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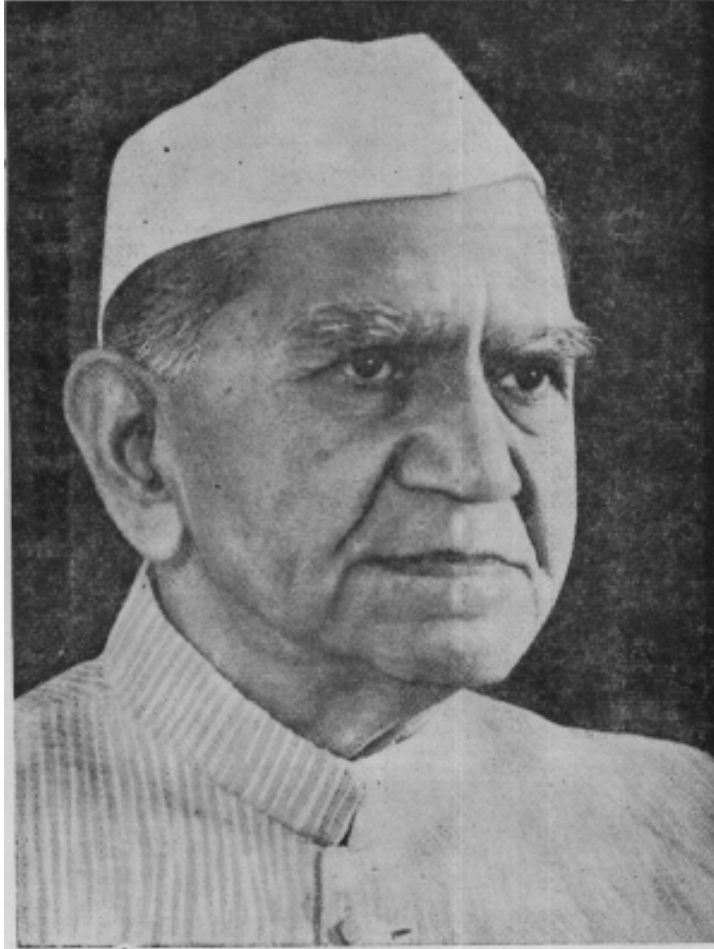
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As we go to the press the nation is plunged in sorrow over the sad news that Shri Fakhruddin AH Ahmed, President of India, passed away.

The Tuberculosis Association of India joins the nation in mourning. Shri Ahmed was the Patron of the Association from 1974. In his death the country has lost an illustrious President and the Association its Patron. We offer our deepfelt condolences to the bereaved family of the late President.

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SPUTUM EXAMINATION BY DIRECT MICROSCOPY

When Robert Koch discovered tubercle bacillus as the causative micro-organism of pulmonary tuberculosis and demonstrated its presence in the sputum, it became a specific and the only authentic diagnostic criterion. But the difficulty was that there were many cases, undoubtedly, of tuberculosis in whose sputum the bacilli could not be demonstrated. Firstly, unless the thick exudate liquifies, the bacilli are not expelled in sufficiently large numbers. Secondly, our methods of direct examination are so crude, and still continue to be so, that if the number of bacilli in the sputum is not sufficiently large, one may fail to demonstrate these leading to a false negative report. In other words, sputum examination, though specific, does not exclude under-diagnosis.

When radiography became available in the diagnosis of disease, the pendulum, as far as pulmonary tuberculosis is concerned, swung to the other extreme. Many shadows in the chest though non-tuberculous were considered tuberculous simply because x-ray examination was tidy and convenient and, therefore, sputum examination, being considered cumbersome and messy, was usually neglected. This phase too is fortunately over to-day and most chest workers agree that the x-ray examination though highly sensitive in the sense that, at least theoretically, there is no case missed, the diagnosis is confirmed by the specific method of demonstration of bacilli in the sputum of persons with abnormal shadows in the chest.

It is only very recently that due attention has begun to be paid to the technique of sputum examination in order to make it most rewarding. A study from the National Tuberculosis Institute has shown that although most of the sputum positives can be found out only by the examination of a single specimen yet examination of even the eighth specimen contributes something to the positively. However, the bulk of the positives can be found by examination of two or three specimens and the contribution of the subsequent ones is nominal. Whatever may be its value as a research or an epidemiological study, in a service organisation it is obviously impossible to examine such a large number of specimens from a single patient as a routine. Most institutions, therefore, examine only two specimens as a routine though many more may be examined in cases which are diagnostic problems.

The next question that arises is the method of collection of sputum. Should it be a spot or an over-night collection? Each of these methods has given better results in the hands of different workers. A logical and organisationally convenient procedure would appear to be to collect two specimens from a patient, one spot and one over-night collection. It is also to be emphasised that collection of sputum in many places does not get the care it deserves. Many patients consider spit and sputum synonymous. A little care on the part of the para-medical staff in teaching the patient how to produce sputum will make a lot of difference. Similarly, selecting the part of sputum to be smeared

on the slide, the staining technique and the diligence with which microscopy is carried out are all very essential and often make the difference between success and failure.

Comparison is also some times made between the two popular methods of direct microscopy viz. Ziehl Neelsen technique and fluorescence microscopy. No doubt the latter is much more sensitive and time saving but it also requires a very sophisticated equipment and, therefore, in situations where the number of sputum examinations to be handled per day is not large and the technician's time is not as costly as in the developing countries, Ziehl Neelsen method should be preferred in majority of the service institutions.

Disposal of a patient whose two specimens of sputum are negative by direct microscopy poses another problem. No doubt culture will prove some of these to be positive but then culture itself requires costly equipment which cannot be made available except in a few large places in the country. Nor is the yield from culture much. Furthermore, if a person is definitely suffering from tuberculosis and direct smear is negative, the sputum in most cases is bound to become positive soon if repeatedly examined and the culture result too becomes available in about six weeks. This little delay in diagnosis is really of no consequence, neither for the patient nor the community. A little delay in starting the treatment does not jeopardize the success of treatment *per se*. As for the community is concerned, it has been conclusively shown by workers like Riley and Associates and more recently by Rouillon *et al* that strictly speaking it is only a person whose sputum is positive by direct smear i. e. who is excreting a large number of tubercle bacilli, is responsible for spreading infection in the community. The 'infective' potential of a direct smear negative culture positive patient is practically nil. Thus, no matter from what angle you look, direct microscopy of the sputum is an efficient diagnostic and preventive tool in our hands. It is cheap and simple, but the pity is that it is so often neglected and very often carried out perfunctorily.

Ours is a big country and the prevalence of disease is nearly uniform all over the country. The microscopy centres in the rural areas are extremely few. While attempts should be made to increase the microscopy centres, something has to be done in the interim period. It should be a good strategy to teach collection of sputum, preparation of smear and fixing it on a slide to all the A.N.M.S. and Multi-purpose Health Workers. Those slides can then be sent to the nearest microscopy centres where staining and microscopy can be done. This would be more convenient and efficient than carrying sputum to different microscopy centres.

Lastly, direct microscopy of sputum is equally unexcelled in monitoring treatment. If the treatment is successful, the number of bacilli in the sputum start falling rapidly and very soon the sputum is negative by direct smear and as long as it remains negative it is a proof that the treatment is effective. In other words, direct microscopy of the sputum must be continued during the course of treatment. For if at any time tubercle bacilli appear again in the sputum, the so called 'fall and rise phenomenon', no other evidence is needed to show that the treatment is no longer effective whatever be the reason thereof. Culture and sensitivity testing may show which drugs have become ineffective but then this information becomes available 8 to 10 weeks later whereas the direct microscopy gives an immediate answer for the regimen as a whole.

CHRONIC BRONCHITIS AND TUBERCULOSIS

T.G. RADHA and R. VISWANAIHAN

(From Vallabhbai Patel Chest Institute, University of Delhi, Delhi)

Obstructive airways disease is known to develop in some cases of pulmonary tuberculosis. However the mechanism of obstruction remains largely speculative.

While there are a few reports on the prevalence and severity of obstructive airways disease among patients with pulmonary tuberculosis, there is so far no report in English literature on the prevalence of healed pulmonary tuberculosis in patients with chronic bronchitis.

A study was therefore carried out to determine the prevalence of healed pulmonary tuberculosis in patients with chronic bronchitis. An attempt was made to compare the pattern of the illness in patients of chronic bronchitis with and without healed pulmonary tuberculosis.

In conjunction with this study, data regarding the prevalence of possible chronic bronchitis in cases of pulmonary tuberculosis was also collected. As far as we are aware no report has so far been published from India.

Material & Methods

V.P.C.I. study:

Clinical records of 2,350 patients admitted to the outpatient clinic of V.P. Chest Institute, Delhi as cases of chronic bronchitis between 1971 and 1975 were scrutinised. Skiagrams of the chest were read with special attention to the extent and nature of tuberculosis. The presence or absence of emphysema was ascertained after the method described by Simon (1970). In all those patients where there was evidence of healed pulmonary tuberculosis, a detailed clinical history was recorded. 24 hours' sputum was sent to the laboratory for exclusion of active disease. Pulmonary function tests, however, could be carried out in only 35 patients.

For study of the difference, if any, of the pattern of illness in patients of chronic bronchitis with healed pulmonary tuberculosis, patients of more or less the same age and sex were randomly selected from the group with chronic bronchitis alone and compared.

