Martin, Amer. Rev. Resp. Dis.: 1959, WO, 13.

One hundred and eighteen patients with active pulmonary tuberculosis were alternately assigned to a course of chemotherapy and corticosteroids or chemotherapy alone. Those receiving steroids showed an initial advantage in weight gain and a sense of well being. Clearing of pulmonary infiltrate and the speed of sputum conversion was significantly greater in the steroid group up to 12 weeks. After 24 weeks the steroid group had no advantage over (he other.

The vital capacity and pulmonary diffusing capacity were reduced equally in both groups before the study. Following treatment, the vital capacity improved significantly in both groups but no change was found in the diffusing capacity. The incidence of abnormal flow rates was the same in both groups, and the underlying airway obstruction did not change with one year's treatment. Ventilation at rest, exercise tolerance, seven minute nitrogen washout, and blood gas tensions at rest and during exercise were similar in both groups initially and after treatment.

S.P.P.

B. C. G. Vaccination of Tuberculin-Positive (Heaf-Test Grade I) Children.

A Report of Newham Health Department, London. Lancet; 1969, ii, 537.

As part of routine BCG vaccination in schools, 239 London children, aged 13-14 years, who were Heaf-test-positive grade I were given BCG vaccine, and the lesions were compared with those in 335 Heaf-test-negative children who were vaccinated at the same time. The children were seen 5—8 days and again 42—56 days after vaccination; there was no clinically significant difference between the lesions on either of these occasions. It is recommended that in the United Kingdom, BCG vaccine should be given to both Heaf-test-negative and Heaf-test-positive grade I reactors in the BCG vaccination programme in schools. Vaccination should be omitted only if there is a previous history of BCG vaccination within the previous ten years and if this can be confirmed by the presence of a scar.

S.P.P.

Two-reading technique for elimination of false readings in delayed type skin tests.

American Thoracic Society, Amer. Rev. Resp. Dis.; 1969, 99, 961.

Four types of reactions can be obtained with tuberculin— the typical delayed, the local sensitization, the Boa-specific and the tissue injury reactions. These reactions may also be present in combination. Two readings of the tuberculin test, the first 24 hours and the second 48 hours after the tuberculin injection are recommended for differentiation of the type of reaction.

If the reaction increases from 24 to 48 hours, it is a typical delayed reaction. If it decreases, it may be a local sensitization, a non-specific, a tissue injury reaction or a combination. In these cases, the test should be repeated in an area where the tuberculin test has not been performed earlier. If the reaction was produced by local sensitization, either no reaction or a small non-specific reaction will be obtained at the new site; but if it was result of a non-specific sensitivity or tissue injury, the same size and type of reaction will develop at the new area. In the case of a combined reaction, a typical delayed reaction will be elicited at the new area.

S.P.P.

Drug induced lung discuses

Editorial, The Lancet; 1969, ii, 628.

New drug-induced respiratory syndromes are constantly appearing. No matter how drugs are given, they may reach the lung by the venous return, and adverse respiratory reactions to drugs may follow administration by the most unlikely routes. Drugs may induce specific respiratory reactions or the lungs may be affected as a part of a generalised response. The mechanisms of most drug-induced lung diseases are poorly understood. It may consist of alveolitis or asthma — like hypersensitivity reaction. The increasingly recognised toxic effects of high concentrations of oxygen on the lung are not only surprising but quite mysterious. In some cases the evidence that reaction in the lung are drug-induced is circumstantial only— for instance, the appearance of pulmonary polyarthritis after the administration of drugs.

S.P.P.

ABSTRACTS

Glucose Intolerance in Pulmonary Tuberculosis

Joseph D. Bloom. Amer. Rev. Resp. Dis.; 1969, 100, 38.

Glucose intolerance tests were performed on 47 male patients with active pulmonary tuberculosis. The patients ranged in age from 19 to 73 years. In 16 patients (34 per cent) glucose intolerance curves were abnormal. This abnormality was not related to age, ethnic background, extent of disease, degree of weight loss, abnormality of hepatic function or family history of diabetes. The data presented does not establish whether occult glucose intolerance pre-disposes to tuberculosis or whether some underlying tissue or endocrine abnormality pre-disposes to both latent diabetes and tuberculosis. Such a relationship however appears to be compatible with the data presented and warrants further investigations in a larger group.

S.P.P.

