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News and Notes * **Abstracts**

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RAJKUMAJU AMRIT KAUR

The news of the sudden passing away of Rajkumari Amrit Kaur on 6th February after a heart attack must have come as a shock to many of our readers. The loss sustained by the tuberculosis workers in the country at large and the Tuberculosis Association of India in particular is irrepairable and it would be extremely difficult to fill the void created by her death.

Rajkumariji was associated with the Tuberculosis Association of India in one way or other from its inception and she had been its elected President for the last many years. Her passing away is a grievous loss and the tragedy of it is that this has happened a few days before the 25th Anniversary of the Tuberculosis Association of India, the celebration of which she was looking forward to.

Tuberculosis workers in India, and in fact many in other countries also have known what an active part she had played to stimulate and carry out anti-tuberculosis work. During the ten years, she was the Union Health Minister, she had contributed a great deal to placing tuberculosis on the map of India. During this period, the foundation for a National Tuberculosis Programme was laid and the achievements even during the short period were remarkable. Her intelligent understanding, dynamism and charm have contributed not a little to this. Big schemes such as National BCG Programmes were started and implemented and this with tenacity in spite of opposition to it from some quarters. The expansion of domiciliary treatment of tuberculous patients was also planned

and started during her tenure, and these were later accepted by the Government as part of its National Tuberculosis Control Programme.

Research schemes on tuberculosis such as the Chemotherapy Centre in Madras, the Madanapalle Field Research Project and the National Survey of Tuberculosis were all started and carried out when she was at the helm of health affairs at the Union Ministry, and the scheme for the establishment of a National Institute of Tuberculosis for training the personnel for this expanded programme was also formulated during her period, though the implementation of it could be done only after she left the Ministry. During the same period co-operation and assistance for tuberculosis programmes came in large measure, from International Organizations, such as W.H.O., UNICEF, Colombo Plan etc. Rajkumari's ability to get things done expeditiously and the confidence she created in all who came in contact with her, both Indian and foreign has given the impetus needed to secure help from International bodies. These organizations held Rajkumari in high esteem and any scheme that came through her could not easily be brushed aside.

While the contribution she has made to the tuberculosis cause in India is great indeed, we will be doing a great dis-service to her, if we do not consider that the cause for which she worked is greater than the individuals behind it. We will be perpetuating her memory, in some fitting way, if only we dedicate ourselves to give our best selfless service for the cause. This is one of the ways, we can pay homage to our departed leader and perpetuate her memory.

INH RESISTANT HUMAN TUBERCLE BACILLI

B. MAHAPATRA

* *(Department of Pathology, Medical College, Burla, District Sambalpur, Orissa)*

Introduction

Mycobacterium tuberculosis shows a wide range of drug sensitivity. In a population of growth, strains may exhibit different degrees of sensitivity to same drug (Yegian and Vanderlinde 1950) and tubercle bacilli isolated from different clinical lesions in the same patient may show different degrees of drug susceptibility (Allen and Roseberg 1958).

Resistance to isoniazid is more frequently seen in human tubercle bacilli isolated from Indian patients, which may be partly due to indiscriminate and extensive use of the drug for its cheapness, and partly due to the rapid emergence of INH resistant variants (Singh 1956-57).

INH resistant human tubercle bacilli differ in many ways from their sensitive counterparts and from those which are resistant to other antitubercular drugs. They may arise as a result of spontaneous mutation (Stakemann 1952, Tsukamura *et at.,* 1959). Lack of virulence to guinea-pigs and rabbits, loss of enzymes like catalase and peroxidase by these resistant "variants have been noted by many workers. Their morphological differences from the sensitive strains have been studied (Takahasi and Kuzi 1956). They may possess very weak or even negative niacin synthesising power (Marks and Trollope 1960) for which it may be difficult to consider them as human types of tubercle bacilli, and sometimes thought to be precursors of 'atypical mycobacteria' (Tarshis 1960).

The anomalous behaviour of the INH resistant variants prompted us to undertake the present study to note their relative frequency and to compare their behaviour with the sensitive ones.

Materials and Methods

Materials: One hundred and nine strains of mycobacterium tuberculosis (human type) were isolated from the sputa of pulmonary tuberculosis patients. These strains were further studied for their INH sensitivity, catalase and peroxidase activity and virulence.

Method to note INH sensitivity

Varying amounts of INH were incorporated in the modified Lowenstein-Jenson media prior to coagulation so that the final concentration in the media was 0.02, 0.04, 0.08, 0.32 and 1.28 mic.gm./ml. (Bull. I.U.T. 1954).

A bacterial suspension having 1 mg. per ml. of semi-dried weight of tubercle bacilli was prepared (Bull. I.U.T. 1955). A loopful of this suspension was cultured in two control tubes and tubes of each concentration of the drug. The results were noted after two weeks incubation at 37°C and then after each week of further incubation up to 8 weeks.

When the growth was not confluent the exact number of colonies were counted by means of hand lens. When there was growth in the media containing 0.08 (or more) mic.gm. of INH per ml., the strain was considered resistant. When only a few colonies developed in media with drug, it was inferred that only a few of the bacilli were resistant. When there was no growth in drug-containing media, the strain was considered to be sensitive.

Method used to note animal pathogenicity

For inoculating the animals the 1 mg. per ml. suspension of tubercle bacilli was used in doses of 1 ml. intramuscular to guinea-pigs and 0.5 ml. intravenous to mice. These animals if not dead within 12 weeks were opened up for microscopic study.

A particular strain was considered pathogenic to an animal if the latter died within eight weeks of inoculation, and there was macroscopic or microscopic evidence of tuberculosis and of presence of A.F.B. in tissue sections. It was thought less pathogenic if the animal died or was sacrificed after 12 weeks and showed evidence of the disease.

Method to note Catalase and Peroxidase activity

Method used by Tirunarayan and Vischer (1957) was followed with certain modifications. Equal parts of 5 per cent solution of Tween 80,

* Present address: Asst. Professor Pathology, S. C. B. Medical College, Cuttack, Orissa.

2 per cent catachol, and 30 per cent hydrogen-peroxide gave the best result and was used for the test. Sufficient amount of the mixture was added to cover the surface of the culture. Presence of catalase was noted by immediate effervescence of gas bubbles and colonies containing peroxidase became brown to black within ten minutes time. When only some of the colonies showed change in the colour, the growth was considered to contain a mixed population of both peroxidase positive and negative bacilli.

Observations

(1) *Relative frequency of INH resistant Strains*
Out of 109 strains, 18 (16.51 per cent) were sensitive and 91 (83.45 per cent) were either fully or partially resistant to INH. Unfortunately most of the patients were treated with one or more of the antitubercular drugs before their sputa could be bacteriologically analysed. Among the persons having INH resistant strains, 14 had no previous history of exposure to this drug and in 18 no definite history of drug exposure was available.

TABLE I

Showing correlation between INH reactivity and Niacin Synthesis

INH Reactivity	No. of strains tested	Niacin action	
		+VE	-VE
		strain	strain
Sensitive	18	16	2
Resistant	91	86	5

(2) *Niacin Synthesising Power*

Table I shows the niacin synthesising power where no difference is found among the INH sensitive and resistant strains as regards niacin synthesis.

(3) *Catalase and Peroxidase action*

The result is given in Table II.

It was observed that none of the sensitive strains showed absence of both the enzymes and none of the resistant strains possessed both of them. Mixed reaction to peroxidase meant that bacilli of some of the colonies possessed the enzyme while others did not and with all probability these cultures showed similar reaction to catalase. Absence of peroxidase ran more in parallel with INH resistance.

(4) *Animal pathogenicity*

The result on animal pathogenicity is shown in Table III which shows that the INH resistant variants are more virulent to mice than guineapigs.

The different characters of INH sensitive and resistant strains are summarised in Table IV.

Discussion

Action of isoniazide on tubercle bacillus is specific (Knox *et al.,* 1952). It acts on growing and not resting bacilli and the action depends on concentration, duration of exposure and temperature (Schaefer 1954). Isoniazid resistance is thought to be developed by induction rather than selection or adaptation (Schaefer *loc. cit.,* Takahasi and Nagayama 1956). The cause of frequent development of INH resistant variants in our country appears to be exposure to the drug before the tests. The possibility

TABLE II

Showing correlation between INH reactivity and Catalase and Peroxidase action

INH reactivity	No. of strains tested	C+ P+.	C+ P±	C+ P-	C- P±	C- P+	C- P+
Sensitive	18	7	8	3	—		—
Resistant	91	—	34	42	1	—	14

Note: C = Catalase. P = Peroxidase. + = Present. — = Absent. ± = Mixed reaction.

TABLE III

Showing correlation between INH reactivity and Animal Pathogenicity

INH reactivity ...	No. of strains tested	G + M +	G + M ±	G + M -	G ± M +	G ± M ±	G ± M -	G - M +	G - M ±	G - M -
Sensitive ...	18	8	...	1	4	2		1	1	1
Resistant ...	91	36	9	...	19	6	1	13	6	1

Note : G = Guinea-pig, M = Mice, + = Pathogenic, ± = Less pathogenic, — = Non-pathogenic.

TABLE IV

Showing different characters of INH sensitive and resistant strains

Type of reaction	Nature of reaction	Sensitive Strains (18)	Per cent	Resistant Strains (19)	Per cent
Niacin Synthesis ...	*Positive*	16	88.88	86	94.50
	Negative	2	11.11	5	5.49
Catalase activity	*Positive*	17	94.44	76	83.51
	Negative	1	5.55	15	16.48
Peroxidase action ...	*Positive*	7	38.88	2	2.27
	Mixed	7	38.88	37	40.65
	Negative	4	22.22	52	57.14
Guinea-pig	*Pathogenic*	.9	50.00	45	49.45
pathogenicity ...	*Less pathogenic*	6 3	33.33	26	28.57
	Non-pathogenic		16.66	20	21.97
Mice pathogenicity	*Pathogenic Less pathogenic*	133	72.22 16.66	68 21	74.72 23.07
	Non-pathogenic	2	11.11	2	2.21

of infection with INH resistant strain is there, but, in the absence of reliable history it can not be of any definite significance.

Niacin synthesis by human tubercle bacilli is much more than with other mycobacteria. Kono (1960) got 98 per cent positive result among 1,084 strains and recommended a simple qualitative method of differentiating this type from other types of mycobacteria. Gilani and Selkon (1958), Runyon *et al.* (1959), Gutierrez-Vaquez (1960) and many others have reported about the reliability of this simple test of identification of human tubercle bacilli. Niacin synthesis by INH resistant human tubercle bacilli is much diminished and sometimes the qualitative test may show negative result (Marks and Trollope, *loc. cit.).* In our study niacin negativity was not increased in INH resistant strains.

Catalase negativity (Middlebrook 1954, Marseille 1955, Nassau *et al.,* 1955, Beck 1927) and loss of peroxidase action (Tirunarayan *et al.,* 1927, Von Bertrab 1959), has been found to be associated with INH resistance in tubercle bacilli. Hauduroy 1957, has observed various degrees of INH sensitivity and catalase activity in the cultures of INH resistant strains. In the present, study all the 18 INH sensitive strains showed strong catalase activity but peroxidase action was absent in 3 of them,

Out of 91 resistant strains none showed the presence of both the enzymes. In 76 strains although catalase action was observed, there was mixed type of reaction to peroxidase in 34 strains and in others the enzyme was absent. Out of 15 catalase negative strains, mixed reaction to peroxidase was seen in one. Peroxidase activity and INH resistance was seen to be more correlated.

Reduced virulence to guinea-pigs is associated with catalase negativity of INH resistant human tubercle bacilli (Wolinsky *et al.,* 1956, Le Joubioux *et al.,* 1956, Lacroix *et al.,* 1956 and Desbordes *et al.,* 1956), but all catalase negative mycobacteria are not of low virulence (Viallior *et al.,* 1955, Winder 1956, Desbordes *loc cit).* Seri *et al.,* (1959) found that possession of both the enzvmes dose not make the mycobacteria pathogenic.

INH resistant and catalase negative mutants show attenuated virulence not only for guinea-pigs but also to rabbits but not for mice (Middlebrook and Cohn 1953-55, Bernard *et al* 1955 and Libermann 1958). Catalase positive variants of INH resistant strains have been observed to produce generalised lesion in guinea-pigs especially in presence of concomitant infection (Peizer *et al* 1955). In our study among the 91 INH resistant strains 78.02 per cent were pathogenic to guinea-pigs and 97.79 per cent to mice. The lesions produced by them were in no way different from those produced by the sensitive strains. The results however, show a definite reduction of virulence for guinea-pigs in INH resistant strains.

Summary

One hundred and nine strains of human tubercle bacilli were studied of whom 91 were INH resistant. These resistant variants in most cases developed in the patients during the course of treatment. These resistant strains did not show an increased degree of loss of niacin synthesising power. None of them possessed both catalase and peroxidase. 16.48 per cent of them lost their catalase activity whereas peroxidase action was lost in 97.79 per cent. Out of the latter group 57.14 per cent showed mixed type of colonies in their culture, some still possessing the peroxidase activity. These resistant variants were virulent to mice in (97.79 per cent) and to guinea-pigs in (78.02 per cent). There was no correlation between the pathogenicity and the production of catalase and peroxidase.

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RESULTS OF DOMICILIARY TREATMENT IN AN URBAN T.B. CLINIC †

K. C. MATHUR, K. D. SINGH, A. CHAKRAVARTY, N. BASU AND M. L. KHANDELWAL *

Introduction

The Madras trial proved that domiciliary treatment is as effective and as safe as hospital treatment. As regards sputum coversion, a rate as high as 90 per cent can be achieved in patients with sensitive bacilli. But the critics have pointed out that in above trial supervision over drug taking was so expensive and exhaustive, that it is beyond the scope of the existing clinics in our country. We Were therefore, keen to find out what could be achieved in a clinic with average facilities in our country, both as far as regularity and conversion rates were concerned.

This opportunity was provided for us during our stay at the New Delhi Tuberculosis Centre as post-graduate internees from April to July, 1963. This Centre operates the domiciliary treatment programme in an urban population of 7 lakhs spread over an area with a radius of five miles. The facilities provided for this programme at the New Delhi T.B. Centre (NDTBC) are following:

(1) Free drug supply to all patients with income below Rs 300 p.m.
(2) Clinic routine provides drug supply once in six months.
(3) Domiciliary supervision of one health visitor for 50,000 population.
(4) Case register and attendance register for the follow up and supervision of the patients are in great detail.
(5) Assessing the patients condition with skiagraphic examination and sputum examination by direct smear (D.S.) or/L.S. culture.
(6) Social welfare programme through a medico-social worker and help of Care and after Care Committees, is a prominent feature of the Centre's programme.

The above facilities are generally accepted as essential requisites of an average clinic in India to manage domiciliary treatment effectively.

† From New Delhi, T.B. Centre.

Aims and Objects of the Study

(1) To find out the conversion rate which was achieved and the regularity maintained among patients treated over a certain period.
(2) To study as to what extent regularity in drug-taking influences the rate of sputum conversion among the patients as a whole.
(3) To find out what degree of irregularity is incompatible with sputum conversion among such patients.

Methods and Material

A retrospective study was made of the recorded results of treatments of all those pulmonary tuberculosis cases whose antimicrobial treatment was started in the first six months of 1961 and who:

(1) Were living in the area covered by the Public Health Control Programme of Centre;
(2) Were sputum positive (D.S. or culture) before the start of treatment;
(3) Had not taken previous treatment for more than a week;
(4) Were not admitted in Hospital during the period of study, and
(5) Continued treatment at the Centre for at least 3 months.

This Centre's experience over the years has shown that people who leave the locality within 3 months are mainly outsiders who come to Delhi in search of admission and leave the area soon after. These were not therefore taken into account.

The period of observation for each patient in the study was one year from the start of his treatment. Total cases under study were 162. All the patients were treated on 2-drug schedule (Streptomycin 1 g. with INH 300 mg. daily; or PAS 8 g. with INH 300 mg. daily; or Siocarbazone 150 mg. with INH 300 mg. daily). In analysing results for this paper, differences in drug schedules have been ignored.

* Delhi University D.T.C.D. Internees.

Definitions

For purposes of this study the following definitions have been followed:

(1) *Sputum Conversion*—The earliest two consecutive negative cultures (sputum or laryngeal swab) at intervals of 4 to 6 weeks and maintained negative till the end of 12 months or till end of treatment (if it was less than 12 months) has been considered as sputum conversion.

(2) *Regularity*—This was judged by the date of reporting of the patient to the Centre and during occasional supervision by the health visitor on counting pills. It is expressed in terms of percentage as follows:
R=Regularity.
T=Period in which the patient was scheduled to take specified drugs.
T_1=Period which was actually taken by the patient to complete the above quantity of medicine.
Hence R=100 T/%
(A) Regular—Patients with 80-100 per cent regularity.
(B) Irregular—Patients with 0-79 per cent regularity.
(a) Moderately, irregular 60-79 per cent regularity.
(b) Grossly irregular, 0-59 per cent regularity.

(3) *Length of Treatment*—-A minimum period of 12 months' treatment has been taken as adequate treatment. Patients taking treatment short of the optimum period are indicated accordingly. Patients completing different periods of treatment are as shown below:

Length of Treatment	Up to 3 months	3 to 6 months	6 to 9 months	9 to 12 months	12 months and over	Total
No. of Patients	5	14	11	7	115	162
Percentage	3.7%	8.5%	6.6%	4.3%	77%	100%

Results

In the tables that follow, the conversion rates have been analysed in relation to other factors, notably regularity of treatment, which may have influenced them.

TABLE 1

Conversion Rates during successive quarters

	Converted			
	Ist Quarter	IInd Quarter	IIIrd Quarter	IVth Quarter
Sputum positive at start of period	162	82	41	22
Number Converted	76	32	15	*6*
Rate of Conversion during quarter	47.0%	39.0%	36.6%	27.3%
Rate of Conversion up to end of quarter	47.0%	66.6%	75.9%	79.6%
Stopped treatment and remained unconverted by the end of quarter	4	9	4	---

Expected conversion rate by the end of IVth quarter if all the cases had continued treatment = 84.3 per cent.