R.B.T.B. Hospital Data:

201 adult patients who have had sputum conversion after treatment were selected from the

indoor patients of Rajen Babu TB Hospital, Delhi, for ascertaining the prevalence of airways obstruction. The duration of cough and phlegm, the duration of hospitalization and the duration of absence of cough and phlegm were recorded. History of dyspnoea on exertion, wheezing and smoking habits was elicited in all the patients. Peak expiratory flow rate was measured with a Wright's peak flow meter, and the maximum of five readings was taken as the reading for the subject under study.

The skiagrams of the chest were scrutinized and the extent of the disease was classified as stage I, stage II and stage III according to American Thoracic Society classification. The presence or absence of radiological evidence of emphysema was also noted. Since in majority of the cases of pulmonary tuberculosis, the symptoms of cough and phlegm disappear after 12 weeks of supervised chemotherapy, those tuberculous patients who gave history of having had cough and sputum with or without dyspnoea for over two years and who continued to have such symptoms even after becoming sputum negative after antituberculosis therapy were categorised as possibly suffering from chronic bronchitis. The patients of possible chronic bronchitis, who in addition had a peak expiratory flow rate less than 200 lit/min were categorised as having probable chronic bronchitis.

Results

Of the 2,350 patients of chronic bronchitis studied at V.P. Chest Institute, 135 (5.7%) had evidence of healed tuberculosis on the chest X-ray. However, in only 22.9% of these cases past history of tuberculosis could be obtained. In 54.8 % of such cases, cough and phlegm reappeared sometime after the successful completion of anti-tuberculous therapy and in 12.5% of cases it started with the onset of tuberculosis and persisted even though tuberculosis had been arrested.

The age and sex wise distribution of cases of chronic bronchitis and chronic bronchitis with healed pulmonary tuberculosis is shown in Table I.

79.8% of patients of chronic bronchitis with healed pulmonary tuberculosis were over the age of 41 years, while only 56.6% of patients with

Table I

Age and sex wise distribution of patients with chronic bronchitis and chronic bronchitis with healed Pulmonary TB.

Age group in years	Chronic Bronchitis			Chronic bronchitis with healed TB.		
	M	F	Total	M	F	Total
<20	135 (5.7)	76 (3.2)	211 (8.9)	0 (-)	1(1.1)	1 (1.1)
21—30	218 (9.3)	111 (4.7)	329 (14.0)	5 (3.7)	5(3.7)	10 (7.4)
31-40	284 (12.1)	149 (6.6)	433 (18.4)	11 (8.1)	5(3.7)	16(11.8)
41—50	405 (17.1)	129 (5.3)	534 (22.7)	21 (15.3)	6(4.4)	27(19.7)
>50	708 (30.1)	135 (5.7)	843 (35.8)	76 (56.3)	5(3.7)	81 (60.0)
Total	1750 (74.4)	600 (25.5)	2350 (100.0)	113 (83.5)	22 (16.5)	135(100.0)

chronic bronchitis alone were over that age. This difference in age wise prevalence was statistically significant ($P < 0.05$). The difference in the prevalence between males and females in both the groups was statistically significant. The prevalence in males was significantly higher ($P < 0.05$) in patients with chronic bronchitis with healed pulmonary tuberculosis than in those with chronic bronchitis alone.

The radiological features in cases of chronic bronchitis with healed pulmonary tuberculosis were then studied. The tuberculous lesion was unilateral in 53.3% of patients and bilateral in 46.7%. In 49.5% of patients only one zone was involved, in 31.1% two zones were involved and involvement of more than 3 zones was seen in only 19.4% of patients. Fibrosis was the predominant lesion in 74.0% of patients, calcification was seen in 22.8% and cavity in 7.4%. 3.7% of patients had had lobectomy. While localised emphysema was seen in only 1.6% of patients of chronic bronchitis alone, it was seen in 9.11% of bronchitics with healed pulmonary tuberculosis. Surprisingly prevalence of generalised emphysema was equal in both groups (54.0%). The duration of cough and phlegm and the grades of exertional dyspnoea in both the groups were as seen in Table II.

The difference in duration of symptoms of persistent cough and sputum in the two groups however was not significant. Though the prevalence of Grade I, Grade II and Grade III dyspnoea was more in patients with chronic bronchitis with pulmonary tuberculosis, the difference

between the two groups was not statistically significant ($P > 0.05$).

The smoking habits in the two groups of patients were as seen in Table III.

The prevalence of smoking was significantly higher ($P < 0.05$) in patients with chronic bronchitis with healed pulmonary tuberculosis as compared to patients with chronic bronchitis alone.

The values of pulmonary function tests in the two groups of patients are given in Table IV.

There was a highly significant reduction in the vital capacity of patients with healed pulmonary tuberculosis as compared to patients with tuberculosis alone. While moderate degree of airways obstruction was demonstrated in both the groups, the difference was not statistically significant. Similar findings were observed with respect to RV/TLC.

R.B.T.B. Hospital data

Of 201 sputum negative patients with pulmonary tuberculosis studied, 36.3% continued to have cough and phlegm even after 12 weeks of hospitalization and supervised chemotherapy.

Of the 201 patients studied 48 (23.6%) were categorised as having possible chronic bronchitis. Since 30 (14.2%) of such patients had a peak expiratory flow rate less than 200 lit/min they have been categorised as having probable chronic bronchitis.

Table II
Duration of symptoms of cough and phlegm and severity of dyspnoea in patients with chronic bronchitis and chronic bronchitis with healed pulmonary TB. (V.P.C.I. Data)

Duration of Cough Phlegm	Grades of Dyspnoea								Total	
	0		1		2		3			
	CB %	CB+TB %	CB %	CB+TB %	CB %	CB+TB %	CB %	CB+TB %	CB %	CB+TB %
	29 (23.57)	17 (13.82)	24 (19.51)	31 (22.90)	10 (8.13)	12 (8.88)	3 (2.43)	7 (5.18)	66 (53.65)	67 (50.78)
5—10 years	4 (3.25)	7 (5.18)	11 (8.94)	16 (11.85)	11 (8.94)	13 (8.62)	2 (1.62)	0 (-)	28 (22.76)	36 (26.65)
> 10 years	5 (4.06)	5 (3.60)	13 (10.57)	12 (8.88)	9 (7.32)	11 (8.14)	2 (1.62)	4 (2.96)	29 (23.57)	32 (23.50)
	38 (30.89)	29 (22.60)	48 (39.03)	59 (43.63)	30 (24.39)	36 (25.04)	7 (5.67)	11 (8.14)	123 (100%)	135 (100%)

Table III
Smoking habits of patients with chronic bronchitis and chronic bronchitis with healed tuberculosis
V.P.C.I. Data

	CHR. BR. with TB.	CH. BR.	Value of paired 't'
Smoker	44.4%	35.2%	P<0.05
Ex-Smoker	11.1%	21.3%	P>0.05
Never Smoked	55.5%	43.5%	P>0.05

Table IV
Pulmonary function tests in patients with Chronic Bronchitis and Chronic Bronchitis with healed pulmonary tuberculosis
V.P.C.I. Data

P.F.T.	n	CH.BR. + TB. m ± S.D.	n	m	CH.BR. + TB. m ± S.D.	Value of paired 't'
FVC	35	2197 .25 ± 709.96	29	3268 .34 ± 915.65		P<0.01 (Sig)
FEV _a %	35	48 .75 ± 4.40	29	49 .66 ± 11.80		P>0.05(NS)
RV/TLC	35	56 .54 ± 3.44	29	53 .71 ± 15.55		P>0.05(NS)
Age	35	49 .40 ± 11.79	29	57 .03 ± 9.87		P>0.05(NS)

n.=number of subjects; m=mean value; S.D.=Standard Deviation

Table V

Age and sex wise distribution of patients of possible and probable chronic bronchitis amongst patients of pulmonary tuberculosis

R.B.T.B.H. Data

Age Group	Pul. TB patients			Possible Chr. Br.			Probable Chr. Br.		
—20	13(6.46)	23(11.44)	36(17.90)	1(0.49)	7(3.43)	8(3.92)	0(—)	5(2.45)	5(2.45)
21—30	29(14.40)	43(21.39)	72(35.70)	7(3.43)	7(3.43)	14(6.86)	2.(0.98)	5(2.45)	7(3.43)
31—40	26(12.93)	24(11.98)	50(24.91)	7(3.43)	9(4.47)	16(7.90)	5(2.45)	8(3.40)	13(5.85)
41—50	17(8.45)	10(4.97)	27(13.42)	2(0.98)	2(0.98)	4(1.96)	2(0.98)	0(—)	2(0.98)
50—	11(5.47)	5(2.48)	16(7.95)	5(2.45)	1(0.49)	6(2.94)	2(0.98)	1(0.49)	3(1.47)
Total	96(47.71)	105(52.26)	201(100%)	22(10.94)	26(12.4)	48(23.58)	11(5.39)	19(8.79)	30(14.18)

Percentages calculated with 201 as base.

Table VI

Smoking habits of patients with pulmonary tuberculosis! n ith probable and possible chronic bronhi hitis

R.B.T.B.H. Data

Smoking Habit	Pul. T.B.	Possible Chr. Br.	Probable Chr. Br.	Total
Smoker (%)	15 (7.46)	12 (5.97)	3 (1.49)	30 (14.92)
Ex Smoker (%)	23 (11.44)	12 (5.97)	10 (4.97)	45 (22.38)
Never Smoked (%)	85 (42.28)	24 (11.94)	17 (8.45)	126 (62.64)
Total	123 (61.19)	48 (23.88)	30 (14.92)	201 (100%)

Age and sex wise distribution of patients with possible and probable chronic bronchitis is given in Table V.