Pulmonary Edema of High Altitude I, II & III

R. Viswanathan et al. Amer. Rev. Resp. Dis.; 1969, 327-349.

Experimental studies have shown that there is a species difference in the development of pulmonary oedema of high altitude (POHA) and that within the same species of animals, susceptibility to POHA is variable. That POHA occurs only in a few of the persons who go to higher altitudes suggests that there are certain constitutional factors underlying the development of this condition. Most of the cases occurred at heights above 3,600 metres. In 75 per cent of the patients, the diseases occurred on re-entry to high altitudes, after spending home leave in the plains for 30 to 60 days. Persons who were susceptible had shorter chests, smaller lung volumes, increased pulmonary arterial pressure and higher pulse rate. Hypoxic breathing lowered the oxygen saturation of the arterial blood to a greater extent in susceptible persons than in normal subjects. They were hyper reactors to hypoxic stress. Their pulmonary arterial pressure rose significantly more than in normal subjects. The rise in pulse rate was also greater. On the other hand, they were hypo-reactors to the cold pressure test.

The basis mechanism underlying the development of POHA is an abnormal reaction of certain parts of the pulmonary vasculature to low PO₂ at high altitudes in susceptible individuals. Whereas susceptibility may be determined genetically, it becomes manifest in

the form of greater pulmonary vascular resistance at the pre-capillary level, presumably as a result of an increased amount of circular muscle fibres in the arterioles of certain areas within the lungs.

The abnormal reaction consisting of severe contraction of muscular arterioles might result in wider opening of perpendicular non-muscular arterioles and consequent loading of capillaries supplied by them, and the resulting rise in capillary hydrostatic pressure might lead to exudation of fluid into alveoli. Alternatively, constriction to the point of occlusion of the terminal branches causes capillary blood stasis, that, with concomitant regional hypoxia, leads to increased permeability and seepage of fluid into the interstitial spaces and alveoli. It is possible that both mechanisms operate in certain cases.

S.P.P.

Aspergillosis

Stephen R. Zellner, John B. Selby & John J. Loughrin Amer. Rev. Resp. Dis.; 1969, 100, 217.

The presence of aspergillus species as a contaminant in sputum cultures is well recognised. Although usually considered a saprophyte, recovery of this organism from sputum of susceptible patients necessitates full evaluation. Aspergillosis should be suspected in patients with obscure respiratory illnesses when other more obvious pathogens are absent. The protean manifestations of aspergillosis, the rarity of the disease, and the low index of suspicion make diagnosis difficult.

Adjuncts sometimes used in establishing diagnosis are skin tests and serologic studies; however, the results of these tests are inconsistent. Radiological findings are variable and may simulate other disease processes. Pulmonary mycetoma with characteristic appearance occurs only rarely. Treatment with Amphotericin B is successful if diagnosis is made early. Characteristic features in a 35 years old man with invasive aspergillosis ending in death are described.

S.P.P.

Pulmonary Arteriovenous Fistula

H. Sluiter-Eringa, N.G.M. Orie and H.J. Sluiter Amer. Rev. Resp. Dis.; 1969, 100, 177.

Pulmonary arterio-venous fistula is a rare disease and diagnosis may elude the unwary

physician especially in the case of non-complainant patient. Data are reported on 27 patients; 18 were members of one family who were suffering from hereditary hamorrhagic telangiectasia. Only two of them had consulted their doctors because of the complaint and in other 25 the condition was discovered accidentally as a result of mass radiographic survey. The tentative diagnosis was made when hereditary hamorrhagic telangiectasia and an extracardiac murmur were present. Angiography is necessary to confirm the diagnosis. An abnormal right-left shunt (calculated with the aid of arterial oxygen tension measurement) was often demonstrated. Progression of lesions was mainly confined to patients with multiple fistulas. In two patients, serious complications possibly iatrogenic, occurred. Indications for and results of surgical treatment are discussed.

S.P.P.

Leiomyoma of the Lung

Stanley Weitzner, Amer. Rev. Resp. Dis. ; 1969, 100, 63.

A coin lesion in the right upper lobe of a 40 years old man proved to be a leiomyoma. A skiagram of his chest taken 3 years earlier was negative. Whereas leiomyomas arising in the bronchi are well known, pulmonary parenchymal leiomyoma is rare. It is supposed to develop from a heterotopic focus of smooth muscle or from the smooth muscle of a peripheral ramification of the bronchial or vascular tree. The possibility of this neoplasm representing a benign-appearing metastasis of a leiomyosarcoma of the gastrointestinal tract or retroperitoneum was excluded because the patient remained asymptomatic and no other neoplasms were discovered during the subsequent 9 years.