TABLE 2

Conversion rates in different age groups

Age groups	Converted	Non-converted	Total
0-15 Years	9	...	9
16-25 Years	50(76.0%)	16(24.0%)	66(100.0%)
26-35 Years	41 (85.4%)	7(14.6%)	48(100.0%)
36-45 Years	17(66.9%)	9 (33.1%)	26(100.0%)
Over 45 Years	12	1	13
Total ...	129(79.6%)	33 (20.4%)	162(100.0%)

TABLE 3

Conversion rates in relation to sex

Sex	Converted	Non-converted	Total
Male	73 (77.6%)	21 (22.4%)	94(100.0%)
Female	56 (82.3%)	12 (17.7%)	68 (100.0%)
Total	129 (79.6%)	33 (20.4%)	162 (100.0%)

TABLE 4

Conversion rates in relation to initial extent of disease

	Converted	Non-converted	Total
Unilateral	75(81.5%)	17 (18.5%)	92 (100.0%)
Bilateral	54(77.0%)	16 (23.0%)	70(100.0%)
Total	129(79.6%)	33 (20.4%)	162 (100-0%)

TABLE 5

Conversion rates by initial cavitary status

	No Cavity	Single Cavity	Multiple Cavity	Total
Converted …	66 (86.8%)	48(73.8%)	15 (71.4%)	129 (79.6%)
Non-converted …	10 (13.2%)	17 (26.2%)	6(28.6%)	33(20.4%)
Total …	76 (100.0%)	65(100.0%)	21 (100.0%)	162 (100.0%)

TABLE 6

Conversion rates in relation to number of zones involved

	1-Zone	2-Zones	3-Zones	4-Zones	5-Zones	Total
Converted	66 (86.0%)	37 (75.5%)	14 (82.0%)	9 (55.0%)	3	129 (79.6%)
Non-converted	10 (14.0%)	12 (24.5%)	3 (18.0%)	8 (45.0%)	...	33 (20.4%)
Total	76 (100.0%)	49 (100.0%)	17 (100.0%)	17 (100.0%)	3	162(100.0%)

TABLE 7

Pattern of regularity

Total Cases..... 162 (100.0%)

Regular..... 116(71.6%)

Irregular ..... 46(28.4%)

(a) Moderately irregular … 31 (19.0%)

(b) Grossly irregular 15 (9.4%)

This study report only immediate results of treatment in conversion rates and is irrespective of the drug schedule followed. The conversion rate on the whole at the end of 12 months was 79.6 per cent (Table 1), but the projected figure by that period , of all the cases had continued treatment would be 84.3 per cent (Table 1), (on the assumption that those who left off treatment at any stage would have fared a wall in subsequent quarters as those who

continued treatment beyond that stage), compared to 90 per cent obtained in the Madras trial. In terms of epidemiological effect on the community, the success of treatment of tuberculosis is judged by the conversion rate of the sputum, and any figure in the range of 80 per cent a highly significant achievement. On further analysis of the conversion rate following observations are possible:

(a) There is no difference in conversion rate in the two sexes or between different age groups (Table 2 and 3).

(b) Extent of the disease in terms of number of zones involved does not appear to influence the conversion rate.-

(c) Difference between the conversion rates of patients with unilateral and bilateral disease is not significant. Whether a disease is bilateral or unilateral used to be of great significance for purposes of success of treatment in pre-antimicrobial are but now this difference seems to be washed away to some extent (Table 5).

TABLE 8

Regularity in relation to age

Age	Irregular	Regular	Total
0—15 Years	2 (22%)	7 (78%)	9(100%)
16—25 Years	23 (35%)	43 (65%)	66(100%)
26—35 Years	11 (23%)	37 (77%)	48(100%)
36—45 Years	8 (30%)	18 (70%)	26 (100%)
Over 45 Years	2 (15%)	11 (85%)	13 (100%)

TABLE 9

Regularity in relation to sex

	Irregular			Regular			Total
Regularity	0-59%	60-79%	Total	80-99%	100%	Total	
Male	8 (8.5%)	17(17.5%)	25 (26%)	34 (36%)	35 (38%)	69 (74%)	94(100%)
Female	7 (10%)	14(20%)	21 (30%)	17 (28%)	30 (42%)	47 (70%)	68(100%)

TABLE 10

Regularity in relation to Sputum Conversion irrespective of length of treatment

	Regularity				
	upto 59%	60% to 79%	80% to 99%	100%	Total
Total Cases	15 100.0%	31 100.0%	51 100.0%	65	162
Converted	5 33.3%	25 80.6%	37 72.6%	62 95.4%	129 79.6%
Non-converted	10 66-7%	6 19.4%	14 27.4%	3 4.6%	33 20.4%

TABLE 11

Conversion Rates in successive quarters according to Regularity of Treatment

Sputum + Cases at start of Quarter	Regularity 0-59%				Regularity 60-79%				Regularity 80-100%			
	Quarter				Quarter				Quarter			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
	15	13	9	6	31	19	12	6	116	50	20	10
Converted during quarter	1 (6.7%)	2 (15-4%)	1 (11.1%)	1 (16.7%)	12 (36.1%)	6 (31-5%)	5 (41.7%)	2 (33.3%)	63 (54.3%)	24 (48%)	9 (45%)	3 (33.3%)
Not converted Continued treatment	13	9	6	5	19	12	6	4	50	20	10	7
Stopped treatment	1	2	2	...	...	1	1	...	3	6	1	...
Expected conversion rate if all the cases had continued treatment till end of 4th Quarter	41.6%				83.0%				91.3%			

TABLE 12

Conversion in relation to length of treatment

	Converted	Non-Converted	Total
3 months	1 (20%)	4 (80%)	5 (100%)
Over 3 months to 6 months ...	5 (35.7%)	9 (64.5%)	14 (100%)
Over 6 months to 9 months ...	7 (63.6%)	4 (36.4%)	11 (100%)
Over 9 months to below 12 months ...	4(57.1%)	3 (42.9%)	7 (100%)
Up to end of 12 months ...	112 (89.6%)	13(10.4%)	125 (100%)

(d) Conversion rate in non-cavitary cases is higher than in cavitary cases (Table 6). But this difference used to be much more significant in pre-antimicrobial era. On further analysis this is shown that 71.4 per cent cases with even multiple cavities are converted only with the antimicrobial drugs, and this adjuvant therapy may be needed only in 28.6 per cent of such cases,

TABLE 13

Conversion in relation to regularity among cases who had adequate treatment (12 months)

Regularity	0-59%	60-79%	80-99%	100%	Total number who took treatment for 12 months
Converted	5 (55.5%)	20 (87%)	31 (86.1%)	56 (98.2%)	112(89.6%)
Non-converted	4 (44.5%)	3 (13%)	5 (13.9%)	1 (1.8%)	13 (10.4%)
Total	9 (100%)	23 (100%)	36 (100%)	57 (100%)	125 (100%)

TABLE 14

Analysis of non-converted cases and possible causes

1. Total No. of non-converted cases 33
2. Regularity (a) Regular (80-100%) 17 (51.5%)
   (6) Irregular (0-79%) 16 (48.5%)

   Total ... 33(100%)
3. Adequacy (a) Inadequate 20 (60.6%)
   (6) Adequate 13 (39.4%)

   Total , 33(100%)
4. Analysis of 17 regular cases—
   (a) 11 had inadequate treatment & 6 had adequate treatment (6) Out of 6 who had adequate treatment (i) 2 refused surgery
   (ii) 1 had primary resistance to INH
   (iii) 1 had secondary resistance to INH
   (iv) 2 had no obvious cause.

Out of 162 patients 125 i.e. 77 per cent had treatment at least for 12 months. This again is a significant figure from a community basis looking to the existing facilities for supervision.

Again there is association of length of treatment and rate of conversion, which is 89.6 per cent among these patients who had 12 ‘months treatment compared to 35.7 per cent conversion among patients who had treatment for less than 6 months (Table 13).

Regularity

All patients did not take the full 12 months treatment and hence regularity is in relation to the period that they took treatment. Table 8 shows that 71.6 per cent of the patients took treatment with regularity above 80 per cent i.e., they were regular.

Age and sex (Table 8 and 9) in this study have no influence on the pattern of regularity. The findings of other investigators like Khaneju (1963) who reported that females were more regular than males, while reverse is findings of Madras trial (TCC 1959).

Looking from community point of view it may be said to be a satisfactory figure. To what extent and at what cost this regularity pattern with increased supervision is not clear. Human nature has a hard core of 10 per cent or so, who will not be amenable to any discipline, no matter to whatever extent the supervision and education may be. Thus the effect of improved service could be expected to influence

the regularity of 19 per cent who were moderately irregular. Till these difficulties are surmounted, we may have to be satisfied with this regularity of the order of 71.6 per cent yielding 79.6 per cent conversion in the community, though our ultimate arm should be cent per cent conversion and cent per cent regularity, so long as the patient lives in the area.

Regularity and Conversion

Tables 10 and 13 indicate the association of increased conversion rate with increased regularity. So much so that with 100 per cent regularity, the conversion rate is 95.4 per cent, compared to 33 per cent with regularity below 59 per cent. This fact brings out the importance of regularity in the treatment of pulmonary tuberculosis. To keep our weapon of Antimicrobials sharp one should use it regularly otherwise, it becomes blunted. This is in keeping with experience elsewhere. Crofton states that 'doctors and patients due to their carelessness are responsible for the failure of drug treatment. It is the doctor's duty to enlist fullest co-operation of the patient and then that to be supervised to minimise the failure rate'.

The same table also shows that to achieve the conversion rate of the order of 80 per cent and above, one should observe regularity of at least 80 per cent. If this conversion rate was the immediate target then it means that human body can condone irregularity to the tune of 20 per cent as maximum.

It has already been pointed out that there is a high association between conversion rate and standard of regularity on one hand, and conversion rate and standard of adequacy on the other hand. But if we analyse the conversion rate of those patients who took treatment for full 12 months (adequate with cent per cent regularity 98.2 per cent are found to be converted compared to 90 per cent of Madras trial 1959). This means that with improved facilities of supervision we can have conversion rate as much as above 98 per cent only with antimicrobials. In other words with adequate and regular treatment with the antimicrobials, the importance of adjuvant therapy becomes insignificant irrespective of the extent of disease. One is therefore inclined to suggest that the cost of finding beds for domiciliary treatment would be offset by a larger supervisory staff in this service.

Table 14 shows that out of 33 cases, irregularity and inadequacy of treatment can account for non-conversion in 16+11=27 cases (79 per cent). This again emphasises the value of a regular and adequate treatment. Out of the rest (21 per cent) i.e. 6 cases, 2 had bacilli resistant to INH and 2 refused surgery. It is only in 2 cases that no cause is evident. Some personal factor like metabolism of drugs in the individual may be responsible for non-conversion in these two cases. An alternative possibility can be that these patients are regular on papers but they may not be actually taking the drugs regularly. This possibility is being studied separately in a different group of patients.

Discussion

The object of the study was to determine what results can be expected from the domiciliary treatment scheme organised from an urban clinic and to measure shortfalls from standards achieved in Research Centre like the Madras Chemotherapy Centre where standard of supervisory staff is several times more than that assigned to an average district TB clinic in India. If any comparison of results is to be attempted, it would be reasonable to assume that the same results would obtain amongst those who non-co-operate in treatment as among those who follow advice regarding treatment. The projected figures given in this paper are based on this assumption.

Conclusion

(1) In an urban clinic with average facilities 79.6 per cent of the patients can be made non-infective in 12 months. Of the total cases 71.6 per cent can be made to take regular treatment. (The treatment can be made to continue for at least 12 months in 77 per cent of the cases).

Theoretically speaking 98.2 per cent of patients can be converted in 12 months, if with improved supervision all patients are made to take treatment with cent per cent regularity for at least 12 months. But looking at the cost involved in providing a larger supervisor staff and realising some weakness of human nature, one may for the present be content with above figures viz., conversion rate (79.6 per cent) regularity and adequacy (77 per cent) in a

community as a whole, though we should aim at 100 per cent results especially in individual cases.

(2) Conversion rate increases with the increase in the standard of regularity of treatment.

(3) To achieve conversion rate at 80 per cent or above, regularity in medicine taking should be at least of the order of 80 per cent. It means body condones irregularity of the order of 20 per cent to the maximum.

This study has convinced us that if average facilities are provided in the district clinic, a reasonable and satisfactory beginning can be made for TB control programme and thus the experience we have gained in this Institution will help us in making our work in the TB clinic more effective.

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CORTICOSTEROID THERAPY IN CHRONIC DRUG RESISTANT TUBERCULOSIS

N. K. MENON

(Institute of T.B. and diseases of Chest, Hyderabad, A.P.)

Planned investigations have confirmed the initial benefits of corticosteroid therapy—improved sense of well being, increased weight, reduced erythrocyte-sedimentation rate and accelerated X-ray regression—in tuberculosis patients with cultures sensitive to the three standard antituberculosis drugs employed. (Tuberculosis Society of Scotland 1957; British Tuberculosis Association 1961). Its effect in patients with cultures resistant to one or more of the standard drugs is less certain.

There is some evidence to show that these hormones may be beneficial also in drug resistant cases. (Turner 1959; Mathur *et al* 1961).

The present communication is based on a study of 20 patients with chronic far advanced cavitary disease and resistant cultures, treated with prednisolone along with the three standard drugs, as indoor, under the author's care at the Hospital for Diseases of Chest and Tuberculosis, Hyderabad during 1959-61.

Patients treated

Twenty patients—9 men and 11 women aged between 30 and 45 years—with chronic bilateral extensive cavitary pulmonary tuberculosis who have had anti-tuberculosis drug therapy in different combinations during the past 30-48 months and had been receiving alternate day Streptomycin injections and daily Isoniazid 200 mgm. and Sod. PAS 10 G. in two divided doses during the preceding 6 weeks without benefit, were chosen for the study. At the tune of starting prednisolone ten patients had come to a clinical and radiographic stalemate and the remaining ten were steadily deteriorating. All patients had sputum cultures persistently resistant to streptomycin (10μ/ml) Isoniazid (5μ/ml) and PAS (10μml.)

The method of swab culture and sensitivity testing described by Nassau (1954) was employed with some modifications in the present study (Menon 1963).

Treatment and Investigations

All patients were continued on the three antituberculosis drugs as they were receiving during the preceding six weeks and in addition prednisolone 5 mg. was given t.i.d. during the first month, b.d. during the second month and o.d. during the third month. Routine records of temperature, pulse and general condition were maintained daily, blood pressure readings once weekly, weight, E.S.R. and urine results, once a month and chest X-ray and sputum culture and sensitivity testing once in 6 weeks.

Results of Treatment

Final assessment was made on completion of three months prednisolone therapy.

Clinical condition

All patients reported improved sense of well being, improved appetite and reduction in cough and expectoration. 19 patients gained weight and one remained stationary. Nine patients who were pyrexial (100-103°F) initially, recorded normal temperature within 10-14 days and remained normal throughout the three month period.

Radiographic and Bacteriological status

Nine out of the 10 cases who were at a radiographic stand still, showed slight to moderate X-ray regression while one showed slight deterioration. 8 out of the 10 who were steadily deteriorating, showed arrest of further deterioration, but two continued to deteriorate as before. Cavity closure, sputum conversion or alteration of drug sensitivity was not noted in any of the twenty cases.

Toxic side effect

Apart from slight mooning of the face in a few cases no serious side effects were seen in the present series.

Follow-Up

When reviewed 3 months after prednisolone had been stopped, of the 17 patients who had shown clinical and radiographic benefits at the end of prednisolone therapy 15 were found to have maintained the same clinical and radiographic status. The remaining two whose progressive deterioration had been arrested failed to maintain the initial benefits and showed clinical and radiographic deterioration. One patient who had slight spread of disease on prednisolone had regained the original radiographic status. The two patients who were deteriorating initially and also during prednisolone treatment continued to deteriorate and one died two months after stopping prednisolone.

Thus, when assessed 3 months after prednisolone had been stopped, 15 of the 20 patients were found to have benefited from prednisolone therapy while the remaining 5 were not significantly affected. No instance of serious deterioration attributable to prednisolone therapy had been noticed in any of the 20 cases treated.

Discussion

There is well established experimental and clinical evidence to show that administration of corticosteroids without adequate chemotherapeutic coverage might lead to spread of tuberculosis without overt symptoms. For this reason, it is generally believed that addition of these hormones to antituberculosis drugs should be restricted to patients with cultures sensitive to all the three standard drugs and that if the cultures were resistant to one or more of the standard drugs the result might not be beneficial and could even be disastrous. (American Trudean Society 1957; Lancet 1962).

The results of the present investigation indicate that adjunctive corticosteroid therapy in patients with resistant cultures need not be harmful as would theoretically be expected but can even be beneficial. For instance, 17 such patients were found to have benefited at the end of prednisolone therapy and 15 of them were found to have maintained the clinical and radiographic gains when reviewed three months later. All the 20 patients had experienced considerable subjective improvement and none had significant radiographic deterioration attributable to the addition of prednisolone. The type of patients in the present study is quite different from that reported by Mathur *et al* (1961) in that, none of the patients in their series had cultures resistant to two of the antituberculosis drugs together.

Why corticosteroids can be safe and even beneficial in drug resistant cases when the covering chemotherapy is expected to be ineffective or only partially effective, due to drug resistance, is difficult to explain. The over all clinical improvement might be attributable to the specific effect of these hormones, particularly in view of the fact that adrenocortical hypofunction is known to occur in chronic tuberculosis but this does not explain radiographic regression in the presence of drug resistance.

Summary

Twenty patients with chronic far advanced disease and cultures resistant to all the three standard drugs were given prednisolone for 3 months in addition to the three antituberculosis drugs which they were already receiving. 9 patients showed slight to moderate X-ray regression; 8 had their radiographic deterioration arrested and all reported considerable subjective improvement. When reviewed 3 months after prednisolone had been stopped, 15 out of these 17 cases were found to have maintained their clinical and radiographic gains. No instance of significant radiographic deterioration attributable to prednisolone was seen.

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PREGNANCY AND TUBERCULOSIS *

M. D. DESHMUKH, T. B. MASTER, K. G. KULKARNI AND H. V. BAHULKAR

Introduction

As regards the effect of pregnancy on pulmonary tuberculosis ideas have changed from time to time. Hippocrates believed that pregnancy was the best cure for consumption and his opinion was followed blindly along many centuries and pregnancy was recommended as a therapeutic measure for tuberculous girls. From the middle of the nineteenth century there was an increasing tendency to regard pulmonary tuberculosis even when quiescent or arrested as an indication for therapeutic abortion. Pregnancy in tuberculosis was thought to be disastrous and it was propounded that 'for virgin no marriage, for married no pregnancy, for pregnant no confinement and for mother no suckling'. Young in early parts of this century, condemned this dictum as illogical and supported Pinard's opinion, 'treat the disease, manage pregnancy', introduced his own 'prevention is better than abortion'. Change in medical opinion has taken place gradually and it is not now believed that tuberculosis need be a bar to marriage or that pregnancy should not be allowed or even encouraged in a quiescent case of tuberculosis, and lactation is only contraindicated where there *is* a danger of infecting the baby (Turner 1950).

Review of Literature

Williams, Whitridge (1916 and 1930) with extensive obstetrical experience, regarded the occurrence of pregnancy in women with tuberculosis as a great misfortune and consequently recommended prevention of pregnancy by the most available contraceptive methods.

Rist (1927) observed that pregnancy was a determining factor in onset of tuberculosis in women. He also observed that pregnancy in tuberculous women leads to extension of existing tuberculous lesion and to production of fresh ones. But successful treatment with A.P. had considerable advantage in restoring patient's health. A.P. also had advantage over abortion in that it saved child's life.

Alice Hill (1928) challenged the old view that pregnancy aggravates pulmonary tuberculosis. In a controlled study of pregnant and non-pregnant tuberculous women she observed that pregnancy had no appreciable effect on the progress of tuberculous disease.

Cohen (1943-1946) and Cohen and associates (1952) observed that by placing the woman under most favourable conditions the risk attached to the pregnancy can be much reduced, the governing factor being whether the pulmonary disease can be brought under control and under such care active pulmonary tuberculosis is seldom accelerated by pregnancy and labour.