While there was no difference between the patients under and over the age of 40 years amongst the patients of pulmonary tuberculosis studied, the difference between those under 40 years and over 40 years amongst the possible and probable chronic bronchitis was statistically significant, the latter greater than the former.

There was however no sex wise difference in prevalence between possible and probable chronic bronchitis ($P > 0.05$).

The prevalence of smoking amongst the three groups, tuberculosis alone, tuberculosis with possible bronchitis and tuberculosis with probable chronic bronchitis is shown in Table VI.

Of the 153 cases with pulmonary tuberculosis alone only 10 (6.5%) had either focal or general-

Table VII Peak Expiratory flow, rate of patients studied at R.B.T.B. Hospital

Sex	Male			Female		
	Disease Group	P.E.F.R.			P.E.F.R.	
N		X±SE (X)	S.D.	N	X±SE(X)	S.D.
Pul. T.B.	69	295.9±16.42	136.44	78	217.4±11.37	100.43
Possible Chr. Br.	12	N.S. 357.9±32.28 ***	113.85	6	N.S. 258.3±17.20 **	42.15
Prob. Chr. Br.	10	128.5±10.59	33.51	19	142.1±10.52	45.89

X Mean
N no. of subjects
N.S Net significant (P>.05)
** Highly significant (P<0.01)

S.F.(X) : Standard error of mean
S.D. : Standard deviation
* : Significant (0.01 <P<.05)
*** : Very highly significant (P<0.001)

ised emphysema. On the other hand, 24 (30.7 %) of patients with possible chronic bronchitis and 18 (60%) of patients with probable chronic bronchitis had emphysema. Of the latter group while 5 (16.6 %) had focal emphysema, 13 (83.4%) had generalised emphysema.

Table VII shows the peak expiratory flow rates in patients of pulmonary tuberculosis and patients with chronic bronchitis (possible and probable) amongst them.

It was seen that there was no significant difference between the mean peak expiratory flow rates of patients with pulmonary tuberculosis alone and patients of pulmonary tuberculosis with possible chronic bronchitis. The difference between pulmonary tuberculosis patients and

those with probable chronic bronchitis was however very highly significant (P<0.05).

The peak expiratory flow rates in 81% of all the tuberculous patients (with and without chronic bronchitis) studied was below the normal values predicted for their age and sex. However in only 45% of the patients was the airways obstruction moderately severe (peak expiratory flow less than 200 litres/min).

Except in the age group under 20 years in males and 21-30 in females, in whom there was significant difference between the mean peak expiratory flow rates between stage II and stage III (Radiological extent) there was no significant difference between the three stages in both sexes and in all age groups.

Table VIII
Emphysema, extent of tuberculous lesion and peak expiratory flow rate
R.B.T.B.H. Data

Peak Expiratory flow rate					
Radiology	Without Emphysema		With Emphysema		Significance of Difference
	n	X±S.D.	n	X±S.D.	
I	17	319.1±137.0	2	120.0± 56.6	P>0.05
II	58	260.5±136.6	13	171.0±108.3	P>0.05
III	122	215.6± 33.5	17	145.0± 54.8	P<0.01

An attempt was therefore made to see if there was any correlation between the radiological evidence of emphysema and peak expiratory flow rate in three stages of pulmonary tuberculosis. The results are summarized in the next table (Table VIII).

It was seen that though the mean peak expiratory flow rates were considerably reduced in those with emphysema in all the three stages of pulmonary tuberculosis, the difference was statistically significant only in those in stage III.

Discussion

Gaensler 1959, Martin 1961, Birath 1966, Anno and Tomaschewski 1958, Hirasawa 1966, Snider 1971 have all reported diffuse airways obstruction in patients with pulmonary tuberculosis. The percentage of patients with obstruction however has varied from 25 % to 50 % depending upon the population studied. As there has so far been no prospective study on these patients with airways obstruction, it is difficult to predict the course of illness in such patients.

A retrospective study was therefore carried out in patients with chronic bronchitis, attending a non tuberculous chest clinic to find out the number of bronchitis who had radiological evidence of healed pulmonary tuberculosis and to study the pattern of illness in those patients. While 5.61 % of the patients of chronic bronchitis had radiological evidence of pulmonary tuberculosis, history of tuberculosis could be obtained in only a few cases despite leading questions. The inability to elicit a history may perhaps be due to: (1) the milder form of the disease seen in these patients, as in majority of the patients the lesion was unilateral and involved only one zone of the lung, chiefly the apex which might have healed on its own, (2) a long interval between the onset of tuberculosis and visit to a chest clinic due to symptoms of dyspnoea etc. (3) reluctance to admit past history of tuberculosis.

The increased prevalence in men over the age of 51 years, a high prevalence of smoking, equal prevalence of generalised emphysema and the same degree of airways obstruction in both the groups, do not justify classifying the patients separately.

Martin (1961) reported hypoxaemia in 4.3% of tuberculous patients with airways obstruction, 1.9% of whom also had CO₂ retention. Despite the longer duration of illness in patients with chronic bronchitis and tuberculosis, while chronic cor pulmonale was seen in 3 % of cases of chronic

bronchitis, it was present in only 1 % of chronic bronchitis with healed pulmonary tuberculosis. The coexistence of pulmonary T.B. therefore did not seem to have had an adverse effect on the course of chronic bronchitis in our patients. Prevalence of possible and probable chronic bronchitis in tuberculous patients, determined on the basis of criteria mentioned earlier, are significantly higher than the rates observed in the general population in a few areas of Delhi.

It might be argued that tuberculous patients with airway obstruction as shown by diminished PEFr might be having endobronchial tuberculosis, emphysema as a result of scarring or a marked reduction in the vital capacity due to an extensive lesion. The presence of endobronchial tuberculosis is only likely in those patients with a short history of cough and sputum who subsequently developed dyspnoea and airway obstruction inspite of antituberculous therapy. The criteria adopted in this study for diagnosing probable chronic bronchitis however excludes such cases.

Of the tuberculous patients studied the prevalence of generalised emphysema and also the extent of the disease was significantly higher in patients with probable chronic bronchitis. While focal emphysema might result as a result of scarring due to long standing tuberculosis, generalised emphysema is possibly due to chronic bronchitis. Since most of them were smokers, it is very likely that they would have been raising sputum long before they developed tuberculosis. A regular follow up of these patients can only confirm the findings of the present study.

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NATIONAL TUBERCULOSIS PROGRAMME: HEALTH BENEFIT FROM CASE FINDING IN PERIPHERAL HEALTH INSTITUTIONS AND DISTRICT TUBERCULOSIS CENTRES

V. SIVARAMAN

(From T.B. Sanatorium, Pondicherry)

The World Health Organisation Expert Committee on Tuberculosis in its ninth report has pointed out that case finding *per se* is not a tuberculosis control measure and any health benefit depends on the ensuing treatment. It has also emphasized that attention must be paid both to the cases that have been discovered and to those individuals incorrectly diagnosed as having tuberculosis.

Under conditions of District Tuberculosis Programme in India, cases that have been discovered and to those individuals incorrectly diagnosed as having tuberculosis.

Under conditions of District Tuberculosis programme in India, cases incorrectly diagnosed as having tuberculosis include:

1. *In Peripheral Health Institutions.* Cases whose sputum is wrongly interpreted as positive (microscopy, some times by paramedical personnel having undergone a short in-service training, being the only diagnostic tool).

2. *In District Tuberculosis Centres.* Due to availability of an experienced laboratory technician and countercheck provided by photofluorography, most, if not all, of the smear positive cases are likely to suffer from the disease but the same may not be true of all X-ray positive smear negative patients. A proportion among them is likely to belong to the category of "incorrectly diagnosed cases".

The purpose of the present paper is to estimate the proportion of patients benefitting from case finding in peripheral health institutions and study the management of smear negative X-ray positive suspects in District Tuberculosis Centres.

Part A—Accuracy of case finding in P.H.Is.

As pointed out earlier only genuine cases of tuberculosis will derive any benefit from anti-tubercular treatment. However there is considerable difficulty in denning a case of tuberculosis. Raj Narain *et al* (1968) have shown that those negative on culture and showing only 1, 2 or 3 bacilli on smear should not be regarded as cases of tuberculosis and that even definite positives on smear which are not confirmed by culture on

radiology may be doubtful cases. Therefore culture positivity shall be the yardstick of disease in the first part of this paper (the second part will deal with merits of treatment based on radiology.)

Rao *et al* (1971) have assessed the standard of microscopy in nine peripheral health institutions. Their data are rearranged in the form of a decision matrix (Macneil *et al*, 1975) in Table I.

By referring to table I we can see that out of 179 declared as smear positive by the PHI personnel 141 were genuine cases i.e. 78 per cent of cases found positive by an average centre are likely to be actually suffering from disease and hence derive benefit from anti-tubercular treatment. On the basis of the erroneous smear result 22 per cent are likely to be treated unnecessarily. We can also estimate the percentage of patients in whom the diagnosis has been missed. Out of 1,502 declared smear negative by the centre 87 have positive culture i.e. 6% of the smear negatives may still have disease.

Rao and Nagpaul (1970) have pointed out that sensitivity and specificity of sputum microscopy would vary under different diagnostic situations. It might therefore be interesting to apply the above calculation to data from different diagnostic situations.