S.P.P.

A Sputum Swab Culture Method for Tubercle Bacilli using Cetrinide Compared with two Swan Culture Methods and the Concentration Culture Method

S. Joseph, N.G.K. Nair and P.R.J. Gangadharan. Tub. Land., (1969), 50, 299.

In smear positive specimens, the cetrinide method was as sensitive as the other methods in detecting tubercle bacilli, but in smear negative specimens, it was less sensitive than the concentration method, although at least as sensitive as the other two swab methods.

The incidence of contamination was least with the cetrinide method.

H. B. D.

Rifampicin in Treatment of Experimental Tuberculosis in Mice

John Batten. Tubercle, Lond., (1969), 50, 294.

Mice injected intravenously with *M. Tuberculosis* and treated with rifampicin (40 mgm/Kgm) alone, isoniazid (25 mgm/Kgm) alone or both drugs showed that neither rifampicin nor isoniazid given daily for 12 weeks reduced the population of tubercle bacilli in lungs and spleen, but when both drugs were given together for the same period, the lungs and spleen of all but one of 30 animals appear to be sterilized of tubercle bacilli.

H. B. D.

Rifampicin in Daily and Intermittent Treatment of Experimental Murine Tuberculosis with Emphasis on Late Results

F. Grumbach, G. Canetti and M. Le Lirzm. Tubercle, Land., (1969), 50, 280.

For comparing the efficacy of the combinations rifampicin-isoniazid, rifampicin-elhambutol and isoniazid-ethambutol given daily, twice weekly and once weekly for six months, in both the daily and intermittent regimen rifampicin-isoniazid was the most effective, with this combination the results produced by twice weekly treatment after an initial daily treatment of one month were almost as good as those produced by daily treatment throughout.

In the second experiment, addition of streptomycin to the required rifampicin-isoniazid, whether given daily or intermittently carried no clear cut benefit.

In the third experiment, addition of rifampicin to isoniazid-streptomycin for a short period (one month) produced a long lasting benefit.

H. B. D.

The Results From Twelve to Thirty Six Months in Patients Submitted to Two Studies of Primary Chemotherapy for Pulmonary Tuberculosis in East Africa

Tubercle, Land., (196), 50, 233

Results from 12 to 36 months of chemotherapy with the following three regimens for 18 months :—

STH :

Thiacetazone 150 mgm plus isoniazid 300 mgm daily with streptomycin sulphate Ig daily for the first two months.

ABSTRACTS

TH 300 : Thiacetazone 150 mgm plus isoniazide 300 mgm daily.

TH 450 : Thiacetazone 150 mgm plus isoniazid 450 mgm plus pyridoxin 6 mgm daily.

Patients- with bacteriological pulmonary tuberculosis were allocated to one or other group.

The patients were also allocated to : —

HV Series : These patients had two surprise visits a month upto 18 months.

No. HV Series : These patients had no surprise home visits.

In one of the two studies, the patients were also allocated at random to :—

IN Series : These patients had an initial two months of treatment in Hospital.

On T Series : These patients were treated as out patients from the start.

At 18 months 92% of 141 STH patients

had a favourable status compared with 80% of the 249 TH 300 and 70% of 83 TH 450 patients, the advantage to STH regimen attaining significance. ($P=0.002$ and $P=0.00003$ respectively). At 36 months, 87% of 109 STH patients, 72% of 209 TH 300 patients and 65% of 65 TH 450 patients had favourable results, again the benefit to the STH regimen was statistically significant ($P=0.004$ and $p=0.0009$).

There was no evidence that the HV series fared better than the No. HV. 82% 213 HV patients, had a favourable status at 18 months compared with 89% of 229 No. HV patients, the corresponding proportions at 36 months were 81% of 187 and 77% of 166 respectively.

There was no evidence that the initial period of in-patient treatment influenced the response, 74% of 91 in the IN series had a favourable status at 18 months compared with 74% of 86 in the Out series, the corresponding proportion at 36 months were 66% of 77 and 72% of 69 respectively.

A co-operative controlled study in East African Hospital and Laboratories with the collaboration of the East African and British Medical Research Councils.

H. B. D.