Schaefer (1949) observed that tuberculosis which is discovered in puerperium had probably existed many months during and even before pregnancy and it was from this group that the unwarranted accusation that pregnancy disposed tuberculosis was made. He showed that equal number of primigravida and multigravida died (19 and 21 per cent), 4 per cent in each deteriorated and 37 per cent of primgravida and 39 per cent of multigravida showed no change and 37 per cent of each improved. Thus parity had no influence on the disease during and after pregnancy. These results compared favourably well with those obtained in non-pregnant women indicating that pregnancy and labour had no adverse effect on pulmonary tuberculosis.

Soldenhoff and Thornberry (1959) stress that in obstetrics, a change of attitude towards pregnant women suffering from pulmonary tuberculosis has occurred. It is directly attributable to the evolution in treatment of tuberculosis. They also believe that necessity of abortion has vanished with advent of chemotherapy. A woman with active tuberculosis can have it arrested in a short tune and become, pregnant and can be offered continuance of pregnancy, with every prospect of her tuberculosis being cured afterwards. However, in mothers in whom tuberculosis has been discovered when she is advanced in pregnancy, in spite of all therapy there may be considerable risk, still she can be assured a healthy baby. These authors stress that as tuberculosis death rate has gone down so have the deaths occurring in those cases with pregnancy. They stress

* From Department of Tuberculosis—J. J. Govt. Hospital, Bombay 8.

that obstetric management resolves itself now in treating the patient as prospective mother rather than a sick woman menaced with pregnancy. Such a patient has every chance of carrying the pregnancy through to its conclusion without any danger to herself or child.

Theories Explaining adverse effect of Pregnancy on Tuberculosis

In discussing these theories, various stages of pregnancy should be differentiated. Pregnancy consists of prenatal period, labour and puerperium. The prenatal period is divided into 3 trimesters during which reaction of pregnancy varies. Graveson (1936) observed that there were two critical periods in pregnancy associated with pulmonary tuberculosis: (*i*) during first trimester and (*ii*) during and after labour (puerperium).

First Trimester: Vomiting in early months of pregnancy resulting in weakness and weight loss, loss of calcium, elevation of blood cholesterol, hormonal imbalance (low estrogen and high gonadotropin levels in blood), state of hypersensitivity and increased demand of metabolism are the factors which might have adverse effect during first trimester of pregnancy. One of the serious complications in first trimester is hyperemesis gravidarum. Falls (1941) states that the dehydration, depletion of nutrition, starvation, acidosis, avitaminosis and serious toxic neuritis and neurosis occur in some of the cases of hyperemesis gravidarum. These when extreme might be having a damaging effect on any reparative process (tuberculosis in present case) which depends on rest—physical and mental and good nutrition.

Second and Third Trimester: In uncomplicated pregnancy, second and third trimesters are not dangerous periods except possibly presence of gravid uterus interfering with rest and aeration of blood. But complications such as renal damage, eclampsia and antepartum haemorrhage during second and third trimester may have adverse effect on pulmonary tuberculosis.

Labour and Puerperium: Progression of lesions of pulmonary tuberculosis in puerperium has been ascribed to such factors as blood loss during and after labour, use of general anesthetics, strain of labour, loss of calcium, hormonal imbalance, sudden descent of diaphragm, lysins of involuting uterus and breast feeding. Socio-economic factors have also been blamed and they appear to be less important.

Controlled studies have shown that pregnancy has no adverse effect on pulmonary tuberculosis. Steward and Simmonds (1947) are of the opinion that child rearing and not child bearing is the major determining factor. Former includes care of infant and its nutrition. The latter is a physiological process of conception, maturation of foetus and parturition with associated metabolic, endocrine and mechanical changes in the mother. Schaefer (1956) states that the months and years following delivery are a more dangerous period for the tuberculous mother than the period of gestation and delivery. Care of the baby after delivery is a social problem and domestic help and financial assistance in the home must be provided ‘ when necessary. The work, neglect of patients’ own rest and the broken sleep while the mother is below par physically, constitute a serious strain for many tuberculous women and decrease their resistance so as to cause reactivation of tuberculosis and for economic reasons they cannot be relieved of these burdens.

Discovery of active tuberculosis in puerperium is a traumatic shock to all concerned. Tendency was to place the blame for the progression on the pregnancy and puerperium. Type, duration and degree of activity of pulmonary lesion, the period of pregnancy at which tuberculosis is discovered, the possibility of providing chemotherapy before and after labour and the nature of individual case are more important factors which may bring about the relapse of the disease. The additional expenses attendant upon the increase in the size of family may, in low income levels place a strain on the budget which will result in a decreased amount of food to a tuberculous mother which may also bring about relapse of the disease. In countries like India repeated pregnancies occurring at close intervals giving no chance to recuperate may also be a factor responsible for break down of already existing tuberculous lesions.

Present Material

I. Incidence of Tuberculosis in Antenatal patients

During 1959-60 1000 antenatal patients who attended the Bai Motlibai Hospital, Bombay 8, and 1000 who attended Cama Hospital,

TABLE 1

Centre	Total Patients x-rayed	Pulmonary Tuberculosis							
		Active		Probably active		Inactive		Total Abnormal	
		No.	%	No.	%	No.	%	No.	%
Bai Motlibai Hospital …	1000	SO	5.0	37	3.7	82	8.2	169	16-9
Cama & Albless Hospital …	1000	49	4-9	47	4.7	84	8.4	180	18.0

Bombay were X-rayed as a routine during their first visit to the antenatal department. The incidence of active, probably active cases requiring further investigations _and inactive cases at the two Centres was as follows: It is quite obvious that there is a high incidence of tuberculosis amongst the pregnant women attending the antenatal department of Bai Motlibai Hospital and Cama and Albless Hospital. Altogether there were 5.0 per cent active cases in the whole series, another 4.2 per cent of the mothers had doubtful shadows needing further investigations and a further 8.3 per cent showed evidence of old healed lesions of the reinfection type of disease or healed Ghon's Focus. A considerable number of the lesions discovered during this examination of the chest in the antenatal clinic becomes obvious. Routine screening of pregnant women has been started at T.B. Clinic, J. J. Govt. Hospital since 1958. Of the total 2063 women screened 93 (4.5 per cent) showed active pulmonary tuberculosis needing treatment. The 1000 mothers from Bai Motlibai Hospital who were X-rayed, were also screened before being X-rayed and only in 5 out of 50 active cases, the lesions were missed on screening and spotted on X-ray plates.

II. Observation of patients with active tuberculosis during pregnancy and after delivery

The study was undertaken during the year 1959-60. Patients in this study were from the poor class of society, living in crowded, one room tenaments in chawls. Ignorance, illiteracy and poverty played a major role in their lives.

These patients were classified in 3 main groups as follows:

Group I: Patients known to be suffering from pulmonary tuberculosis before the onset of pregnancy.

Group II: Patients having symptoms suggestive of pulmonary tuberculosis during their pregnancy.

Group III: Patients detected only because of routine X-ray of chest in antenatal period. In these patients special efforts were made to elicit the history of symptoms by repeated questioning but none of the patients gave such history.

1. Initial Observation

Table 2 shows the distributions of patients in 3 main groups and also according to the activity of the disease present when tuberculosis was first diagnosed during pregnancy.

TABLE 2

Main group	Activity of disease			
	Active	Probably Inactive	Total	Percentage
I	26	5	31	52.5
II	19	0	19	32.2
III	6	3	9	15.3
Total	51	8	59	100.0

31 (52.5 per cent) of 59 patients were previously known cases of tuberculosis and were taking treatment for some time before they

conceived (Group I). There was history of onset of symptoms of tuberculosis in relation to some previous pregnancy in 14 patients from this group. 17 patients did not give such history. 19 patients (32.2 per cent) have symptoms such as cough, expectoration, low fever, loss of weight, etc., sometimes during pregnancy (Group II). All but one patient from this group denied any history of pulmonary tuberculosis before the pregnancy supervened. One patient gave history of pleurisy with effusion 6 years prior to this attack. Diagnosis of pulmonary tuberculosis in all these patients was suspected from symptoms and confirmed by chest X-ray. 9 patients (15.3 per cent) were diagnosed as suffering from pulmonary tuberculosis during routine radiographic examination of the chest (Group III). On repeated questioning to these patients, it was confirmed that they did not have any symptoms of pulmonary tuberculosis.

Age: 58 of 59 patients were in the age group of 15-35 years. Majority of them i.e., 49 (83 per cent) of 59 patients were in the age group of 21-30 years.

Parity: 6 (10.2 per cent) of the 59 patients were primigravida and 53 (89.8 per cent) were multigravida. The maximum number of cases were seen as II, III, IV and V gravida.

Duration of Pregnancy when first attended the Clinic:

Only 8 (13.6 per cent) of 59 patients came under observation during first trimester of pregnancy, 22 (37.2 per cent) of the patients came under observation during second trimester and 29 (49.2 per cent) during third trimester of pregnancy. Thus majority of patients came under observation when the pregnancy was well advanced.

Radiographic extent of disease at first presentation:

Of the 59 patients 8 patients had probably inactive disease as assessed by their chest radiographs. 51 patients had active disease. The distribution of patients according to the radiographic extent of disease was as follows:

11 (21.6 percentage) of 51 patients had 'MINIMAL' disease. Of these 5 were detected as suffering from pulmonary tuberculosis on routine chest radiography, 5 had symptoms suggestive of pulmonary tuberculosis and one was already on treatment for tuberculosis.

TABLE 3

Group of Patients	Radiographic extent of disease		
	Minimal	Moderately advanced	Far advanced
I	1	14 (9)*	11 (11)
II	5	11(6)	3 (3)
III	5	1	0
Total	11	26 (15)	14 (14)
Percentage	21.6	51.0	27.4

* Parenthesis indicate number of patients with cavitary disease.

26 (51.0 per cent) of 51 patients had 'MODERATELY ADVANCED' disease. Of these only one was diagnosed on routine chest radiography examination, 11 had some symptoms during pregnancy and 14 were already on treatment. 14 (27.4 per cent) of 51 patients had 'FAR ADVANCED' disease. Of these 3 had symptoms during pregnancy and 11 patients were already under treatment when pregnancy supervened.

Sputum Examination: Of the 51 patients with active disease only 18 (35.3 per cent) showed acid fast bacilli on direct smear examination. Repeated smear examination and cultural studies would have definitely yielded more positive results, but such studies were not possible (8 patients with probably inactive disease are not included here).

Erythrocyte sedimentation Rate: E.S.R. at time of first examination is shown in Table 4.

In pregnancy also the E.S.R. increases so it is very difficult to assess the activity of disease on the basis of E.S.R. Even here the E.S.R. does not show any relation to activity of disease or its extent. 45 patients had E.S.R. values 31 to 60 mm., only one had E.S.R. values between 11-20 mm. and his disease was 'probably inactive'. 6 patients had E.S.R. value between 21-30 mm. of, these 3 patients probably inactive disease. 7 patients had E.S.R. value between 61 to 70 mm.

TABLE 4

E.S.R. in mm.	Active disease			Probable Inactive disease	Total
	Minimal	Moderate Advanced	Far Advanced		
0-10	0	0	0	0	0
11-20	0	0	0	1	1
21-30	0	*	‘	3	6
31-40	*	5	2	1	13
41-50	2	8	1	1	12
51-60	4	9	5	2	20
61-70	0	2	5	0	7

Previous Treatment: 28 (47.5 per cent) of 59 patients had not taken any antituberculosis chemotherapy before. Of these 3 patients had probably inactive disease. 11 (18.6 per cent) were taking chemotherapy at the tuberculosis clinic when pregnancy supervened. Of these one had probably inactive disease which must be the result of continuous treatment for one year prior to time pregnancy was diagnosed. Her previous X-ray had shown active disease. 20 (33.9 per cent) patients had taken treatment sometime back (period varying from 1 to 6 years). At that time when pregnancy was confirmed they were not under treatment. All these patients had irregular treatment. Of these 4 patients had probably inactive disease.

2. Response to Treatment

Majority of patients received isoniazid 100 mg twice a day and streptomycin 1 Gm twice a week. In very few cases PAS was added. One patient received isoniazid only. Patients continued treatment for a varying period from 6 to 12 months.

There were 6 patients whose period of observation was less than 6 months and there was one patient whose observation was continued for more than one year. 24 of 51 patients with active disease were regular in attendance for treatment and 27 were irregular. 8 patients with probably inactive disease were also irregular. Majority of these patients did not attend for a month or two after delivery as they left the place and some were irregular for no obvious reason. All patients delivered normally and then again started attending the clinic, after a variable period of 2 to 6 weeks.

Radiographic changes:

The two, radiographs from each of the 8 patients with probably inactive disease did not show any change in the lesion. This confirmed that the disease was inactive from the beginning of the observation period. These patients have been excluded from the subsequent analysis.

Of the 51 patients with active disease, 30 (58.8 per cent) improved, 4 (7.8 per cent) showed no change in radiographic shadows and 17 (33.3 per cent) deteriorated.

Relation of radiographic changes to the initial extent of the disease:

Of the 11 patients with minimal disease 10 (90.9 per cent) improved and only 1 (9.1 per cent) deteriorated. Of the 26 patients with moderately advanced disease 15 (57.7 per cent) improved 2 (7.7 per cent) showed no change and 9 (34.6 per cent) deteriorated. Of the 14 patients with far advanced disease 5 (35.7 per cent) improved 2 (14.3 per cent) showed no change and 7 (50.0 per cent) deteriorated. Thus it is obvious that there is definite correlation between response to treatment and the initial extent of disease.

Relation of radiographic changes to the regularity of treatment:

Of 51 patients, 24 were regular in treatment. Of these 19 (79.2 per cent) improved, 2 (8.3 per cent) showed no change and 3 (12.5 per cent) deteriorated. Of the 27 patients who were irregular in treatment, 11 (40.7 per cent) improved, 2 (7.4 per cent) showed no change and 14 (51.9 per cent) deteriorated. The relation of initial extent of disease, radiographic response and the regularity of treatment is shown in Table 6.

TABLE 5

Extent of the disease	Radiographic changes						Total	
	Improved		No change		Deterioration			
	No.	%	No.	%	No.	%	No.	%
Minimal	10	90.9	0	0-0	1	9.1	11	100.0
Moderately Advanced	15	57-7	2	7.7	9	34.6	26	100.0
Far Advanced	5	36-7	2	14.3	7	50.0	14	100.0
Total	30	58.8	4	7.8	17	33.3	51	100.0

TABLE 6

Initial extent of disease	Radiographic change					
	Improved		No change		Deterioration	
	Regular	Irregular	Regular	Irregular	Regular	Irregular
Minimal	5	5	0	0	1	0
Moderately advanced	9	6	1	1	0	9
Far advanced	5	0	1	1	2	5
Total	19	11	2	2	3	14
Percentage	63.3	36.7	50.0	50.0	17.6	82.4

TABLE 7

Main group	Radiographic changes						Total	
	Improved		No change		Deterioration			
	No.	%	No.	%	No.	%	No.	%
I	10	38.5	4	15.4	12	46.2	26	100.0
II	15	78.9	0	0	4	21.1	19	100.0
III	5	83.3	0	0	1	16.7	6	100.0

Of the 30 patients who improved, 19 (63.3 per cent) were regular and 11 (36.7 per cent) were irregular in treatment. In 4 patients who showed no radiographic change, the regularity of treatment was not an important factor at all. Of the 17 patients who deteriorated, 14 (82.4 per cent) were irregular in their treatment, only 3 (17.6 per cent) being regular in their treatment. This is a significant observation especially in patients with moderately advanced and far advanced disease.

Radiographic response and mode and time of diagnosis of pulmonary tuberculosis:

Of the 26 previously known active pulmonary tuberculosis (Group I) 10 (38.5 per cent) improved, 4 (15.3 per cent) showed no change and 12 (46.2 per cent) deteriorated. Of the 19 patients who had some symptoms during pregnancy (suspected to be suffering from tuberculosis and confirmed by radiography—Group II) 15 (78. 9 per cent) improved while 4 (21.1 per cent) deteriorated. Of the 6 patients in whom diagnosis was made on routine chest X-ray examination (Group III) 5 (83.3 per cent) improved while only 1 (16.7 per cent) deteriorated. This necessarily indicates that patients who have taken irregular treatment for long time do not respond very well to the treatment. Patients who have some symptoms suggestive of pulmonary tuberculosis fared better than above group. But patients who have been diagnosed in presymptomatic stage fare best barring few cases which were irregular in treatment or which might be excreting drug resistant organisms.

Relation of Descent of Diaphragm after parturition to Radiographic Response:

Of the 59 patients in 32 the diaphragm descended by one or two intercostal spaces after delivery. In spite of this descent, 17 of 32 (53 per cent) patients showed radiographic improvement. 8 (25 per cent) patients showed ,no radiographic change. In 6 of these the disease was radiographically inactive at the beginning and descent of diagphragm did not cause any reactivation. 7 patients (22 per cent) showed deterioration. This was attributed more to the irregularity of treatment than the descent of the diaphragm. In 27 patients the diaphragm did not descend after delivery. Of these 13 (48 per cent) improved, 4 (15 per cent) showed no change and 10 (37 per cent) deteriorated radiographically. This shows that deterioration is not necessarily associated with descent of diaphragm.

Sputum Conversion in relation to radiographic changes at the end of observation period: At the beginning sputum from 18 out of 51 patients (35 per cent) showed acid fast bacilli on direct microscopic examination of one smear, while that of 33 patients (65 per cent) did not show acid fast bacilli. At the end of observation period there was no significant change in the incidence of sputum positivity, 16 patients (31 per cent) having positive" sputum and 43 (69 per cent) having negative sputum. Apparently only 2 patients converted to negativity. But if sputum result and the radiographic response are related it is observed that of the 6 patients who showed radiographic improvement

TABLE 8

Level of Diaphragm	Radiographic changes						Total	
	Improved		No change		Deterioration			
	No.	%	No.	%	No.	%	No.	%
Descend	17 13	53	8(6)*	25		22	32	100.0
Non-Descend		48	4(2)	15	10	37	27	100.0
Total	30	...	12(8)		17		59	

* Parenthesis indicate number of patients with probably inactive disease.

TABLE 9

Radiographic change	State of sputum at onset	No. of Patients	State of sputum at the end of observation period	
			Positive	Negative
Improved … …	Positive Negative	6 24	0	5 24
No change … …	Positive Negative	2 2	*I*	0 2
Deterioration … …	Positive Negative	10 7	103	0 4
All patients … …	Positive Negative	18 35.0% 33 65-0%	16 31%	35 69.0%

(8 patients with probably inactive disease had negative sputum throughout and are not included here)

and had positive sputum at the onset, 5 converted to negative status and one maintained positive status at the end of observation period. On the other hand, of the patients who showed radiographic deterioration, 10 maintained the positive status of sputum at the end of observation period. In addition, of the 7 patients who had negative sputum at the beginning 3 became positive thus increasing the number of patients with positive sputum to 13 at the end.

Changes in E.S.R. at the end of Observation period:

It was observed that there was a fall in ESR in majority of patients because the number of patients with high ESR values decreased and that with low ESR values increased at the end of observation period as compared with the distribution of patients according to ESR values at the onset.