The results of the calculations are presented in Table II.

A perusal of the table shows that smear surveys with mass chemotherapy amongst those found positive, even if otherwise feasible, might result in quite a high proportion namely 45 percent of patients being treated unnecessarily.

It may also be concluded that optimising the technical efficiency of sputum microscopy in PHIs will result in reduction in the number of patients unnecessarily treated from 22% to 9%.

The improvement of technical efficiency may be obtained either by posting trained technicians in place of paramedical personnel or laying greater emphasis to the in-service training of the latter. The question deserves further study by programme planners.

Table I

Decision matrix correlating smear result and culture result: Smear prepared and read by non-technicians in PHJs

	Culture		Total
	C+	C—	
Smear positive	141	38	179
Smear negative	87	1415	1502
	228	1453	1681

Table II

Effectiveness of microscopy under different conditions

	Clinical situation		Epidemiological situation
	Smear report by technician	Smear report by non-experienced technician	
	(1)	(2)	(3)
No correctly diagnosed expressed as percentage of total declared positive	78%	91%	55%
No. in whom diagnosis is missed expressed as percentage of total declared negative.	6%	2%	1%

Note :- Column (1) Refers to microscopy carried out by paramedical personnel after a short period of training. Data from Rao *et al* (1971).
Column (2) is obtained from the same data as above but microscopy carried out by N.T.I. Personnel.
Column (3) from Raj Narair *et al.* 1968.

In terms of probability, the figures derived could be interpreted thus: Any patient found positive by a PHI has 0.78 probability of being actually tuberculous, and any patient found negative has 0.06 probability of having a positive culture. This figure will be used in the second part of the paper,

Part B—Management of Smear Negative, X-ray positive “Suspect Tuberculous” Patient—A decision analysis approach.

The national tuberculosis programme envisages case finding in District Tuberculosis Centres through photofluorography and sputum microscopy. Often a case is seen in which the

radiological diagnosis is tuberculosis but the sputum smear is negative for AFB. As culture facilities are not available in most District Tuberculosis Centres, considerable uncertainty exists in deciding the line of treatment in such cases. It is common to see in many centres anti-tubercular treatment being started in such instances. The expected “benefits” of such therapy are:

(1) Improvement in persons who though smear negative would have been positive by culture,

(2) Prevention of breakdown in “early” cases i.e. the contention being that such cases

represent pre-culture positive stage of the pathogenesis of pulmonary tuberculosis. At the same time one must remember that such therapy involves the following "risks" also.

(0) It is likely that some patients are suffering from non-tubercular chest conditions and failure of anti-tubercular chemotherapy may mean dissatisfaction of the patient whose felt need is not satisfied.

(z7) Through "overdiagnosis" the objective of the programme is not attained and there may be wastage of resources.

The purpose of the present paper is to evolve a model for decision making to enable us to arrive at a rational formula to solve the problem.

I. Modern Techniques of Decision Analysis

1. *Decision Tree* : Decision analysis includes construction of a decision tree that describes the possible courses of action available and the consequences of each, obtaining a quantitative estimate of probability and utility (value) of each outcome and combining the estimates by a method that provides a measure of the expected value or worth of each course of action.

A decision tree consists of nodes and branches. For the problem under discussion a decision tree is represented in Fig. 1. Referring to the figure one can see that the decision to be made is whether to administer antitubercular treatment (hereinafter called treatment) or observe. (Observation will include repeating sputum smear examination thus increasing its reliability, formulating an alternative diagnosis and starting treatment for this diagnosis). In either case there is some chance (square node) that the culture, if performed would have been positive or negative. Amongst culture negative cases some may in fact be in "early" pathogenesis

phase of tuberculosis (TBP) and others will be having non tubercular chest conditions (NT). The outcome of treatment or observation may be favourable (F) or unfavourable (U).

2. *Quantitative Analysis* : It is well to remember one of the rules of decision analysis enabling us to calculate the expected value of a decision course. The expected value (EV) of a chance node reflects both the probability and the value of each possible outcome.

Thus, for example, a course of action may have two probable outcomes 01 and 02. The expected value of this course of action is given by the formula:

$$EV = P(01) \times V(01) + P(02) \times V(02)$$

wherein

P(01) = Probability of outcome 01; V(01) = Value of outcome 01

P(02) = Probability of 02; (V02) = Value of outcome 02.

In our discussion we shall assign a value of + 100 to each favourable outcome V(F) =100 and -100 to each unfavourable outcome V(U) = -100).

Assumptions Made:

(1) The discussion is solely centered around new patients aged 10 years and above.

(2) (a) 90% of culture positive patients treated with anti-tubercular drugs will have a favourable outcome. (This is above the reported 65% results obtainable under programme conditions but slightly less than those obtainable in controlled trials). But it must be remembered that controlled trials deal with patients who are regular and harbour bacilli sensitive to the drugs used. In fact it represents the maximum that could be achieved.

(b) 100% of culture negative early tuberculous cases will respond favourably to anti-tubercular treatment (Banerjee in 1967 reported that 98.3% of such cases remained negative after 3 years of treatment).

(3) 15% of culture negative cases are early cases of tuberculosis (Based upon the fact that 8-15% of such cases breakdown annually. Raj Narain and Frimodt Moller quoted by Nagpaul, 1967).

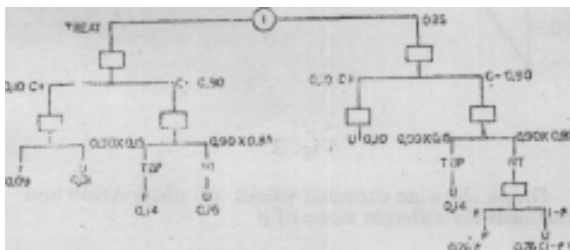


Fig. 1

Decision tree describing alternative strategies available to the physician and their potential outcomes

(4) All observed cases of culture positive tuberculosis will have an unfavorable outcome.

(5) All non-tubercular patients offered anti-tubercular treatment will have an unfavorable outcome. (Isoniazid, P.A.S. and thiacetazone are useless in chronic non-tuberculous bronchopulmonary infections.) (Leading article *Tubercle* 1969, 50, 68).

A. Expected Value of Treatment:

Favourable outcome can be expected in the following cases when the strategy “treat” is adopted.

- (1) 90% of culture positive cases and
- (2) 15 % of culture negative cases.

It is therefore essential to find out the probability of culture being positive when smear is negative. The exact calculations have been explained earlier. The value may vary from 0.01 to 0.06. For simplification we may take 0.10-90% of this and 15 % of 0.90 as the likely chances of a favourable outcome. By designating as P (FT) the probability of favourable outcome with treatment we get :

$$P(FT) = (0.10 \times 0.90) + (0.90 \times 0.15)$$

$$P(FT) = 0.23.$$

Treatment yields an unfavourable outcome in culture negative non-tuberculous cases. Using similar notations i.e. designating as P (UT) the probability of unfavourable response to treatment :

$$p(UT) = (0.10 \times 0.10) + (0.90 \times 0.85) = 0.77$$

Following the principle enunciated earlier regarding the calculation of expected value :

$$EV(T) = P(FT) V(FT) + P(UT) V(UT)$$

with numerical values

$$EV(T) = (0.23 \times 100) + (0.77) (-100)$$

$$EV(T) = -54$$

B. Expected values of observation:

Observation (which by definition includes treatment for alternative diagnosis) yields a favourable outcome only in a certain proportion of non-tuberculous cases. Let us designate this probability as p. Then.

$$P(F\text{ obs}) = 0.90 \times 0.85 \times p$$

$$P(F\text{ obs}) = 0.76 p$$

In the following eventualities we may have

unfavorable outcome when the strategy “obs” is adopted :

- (1) All the culture positive cases.
- (2) 15% of culture negative early tuberculous cases
- (3) a certain proportion (1-p) of non-tuberculous cases.

$$P(U\text{ obs}) = 0.10 + (0.15 \times 0.90) +$$

$$(0.90 \times 0.85) (1-p) = 1 - 0.76 p$$

$$EV(\text{obs}) = P(F\text{ obs}) V(F\text{ obs}) + P(U\text{ obs})$$

$$\times V(U\text{ obs})$$

$$= 76 p + (1 - 0.76 p) (-100) =$$

$$152p - 100$$

The expected values of treatment and observation may be plotted in the form of a graph. P is taken as abscissa (in the X axis) and E.V. as ordinate (in the Y axis). The expected value of treatment is not influenced by p and for all values of p-EVT, -54. It is therefore represented by a line parallel to the X axis and intersecting the Y axis at -54 (Fig. 2).

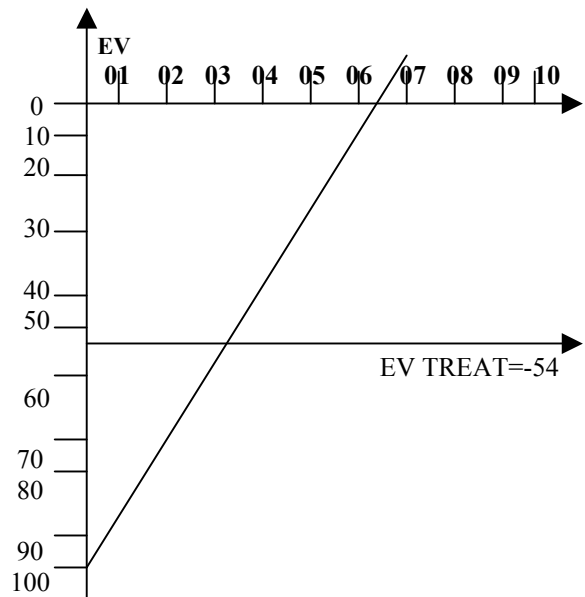


Fig. 2

Graph showing expected values of observation and treatment for different value of p

To plot EV (obs) we may assign different values to p and obtain corresponding values for EV obs from the equation $EV\text{ obs} = 152p - 100$. By joining these points we obtain another straight line representing EV obs.

From the graph (Fig. 2) we see that for values of p less than 0.3, EV treat is higher than EV obs. whereas if p is more than 0.3, EV obs has a higher value than EV treat. In terms of the problem we are facing, this means the following :

Confronted with a patient presenting an x-ray lesion suggestive of pulmonary tuberculosis whose sputum is negative, the physician asks himself what else it could be, and formulates an alternative diagnosis. He then assesses the chances of cure for this disease. If such chances were more than 30 %, it is better to withhold anti-tubercular treatment and manage the case proceeding on the assumption that the second diagnosis is correct.

II. Discussion

1. The decision analysis approach adopted in the present paper is finding application in industrial management economics and government. A few studies have been carried out abroad in an attempt to apply the same approach to medicine (Parker & Kassirer 1975, Schwartz *et al* 1973).

2. The analysis shows that administration of anti-tubercular treatment to x-ray positive sputum negative patients is not always a good strategy.

3. p in the above discussion is a vague concept because there are no data to calculate the prevalence of chest diseases other than tuberculosis and their cure rates. The general impression is that most of the non-tuberculous chest diseases encountered in India are inflammatory and miscellaneous lesions such as pulmonary eosinophilia. These lend themselves well to specific therapy and the cure rate may be definitely higher than 30%. Therefore, observation is likely to be the better choice in the prevailing circumstances. However, if bronchogenic carcinoma were widely prevalent an altogether grim prospect is in store.

4. It may be concluded that it would be worthwhile to undertake field studies designed to identify different chest conditions often mistaken for tuberculosis and the efficiency of treatment thereof. These studies will indirectly help the national tuberculosis programme by minimising the wastage of anti TB drugs. The tendency to condemn non-tuberculous patients to long continued chemotherapy on the basis of x-ray suspicion may be curbed. The W.H.O. expert committee on tuberculosis in its ninth report pointed out that when treatment is initiated on the basis of radiographic findings alone, a substantial proportion of patients are treated unnecessarily.

This wastes resources, throws strain on understaffed and under-financed treatment services and unnecessarily exposes many patients to loss of their job, loss of their home and to serious social stigma.

5. It might be argued that the above conclusions are reached proceeding from certain assumptions. A question may arise whether these conclusions would still be valid if some of the assumptions were wrong. It must be pointed out here that despite the fact that our assumptions 2 (a) & (b) and (4) are weighted in favour of treatment, and the value 0.10 (for probability of culture being positive when smear is negative) is on the high side, this strategy is better only for a small range of p values.

6. The contention that 8-15% of bacteriologically negative suspects breakdown per year might be challenged and some may place this figure higher. It would be interesting to find out how far this figure influences the conclusion reached. For the purpose it is useful to substitute by "b", the value 0.15 (the probability of a culture negative patient being an early case of P.T.). It is possible to calculate the expected values of treatment and observation, by applying the same principles outlined earlier we get: EV (treat) = 180 Ob - - 82.

EV (Obs) = 180 p — 180 p b — 100 when the expected values of the two principal courses of action are equal, the physician should be indifferent to choosing either course (Parker & Kassirer 1975). Thus indifference to either option exists when EV treat = EV obs.

Substituting the equation given above makes it possible to derive an expression containing a probability value at which the physician should be indifferent to treating or observing this probability value at the indifference point is derived as follows :

$$EV \text{ treat} = EV \text{ obs.}$$

$$180 b - 82 = 180 p - 180 p b - 100 \text{ and solving for } b$$

$$p - 0.1$$

$$1 + P$$

Thus b is a threshold probability that will be denoted hereafter as B to avoid confusing this threshold level with the probability that a given bacteriologically negative suspect is actually suffering from tuberculosis.

The relation between the efficiency of observa-

tion and B is plotted in Fig. 3. At one extreme if none of the bacteriologically negative suspect is likely to breakdown observation is a better strategy provided the efficiency of treatment of non-tubercular chest disease is more than 10%. At the other extreme if the breakdown rate is more than 45 % treatment is to be chosen even if the efficiency of treatment of non tubercular chest diseases is 100%.

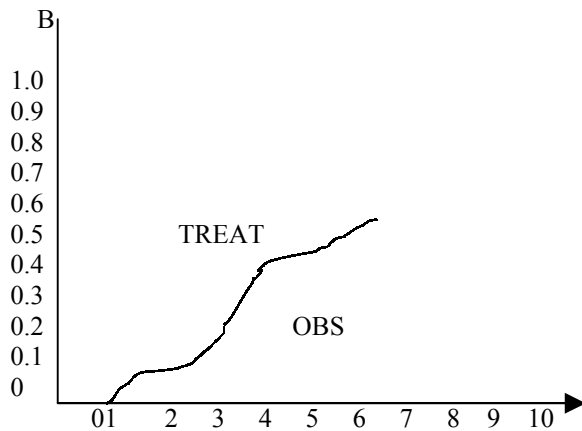


Fig. 3
Relationship between efficiency of treatment and breakdown rate among suspects

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A SOCIOLOGICAL STUDY OF AWARENESS OF SYMPTOMS OF PULMONARY TUBERCULOSIS AND ACTION TAKEN BY THE PATIENTS TO SEEK RELIEF

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Introduction

The National Tuberculosis Control Programme is based on the concept of responding to the felt-need of the community by relieving the sufferings of the patients. The socio-economic situation in the community has its impact on the efficient implementation of the programme. The present study was undertaken to assess the response of the patients to the suffering they undergo on account of pulmonary tuberculosis and the factors influencing the promptness with which they sought medical aid to alleviate their suffering.

Material and Methods

Cases of pulmonary tuberculosis among over 15 years olds, diagnosed in the course of 3 months on radiographic evidence and comprising of bacillary and abacillary cases, were selected for the study.

The Government Chest Institute and Tuberculosis Demonstration and Training Centre functions as the District Tuberculosis Centre for Madras city. Besides this institute there are 18 affiliated peripheral centres whose areas of

service are well denned. Symptomatics from not only the area served by this Centre (area cases—AC) but also from other areas within (out of area—OA) and outside (out-station—OS) the city do report here initially.

A questionnaire was evolved to ensure the required information from the patients. Due care was taken to obviate any bias or ambiguity in the form. The social workers, who conducted the interviews were clearly apprised of the modus operandi and aim of the study. The questioning of the subjects was done, individually in a cubicle, after diagnosis. Necessary information was elicited from patients, while encouraging them to talk freely on the various aspects during the private interviews. Information regarding earliest action taken by them either by attending this centre or other medical facilities prior to attending this institute was recorded.

Analysis

A total of 796 patients were studied of whom 600 were men and 196 were women. The mean age for men and women was 37 years and 32 years respectively.

Table I *Distribution of cases according to age, sex and*

sputum status

Age group in years	Sputum status and Sex					
	Bacillary			Abacillary		
	Men	Women	Total	Men	Women	Total
15—24	41	10	51	51	38	89
25—34	67	23	90	81	47	128
35—44	74	18	92	100	35	135
45 +	67	7	74	119	18	137
Total	249	58	307	351	138	489

The proportion of bacillary cases among males was 42% as against 30% among females, a statistically significant difference. Similar difference was not noticed in the different age groups studied.

The proportion of male patients from OS is significantly higher and correspondingly the proportion of female patients is significantly less. There is no statistically significant difference among the bacillary and abacillary cases with reference to the area from which they come.

Table II
Distribution according to domiciliary status, sex and sputum status

	AC	OA	OS	Total
Men	269 73%	199 73%	132 88%	600 75%
Women	101 27%	74 27%	21 12%	196 25%
Total	370	273	153	796
Bacillary	140 38%	105 39%	62 40%	307 39%
Abacillary	230 62%	168 61%	91 60%	489 61%

Table III
Distribution of the Symptoms

Symptoms	No. of persons	Percentage	Percentage to the total No. of subjects studied (796)
Cough	734	35	92
Fever	412	20	52
Haemoptysis	257	13	32
Chest Pain	162	8	20
Breathlessness	80	4	10
Loss of Appetite	201	10	25
Loss of Weight	123	6	16
Others	105	5	13
Total	2074	101	

The highest prevalent symptom observed is cough (35%), which was complained of by the largest number of patients (92 %). The other two prominent symptoms were fever and haemoptysis complained of by 52% and 32% of patients respectively.

The mode of this distribution is obviously 2 symptoms, a peak of 38 % of the patients having had 2 symptoms. 40% had taken action within 1 month, 65% within 3 months and 84% within 6 months.

The correlation co-efficient between the number of symptoms and the time lag *In* months works out to 0.1 with a standard error of 0.036. This evidences there being a fair and statistically significant direct correlation. An explanation hereof would be that the patients who seek medical aid at a later stage have more symptoms than those who seek aid earlier. Obviously these have ignored the fewer symptoms they had during the initial phases of the disease.