TABLE 10

E.S.R.	At the Onset		At the end	
	No.	%	No.	%
11-20	1	1.7	10	16.9
21-30	6	10.2	10	16.9
31-40	13	22.0	17	28.8
41-50	12	20.3	5	8.5
51-60	20	33.9	13	22.0
61-70	7	11.9	4	6-8
Total	59	100.0	59	99.9

3. Fate of Infants

Of the 60 infants born (one was twin pregnancy) 6 infants died, 4 within one month of their birth and 2 later. One was a prematurely born (8| months) and died on the 3rd day after delivery, cause of death being prematurity and dehydration, one had some congenital anomaly and died immediately after birth; two died on 7th day after delivery due to diarrhoea and vomiting. Of the later two infants, one died two months and another 8 months after delivery. Exact cause of death could not be ascertained in 4 of the 6 deaths.

Most of infants were given B.C.G. vaccine within 24 hours of birth. Those who missed B.C.G. vaccine at birth were vaccinated within one month after tuberculin testing. The mothers who were expectorating acid-fast bacilli and having active disease were advised to avoid breast feeding of their infants and to separate the infants from them. Such measures were not adopted for the infants of the mothers who were showing signs of quiescence and those who had become non-infective.

Discussion

Incidence of active pulmonary tuberculosis as assessed by routine X-rays of 2,000 patients is 5.0 per cent. On screening 1,000 women attending Bai Motlibai Hospital, 5 out of 50 active cases were missed. These could be spotted only by chest X-rays. Thus screening is quite comparable with X-ray examination and can save the cost of X-raying all antenatal women. Those who show suspicious shadows on screening should be X-rayed for confirmation. In places where Mass Miniature Radiography is possible, it could be successfully and economically used instead of screening.

The prevalance of active tuberculosis as observed in present study is quite high as compared with the prevalance of disease in general population. According to the National Sample Survey carried out in our country the prevalance of active or probably active disease in India is about 1.3 to 2.5 per cent.

Schaefer (1956) says that the reported incidence of tuberculosis in pregnancy is dependent on the efforts made to diagnose it. According to his observations by routine X-raying of women in antenatal period the incidence of significant tuberculosis is about 3 times more than is observed by history taking and physical examination.

Heaf and Rusby (1948) stress that risk to the mother is directly related to the extent and severity of the disease so it is desirable that tuberculosis, if present should be detected as early as possible. The best method of doing this is X-raying the chest of every pregnant woman at her first attendance to antenatal clinic and that the antenatal group of women should be on a high priority list of Mass Radiographic surveys.

In this study it has also been attempted to assess the effect of pregnancy upon pulmonary tuberculous lesion—active and probably inactive. It summarises the effects as observed on a poor class of patients attending general hospitals in Bombay. These patients were mostly illiterate, poor and living in unhygienic crowded localities. All patients were ambulatory.

It was not possible to compare these patients with a group of non-pregnant tuberculous women of same age group, socio-economic standards and having similar type of disease and treated in the same way. This would have given us the exact idea of effect of pregnancy on pulmonary tuberculosis. Another drawback is that the observation period was very short, as it is now accepted that the minimum period of treatment should be at least one year.

Most of the patients reported themselves for antenatal supervision during second and third trimester of pregnancy, so effect of early pregnancy on tuberculous lesions could not be studied and therapeutic abortion was out of the question here.

The important age group in which the majority of the patients were seen in present study was 21 to 30 years of age. 49 (83.0 per cent) of the 59 patients were seen in this age group. It has been observed that the morbidity and mortality rates in females are at their peak in this particular age group and then there is an abrupt fall. Pregnancy and child bearing have been blamed for this.

Majority of the patients in present study were multigravida. 42 (71.1 per cent) of 59 patients were seen 2nd 3rd 4th or 5th gravida as against only 6 (10.2 per cent) in primigravida. Schaefer (1949) has observed almost equal incidence of pulmonary tuberculosis in primigravida and multigravida. Higher incidence in multigravida in our series may be explained by the fact that in India marriages take place at early age and there are repeated and unplanned pregnancies.

Results in this study point out the effects of inadequate and irregular treatment of tuberculosis for want of drugs and non-co-operation, poverty and ignorance of patients in general and about tuberculosis in particular.

Patients have been classified in different groups to assess the effect on pregnancy on pulmonary tuberculosis. This type of classification was adopted by Turner (1950).

Cohen (1936) reported that in women with questionable tuberculosis or with definite but inactive tuberculosis, child bearing did not have any adverse effect even in adverse social circumstances. Steward and Simmonds (1943) and Turner (1950) also demonstrated that prognosis of quiescent tuberculosis is not adversely affected by pregnancy. In the present study there were eight cases of 'probably inactive disease' and none of them was affected adversely by pregnancy.

In the present study 31 (52.5 per cent) of 59 patients were suffering from pulmonary tuberculosis before they had conceived. The disease

was active in 26 of these 31 patients. The best advice for these patients would have been to avoid pregnancy till the lesion heals. This was not possible because of sheer negligence as well as ignorance about tuberculosis on the part of these patients. 12 (46.2 per cent) of 26 patients with active disease from this group deteriorated, the main causes of deterioration being irregularity of treatment and the chronicity of the disease. The probability of the emergence of drug resistant strains of tubercle bacilli cannot be ruled out. But as it was not possible to do drug sensitivity test studies due to lack of facilities for doing so this could not be confirmed. In some cases the lesions were such that only surgery would have helped to get rid of the disease and final healing. In the other two groups of patients whose tuberculosis was detected for the first time during pregnancy fared well as compared with the above group.

The majority of patients in the present study were seen with moderately advanced and far advanced disease, only 11 (21.6 per cent) of the 51 patients with active disease having minimal tuberculosis. It was observed that the prognosis of patients was definitely related to extent of disease. 90.9 per cent of the patients with minimal disease improved as against 57.7 per cent and 35.7 per cent of those having moderately advanced and far advanced disease respectively. 9.1 per cent, 34.6 per cent and 50.0 per cent patients with minimal, moderately advanced and far advanced disease respectively deteriorated.

Observations relating response to the regularity of treatment were equally important. It was observed that the patients who were regular for treatment have fared better than those who were irregular. Hence one should stress regularity of treatment to every patient whatever may be the extent of the disease.

It was obvious in present study that the descent of diaphragm was not of any importance as far as prognosis of tuberculous patients after parturition. Of the 17 patients who deteriorated only in 7 the descent of diaphragm was seen. On the other hand of the 30 patients who showed improvement, 17 had shown descent of diaphragm. In 6 out of 8 patients with probably inactive disease the diaphragm descended but there was no reactivation of disease. This disproves the observation of many workers that descent of diaphragm is the cause of deterioration in the postpartum period.

Follow up of the infants was not up to date. 6 of the 60 infants died, 4 within first month of their birth, 1 in the second month and 1 in the eighth month. In two infants the cause of death was obvious (one prematurity and dehydration; another congential anomaly). Pulmonary lesion in the mothers of these two infants was showing improvement radiographically and their sputum was persistently negative. In the other four infants who died it was difficult to assess the cause of death. Mothers of two children had probably active disease (Sputum negative) and in third the disease was active but had responded well to treatment and sputum was negative from the beginning. Mother of the 4th child had active disease with positive sputum at the beginning. She deteriorated in spite of treatment and sputum remained positive. It is probable that the cause of death of infant of this mother may be tuberculosis but there was no definite proof for it.

Rest of children fared well. All were B.C.G. vaccinated.

Summary and Conclusion

59 patients of pregnancy associated pulmonary tuberculosis are studied. 31 patients (52.5 per cent; were previously known cases of pulmonary tuberculosis when they first attended the antenatal clinic. 19 patients (32.2 per cent) were suspected to be suffering from pulmonary tuberculosis when they attended the antenatal clinic and diagnosis confirmed by chest X-ray examination. 9 patients (15.3 per cent) were diagnosed on routine antenatal chest X-ray examinations.

Majority of patients (48 of 59) were from the age group 21 to 35 years.

53 patients (90 per cent) of them were multigravida.

Most of them came under observation for first time in the later half of pregnancy.

8 patients had probably inactive disease and 51 had active disease. Of these 51 patients, 11 (22 per cent) had minimal disease. 26 (51 per cent) had moderately advanced disease and 14 (28 per cent) had far advanced disease. 18 of 51 patients (36 per cent) showed A.F.B. on direct smear examination of the sputum.

Response to treatment as assessed by radiography was related to initial extent of disease, regularity of treatment and relation of onset of disease to pregnancy. At the end of observa-

tion period, of the 51 patients with active disease, 30 (58.8 per cent) showed improvement, 4 (7.18 per cent) showed no change, 17 (33.4 per cent) deteriorated. The 8 patients with probably inactive disease did not show any radiographic changes.

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A REVIEW OF 1,000 CASES OF CHILDHOOD TUBERCULOSIS AT TRIVANDRUM (KERALA)

N. S. NAIR *(Tutor),* KURIAN THOMAS *(Resident),* T. P. JOHN
(Assistant Professor), AND OMANA MATHEW *(Professor)*
The Department of Paediatrics, Medical College, Trivandrum

Tuberculosis has been a perennial scourge for mankind from time immemorial. Signs of the ravages of the disease were found in bodied mummified centuries before the birth of Christ. (Arora) 2. Mention about the condition had been made in 600 B.C. by Sushrutha and Charaka (Benjamin) 7.

The high prevalence rate of infection in India is well known. Tuberculosis accounted for 8.9 per cent of the total deaths in Bombay in 1950. (Udani) 56. No fewer than 40,000 deaths annually among the paediatric age group were officially attributed to Tuberculosis. (Udani and Sheth) 60. Benjamin 8 assessed the morbidity of Tuberculosis in Indian children at 2.5 per cent (urban) and 0.4 per cent (rural). Udani 58 observed that 83 per cent of children from the poor and low middle class socio-economic groups showed a positive tuberculin reaction. In India, Tuberculosis is the second major cause of death in the age group 1—4 years (Athavale) 5. The present study was undertaken with a view to assess the patterns of the disease met with in Trivandrum in the paediatric age group.

Materials and Methods

The study is based on 1,000 consecutive cases seen at the T.B. Clinic of the S.A.T. Children's Hospital, Trivandrum.

The age of the subjects ranged from 2½ months to 12 years. The Clinic is run on an out-patient basis. The subjects included patients discharged from the Wards, cases detected at the General Out-patient Department, and those seen at the Peripheral Centres attached to the Hospital. Tuberculin Test was carried out in all cases with 1 T.U. of Old Tuberculin, or equivalent dose of PPD, an induration of 8 m.m. or more, being considered as Positive reaction. Skiagrams of the chest were obtained in all subjects, and were periodically repeated. In addition to a complete physical examination, relevant haematological and ancillary methods of investigation were carried out in all cases, wherever necessary. Depending on the total monthly family income, the subjects were classified into 4 groups: Group 1—below Rs 50, Group 2 Rs 50-99, Group 3 Rs 100-199 and Group 4 over Rs 200 per month. On the basis of their nutritional status, the subjects were divided into four groups: Taking the expected average weight of the child to be 100 per cent, the nutritional status was adjudged 'Fair' (70-110 per cent), 'Poor' (below 70 per cent) and 'Good' (above 110 per cent). The figures given by Phadke 50 for infants and children (upto 3 year of age) and by Athavale 4 (over 3 years of age), for average weight have been adopted.

Limitations and Drawbacks

It is well known that Hospital data do not necessarily indicate conditions in the community at large. In the absence of relative data, it has not been possible to assess the extent to which our observations reflect, or differ from conditions in the overall population of Trivandrum.

A Mass Miniature Radiographic Survey in Bombay, revealed the existence of Pulmonary Tuberculosis in 2.5 per cent of children examined (Udani 57). Based on this figure, Udani assessed the number of children in Bombay who would reveal evidence of Intrathoracic Tuberculosis radiologically at 7,500. Assuming the paediatric age group, to constitute 40 per cent of the population, the number of children in Trivandrum would be 95,926. The figure of 2.5 per cent can be expected to hold good in other parts of the country as well. Hence it would be reasonable to assume that no fewer than 2,398 children in Trivandrum City would show evidence of the disease radiologically. Only 798 of these subjects have been seen by us. It is evident that only a minority of the affected paediatric population locally, have passed through our hands.

Hospital income data are notoriously unreliable. Our subjects belonged almost exclusively to the lower income groups, the family income being less than Rs 100 per mensem, in an overwhelming majority of cases. Due to the strictly limited number of subjects from the higher

income groups, no valid conclusions can be drawn regarding the relationship between socioeconomic status and Tuberculosis. Due to administrative reasons, children above 12 years of age, have had to be excluded from the study. Since the subjects were seen on an out-patient basis, bacteriological investigations have not been routinely possible. Much credulence cannot be attached to the Contact History since the incriminated subjects have not been screened radiologically.

Analysis of Results

Sex Distribution

Table No. 1 shows the sex distribution in our subjects.

TABLE 1

Age Group	Males		Females		Total
	Number	Per cent	Number	Per cent	
0-2 years	167	56	130	44	297
2-5 years	225	64.3	125	35.7	350
5-8 years	120	61	77	39	197
8 years & Over	66	42	90	58	156
Total	578	...	422	...	1000

Boys (588 cases) outnumbered girls. The National Tuberculosis Survey 47 showed a predeliction for the disease among females. It is to be assumed that the greater prevalence of the disease among females has some causal relationship to the stresses and strains of rigorous household activities in our female population. Evidently, this deleterious influence could not be expected to hold good in the paediatric age group. However our observations seem surprising in view of the fact, that females outnumber males in Kerala. This could possibly be due to the differential regard for boys and girls as suggested by Paffenberger and Verma 49 in their study of Morbidity in Children in Gujerat. They also point out that the relatively high value of the male child results in a differential perception of self along sex lines.

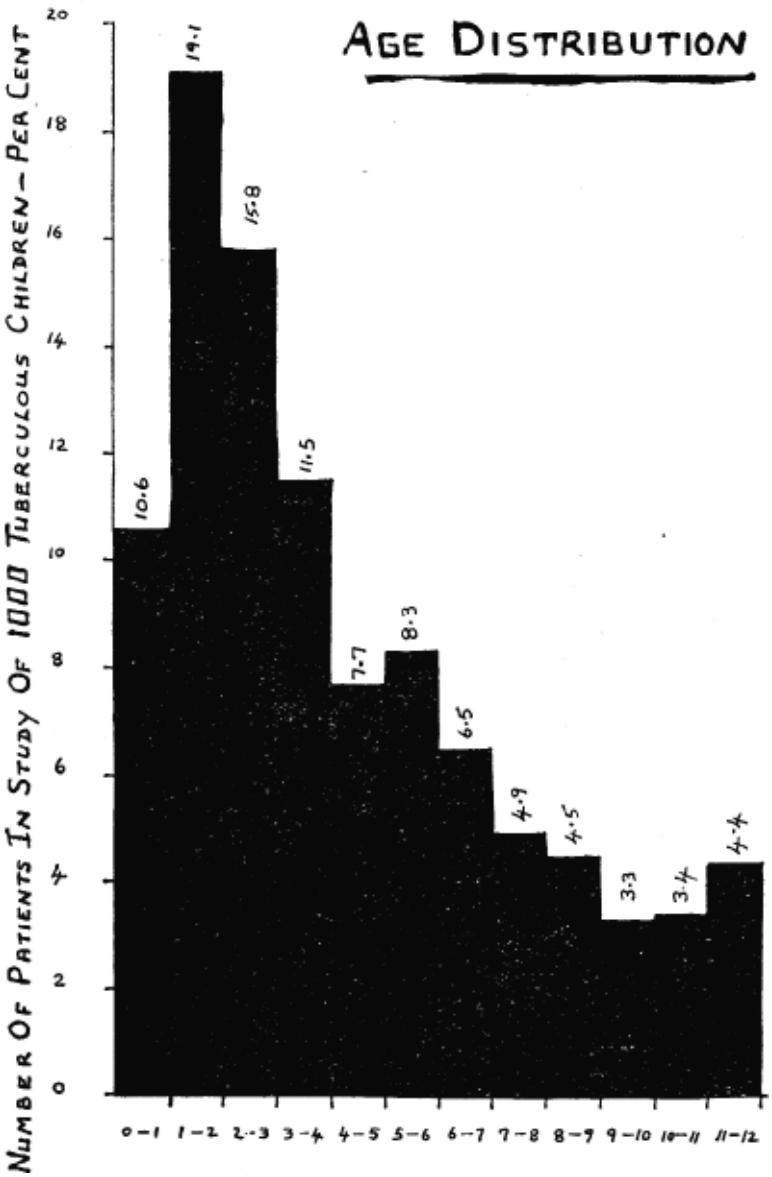
There was a decidedly greater morbidity among girls of the higher age group. Girls constituted 58 per cent of patients over 8 years of age. The metabolically labile environment of the prepuberal female, presumably renders her vulnerable to infection and illness. It is well known that Menarche tends to occur much earlier in our children.

Age Distribution

Table No. 2 shows the age patterns in our study.

TABLE 2

Age in Years	Number of cases	Per cent
0-1	106	10.6
1-2	191	19.1
2-3	158	15.8
3-4	115	11.5
4-5	77	7.7
5-6	83	8.3
6-7	65	6.5
7-8	49	4.9
8-9	45	4.5
9-10	33	3.3
10-11	34	3.4
11-12	44	4.4



In general, a decrease in number of affected children was observed with advancing age. It is well known, that the younger age groups account for the larger number among the paediatric population. It is also reasonable to assume, that deviations from health would be more promptly observed, and hospitalization hastened in the case of younger children, due to the greater parental regard for their younger offsprings.

Infants between 1-2 years of age were the most vulnerable, accounting for nearly a fifth 19.1 per cent of the total number of cases. The lowest incidence was met with at 9-10 years

of age, 3.3 per cent. The maximum number of cases were between 0-3 years of age, but no age was immune. In the so called 'Safe' period of 3 years to puberty, we had no fewer than 545 cases. Despite the exclusion of children above 12 years of age, the incidence of the disease in the prepuberal period of 11-12 years rose from 3.35 per cent at 9-11 years of age, to 4.4 per cent Shah *et al.*, 52 in a radiological survey of the prevalence of pulmonary tuberculosis in Bombay children, found a minimal incidence of 0.4 per cent in school children (4-14) years. Their figure for the incidence of the disease among children below 4 years of age was 2.5 per cent.

Socioeeonomic Status

Our patients were drawn mainly from the lower income groups. The family monthly income was less than Rs 50 per mensem in 59.2 per cent of cases. In fewer than 1 in 25 cases (38 subjects) was the family income over Rs 200 per mensem. Benjamin has stated that poverty is one of the factors, which influences the incidence of Tuberculosis in a community. Almost without exception, housing conditions were eminently unsatisfactory.

Occupation of Parents

In relation to Childhood Tuberculosis, this is relevant, mainly as regards the *per capita* income of the family. The parents of our patients were from different professions and walks of life. Benjamin 7 has pointed out that the disease spares no ethnic or social group. Unskilled workers accounted for 59.1 per cent. 7.2 per cent were farmers, and presumably were from the rural areas on the outskirts of the City. The National Tuberculosis Survey revealed that contrary to popular opinion, the morbidity of the disease is quite high in rural areas. Hospital personnel accounted for 2.8 per cent. It would have interesting to screen these subjects radiologically for evidence of the disease.

Nutritional Status

Table No. 3 shows the nutritional status in our subjects.