Table IV

Distribution of patients according to number of symptoms and duration (time-lag) before taking action

No. of symptoms	Time lag in months				Total
	0—1	1—3	3—6	6+	
1	41	25	13	6	85
2	133	64	58	46	301
3	88	74	50	54	266
4	52	35	28	25	140
Asymptomatic	4				4
Total	318	198	149	131	796

Table V

Distribution of patients according to the time, lag and sputum status

	Time lag in months				Total
	0—1	1—3	3—6	6+	
Bacillary	99 31%	100 51%	70 47%	38 29%	307 39%
Abacillary	219 69%	98 49%	79 53%	95 71%	489 61%
Total	318 100%	198 100%	149 100%	133 100%	796 100%

Table VI
Distribution according to sputum status, time lag and area

	No. of patients	0—1 months		1—3 months		3—6 months		months									
		Total No.	%	Positive No.	%	Total No.	%	Positive No.	%	Total No.	%	Positive No.	%				
A.C.	370	194	53%	63	33%	92	25%	47	51%	45	12%	19	42%	39	10%	11	28%
O.A.	273	94	34%	27	29%	68	25%	34	50%	63	23%	33	52%	48	18%	11	23%
O.S.	153	30	20%	9	30%	38	25%	19	50%	41	27%	18	44%	44	29%	16	36%
Total	796	318	40%	99	31%	198	25%	100	51%	149	19%	70	47%	131	17%	38	25%

Among those who have taken action during the 1st month of their developing symptoms a large proportion are abacillary. The proportion of bacillary cases seems to increase as the time lag advances upto 3 months and then declines with a corresponding increase in abacillary proportions after six months. The differences are highly significant. ($P < .01$).

The earlier the patients report the less is the scope for them to be bacillary. That the small proportion of bacillary cases took action after 6 months could possibly be due to a major portion of the patients' developing bacillary status during the range of 1-6 months of their time lag and their taking action in that very span, due to acute suffering.

Among the patients from 3 areas studied, those from AC and OA show that the proportion of patients taking action during the different

spans is of a descending order with lapse of time whereas the reverse is the case in the OS cases. The nearness of the medical facility has caused a larger proportion of tuberculous patients to seek relief earlier.

There is very little difference between the proportion of sputum positives attending from AC and OA during 0-1 month and 1-3 months.

Between 3-6 months time lag there is a conspicuously higher proportion of sputum positives among OA cases than the other two. It is also observed that beyond 6 months there is a higher percentage of sputum positives in the OS group than in the other two.

Obviously the higher proportion of sputum positives among the OA and OS cases with increase in time lag is due to progression of the disease consequent on the delay in seeking medical aid.

Table VII

Attitude of nearest relatives towards the patients

Relationship	Total	Good	%	Hostile	%
Father	91	84	92%	7	8%
Mother	143	139	97%	4	3%
Wife	404	374	93%	30	7%
Husband	133	114	86%	19	14%
Son/Daughter (Children)	294	268	91%	26	9%
In-laws	36	26	72%	10	28%
Brothers/Sisters	134	113	84%	21	16%
Others	41	35	85%	6	15%
Total	1276	1153	90%	123	10%

Table VIII

Analysis of the attitude of patients

Sex	Sputum status	Optimistic	Pessimistic	Total
Men	Positive	225	27	252
		89%	11%	100%
	Negative	316	32	348
		91%	9%	100%
Women	Positive	46	9	55
		84%	16%	100%
	Negative	125	15	140
		89%	11%	100%
Total	Positive	271	36	307
		88%	12%	100%
	Negative	441	47	488
		90%	10%	100%
Grand Total		712	83	795
		90%	10%	100%

In-laws have more tendency to turn hostile towards the patient (28%).

Brothers or sisters and husbands fall in the next order (16% and 14% respectively).

Comparison between wife turning hostile towards her husband or the husband turning hostile towards wife reveals that more husbands had been hostile towards their ailing wives.

The mother's attitude towards their ailing children has outstandingly remained good and sympathetic (97%).

84 to 91% of the patients have shown an optimistic attitude (both men and women or bacillary and abacillary cases). Furthermore among those who are inclined to be pessimistic there is no statistical difference in all the groups. This attitude is presumably due to the knowledge that Tuberculosis is curable in view of availability of effective treatment with drugs.

Discussion

An assessment of the human suffering brought about by pulmonary tuberculosis and the

promptness of the response of the patients to seek relief will help proper orientation of services under the N.T.P. with maximal expedition. Such a sociological approach to a major health problem in the community is sure to reap its benefits. The present study which had its aim firstly, to study the symptom awareness among patients, secondly their response to the suffering they are subjected to on account of the disease, and thirdly the psychological impact of the disease on themselves and the attitude of their near relatives towards them in the present context of efficacious treatment available to them.

A survey through interviews in Delhi and New Delhi area conducted by Sikand and Raj Narain (1957) lead to the conclusion that consciousness of the disease is not sufficiently widespread for control measures to be based on it and that the "unknown" cases constitute a major public health hazard. In a sociological study of awareness of symptoms among persons with pulmonary tuberculosis by Banerji and Anderson (1963) approximately 70% of sputum positive patients and approximately 80% of persons considered to suffer from Radiologically active tuberculosis were found to be aware of the symptoms.

The above two studies were more in the nature of health surveys through interviews supplemented by the objective use of diagnostic tools with a possible variation in the interview techniques used. However, the difference in interviewing techniques plays a much less important role, the more definite the diagnosis. When the case is sputum positive or found active Radiologically, the type of interview technique is apparently of little importance.

Pamra, Pathak and Mathur in their study on new patients attending New Delhi Tuberculosis Centre, found that nearly 80% of the patients took remedial action within one month of the appearance of the symptoms. A larger proportion of out-station patients seem to have taken over 3 months before seeking medical aid as compared to those from domiciliary area.

Whereas 53% of the patients among our area cases took action within a month only 20% of the OS had sought relief in a similar period. It was also observed that with lapse of time a larger proportion of OS cases and comparatively lesser proportion of AC and OA cases have taken action. Presumably this is due to the proximity of the medical facility which has caused the AC and OA cases to take earlier action than the OS cases.

When all the patients from the 3 areas are analysed, it is observed that 40% had taken action within 1 month, 65% within 3 months and 84% within 6 months.

Another interesting observation is that among patients reporting within less than a month, a larger proportion are abacillary. The proportion of bacillary cases increases with further lapse of time before they seek medical aid. This definitely correlates with the progress of the disease.

The proportion of in-laws tending to be hostile is highest whereas the mother had remained sympathetic, both the above confirming to the traditional pattern of behaviour. The optimism effused by the patients speaks well of not only their awareness of the symptoms of the disease resulting in their taking early action to seek relief but also in their confidence in the modern treatment to get well and back to their normal life.

Summary

Awareness of symptoms of Pulmonary Tuberculosis and promptness of action taken to seek the treatment by the sufferers in an urban area was studied. The proximity of the medical facility enabled a sizable proportion (53%) to take action within less than a month. The proportion of patients drawn from all the 3 areas (AC, OA & OS) who took action within a month was 40%, within 3 months 65% and within 6 months 84%. It was also observed that among symptomatics reporting within a month, the bacillary cases are proportionately low which tends to increase as the time elapses. Analysis of the psychological impact of the disease on the patients elicited a sense of optimism in a large proportion of patients obviously due to a very favourable response to good treatment. The attitudes of the relatives towards the patients tended to be on traditional lines, a large proportion of the in-laws being hostile and confirming the mother's sympathy to her offspring.

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COMPARISON OF HYPERSENSITIVITY REACTIONS TO HEAT-CONCENTRATED AND PURIFIED PROTEIN DERIVATIVE TUBERCULINS IN AN INFECTED HERD

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Introduction

In order to obviate the problem of no-visible-lesion (NVL) reactors, improvements in the tuberculin test have been suggested from time to time. One of the lines of attack has been the development of a more purified form of sensitin. Thus, Koch's Old Tuberculin (O.T.), which used to contain foreign protein derived from meat extract, was replaced by the allergin prepared from the growth of tubercle bacilli on synthetic medium (Long and Seibert, 1926a; Dorset, 1934). The heat-concentrated-synthetic-medium (HCSM) tuberculin quickly gained popularity and is till this day employed for veterinary use in the U.S.A. and several other countries, including India. It may, however, be mentioned here that in the present-day literature all tuberculins concentrated by heat, including those prepared on synthetic media, are referred to as O.T.

Long and Seibert (1926 b) also showed that the active principle of tuberculin was a protein. Since tuberculin could now be prepared from growth of tubercle bacilli on synthetic media, which contained no protein, it became feasible to precipitate it out without fear of admixture with extraneous protein. This was accomplished in 1934; and methods of preparation, testing and use of purified protein derivative (PPD) of tuberculin were described in detail (Long, 1934; Seibert, 1934).

The purpose of the present investigation was to compare the reactions evoked by PPD tuberculin and HCSM tuberculin, with a view to explore the possibility of eliminating the NVL reactions in cattle and buffaloes.

Material and Methods

Mammalian tuberculin prepared on synthetic medium at the Indian Veterinary Research Institute (I.V.R.I.) and mammalian and avian PPD tuberculins (of comparable potency) obtained from the Central Veterinary Laboratory, Weybridge, England, were employed in this study.

Tests with the three products were conducted simultaneously, on the same side of the neck, at 3 different, shaved areas of the skin, with a distance of at least 10 cm in between them. The

test sites used for the local tuberculin and mammalian PPD tuberculin were alternated in approximately 2 equal groups of animals. The skin-fold was lifted and its thickness measured with Vernier callipers. The concerned sensitin was injected into the deeper layer of dermis, taking care not to deposit it too superficially in the epidermal region or to pierce it deeply so as to reach the subcutis. Observation of reactions was made 72 hours after injection and thickness of the double-fold of skin at the site of injection recorded, if any appreciable increase therein was noticed. Whenever measurement of skin thickness at the site of injection of one sensitin was considered necessary, the reaction to the other sensitin was also measured with callipers, even if totally absent. Two and a half-fold measurement of the original, with a minimum increase of about 8 mm, was reckoned as a reaction if accompanied by other characteristics associated with the true response (diffuseness, oedema, pain and warmth).

Two hundred and thirty seven cattle of different age groups in a herd, which had been known earlier to exhibit many NVL reactions to HCSM tuberculin, were taken under experiment. Another group of 17 buffalo calves kept separately on neighbouring premises, was also included in this study.

Results

Out of the animals tested, 195 cattle and all the 17 buffalo calves did not evince any reaction whatsoever to any of the 3 tuberculins. One bullock reacted frankly to both the mammalian Tuberculins (PPD and HCSM), showing a fairly smaller cross reaction to avian PPD. Of the remaining 41, none reacted to HCSM tuberculin; and in 11 of these, the reactions with mammalian PPD too were small enough to be classified as negative, even though the degree of swelling was in each case somewhat greater with PPD than with the local, heat-concentrated product. Also, eight more animals in the lower range of response reacted only to avian PPD tuberculin. Among the 22 non-reactors to HCSM tuberculin still left over, five showed response with avian PPD which was equal to or greater than that produced by mammalian PPD. However, 17 reactors exhibiting greater response to mammalian PPD than to avian PPD were still left over. By adopting the British standards of comparative test,

Table 1

Correlation Between Reactions to Mammalian PPD and Avian PPD on 237 Animals in Herd A

Reactions to mammalian PPD (Thickening in mms)

		<1.5	2.5	3.5	4.5	5.5	6.5	7.5	8.5	9.5	10.5	11.5	≥12.5	Total
Reaction to avian PPD (Thickening in mm.)	≤ 1.5			1		2		1						4
	2.5			1	2		1							4
	3.5		1	3	1	1	2	2						10
	4.5	4	1	1		1		1			1			10
	5.5	1				1	1		1	1				05
	6.5	1							2		1			02
	7.5			2										02
	8.5										1			01
	9.5			1							1			02
	10.5													
	11.5													
	12.5													
Total		6	2	8	2	5	3	5	5	3	1	1	1	4

Note : 195 animals showing no reaction to any of the sensitins have not been added in this table.

most of these could also be cleared of suspicion in a herd known to abound in non-specific reactors, except for 3 animals that would be categorized doubtful, warranting a retest. In short, PPD tuberculin appeared to elicit uniformly stronger reactions than the HCSM tuberculin, which was, thus, considered not to produce any more non-specific reactions than the former.

The differences in response to intradermal tests with the 3 sensitins are illustrated by means of histograms (Fig. 1). Careful examination of these brings out the following facts:

(i) Mammalian PPD tuberculin elicited greater skin reactions than the HCSM tuberculin used in this trial.

(ii) The response to avian PPD was almost approaching that evinced by mammalian PPD.

(iii) HCSM tuberculin, eliciting milder reactions as it is, cannot be incriminated for producing a larger proportion of non-specific reactions than mammalian PPD. In this study, in fact, no such reactor requiring further elucidation was shown by the HCSM product.

The grades of reactions shown by individual animals that responded to mammalian or avian PPD and the distribution of various combinations of responses in the herd are depicted in the correlation table. It will be observed that different intensities of sensitivity reactions to the two products are fairly dispersed over the whole area, with somewhat greater spattering in the zone of reactions to mammalian PPD. This seems to suggest that cause of sensitization

tested simultaneously with both the products. Van Waveren (1965) observed that PPD gave a better yield but otherwise the purification offered no striking advantage. No wonder, therefore, that the heat-concentrated product continues to be used by both veterinary and medical workers in many countries and the WHO still undertakes to prepare, stock and distribute the standard for old tuberculin from the State Serum Institute, Copenhagen, Denmark.

It has, however, to be conceded that PPD tuberculin is a chemically purer substance and its potency can be measured with far greater accuracy by chemical means than is possible with the heat-concentrated sensitin. It would, therefore, be natural that, in due course of time, O.T. would be replaced by the more refined product everywhere. Until then, the use of HCSM tuberculin in veterinary practice is permissible in developing countries, in view of the lower cost of its production without any significant disadvantage in diagnosis, as compared to the chemically purified product.

Summary

Comparative study in 237 cattle and 18 buffaloes showed the local HCSM tuberculin to evoke milder skin reactions than PPD tuberculin. Among cattle, which formed part of an infected herd known to exhibit a high proportion of NVL reactions, none of those declared non-reacting by the British Comparative test with avian PPD tuberculin gave reaction with the heat-concentrated product so as to be considered as non-specific. The distribution of combinations of responses to mammalian and avian PPD tuberculins was suggestive of the cause of hypersensitivity in this herd being more closely related to the former.

ACKNOWLEDGEMENTS

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operating in this herd is allergenically more closely related to the mammalian type than to the avian type of tubercle bacillus.

Discussion

The results of the present investigation showed that HCSM tuberculin produced uniformly milder reactions as compared to those evoked by mammalian PPD tuberculin. This observation is also supported by the recent findings of Malhotra and Pathak (1974). The former preparation cannot, therefore, be incriminated for showing up false reactions any more than PPD itself. This finding is in accord with expectation in so far as HCSM tuberculin, having been prepared on synthetic medium, contains no extraneous matter other than the active principle(s) or inert metabolites of the tubercle bacillus and left over ingredients of the medium. One of the authors (G.S.) had, on an earlier occasion, ascertained that the constituents of the synthetic medium do not elicit any reaction in animals in the maximum concentration that can possibly be present in the concentrated product.

The experience of earlier workers too has been similar. Thus, Doig *et al.*, (1938) found that reactions with PPD were much the same in character to the response elicited by O.T. in guinea pigs and man, except that PPD was somewhat more potent; and Nielsen and Plum (1940) did not find PPD tuberculin to give any clearer reaction than old tuberculin in cattle

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SERUM PROTEINS IN ANAEMIC PATIENTS OF PULMONARY TUBERCULOSIS

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Introduction

Tubercular lesions in the lungs cause not only local tissue breakdown but also other systemic effects which can get reflected as a change in the serum protein fractions and the blood hemoglobin. Mathur *et al* (1962) studied total serum proteins and its fractions in pulmonary tubercular patients and came to the same conclusion as Dhopeswarker *et al* (1960) who had published that the total serum protein and the albumin levels decreased whereas the levels of alpha-2 and gamma globulin increased. Vyas (1968) also observed decrease of albumin and the increase of alpha-2 and gamma globulins, but he observed an increase in the total serum protein levels in chronic pulmonary tuberculosis. Kuntz (1968) also stressed his observation that there was a rise in alpha-2 globulin level.

Prasad *et al* (1973) observed that with the progress of the disease there was decrease in the total serum proteins and the albumin levels. In 1974, Jha *et al* observed that there was decrease in the albumin associated with the increase in the gamma-globulin so that the total serum protein level remained usually unaffected.

The object of this study was to determine the serum proteins and the blood hemoglobin in pulmonary tuberculosis patients and to compare the observations with those of other workers, besides making some significant observations.

Material and Methods

Sixty patients (40 males and 20 females) of pulmonary tuberculosis admitted in the Chest Disease Hospital attached to S.P. Medical College, Bikaner, were studied, the selection of cases being done as under :

1. Only male cases with hemoglobin of 12 gm or less/100 ml. of blood and female cases with 10 gm or less/100 ml. were included.
2. All cases had sputum positive for A.F.B. (Acid Fast Bacilli) at the time of study.
3. Extrapulmonary tuberculosis and other diseases were excluded on clinical grounds, which included radiography and other routine tests.

4. No iron, copper or hormonal therapy was given to the patients for at least the preceding six months.
5. None of the females was pregnant.

Twenty five controls (15 males and 10 females) were also studied side by side, keeping in view their comparable socio-economic status and the age.

Total serum proteins were estimated by the biuret method (Wootton, 1964) using Spectrophotometer at 540 nm wave length. The serum protein fractions were estimated by agarose electrophoresis (Nerenberg, 1966 and Price, 1969) using barbitone buffer and Systronics type 601-1 power supply and its tank. Densitometric readings were plotted on graph paper and the results calculated as the percent of the total serum proteins. The blood hemoglobin was estimated by acid hematin method.

The statistical analysis included the calculations of mean, standard deviation, standard error of difference, "t" test and the "P" value.

Results

Observations are tabulated as under along with a scattergram, showing relation between blood hemoglobin and the total serum proteins in these cases.

Looking to table 1 it is seen that with the exception of three male cases which fall in the hemoglobin value of 4 to 5.9 gm percent, all the cases of both the sexes show corresponding rise in their total serum protein values along with the rise in their blood hemoglobin values. Table 2 shows absence of any correlation between hemoglobin values and the total serum protein values in the male cases, whereas the females show rising values of hemoglobin for the rising total serum protein values. But looking at figure 1 it is clearly seen that there is no correlation between the blood hemoglobin and the total serum protein values in either of the sexes.