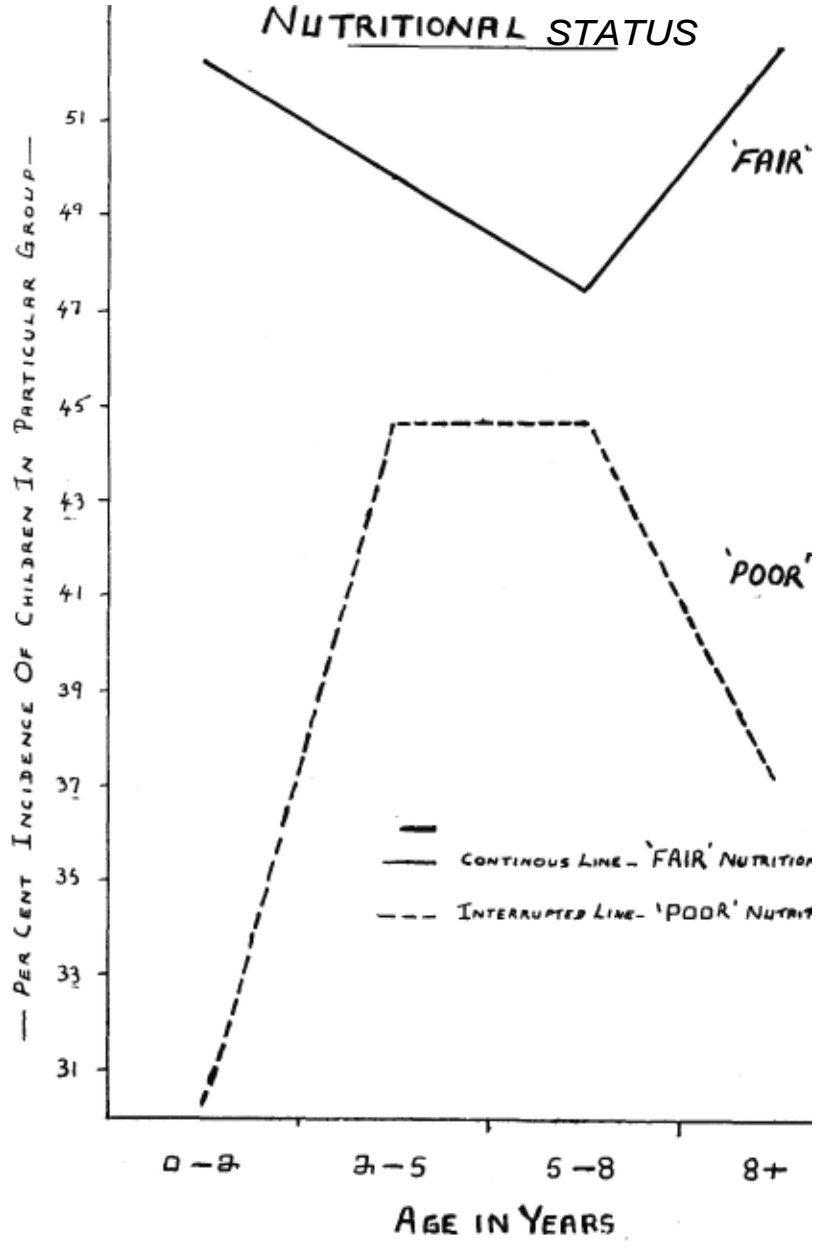
TABLE 3

Age in Years	Fair		Poor		Good	
	Number	Per cent	Number	Per cent	Number	Per cent
0-2 (297)	155	52.2	90	30.3	52	17.3
2-5 (350)	170	49.8	156	44.6	24	7
5-8 (197)	94	47.7	88	44.7	15	7.6
8 years and over 9 (156)	82	52.6	58	37.2	16	10

The nutritional status was adjudged to be 'Poor' in 39.88 per cent, 'Good' nutrition being encountered as infrequently as in 1 in 10 subjects (10.7 per cent). The apparent bearing of Malnutrition on Tuberculosis as revealed in the present study, must however be viewed in the light of the prevalence of unsatisfactory states of nutrition among our children. Discussing the resistance of the child in relation to the Natural History of the Disease, Carter and Trowell (22) state, that the nutritional status of the patient has always been recognized to be of paramount importance. Deshmukh (30) on the other hand asserts, that Malnutrition *per se,* does not make one susceptible to the disease. It appeared as though nutrition had very little bearing on infection in infancy. While 44.7 per cent of subjects between 2-8 years of age, showed 'Poor' nutrition, in only 30.3 per cent of infants below 2 years of age, was the nutritional status deemed to be poor. It is well known that nutrition tends to be unsatisfactory during the postinfancy period.

Contact History

A history of contact was available in 355 subjects. Though infection from a single exposure has been reparted many times, it usually occurs only if the exposure is both intimate and heavy (Miller 40). In 64 cases, the patient had been in contact with more than one affected person. Thus our patients had come into contact with a total of 431 persons afflicted with the disease. In a thickly populated city like Trivandrum, it would have been reasonable to expect, a higher figure for contact history. In fact as Billimoria (17) has pointed out, 'To



find a case who could not have possibly been exposed to the infection, would be like asking for the Moon, in any Indian City, large or small'. Our figure favours comparably with that of Manchanda (38) who obtained a definite history of contact in 37.6 per cent of cases. Sud and Laroia (55) however could elicit such a history in *72* per cent of their cases.

A history of contact was more often forthcoming in the younger age groups-Table No. 4.

While a positive history of contact could be obtained in 45.12 per cent of subjects below *2*

TABLE 4

Age in Years	Total Number	Contact History +	Per cent
0—2	297	134	45.2
2—5	350	126	36
5—8	197	60	30.46
8 years and over	156	35	22.43

years, the corresponding figure for the 8-12 years age group was as low as 23.43 per cent. Deshmukh (26) recalls that Fridot Muller at Madanapalle, confirmed Palmer's view, that a positive history of contact is generally available in practically all cases of infection, in the younger age groups. Deshmukh *et al*., have demonstrated the high rate of infection and of tuberculosis, in contact children. Infected persons outside the patient's home, accounted for only 5.01 per cent of contacts—Table No. 5.

TABLE 5

Age in Years	Father	Mother	Siblings	Grandfather	Grandmother	Uncle	Aunty	Neighbour	Other	Total
0—2	23	22	88	6	7	8	9	5	2	134
2—5	29	21	43	13	11	14	2	9	3	126
5—8	14	11	21	6	2	5	8	3	...	60
8 years and over	3	7	18	1	2	0	3	1	...	35

This could largely have been due to the unfortunate stigma attached to the disease, with consequent concealment. Nevertheless, the fact that 95 per cent of contacts were from the patient's own home, is worthy of note. Wallgren (62) states that with but a few exceptions, tuberculous infants and children acquire their infection from a consumptive member of the family. Our figures draw attention to the usefulness of screening the home contacts of tuberculous children, as a relatively inexpensive public health measure for detection of undiagnosed patients in the Community. From a strictly paediatric point of view also, as Ramakrishnan (51) has pointed out, the major risk to young children, is exposure to infectious persons before the latter have received any treatment.

Grandparents are frequently incriminated as the source of infection Manchanda (37). This however was not the case in the present series, where they accounted for only 11.4 per cent of contacts. It could well be, that a host of—inimical factors like chronic undernutrition, poverty, poor housing conditions, and the low standards of environmental sanitation, all connive to make the illness in elderly subjects rapidly fatal, resulting in shorter periods for possible dissemination of the disease in the community. Siblings of the patients were the most frequent offenders: 39.44 per cent.

Duration of Illness

Deviations from apparent health, as revealed by interrogation of relatives revealed that the duration of illness ranged in our subjects, from 3 days to as long as 18 months. In 43.4 per cent the complaints dated from 1-3 months prior to observation. The duration was over 6 months in 13.5 per cent. Only a quarter of the subjects (251 cases) had presented themselves for examination within a month of onset of symptoms. This is perhaps a reflection of the lamentable sense of complacency of the local population.

Previous Illness

Coelho (24) states that our children suffer from contagious and infectious diseases, like whooping cough, measles and dysentery, which prepare them for a tubercular infection. The common illnesses from which our patients suffered within the past 12 months prior to observation, was as is shown in Table No. 6.

Manchanda (37) observed in a study of tuberculous children, that 62.4 per cent had suffered previously, from some significant illness or other. Only 449 of our cases gave such a history. A history of 'Frequent attacks of cough and cold' was forthcoming in no fewer than 285 cases. The causal relationship, if any, between these attacks of respiratory infection and tuberculosis remains to be elucidated. It could well

TABLE 6

Measles …	67 cases	Whooping Cough	95 cases
Frequent Cough and Cold …	285 cases	'Asthma'	95 cases
Gastroenseris …	35 cases	Pneumonia	11 cases
Enteric Fever	13 cases	Smallpox	7 cases
Inf. Hepatitis ...	11 cases	Otitis Media	12 cases
Diphtheria	7 cases	Lung Abcess	2 cases
Heart Disease ...	5 cases	Mongol	1 case

be, that these episodes marked the onset of the infection in a considerable proportion of children. While 95 subjects had suffered from pertussis, a history of Measles was available in 67 cases; these two conditions have been incriminated as having a baneful influence on the genesis of Tuberculosis in the paediatric age group. Bentley *et al* (12) emphasize the dangers of haematogenous dissemination with Measles and Pertussis, in a child with the primary infection. This relationship could not, however, be demonstrated in the present series. 88 subjects gave a history of previous attacks of 'Asthma'. This high incidence makes us wonder as to whether these children with the 'Asthmatoid Syndrome' represent a group particularly vulnerable to Tuberculosis. In 37 of these 88 cases, there was radiological evidence of intrathoracic regional adenopathy. Further studies are clearly warranted, before any definite conclusions can be drawn as regards the nature of this association. A history of Gastroenteritis was obtained in 35 subjects, Wallgren 63 states that intestinal disorders in infants and small children, undermine the child's powers of resistance, and tend to cause an acquired tuberculous infection to pursue a malignant course.

Presenting Complaints

As pointed at by Macpherson (35), Primary Tuberculosis in children is symptomless in the vast majority of cases. Cammock and Miller (19) estimated that three quarters of about a 1,000 children under five, passed through the primary infection without illness or with illness so mild, that deviations from health were not apparent. The most frequent symptoms were: Fever (69.8 per cent), Cough (79.3 per cent;, Loss of Weight (20.3 per cent), and Anorexia (14.7 per cent). Other significant complaints were: Dyspnoea (10.6 per cent), Pallor (4.1 per cent) and vague chest pains (4.3 per cent). Diarrhoea (5.6 per cent) was more frequent than Constipation (2.3 per cent). Complaints also included Pain in the Abdomen (2.2 per cent), Hyperhidrosis (1.9 per cent), Hoarseness of Voice (0.6 per cent) and Haemoptysis (0.9 per cent). The manifold patterns of the presenting complaints may be explained on the basis of the selective nature of the study, and the fact that over a third of our subjects manifested Postprimary and Extrathoracic forms of the disease.

Clinical Signs

The paucity of clinical signs was a striking feature of our study. While the liver was palpable in 193 subjects, the incidence of splenic palpability was as low as 6.5 per cent. An incidence for palpability of the liver of 19.3 per cent must be viewed in the light of the observation of one of the authors N.S.S. (46) who found the organ to be palpable in 28.3 per cent of children without apparent liver disease. Nadkarni and Gadgil (44) found that 16.3 per cent of the total inflammatory splenomegalies in infants and children were of the chronic variety. Excepting two, all of these cases were of Secondary Tuberculosis. Udani (59) emphasized that hepatosplenomegaly was a not uncommon clinical manifestation of various types of tuberculosis in children. Clinical signs elicited by clinical examination of the chest, were minimal, and were far from commensurate with the extent of pulmonary invlovement revealed radiologically. Bhandari and Kaul (11) consider the absence of physical signs as a characteristic feature of the primary infection. The futility of attempting to arrive at a definite diagnosis based on pre-

senting complaints and clinical signs in Childhood Tuberculosis is obvious.

Types of the Disease

The intrathoracic and the extrathoracic forms of the disease accounted for 929 and 71 cases respectively. Meyer (43) observed that Extrathoracic Tuberculosis occurred in 5-10 per cent of children, infected under three years of age, and in about 3 per cent of older children.

Intrathoracic Tuberculosis

While 648 cases of uncomplicated Primary Tuberculosis were met with, there were 281 cases of Postprimary Intrathoracic Tuberculosis. Indeed, the primary complex in our children is a far from benign lesion.

Table No. 7 shows the incidence of the various forms of Intrathoracic affections in our cases in comparison, to those observed by Bentley *et al.,* in the Highwood Survey in England.

TABLE 7

Primary	Present Study Per cent	Bentley *et al.* Per cent
Typical Primary Complex	3.1	1096
Glandular Component Alone	55.4	19.27
Chest Negative	6.3	...
Post Primary Consolidation	3.3	...
Collapse	0.5	Segmental Lesions 16.11
Infiltration	17.9	...
Calcification	0.6	14.01
Chronic Pulm. T.B.	1.1	11.06
Thickened Pleura	0.1	...
Pleural Effusion	1.1	21.54

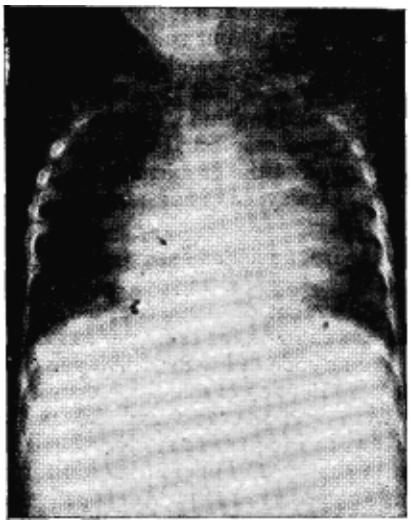
A strikingly high incidence of uncomplicated primary tuberculosis was a feature of our study. While 64.8 per cent of our subjects belonged to this group, the corresponding figure in the study of Bentley *et al* was as low as 30.23 per cent. We would conclude, that the younger age groups are more affected in India. Miller (42) points out that the problem in the Western Hemisphere today, is that of Adolescent Tuberculosis.

A greater frequency of Intrathoracic Lymph Node affection was a feature of our cases. While involvement of the Glandular Component alone, accounted for 19.27 per cent and the typical Primary Complex for 10.96 per cent in the study by Bentley *et al.,* the corresponding figures were 55.4 per cent and 3.1 per cent respectively, in the present study. Deshmukh *et al.,* in a survey of Tuberculous Children in Maharashtra, observed Hilar Adenopathy alone in 581 subjects, and the Typical Primary Complex in 37 cases. It would seem that a greater predeliction for regional adenopathy is a characteristic of Indian children in comparison to their Western counterparts.

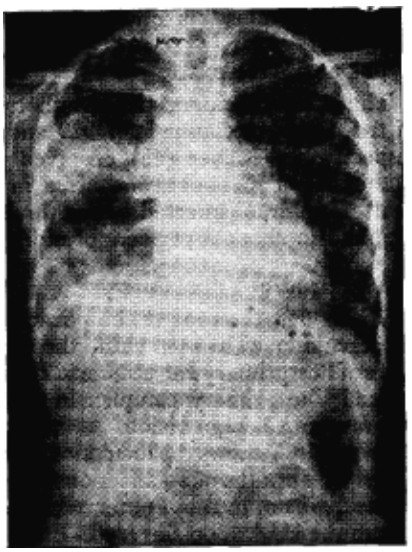
Brookes (18) considers the percentage of significant haemotogenous and lymphogenous spread to be very much greater in India. Our figures, however, do not bear this out. We believe that the true incidence of miliary and meningeal tuberculosis, would have been higher in these parts, as it has been our experience, that a significant number of these patients with the more serious forms of the disease, do not report to the T.B. Clinic for follow up, after discharge from the Wards.

While evidence of calcification was a rarity in our subjects, (0.6 per cent) this was frequently met with in the Highwood Survey 13. Calcification must be considered as the successful culmination of the reparitive mechanisms of the body, and hence as an index of inherent reparative capacity of the individual. The lower incidence of calcification in our subjects may be a reflection of the higher vulnerability of our children, as a racial characteristic. In Africa, Carter (20) saw no cases of calcification of the mediastinal glands in Kikiyu children, while Altmann (1) noted a high incidence of calcification in Bantu children. Benjamin (8) states that Calcification is fairly common in Indian children.

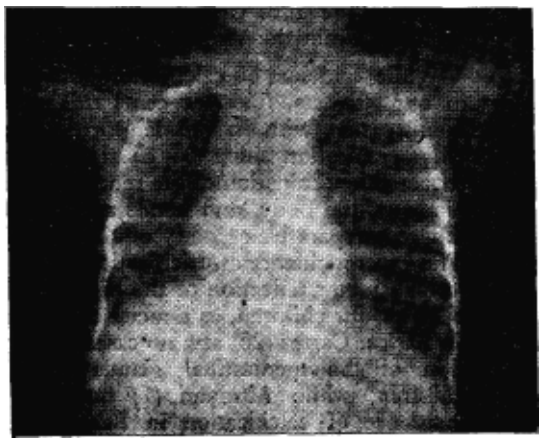
The same explanation holds good for the



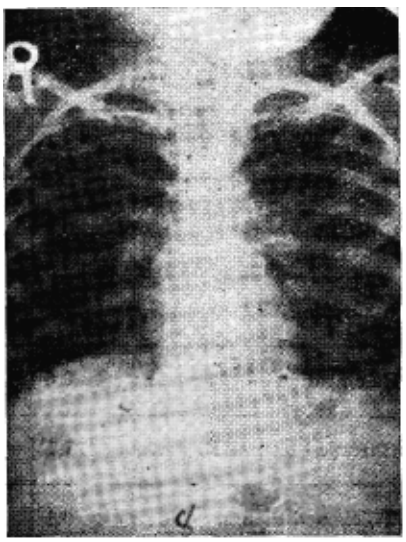
A Case of Tuberculous Pericarditis



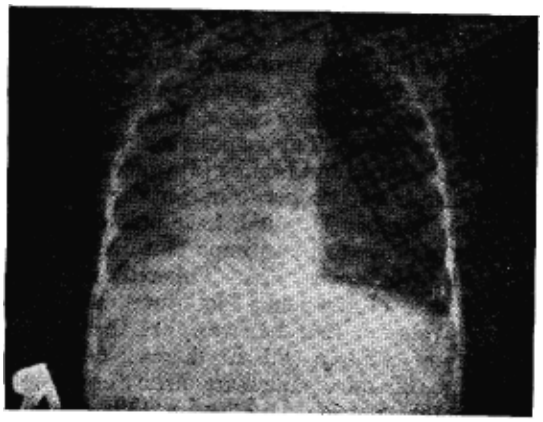
‘ Adult’ type of Tuberculosis with Cavitary Lesions



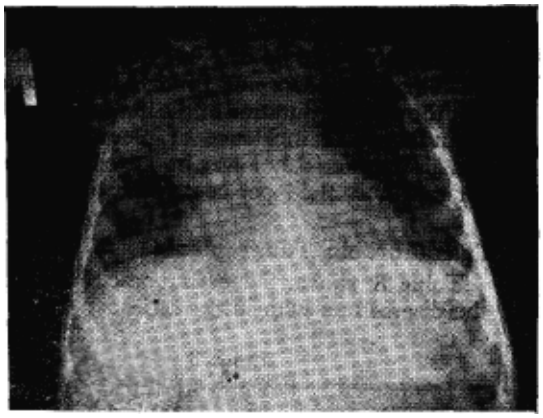
Collapse of the Right Upper Lobe (apical and pectoral segments), presumably due to enlargement of the Right Paratracheal Lymph Glands.



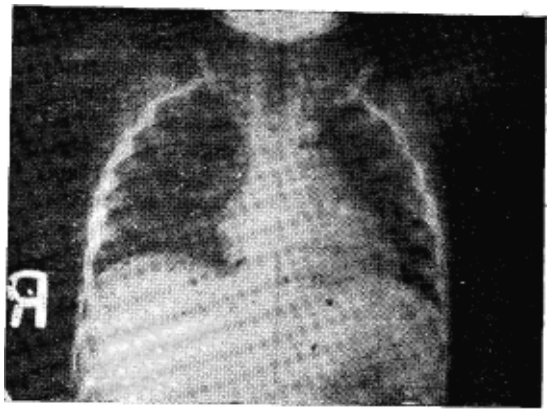
Miliary Infiltration throughout both Lung Fields, with bilateral enlargement of the hilar lymph nodes.



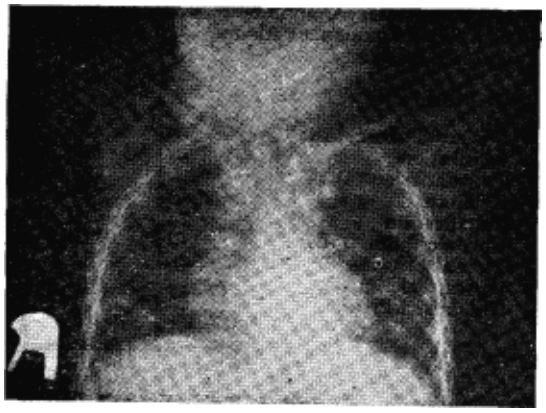
Extensive fibrosis or the Right side, showing marked shift of the trachea and the mediastinum towards the Right,



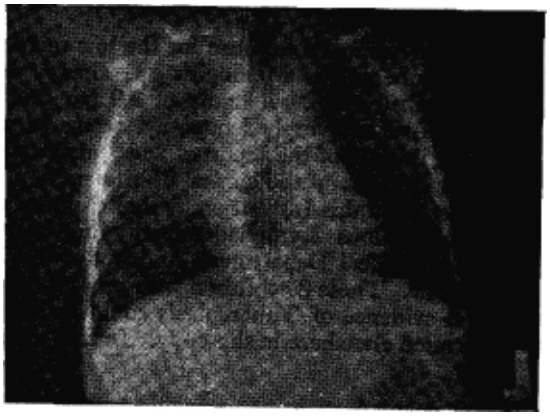
Extensive area of homogenous opacification —involving the Right Upper Lobe, with probable involvement of the Anterior Middle segment of the Right Middle Lobe.



Calcified left hilar and paratracheal lymph nodes. Calcified nodes are also seen in the left supraclavicular region.



Calcified hilar and paratracheal nodes on both sides. Calcification has also occurred in the supraclavicular nodes.



A Calcified Parenchymal Focus is visible in the Right Mid-zone.

appreciably lower incidence of Chronic Pulmonary Tuberculosis locally (1.1 per cent as compared to 11.0 in the Highwood survey.) 13. This also bears out Brooke's observation that the average duration of the illness is shorter in India. The incidence of pleural effusion was also appreciably lower in our children (1.1 per cent and 21.54 per cent respectively).

Extrathoracic Tuberculosis

Table 8 shows the extrathoracic forms of the disease met with in the series:

TABLE 8

	Number	Per cent
Tuberculous, Meningitis ...	20	18.9
T.B. Lymphadenopathy	29	27
Abdominal Tuberculosis ...	6	5.7
Spinal Tuberculosis	4	3.8
T.B. Dactylitis	2	1.8
Erythema Nodosum	1	0.9
Phlyctenular Conjunctivitis	7	0.7
Tuberculous Pericarditis ...	2	1.8
Miliary Tuberculosis	35	3.3

The presumable cause for the low incidence of Tuberculous Meningitis has already been remarked upon. A figure of 2.9 per cent for tuberculous lymphadenopathy, seems surprising, in view of the reported wide prevalence of the disease in the nodes of the neck. The custom in this Institution, is that children with Tuberculous Lymphadenopathy are seen at the Surgical Department, and not at the T.B. Clinic. These 29 children were cases in whom, no evidence of Tuberculosis could be demonstrated elsewhere in the body. In fact, cervical glands were palpable in over a third of our patients (361 cases).

The fact that Phlyctenular Keratoconjunctivitis was met with in 7 children is worthy of note. In four of these cases, there were no other evidence of Tuberculosis elsewhere in the body. Arora and Maniar (3) who recorded an incidence of 0.2 per cent for the condition in a Bombay Hospital, have pointed out, that it can prove to be an important diagnostic sign, in an otherwise silent Tuberculosis. A solitary case of Erythema Nodosum was met with. Wallgren (64) believes that the great majority of children with Erythema Nodosum show signs of active pulmonary disease or extrathoracic processes. Middlemiss (39) found evidence of Tuberculosis in 80 per cent of his cases showing Erythema Nodosum. Our figure for the incidence of Extrathoracic Tuberculosis (including the miliary forms) is slightly higher than that recorded by Sheth (5-7 per cent) (53). The dissimiliarities observed included a higher prevalence of Cervical Adenitis, (26.4 per cent in the present study in comparison to 18 per cent quoted by Sheth), and a lower incidence of the skeletal forms (5.7 per cent and 15 per cent respectively), and of Abdominal Tuberculosis (5.7 per cent and 15 per cent respectively), in our subjects.

Radiological Findings in the Chest

These were as shown in Table No. 9:

TABLE 9

Type of Lesion	Number
Primary	
Typical Primary Complex	31
Glandular Component Alone	554
Chest Negative	132
Post Primary	
Miliary Tuberculosis	35
Infiltiation	179
Consolidation	33
Collapse	5
Calcification	6
Chronic Pulm. T.B.	11
Pleural Effusion	11
Pericardial Effusion	2
Thickened Pleura	1

The Chest was radiologically normal in 132 children. In this connection the limitations of radiological diagnosis have to be kept in mind. Emery and Lorber (33) observed that in Miliary Tuberculosis, the radiographs were positive only, when the majority of tubercles were over 1 mm. in diameter and their number was 5-20 per c. mm. Bhandari and Kaul (9) have stressed that a primary focus may well be concealed by the heart shadow. The different regions of the Lungs, show wide variation in their radiological accessibility. It is evident, that pulmonary affection is not synonymous with positive skiagrams.

Simple Primary Pulmonary Tuberculosis

Bhandari and Kaul (10) have reported 47.5 per cent incidence of uncomplicated primary tuberculosis in their survey of 1060 tuberculous children. Our figure for the condition was 64.8 per cent.

Typical Primary Complex

This was observed in as few as 31 cases. It may be, that in most case the primary focus may be too small to show by present radiological methods, or it might be obscured by the diaphragm or mediastinal shadow. The primary focus was on the right side in 28 out of the 31 cases. This would seem to establish the preponderance of the primary focus in the right lung. Bentley *et al.,* however emphasize that there are no such areas of predeliction. As is to be expected, nearly two thirds (22 subjects) of the cases showing the typical primary complex were under 5 years of age.

Primary Complex Regional Lymphadenopathy alone

In 554 subjects the regional intrathoracic nodes alone were involved. More than one group of glands were involved in 59 cases, accounting for a total of 616 groups of glands. Of these 502 were on the right side, and 114 on the left. In only a quarter of these cases was the glandular involvement noted above 5 years of age—Table No. 10.

The hilar glands were predominantly involved, affection of the paratracheal group being restricted to 66 instances. While the greater ease with which right sided glands are visualized has to be borne in mind, the higher frequency with which rightsided glands are involved is beyond question. Ghon (34) found pleural changes in two thirds of his subjects with primary infection. We failed to come across a single child with evidence of unequivocal pleural affection, in our cases of Simple Primary Tuberculosis.

TABLE 10

Age Group in Years	Right Side		Left Side	
	Hilar	Paratracheal	Hilar	Paratracheal
0—2	145	22	31	3
2—5	151	15	31	6
5—8	89	9	25	1
Over 8 years	62	9	16 .	1
Total ...	447	55	103	11

Post-primary Intrathoracic Tuberculosis

This accounted for 28 cases. The manifestations included mainly the Miliary, the Infiltrative and the Segmental lesions. Pulmonary involvement suggestive of the Adult Forms of Tuberculosis, Calcined lesions and Pleural Effusions contributed the minor share towards this group.

Miliary Tuberculosis

There were 35 cases of Miliary Tuberculosis. Bhandari and Kaul (11) have observed an incidence of 2.3 per cent. The majority (23 cases) were under 5 years of age. The predominance of girls in the latter years of childhood observed by Bentley *et al* (14) was lacking in the present study. Bentley *et al* consider cases of Occult Miliary to be quite common. Since neither sternal marrow nor needle biopsies of the liver, were carried out, no opinion can be expressed as regards the incidence of cases of this type in our series. :

Infiltrative Tuberculosis

Radiological evidence of Infiltration was observed in 179 cases. In 49 of these the infiltration was bilateral. Lesions involving all six zones of the Lungs were seen in 6 children.

Lesions were noted in more than one zone in a number of cases, the total number of infiltrations, being as high as 260. Associated regional adenopathy was a feature in 91 of these 260 lesions. Glandular involvement was most common between 2-5 years of age (43/91). Infiltrative lesions were commoner in the older age groups. Thus while the age group 0-2 years accounted for only 18.7 per cent (55/297) of the total infiltrative lesions, 28.2 per cent (174/547) of lesions occurred between 2-8 years. The majority were on the right side (170/260).

Involvement of the midzone was most frequent (124/260). The right midzone was most frequently affected 89/260. Very few lesions occurred in the left upper zone. Deshmukh (25) considers an isolated basal lesion in males to be rather rare. This however was not the case in the present study. Nor could the predeliction for basal lesions in females noted by him be substantiated.

Table No. 11 shows the infiltrative lesions in the study classified according to the age group of the patients. The salient features were: (1) Involvement of the right upper zone was more frequent over 8 years of age; (2) On the contrary, left upper zone involvement was extremely rare over 8 years of age having been noted in a solitary instance. (3) Left lower zone involvement was commoner during the first two years of life, and (4) children over 5 years of age showed greater affection of the left middle zone. We are unable to offer any valid explanation as regards these regional proclivities.

TABLE 11

Zone	0-2 yrs.	2-5 yrs.	5-8 yrs.	8 yrs. and over
Right Upper	6	10	5	6
Right Middle	18	41	22	9
Right Lower	11	23	13	7
Left Upper	6	10	6	1
Left Middle	5	14	11	5
Left Lower	9	11	8	3

Segmental Lesions

These included 33 cases of Consolidation and 5 cases of Collapse. It has recently been suggested that pure forms of consolidation or Collapse are very infrequent, and that most of these lesions are in the nature of a Consolidation-Collapse. Carter and Trowell (27) consider consolidation-collapse to be the commonest expression of the progressive primary lesion.

Our incidence of regional segmental lesions (3.8 per cent) is appreciably lower than in the West (Bentley *et al* 16.11 per cent 13). This seems inexplicable particularly in view of the role played by tuberculous glands in the pathogenesis of such lesions. The frequency with which Intrathoracic Regional Glands were involved in cases of Primary Tuberculosis will be recalled. Only a third of the patients with segmental lesions were above 5 years of age. The greater frequency of segmental lesions in the younger age groups, has been commented upon by Macpherson and Lutwycha (36).

Calcification

Parenchymal calcification in the right midzone was observed in one case. Calcified hilar, and/or paratracheal glands constituted the rest of the cases. One child also showed calcified cervical nodes. It was interesting to find that in a 9 month old infant, a well calcified right hilar gland was visible radiologically.

Chronic Pulmonary Tuberculosis

Under this heading we have included 9 cases of cavitary lesions and 2 cases of extensive fibrosis. The lesions in 5 of these cases were apical in distribution. No predeliction could be demonstrated for either the left or the right side. 6. out of the 9 subjects were females. In Nalblant's Survey, there were 3 times as many girls as there were boys. (Nalblant 45). The exclusion of children over 12 years of age, presumably accounts for the very low incidence of Adult Tuberculosis in our series.

Pleural Effusion

There were only 11 subjects who showed radiological evidence of pleural effusion, 7 of these being girls. A 1 year old infant had a

massive pleural effusion on the right side. Our figure is at marked variance with the views of Caffey (23) who asserts, that Pleurisy is so common in Primary Tuberculosis, that it is a component rather than a complication of the disease. Send and Das Gupta assessed the frequency of Bronchiectasis in Childhood Tuberculosis at 5 per cent. (Sond and Das Gupta 54). We did not come across a single child with Bronchiectasis. This may be due to the fact that bronchograms were not possible in our study.

Extrathoracic Tuberculosis

Due to the strictly limited number of subjects manifesting with these forms of the disease it would be presumptuous to draw any conclusion as regards the bearing of various factors like sex, age etc., on these types of Tuberculosis in the present study.

It is reasonable to assume that quite a few cases of tuberculous involvement of the abdomen have escaped detection. The diagnostic clinical criteria of the condition has severe limitations. Van Beck and Heck (61) were confident of demonstrating involvement of the liver in even early cases of pulmonary tuberculosis by percutaneous liver biopsy. Desai *et al.,* (31) opine that primary abdominal tuberculosis is probably not common in our children.

We failed to come across a single case of renal involvement. This again, is in agreement with the views of Desai *et al* (32), to whose knowledge, Tuberculosis of the Kidney with it's typical symptomatology is not often seen in the paediatric age group. We would like to draw attention to a 6 month old infant who presented with tuberculous involvement of the Spine.

The Tuberculin Reaction

The reaction was graded into 4 groups: (1) 8-9 mm, (2) 10-14 mm., (3) 15-19 mm. and (4) over 20 mm. The large majority of cases (519 subjects) fell into Group 2. The respective figures for the other groups were: Group 1-74; Group 3-219 and Group 4-163. No definite relationship could be established between the extent of the reaction, and the severity of the illness. Groups 3 and 4 reaction were however more frequent among patients with leural Effusions and Phlyctenular Keratoconjunctivitis. One of our patients showed a positive reaction 80 mm. in extent. The possibility of this having been a nonspecific allergic reaction, was ruled out by the presence of Hilar Adenopathy with parenchyma infiltration in this patient's chest X-ray.

Tuberculin Negativity

There were 25 children in whom the Tuberculin Reaction was consistently negative, despite clinical and/or radiological evidence of Tuberculosis. In 7 of these cases, the subjects were below 3 years of age. The discrepancy could be attributed to extreme inanition in 4 cases, and to extensive forms of the disease in 7 patients—5 cases of Miliary and 2 cases of bilateral Cavitary Tuberculosis. Three were convalescent cases of Tuberculous Meningitis. One of these patients was mentally deficient. In none of these 25 patients was a history of recent attacks of Pertussis or Measles elicited.

The course of the disease in our patients after therapy had been instituted, their subsequent progress gauged radiologically or otherwise and the bearing of a multitude of factors like age, sex, type of the disease, etc., of the behaviour and the ultimate prognosis of the condition, are being compiled and analyzed. It is hoped to present the relevant data and observations in a future communication.

Summary

The study is based on 1,000 infants and children seen at the T.B. Clinic of the S.A.T. Children's Hospital, Trivandrum. The materials and methods of study are described, attention being drawn to the limitations and drawbacks.

In general, a decrease in the number of affected children was observed with advancing age. The morbidity was found to be higher among boys. The large majority of subjects were from the poorer sections of the Community. Nutritional Status was adjudged to be 'Poor' in 39.8 per cent. History of contact with an infected person was available in 355 subjects, such history being much more frequently elicited in the younger age groups. Siblings were the most frequent offenders. The bearing of previous illnesses in our subjects and Tuberculosis is discussed. Presenting complaints were protean. Clinical signs were conspicuous by their absence.

While 648 cases of Uncomplicated Primary Tuberculosis were met with, there were 281

oases of Postprimary Intrathoracic Tuberculosis. The incidence of various forms of intrathoracic tuberculosis met with in .the study is compared with relevant Western figures. The types of Extrathoracic Tuberculosis met with are described. Radiological manifestations in the chest of the subjects are analyzed. The tuberculin Reaction in these children is discussed with particular reference to the false negative reactions observed in 25 cases.

The observations are analyzed in some detail, reference being made to relevant literature on the subject.

Acknowledgement

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SILICOTUBERCULOSIS IN SURFACE WORKERS WITH A CASE REPORT

O. P. MITAL[1], S. K. SINGH[2] AND B. RAJ[3]

Since the time of Hippocrates it has been known that 'asthmatic or phthisic pulmonary disease results from breathing dust in mines and other sources, where the rock crust of the earth is brought into fine powder'. Hence it is that 'In the Carpathian Mountains there were women who had married seven husbands, all of whom, this dreadful disease had brought to an early grave'.

Thousands of active cases of pulmonary tuberculosis are detected every year in this thickly populated industrial city of Kanpur. A large majority of them are drawn from workers like rickshaw-pullers, hawkers and vendors, leather-handlers, textile and jute mill-workers and petty merchants of all trades. Persons working in dusty industries—like potteries, brick-laying (Parmeggiani, L.)[1], stone engraving, knife-grinding, stone cutting etc., have revealed a fairly high incidence of pulmonary tuberculosis, although there are no statistics available (Gupta 1959)[2-3] in India.

Bhagwan Das, 60 years, male, was admitted as medical emergency on June 21, 1961 for treatment of Congestive heart failure. He was soon found to have miliary shadows in the lungs was suspected miliary tuberculosis and was transferred to our care.

He had been working as a stone cutter and engraver for thirty years prior to admission to hospital. He started as an apprentice at the age of 16 years and worked with his chisel and hammer upto the age of 46, engraving and inscribing letters and floral designs on various kinds of stones and marble. He had pleurisy with effusion in the left side six years ago and about a litre of clear straw-coloured fluid was aspirated from the pleural space. He was treated by a general practitioner for about three months, and remained well for about two years. For the last about three years he had cough, sputum and dyspnoea. Short courses of treatment were taken, which gave him some relief. He had haemoptysis of about 200 mls., two months prior to admission.

On admission patient had spasmodic productive cough with dyspnoea and orthopnoea. Expectoration was frothy and contained lot of black pigment in it, and measured about 200 to 300 mls. in 24 hours. He was pyrexial and had oedema on his feet. There was cyanosis and clubbing; coarse rales, and rhonchi were audible all over both lung fields. The liver was enlarged (5 cms.) and was tender smooth and firm. The pulmonary 2nd sound was accentuated. Blood examination revealed poly morphonuclear leucocytosis, E.S.R. 58 mm. for 1st hour (Wintrobe), Haemoglobin; 12.5 Gm per cent, R.B.C. 4.6 mill/cmm., serum proteins 6.8 Gm per cent, Blood cholesterol 210 mgm per cent. Cysts of E. histolytica were found in stool. Urinalysis was normal. Direct smear examination of sputum showed acid fast bacilli.

Radiographic examination: Skiagram chest revealed Egg-shell-calcification in both hila, nodular opacities throughout both lung fields. An area of breakdown in the left upper zone; evidence of pleural thickening on both sides and signs of emphysema. A dense ill-defined rounded opacity was seen below the right hemidiaphragm.

Skiagram of the abdomen after penumoperitoneum revealed a large, discrete, rounded, sharply defined, opacity of 7 cm. X 6 cm. and a smaller one of 2 cm. in diameter in the postero-superior part of the liver, also showing egg-shell calcification.

Lung-Biopsy: An open lung biopsy was performed through the eighth space on the left side. On histopathological examination of the section the tissue showed 'classical silicotic nodules and other lesions compatible with the diagnosis of tuberculosis'. (Personal communication, Prof. A. L. Cochrane, P. R. U. Llandough, and Dr Roger M. E. Seal, Sully hospital Penarth South Wales).

[1] Head of the Department of Tuberculosis and Chest Diseases, G.S.V.M. Medical College, and, Thoracic Surgeon, Tub. Hospital, Kanpur, U.P. India.

[2] Resident Medical Officer, Tub. Hospital, Kanpur, U.P. India.

[3] Registrar, Tub. Hospital, Kanpur, U.P. India.

Skiagram chest showing egg-shell calcification in the root glands on the left side. The haziness in the upper part is due to tuberculous disease—and that in the lower part following thoracotomy for lung biopsy.

Skiagram alter pneumoperitoneum showing a large rounded calcified opacity in the liver.

Discussion

Various kinds of dusts produced in different industries, in turn produce different types of respiratory lesions.

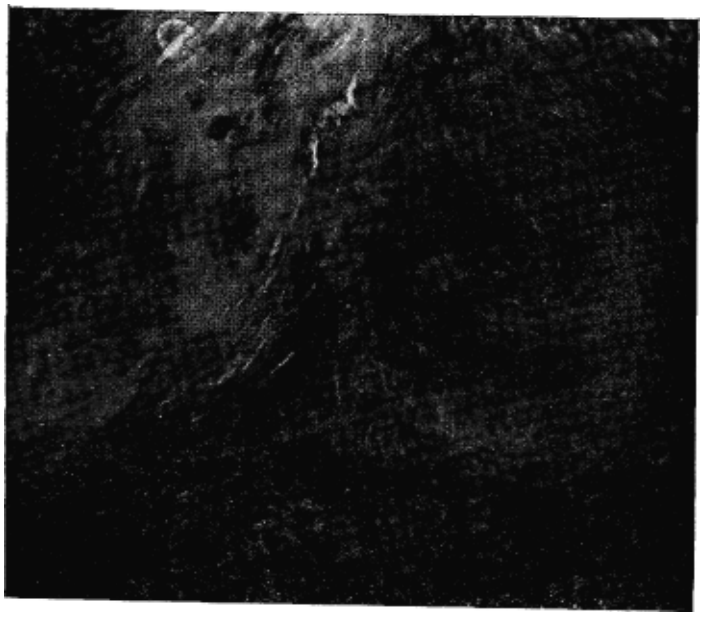
The chemical properties and physical features of dust particles, their concentration in atmosphere inhaled by the workers, the duration of exposure, individual reaction, each play a role in determining the ultimate outcome of the lesion.

In this patient tuberculosis complicated silicosis after he had worked for 30 years as stone-engraver. A complex of silicosis and tuberculosis is no doubt responsible for all but a small minority of the deaths from inhalation of silica dust. The resulting changes are different from those usually described and depend to a large extent on the time of infection with the tubercle bacillus and the size of the dose, in addition to the degree of silicosis.

The microscopic picture of silicotuberculosis represents very interesting stages from a typical silicotic whorl to a true caseous tubercle. As the tuberculosis gradually gains momentum, the nodule becomes more tuberculous. Around its border there is, characteristic tuberculous capsule with here and there accumulation of newly formed lymphoid tissue. Usually they slough into cavities when they involve major part of the lobe.

In old silicotic nodules gradual caseation takes place, and there becomes a peculiar egg-shell like calcification, which is more prone to form around the outside of the nodes than in the centre, giving the appearance of 'exoskeleton' to the lymph nodes as seen in the radiographs. As the process becomes more tuberculous the physical findings become more characteristic of tuberculosis. Silica undoubtedly aggravates tuberculosis in experimental animals (Sweany *et al*).[4]

There is no uniformity of opinion about the time of appearance of silicosis. It seems to vary largely with the source of die silica and the particular nature of the work. In the cases of Pitcher the three stages appeared at the end of 11, 14 and 17 years respectively, and this is a fair average according to the reports in the literature. In some occupations and persons, however, the disease developed in a very short time. Pancoat and Pendergrass (1926)



Photomicrograph showing typical hyaline and silicotic nodule.

Silicotic nodule H. & E. X 100 and in polarized light. (By courtesy Dr Roger M. E. Seal, consultant Pathologist, Sully Hospital, Penarth, Cardiff).

reported a case of acute silicosis appearing one year after the patient had worked in sand pulverising for 35 days. In one patient working in a crushing mill the disease developed after three months. Gartner (1956)[5] described detailed report of a case of confluent silicosis in a man with a history of only 3½ months' exposure to silica as a sand blaster, cleaning metal eating. The average minimal period of exposure for causing silicosis, however, is placed at two and one half years. The commonest complication of silicosis is pulmonary tuberculosis. The incidence was 25.5 per cent in 1612 cases of Gupta (1959).

Likewise, there is no definite opinion with regard to quantity and quality of particles, necessary to cause silicosis. In general it is accepted that more than 5,000,000 particles per cubic feet of air containing 6 per cent or more of silica and less than 10 micron in size are dangerous.

Conclusion

In India no survey has so far been done to determine the incidence of tuberculosis, in industry. Many cases of tuberculosis with pneumoconiosis are reported in coal miners (Kapur[6] 1961; Roy[7] 1956).

There are however no reports available in the recent literature of cases of silicosis developing in surface workers. Proyard, G.[8] (1960) has mentioned that the traditional method of cutting and dressing bricks to size and shape is by hammer and chisel. But in recent years in the building and repair of furnaces there has been a great use of carborundum saw for cutting brick lining. The operation is dusty and dangerous. Two definite cases of rapidly forming silicosis were observed in such a team.

However, this case emphasizes the importance of long term occupational *hazard* of stone engraving even when no machines are being used to raise the silica dust as it is understood to do in the mines. Apparently, the size of the particles that would be raised by a chisel and hammer could not be of such fine dimensions and would appear to be too big to be inhaled and deposited.

Summary

A case of silico-tuberculosis in a stone engraver who was working with chisel and hammer for thirty years is reported, adequately supported by histopathological examination.

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SELECTIVE CHEMOPROPHYLAXIS IN TUBERCULIN POSITIVE CONTACTS WITH ISONTAZID

B. C. SARBADHIKARI*

Primary tuberculosis is the precursor of clinical tuberculosis and some of its complications occurring at a subsequent stage. So in the control of tuberculosis, prevention of primary tuberculosis is of prime importance. It is equally true that prevention of primary tuberculosis is very difficult in a country with very limited segregation facilities for tuberculous patients either in their homes or in hospitals. Tuberculous patients and their associates including children are obliged to live together generally in one or two roomed unhygienic tenements and they cannot escape acquiring the disease in large numbers.

By primary tuberculosis is meant those tuberculin positives who are asymptomatic and are without radiological or bacteriological evidence of the disease.

The Madras Chemotherapy Centre's findings that there are no additional risks for acquiring the disease among the contacts of domiciliary index cases, in this connection is somewhat heartening (Wallace Fox, 1963); but this is conditioned by treatment of index cases. But at the same time it cannot be denied, that the treatment and supervision of index cases, as done at Madras, cannot generally be attained in the domiciliary management of tuberculous patients, from an average Chest Clinic in India. So additional risk to contacts for getting the disease from domiciliary index cases, in general, remain to a greater or lesser extent.

One should therefore face facts and make the best out of the bad situation to prevent the high morbidity from tuberculosis which is common in this country. This can be, in my opinion, done by the extensive use of Isoniazid chemoprophylaxis. This may be considered as secondary chemoprophylaxis. Primary chemoprophylaxis is administration of anti-TB drugs in a tuberculin negative, and this is not rational, as anti-TB drugs have bacteriostatic effects on tubercle bacilli and so in a tuberculin negative the question of doing chemoprophylaxis, by the drug, does not arise. Here B.C.G. Vaccination is more logical.

Experiments in guineapigs (Palmer 1959), in calves (Rosati *et al.,* 1957), in monkeys (Schimidt, 1959) and others have established the value of chemoprophylaxis in the prevention of tuberculosis.

This paper is a continuation of my study on chemoprophylaxis (Sarbadhikari-a, 1960) and paper of mine read at the 7th International Congress on Diseases of the Chest at New Delhi in February 1963 and at the 2nd Maharashtra State Anti-TB and Chest Diseases Workers' Conference at Bombay in December 1963. In this paper an attempt has been made to see whether it is justified to use chemoprophylaxis in pulmonary tuberculosis based on results of isoniazid prophylaxis in our series and in others' and its possibilities in practice, in the context of tuberculosis position in India.

Investigation and Results

At the Calcutta Corporation's Mansatala Chest Clinic we had 1874 tuberculin positive contacts up to the age of 15 years, with no radiographic or fluroscopic evidence of pulmonary tuberculosis in them, in different yearly groups from June 1956 to 1959. They were contacts of 462 index cases of which 162 were open cases by direct smear; Patients and their contacts were obliged under adversity to live together. Amongst these 1874 positive contacts 1047 had isoniazid prophylaxis for a period of six months with daily isoniazid dose of 8 mg. per/kg, body weight in three divided doses along with multivitamin tablets or shark liver oil. The remaining 827 positive contacts had no such prophylaxis.

As to why some had isoniazid prophylaxis and others not, it was a mere chance. It was left to the positive reactors, rather to their guardian's views as the contacts were minors, to decide about long continued drug taking, specially when they were not actually sick requiring their regular and frequent attendance at the clinic. This indirectly facilitated to have some comparable groups with and without chemoprophylaxis.

* Superintendent, Corporation Mansatala Chest Clinic, 17, Mansatala Row, Calcutta-23, INDIA.

TABLE 1

Showing the number and percentage of cases studied with or without Isoniazid prophylaxis, according to age groups

Age Groups	With INH Prophylaxis		Without INH Prophylaxis	
	No. of cases	Percentage	NO. of cases	Percentage
Upto 3 Years	198	18.9	242	29.3
4 to 7 Years	385	36.8	217	26.2
8 to 11 Years	281	26.8	183	22.1
12 to 15 Years	183	17.S	185	22.4
Total	1047	...	827	...

In this retrospective study of tuberculin positive contacts we have reviewed development of tuberculosis in those who had isoniazid prophylaxis and in those who had no such prophylaxis, in each yearly different groups; the maximum period of observation being one year to four years.

Tuberculin Test: Old Tuberculin was used. The dilution used was 1/5000. Before Feb - ruary 1957, 1/10000 O.T. was used and if negative, re-tested with 1/1000 O.T. Re-testing after chemoprophylaxis course was done only in 253 cases of 1958 and 1959 and in 8 cases i.e. in 3.16 per cent was found to be negative.

Discussion

In our series of positive contacts up to 15 years of age, tuberculosis developed in 17.7 per cent within a short period of observation of four years (Table 2). This eventuality of developing tuberculosis and that within a short period perhaps depending upon the varying standards of living of the people and available control measures against the disease is observed by other workers. This is shown in Table 3.

On the other hand beneficial results of chemoprophylaxis in preventing tuberculosis in

TABLE 2

Showing percentage of Dropped cases with No. of cases dropped out of the original and Morbidity percentage with No. of cases developing morbidity amongst the followed-up cases, during Maximum period of observation in each yearly group, with or without Isoniazid prophylaxis

Observation period of Different Groups	With INH Prophylaxis		Without INH Prophylaxis	
	Dropped case % & No.	Morbidity % & No.	Dropped case % & No.	Morbidity % & No.
0 to 1 Year … 1959 Group …	11.4% (47/414)	0.8% (3/367)	14.6% (44/301)	5.1% (13/257)
1 to 2 Years … 1958 Group …	10.8% (38/353)	1.3% (4/315)	16.8% (55/328)	12.1% (33/273)
2 to 3 Years … 1957 Group …	19.5% (50/257)	1.5% (3/207)	11.1% (49/222)	17.9% (31/173)
3 to 4 Years … 1956 Group …	28.1% (62/220)	2.5% (4/158)	31.1% (56/180)	17.7% (22/124)
Total cases (Original) …	1,244	...	1,031	...
Total cases (Followed-up) …	...	1,047	...	827

TABLE 3

Showing Morbidity percentage by OTHER Authors during Maximum period of Observation in their series, with or without chemoprophylaxis

Author Place or Country Observation Period Age of subjects	Morbidity % with Chemoprophylaxis	Morbidity % Without Chemoprophylaxis
Chiba (1959) Japan 4 to 36 Months Children	Nil. (Contacts)	5.6 % (Contacts)
Debre *et al* (1959) France 4 Years up to 25 years	Age Group 1.8 %— Below 5 Years 2.3 %— 5-9 Years 2.3%- 10-14 Years 2.2 %— 15-25 Years	7.5 % 6.1 % 12.1 % 21.0 %
Deshmukh *et al* (1961)a Bombay, India 2Years Children	.6 % (Contacts and Non-contacts) .73% (Contacts) Nil(Non-contacts)	2.5 % (Contacts and Non-contacts) 4.24 % (Contacts) 1.49 % (Non-contacts)
Hsu (1958) U.S.A. (Texas) By the age of 20 Yrs. Children	Not done	12%
Ramakrishnan *et al* (1961) Madras- India 2 Years All age groups	Not done	12 % (Contacts below 5 Yrs.) 7.6 % (Contacts of all age groups)
U.S P.H.S. (1957)	.4 %	2%
U.S.A. Children		
Zorini-a (1959) Italy 3 Years Children	.21 %	1.13 %

tuberculin positive contacts in our series of 2.5 per cent morbidity during an observation period of four years, is less spectacular in its achievements than seen in control studies of Zorini, Deshmukh, Chiba and others who had chemoprophylaxis in their control series (Table 3). Even so, the morbidity with chemoprophylaxis of 2.5 per cent in our series, is significantly lower compared to 17.7 per cent in our comparable series without such chemoprophylaxis during a follow-up period of four years in both.

Regarding chemoprophylaxis in tuberculosis, no one who accepts the principle of chemotherapy in tuberculosis should have any reasonable doubts of its efficacy for chemoprophylaxis also. In this one aims only to treat the subject earlier viz., in its primary disease stage.

TABLE 4

Showing tuberculin positive percentage in general population and in contacts

Age Group	General (%) Benjamin, 1959	Contacts (%)	
		Author	Deshmukh *et al* .b, 1961
Upto 6 Years …	27.3 %	52.7 % (1212/2300)	70.7 %
7 to 14 Years …	47.3 %	74.2 % (1470/1980)	90.2 %
15th Year …	...	87.9 % (660/751)	88.9 %
15 to 25 Years …	71.7%	...	...

Investigations by Arthur Myers has shown that when the sensitivity to tuberculin can first be elicited, X-ray film of chest revealed no abnormality in about 95 per cent of cases. On the other hand the value of positive tuberculin reaction to be the earliest diagnostic criteria of primary tuberculosis, is evidenced by the fact, that Ghon had reported postmortem findings of lesion in lung or regional lymph nodes or both in 96 per cent of bodies of children who died of non-tuberculous conditions and in them, during life, there were no other evidence of tuberculosis except sensitivity to tuberculin (Arthur Myers, 1963).

Accepting the principle of chemoprophylaxis, the crux of the question is who amongst approximately two third of the entire Indian population of tuberculin positives, should have priority in such Isoniazid prophylaxis. This may not be practicable; but it is logical to do it.

The prime criteria to determine such priority in doing chemoprophylaxis is to find out who are 'Recent Converters'. This is because in recent converters the tubercle Bacilli are yet in a multiplying i.e., active stage when Isoniazid exerts its bacteriostatic effects most. This strategy however cannot be utilised in India, in practice now, as it requires a huge Technical organisation to find out recent converters, by doing repeated tuberculin testing at periodic intervals and at all levels.

The next important criteria for chemoprophylaxis, however are tuberculin positives up to 15 years as in our series, and who cannot have adequate home segregation or hospitalisation of the tuberculous index cases, and who are obliged to live with patients, some of whom are open cases. They being exposed to bacillary bombardment are in special risk to contract the disease and they deserve priority.

The rationality in restricting age limits to 15 years, for Isoniazid prophylaxis, is because the vast majority of such contacts, viz., 87.9 per cent as in our series and Deshmukh's Bombay series of 88.9 per cent in that group were tuberculin positives by the age of 15 years (Table 4). Hence such chemoprophylaxis on a selective basis, need only to deal with a small proportion of the entire tuberculin positive population in India.

In a previous series of ours (Sarbadhikari-b, 1960) with three months chemoprophylaxis the morbidity was 3.7 per cent against 1.3 per cent in our present series. This perhaps suggests utility of longer period of chemoprophylaxis. Caroll Palmer's experiment in guineapigs supports this view (Palmer-b, 1959).

Even with higher doses of Isoniazid than the therapeutic doses, toxicity in our series occurred in 8.7 percent of which 1.2 per cent were severe enough to stop Isoniazid prophylaxis. In the rest with mild toxicity, temporary suspension of Isoniazid was all that was necessary.

We had no laboratory facilities to determine drug resistance developing in Isoniazid prophylaxis subjects in our series. But subjects who developed pulmonary tuberculosis in spite of Isoniazid prophylaxis, responded satisfactorily to combined chemotherapy. Zorini's experiment in guineapigs contradicts development of bacterial resistance, the only exception

being a case where chemoprophylaxis and B.C.G. were used together (Zorini-b, 1959).

Chemoprophylaxis and B.C.G. Vaccination are complimentary to each other, requiring prefential use of one or the other under varying epedemiological trends of infection rate as may be present in a community. From this point of view, at a chest clinic, tuberculin positive percentage in contacts being so high even in children (Table 4) limits, the scope of B.C.G. Vaccination, and here the chemo-prophylaxis is the major answer to control programme of tuberculosis in India.

Even the incurable optimist, cannot possibly visualise revolutionary changes in India giving improved sanitation, economic and living conditions for the people, to the extent seen in some of the Western countries. These were considered important factors in the control of tuberculosis in those countries. In case of rejection of Chemoprophylaxis in tuberculosis even on a selective basis, it would be most regretable, as regards tuberculosis.

In conclusion it can be stated that the Isoniazid chemoprophylaxis done at a clinic in tuberculin positives up to 15 years of age to contacts of domiciliary index cases, is a rational and effective measure, to check high tuberculous morbidity, in India.

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INHIBITORY ACTION OF SODIUM AZIDE ON MYCOBACTERIA

K. C. GUPTA AND AMAR NATH

(Department of Microbiology, Regional Research Laboratory, Jammu Tawi)

Sodium azide has been reported to have inhibitory action against various aerobic bacteria (Snyder and Lichstein, 1940-41; Lichstein, 1941 and Lichstein and Soule, 1944). From these studied, there issued several selective media for aerobic bacteria. There does not seem to be any reference in literature on the inhibitory action of sodium azide on the growth of mycobacteria. One of us (Gupta *et al.,* 1963) has already reported that sodium azide has a stimulating action on the respiration of B.C.G. Canadian, B.C.G. Swedish and B.C.G. Moreau, while the respiration of B.C.G. Copenhagen is not affected. This report deals with the antitubercular activity of sodium azide.

Antitubercular activity of sodium azide was tested by serial dilution method in Youmans medium containing 0.02 per cent Tween 80.

The results of inhibitory effect of sodium azide on mycobacteria are shown in Table 1. It is obvious from the perusal of the table that azide inhibits the growth of *M. tuberculosis* $H_{37}RV$, *M. tuberculosis* Ravenel, *M. phlei, M. avium* B 19-2, *M. tuberculosis* ATCC 607 in concentrations ranging from 50 to 100 µg/ml.

TABLE 1

Antitubercular activity of sodium azide

Culture	Minimum inhibitory concentration Mg/ml	
	Complete	Partial
M. tuberculosis H_3,RV	100	50
M. tuberbulosis Ravenel	100	50
M. phlei	50	...
M. tuberculosis ATCC 607	100	50
M. avium B 19-2	100	...

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A SHORT NOTE ON ANTITUBERCULAR ACTIVITY OF AN ACTINOMYCIN PRODUCED BY A NEW SPECIES OF STREPTOMYCES

K. C. GUPTA, AMAR NATH AND I. C. CHOPRA

(From the Department of Microbiology, Regional Research Laboratory, Jammu Tawi)

During the course of a systematic search for new antibiotics, an actinomycin complex was isolated from *Streptomyces regensis* sp. nov. (Gupta *et al.,* 1963). This actinomycin complex differs from other actinomycins described in literature in its amino acid composition and is very highly active agairtst *Staphylococcus aureus* and *Mycobacterium tuberculosis*. The strains of Staph. aureus highly resistant to penicillin, streptomycin, chloramphenicol, tetracyclin and erythromycin are equally susceptible to its action.

This report deals with the antitubercular activity of this actinomycin complex.

Antitubercular activity was tested by serial dilution method in Youman's medium containing Tween 80 and bovine albumin Fraction V. The tubes containing the desired concentration of the drug in the medium were inoculated with 0.03 ml. of 14 days old culture *of Mycobacterium tuberculosis* H_{37} RV, *M. tuberculosis* Ravenel and *M. avium* B 19.2, The results were read after 14 days of incubation at 37°C. In the case of *M. tuberculosis* ATCC 607, the reading were taken after 48 hours.

The results of antitubercular activity of the actinomycin complex are shown in Table 1. It is obvious from the perusal of the table that the actinomycin complex shows a very high antitubercular activity. The growth of *M. tuberculosis* H_{37}RV and *M. tuberculosis* Ravenel is inhibited in a concentration of 1 /μg/ml. There is a partial inhibition of growth in a concentration of 0.25 to 0.5 /ug/ml. The growth of *M. avium* B 19.2 and *M. tuberculosis* 607 is inhibited in concentration of 2 and 10 /μg/ml. respectively.

Summary

The actinomycin complex isolated from *S. regensis* sp. nov. shows very high antitubercular activity which is comparable to that of streptomycin (Table 1).

TABLE 1

Antitubercular activity of an actinomycin complex

Culture	Drug	Minimum inhibitory concentration in μg/ml.	
		Complete inhibition	Partial inhibition
M. tuberculosis H_3,RV	Actinomycin complex	1	0.25-0.5
M. tuberculosis Ravenel	”	1	0.25-0.5
M. tuberculosis ATCC 607	”	10	5
M. avium B 19.2	”	2	0.5 -1
M. tuberculosis H_{37}RV	Streptomycin	0.5	0.25
M. tuberculosis Ravenel	…	1	0.5
M. avium B 19.2	…	1	...

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WORLD HEALTH DAY
April 7th, 1964
'NO TRUCE FOR TUBERCULOSIS'

A Statement

DR M. G. CANDAU
(Director-General, World Health Organization)

At least 15 million people suffer from infectious tuberculosis in the world toady. The disease still claims more than 3 million lives each year: and these are cautious estimates of the situation.

It is true that there has been a spectacular decline in tuberculosis deaths in nearly all economically-developed countries. Between 1950 and 1960 the tuberculosis death rate fell from about 14 to nearly 2 per 100,000 population in the Netherlands, from nearly 21 to well below 6 in the U.S.A., from more than 47 to less than 20 in France, and from 122 to 31 in Japan, to mention only a few examples.

Unfortunately the number of tuberculosis sufferers has not declined nearly as rapidly as the number of deaths, and tuberculosis still remains a grave problem even in the more-favoured countries. In the world as a whole, it can be estimated that between 2 and 3 million new cases still occur each year.

In the less-developed areas of the world, morbidity statistics are not so reliable, but special surveys have indicated that one person in every hundred may suffer from infectious tuberculosis. Even more serious, up to 70 per cent of children may be infected before they reach the age of 14.

In India alone, for instance, there may be as many as 3 million infectious cases. In Latin America there are 600,000 known cases of active tuberculosis and probably 1,800,000 Undeclared ones.

The most recent WHO Expert Committee on tuberculosis laid down a criterion by which a country could judge its progress towards the conquest of tuberculosis. The Committee felt that tuberculosis could not be considered to be eliminated as a public health problem unless the number of children who became infected before the age of 14 fell below one per cent.

Not a single country in the world today satisfied this condition. Yet for the first time in man's history we now possess effective weapons with which to fight tuberculosis. This is why the theme for World Health Day this year is 'No Trace for Tuberculosis'.

Vaccination with B.C.G. can protect large segments of any population from the risks of infection to which it is exposed by the tuberculosis sufferers in its midst. Treatment with the modern drugs—isoniazid, streptomycin and p-aminosalicylic acid (PAS)—can render patients non-infectious and cure the disease. This is possible even in countries where the number of sufferers is a thousand times greater than the number of sanatorium, beds, and where treatment has to be given while patients go on living at home.

These weapons are both powerful and relatively cheap, but they must be properly used. If B.C.G. vaccination is fully to serve its purpose, it must be given to a high proportion of young people before they are exposed to any serious risk of infection. Drug treatment can succeed in reducing the tuberculosis problem only if the majority of infectious cases are detected before they spread the disease, and if those under treatment actually take their pills. Most important therefore is the efficient organization of community-wide services adapted to each country's particular situation. This means that doctors and auxiliary workers of all kinds must be given the right training.

The discrepancy between what could be achieved with the knowledge and tools available today and what is actually being done is both a national and international challenge.

Bodies like the World Health Organization, UNICEF, and the International Union Against Tuberculosis are ready to face the challenge, but the main effort must come from within the countries themselves. It is the duty of every national health service to take advantage of all possibilities and join in a world-wide drive to conquer this scourge which continues to kill millions each year and is a drag on economic progress by weakening and immobilizing tens of millions.

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NEWS AND NOTES

Our New President

Dr Sushila Nayar, the Union Minister for Health, was unanimously elected as the President of the Tuberculosis Association of India in place of the late Rajkumari Amrit Kaur at the joint meeting of the Finance and Executive Sub-Committees held on 27th February, 1964.

Twentyfifth Anniversary of Tuberculosis Association of India

The Tuberculosis Association of India will be completing twentyfive years in February this year. It has been decided to have its twentyfifth anniversary meeting at the time of the next Annual General meeting, Central Committee meetings, Secretaries Conference, the meeting of the Technical Committee and the XlXth TB and Chest Disease's Worker's Conference. These meetings will be held from 3rd to 8th April, 1964.

The twentyfifth anniversary meeting of the Association will be held in Rashtrapati Bhavan, New Delhi, on Saturday the 4th April, 1964 at 3 p.m. The President of India has graciously agreed to address the meeting. The President will be ' At Home' to delegates in the evening of 4th April.

The 15th Conference of Secretaries of State TB Associations and Seal Sale Organisations will be held at 10 a.m. on Friday, the 3rd April, 1964 in the Conference Hall of the Association. The main subject for discussion at this conference will be formation and working of State and District TB Associations.

Publications

To mark the 25th anniversary, the Association has brought out a Special Souvenir. The sixth edition of the Directory of the TB institutions in India has also been brought out and is now on sale at Rs. 6.50. Those who wish to get their copies should book order immediately with the Secretary, TB Association of India, 3 Red Cross Road, New Delhi.

Tuberculosis and Chest Diseases Workers' Conference

The 19th Tuberculosis and Chest Diseases Workers' Conference will be held in Delhi from 5th to 7th April, 1964. Over 300 delegates are expected to attend the conference. On behalf of the Tuberculosis Association of India, The Delhi TB Association is making the necessary arrangements. Intending delegates are requested to correspond with Dr M. M. Singh, Honorary General Secretary, Delhi Tuberculosis Association, Municipal TB Clinic, S. P. Mukherjee Marg, Delhi-6, for detailed information about the conference.

Chest and Heart Association—India Scholarship

The Chest and Heart Association, London has decided to award a Scholarship to the value of £500 to a medical graduate from India for study in Tuberculosis in the United Kingdom in 1964. The candidate will be selected by the Tuberculosis Association of India. The period of study is for three months and the candidate will have to have his training in UK from mid September to mid December, 1964.

Applications should be sponsored by official or non-official bodies who should guarantee that the persons they recommend, if selected will be suitably employed and that the nominee will return to tuberculosis work in India after the training. The travelling expenses to UK and back to India have to be met by the candidate or by the sponsoring authority.

Applications on the prescribed form must reach the Secretary, Tuberculosis Association of India, 3, Red Cross Road, New Delhi, on or before 15th April, 1964. Applications received incomplete or after that date will not be entertained.

TB Health Visitors' Course

The 1964 Health Visitors' Course commenced in the New Delhi TB Centre on 3rd January, 10 candidates are undergoing the prescribed course.

Eastern Regional Committee

The next meeting of the Eastern Regional Committee of the International Union against Tuberculosis will be held in Manila, Philippines, some time in October/November, 1964. The Philippine Tuberculosis Society, Manila, will act as host to this meeting.

The Indian Journal of Tuberculosis

ABSTRACTS

Vol. XI March 1964 Abst. No. 2

The Diagnosis and Treatment of Bronchogenie Carcinoma

50 per cent cases with bronchogenic carcinoma at the time of diagnosis are shown to have a spread beyond the limits of resection. 20 per cent at Thoracotomy will have extensive disease that extirpation is impossible or is only palliative. In the rest 30 per cent, resection yields a 5 year cure rate.

In the small group in whom tumour is confined to lungs with no venous or lymphatic extension, the cure rate is about 50 per cent.

All adults who develop respiratory symptoms should be suspected of having cancer. The characteristic symptoms are worsening cough, haemoptysis, unilateral wheeze, weight loss etc.

In adults Pulmonary infiltrations associated with lower respiratory infections should be viewed as possibly related to neoplasm even if the clinical response to treatment is prompt. If resolution is delayed beyond two or three weeks, complete diagnostic study for bronchogenic carcinoma should be performed. This may include Bronchoscopy, Bronchography, exfoliative cytology, scalene node biopsy, early exploratory Thoracotomy.

Even if clearing is prompt and complete, roentgenograms should be repeated at intervals of six weeks, then three months and if there is no change thereafter semi-annually.

Chest roentgenograms every six months are recommended for men over 40, particularly for heavy cigarette smokers since lung cancer is much uncommon in this group. Lung cancer should be sought deligently in those with thoracic disease, such as tuberculosis, especially when unexplained changes in symptoms or chest films occur. The value of comparing the roentgenograms with all earlier available films cannot be over emphasised since any evidence of change heightens the likelihood of neoplasm.

Total surgical removal is the only curative treatment. Hilar lesions should require Pneumonectomy, while distal lesions may be recovered by lobectomy along with regional node dissection. Curative resection is not possible if there are distant metastasis.

Involvement of Phrenic nerve in the upper mediastinum contradicts surgery, 'whereas invasion of the Phrenic nerve in the lower mediastinum when the Pericardium can be removed with the tumour, may allow complete removal.

In patient with Pleural effusion or with chest wall involvement or diaphragm, indicates invasion, are signs of operatability.

Radiation Therapy even with super-voltage technique or and chemotherapy are Palliative and should be reserved for patient who is not a surgical candidate.

Combined Pre-operative irridiation and surgery appears promising in superior scalene tumours.

Effective palliation and comfortable prolongation of life can be achieved by attention to prevention and therapy for such complications such as retained secretions, atelectasis and infection.

Early diagnosis and prompt surgical therapy provides the only effective means for treating Bronchogenic Carcinoma.

(A Statement of the Sub-committee on Surgery and the Committee on Therapy. Amr. Rev. Resp. Dis., Vol. 88, No. 2, Aug., 1963).

Indications for Resecting Solitary Pulmonary Nodule

A solitary pulmonary nodule is one which is 6 cm., in diameter or less. It is rounded or oval with smooth contours and sharply demarcated edges. Calcification may be present.

The prompt and accurate diagnosis is important because a significant percentage are malignant.

Differentiation between the malignant from the benign nodule has to be done from the point of immediate surgical intervention.

History and physical examination are rarely helpful. *Diagnostic Tests:* 1. Roentgenography: The location, sharpness of margins and density of the lesions are unreliable guides.

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Recent origin, rapid growth revealed by serial roentgenograms and umblication or notching of the surface of the nodule are highly suggestive.

If a lesion excavates, eccentric location of the Cavity or irregularity of the cavity wall suggest malignancy.

Solid character of the lesion with laminated calcification or scattered flecks of calcium within the lesion are suggestive of benignancy but cannot rule out malignancy. Tomography is often essential to establish that calcification is present and it is located within the nodule rather than adjacent to it. Lack of change on serial roentgenograms over a five year period is a strong but not an absolute evidence of a benign lesion.

2. *Skin Tests:* Negative skin tests with tuberculin histo-plasmin and Coccidiodin in creases the probability that pulmonary nodule is cancer.

A positive tuberculin test is an indication for antimicrobial coverage during the surgical period.

3. *Serologic Tests:* Negative serologic tests are a helpful guide in Diagnosis.

4. *Sputum Studies.:* If cytology is positive, operation is indicated because of known malig nancy, if negative, exploration is indicated because of a suspected malignancy.

5. *Bronchoscopy:* This is rarely indicated because of the peripheral location of these nodules, they can be rarely visualized. Bron choscopy to obtain bronchial secretion for cytologic study subjects the patient to un necessary delay and expense.

6. *Scalene node biopsy.* In the absence of mediastinal adenopathy, it has not much place in diagnosis.

7. *Thoracotomy:* Resection is the only definite diagnostic procedure.

(A Statement of the Sub-Committee on Surgery and the Committee on Therapy, Amr. Rev. Resp. Dis., Vol. 88, No. 2, Aug., 1963).

Isoniazid Prophylaxis in Mental Institutions

The effectiveness of Isoniazid Prophylaxis was tested in a Controlled double blind trial among 27924 mental patients.

Pills were given daily for twelve months, Isoniazid in an average dose of approximately 5 mgm. per Kg. of body weight.

During the mediation year 21 cases for active tuberculosis were diagnosed in, the placebo group and only 4 in the isoniazid group.

Two thirds of the placebo group and 3 of the four isoniazid cases occurred among those whose initial roentgenograms showed abnormal findings and the other third among those whose initial Tuberculin reaction were more than 5 mm.

No cases occurred in either group during the medication year among those whose initial tuberculin reaction was 5 mm.

The group has been observed annually since the mediation year. Through May, 1962, 30 additional cases of active tuberculosis have been diagnosed in the placebo group and 15 in the isoniazid group.

Of the placebo cases, nine came from those with initial abnormal roentgenograms, 17 from the tuberculin positive and four from tuberculin negative groups.

Of the Isoniazid cases, five came from the group with roentgenographic abnormalities, five from the tuberculin positive and five from the initially tuberculin negative groups.

Of the four placebo cases and five isoniazid cases from the initially tuberculin negative group, one of the patients who received placebo and four who received isoniazid were still tuberculin negative at the end of medication year.

The trial confirms the findings from the previous trials of the effectiveness of isoniazid prophylaxis.

(Shirley H. Perdue, Frank W. Mount, Francis J. Murray and Veena T. Livesay. Amr. Rev. Resp. Dis., Vol. 88, No. 2, August, 1963).

Increased Resistance of Mycobacterial Tuberculosis to Drug Therapy

In 44 per cent of the New and 46 per cent of the Old patients in a group of 482 Negro patients, were resistant to one or more of the three antituberculous agents.

The patients rate of recovery decreased as the resistance of the organism increased.

Patients with Prior therapy developed chronic disease or died of tuberculosis 3f times more frequently than patients without prior therapy.

(Enreqiu Gerszten, Donald. Brenmer, Marvin J. Allison and Miles E. Ranch. J.A.M.A., July 6, 1963).

Management of Spontaneous Pneumothorax

Rupture of subpleural bleb is the commonest cause of spontaneous pneumothorax. There may be associated emphysema or Tuberculosis.

Four methods of treatment have been used.

(a) Expectant Observation.
(b) Needle aspiration of the intrapleural air.
(c) Closed thoracotomy.
(d) Open thoracotomy.

(a) Expectant Observation is recommended for minimal pneumothorax with few symptoms. The drawback is progressive or persistent pneumothorax or the development of a film encased, unexpandable lung.

(b) Single or multiple needle aspirations may be effective, but puncture of the lung may cause additional air leak or bleaching and aspiration of air is rarely complete and the residual air in the pleural space will prevent approximation of the visceral and parietal pleural surface and the pleural symphsis.

(c) Closed thoracotomy with introduction of a intercostal catheter attached to water seal drainage with or without suction is the treat ment of choice in uncomplicated spontaneous pneumothorax.

If the lung does not re-expand or becomes atelectatic the most common cause is retained secretions obstructing the bronchial airway, the relief of which may require coughing, mycolytic agents, endotrachial suction or bronchoscopy. The thoracotomy tube should remain in place for at least 24 hours after cessation of air leak and re-expansion of the lung. If the pneumothorax does not recur, the tube is removed.

Pondrage, the insufflation of irritants through a trocar to produce adhesive pleurites should be reserved for recurrent pneumothorax when there is roentgenographic pulmonary abnormality and for emphysematous patients unsuitable for thoracotomy. It is not recommended for patients with parenchymal infiltrations or emphysematous bullae for which resection is indicated.

(d) Open thoracotomy is indicated for persistent air leakage not controlled by a closed thoracotomy or for recurrent spontaneous pneumothorax.

At thoracotomy blebs are removed. The visceral and parental pleural surfaces are abranded or parietal pleurectomy done.

(A Statement of the Sub-committee on Surgery and the Committee on Therapy. Amr. Rev. Resp, DM., Vol. 88, No. 2, August, 1963).

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I, B. M. Cariappa, Secretary of the Tuberculosis Association of India, 3 Red Cross Road, New Delhi 2, hereby declare that the particulars given above are true to the best of my knowledge and belief.

(Sd) B. M. CARIAPPA
on behalf of the Tuberculosis Association of India