Table 3 shows that there is a highly significant decrease in the total serum proteins, the albumin and the beta globulin fraction in the male cases. Alpha-2 globulin and the gamma globulin values show highly significant rise. Alpha-1

Table I
Relation of total serum proteins to blood hemoglobin

MALES			
SI. No.	Hemoglobin Gm/100ml. blood	No. of cases	Mean Total Proteins Gm/100 ml. serum
1.	4— 5.9	3	5.86
2.	6— 7.9	5	5.44
3.	8— 9.9	22	5.66
4.	10—11.9	10	5.71
FEMALES			
1.	4— 5.9	3	5.16
2.	6— 7.9	5	5.84
3.	8— 9.9	12	6.70

Table II
Relation of blood hemoglobin to the total serum proteins

MALES			
SI. No.	Total Proteins Gm/100ml Serum	No. of cases	Hemoglobin Gms/100 nil. blood
1.	3—3.9	Nil	—
2.	4—4.9	7	8.48
3.	5—5.9	20	8.33
4.	6—6.9	13	8.769
5.	7—7.9	Nil	—
FEMALES			
1.	3—3.9	1	5.0
2.	4—4.9	Nil	—
3.	5—5.9	6	7.099
4.	6—6.9	6	7.90
5.	7—7.9	7	8.25

Table III

MALES						
S.No.	Investigation	Patients (40) Mean S.D.	Controls (15) Mean & S.D.	't' Value	'P' Value &	Signi- ficance
1.	Total Proteins	5.60	6.64 0.42	6.34	<0.001 .08	H. Sig.
2.	Albumin	43.6	38 3.0	12.0	<0.001 .2	H. Sig.
3.	Alpha-1 Glob.	5.1	3.66 0.49	1.85	>0.05 .4	Nonsig.
4.	Alpha-2 Glob.	13.3	8.13 1.5	7.67	<0.001 .29	H. Sig.
5.	Beta Glob.	8.2	10.93 1.03	5.68	<0.001 .8	H. Sig.
6.	Gamma Glob.	31.6	18.93 2.4	9.9	<0.001 .7	H. Sig.
FEMALES						
1.	Total	6.25 1.05	6.55 0.45	0.40	>0.5	Nonsig.
2.	Albumin	42.45 6.5	58.2 5.1	7.19	<0.001	H. Sig.
3.	Alpha-1 Glob.	5.32 1.8	3.9 .01	2.73	<0.02 1	H. Sig.
4.	Alpha-2 Glob.	11.45 4.18	7.72 1.06	3.76	<0.001	H. Sig.
5.	Beta Glob.	10.55 2.7	10.7 1.14	0.21	>0.1	Nonsig.
6.	Gamma Glob.	30.47 6.4	19.47 3.8	5.82	<0.001	H. Sig.

- Notes:-
1. Total Proteins are in Gms/100 ml. Serum.
 2. Protein fractions are as percent of the Total Proteins.
 3. H. Sig. — Statistically Highly Significant.
 4. Nonsig. — Statistically Not significant.

male cases show significant decrease which may be accounted for by the decreased serum albumin. The female cases do not show any decrease; they show rather an increase (though insignificant) in total serum protein level. And this normal value or insignificant rise may be due to the increase in the globulin fractions which compensate or even overcompensate for the albumin decrease.

Due to the tissue damage by the tubercular lesion we do expect increase in the alpha-2 fraction of the globulins. Some workers (Mathur *et al.*, 1962 and Kuntz, 1968) have preferred the alpha-2 globulin level estimations to E.S.R. in tuberculous patients regarding both the disease status as well as the prognosis. Serum albumin decrease can mainly be explained by the fact that there is depression of liver cell function due to tubercular toxæmia. The additional responsible factors may be dietary deficiency (low socio-economic status) and anorexia. Increased protein catabolism at the site of lesions and the body's attempt for the compensation can have the effect of decreasing the levels in the body albumin pool, i.e. plasma. The hyper-gamma-globulinaemia can be due to the immunological response as can be expected in any chronic granulomatous inflammation.

There is no correlation between the total serum protein and the hemoglobin levels in these cases, which can be explained by the fact that there are other contributory factors for causing anaemia besides the total serum protein levels. Reason for studying only anaemic cases is that other investigations regarding serum iron, serum iron-binding capacity and serum copper were undertaken in these cases with the intention of finding some significant findings in regard to anaemia in pulmonary tubercular patients. These results are being published separately.

Summary

Blood hemoglobin, total serum proteins and its fractions were estimated in sixty anaemic patients of pulmonary tuberculosis and compared with those of twenty five healthy individuals. Statistically highly significant increase in alpha-2 and gamma globulins with highly significant decrease in albumin was found in the sera of these patients. No correlation was found between the blood hemoglobin and the total serum protein levels.

Fig. 1.

Scatterogram showing relation between blood hemoglobin and total serum proteins

globulin shows only insignificant rise in these male cases.

The female cases have insignificant rise in the values for total serum proteins and the beta globulins. There is highly significant decrease in the albumin and highly significant increase in the alpha-2 and the gamma globulins. Alpha-1 globulin shows a significant rise in these cases (Table 3).

Discussion

There is highly significant decrease in albumin and highly significant increase in alpha-2 and the gamma globulin levels in both the sexes. This is in conformity with the observations made by all other workers, though some publications (Heaf & Ruby, 1959; Kuntz, 1968; Prasad *et al.*, 1973; and Jha *et al.*, 1974) do not lay stress on a significant gamma globulin rise in these cases.

Regarding total serum protein levels, the

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CASE REPORTS

TUBERCULOSIS OF BREAST

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Tuberculosis of breast is considered to be a rare condition (Sandison and Walker, 1962). Incidence in Western countries has varied from 0.06 to 1.6% of all breast affections (Dawson and Marvey, 1942; Haagensen, 1956; Aureggi and Picardi, 1963; Sandison and Walker, 1968). Reports from India have described the incidence from 3.0 to 5.38% (Chaudhury, 1957; Dharkar *et al*, 1968; Dube and Agrawal, 1968 and Pratap *et al*, 1971).

We are reporting 4 cases of tuberculous mastitis which we encountered between April 1974 and March 1975.

Case Report 1 :

D.W., 35 years old, married woman was seen in the out-patients' section in August 1974 with the complaints of lump and heaviness in the right breast for three years, discharging sinuses in the right breast and axilla for one year and low grade pyrexia, anorexia and loss of weight for nine months. There was no history of contact. She had two children. She had not taken any specific treatment before reporting to us.

On examination she was found to be slightly anaemic, her pulse rate was 82 per minute and blood pressure 110/74 mm. of mercury. There was a firm, freely mobile lump palpable in the right breast, measuring 5.5cm in size. A sinus was present in the upper part with thin watery discharge from it (Fig. 1). The left breast was normal. Lymph glands in the right axilla were enlarged, matted, firm and nontender with discharging sinuses. There were no abnormal signs in the respiratory and other systems.

Blood examination revealed haemoglobin 9.5 gm% and erythrocyte sedimentation rate 45 mm. in first hour (Wintrobe). Total white cell count was 9,500 per cubic mm., with polymorphs 52 percent, lymphocytes 46 percent- and eosinophils 2 percent. Mantoux test with 2 tuberculin units was positive 18x16 mm. AFB could not be detected in the pus on direct microscopy and on culture. Skiagram chest postero-anterior view did not reveal any abnormality.

A provisional diagnosis of tuberculosis right breast was made and she was advised injection



Fig. 1.

Showing multiple sinuses in the right axilla. Right breast shows diseased area above the areola.

Streptomycin sulphate 0.75 gm. daily, Isoniazid 300 nig. once a day and para-amino salicylic acid 5 gms. twice a day. She improved clinically with marked diminution in the size of the lump and discharge from the sinuses reduced considerably. After three months the treatment was changed to isoniazid (300 mg) and thiacetazone (150mg) once daily. Five months later, the sinuses in axilla healed and the one in breast also became very small but little discharge continued. The lump almost disappeared. At this stage a local surgical excision* of the diseased areas was performed. Histological examination of the tissue revealed tuberculous granulation tissue, confirming the diagnosis of tuberculosis right breast. Chemotherapy was continued and she is progressing well.

Case Report 2 :

G.D., 45 years old, married lady was seen

* Biopsy could have been performed before start of treatment. —Editor

in December 1974 with the complaints of a gradually enlarging lump in left breast since one year. There was history of loss of appetite and weight. No contact could be traced. She had six children and the last delivery was 8 years back. She had not taken any treatment in the past.

On examination there was a lump palpable in the upper inner quadrant of left breast, 4x4cm. in size, firm and mobile. Nipple and areola were normal. Right breast was normal. Lymph glands in the left axilla were enlarged, firm and discrete. Respiratory system examination revealed no abnormal signs. Other systems were normal.

Haemoglobin was 10.5 gm% and erythrocyte sedimentation rate 55 mm in first hour (Wintrobe). Total white cell count was 10,000 per cubic mm. with polymorphs 62%, lymphocytes 36 %, eosinophils 1 % and monocytes 1 %. Mantoux test with 2 tuberculin units was 10 x 10 mm. Skiagram chest did not reveal any abnormality.

A clinical diagnosis of carcinoma of left breast was made and radical mastectomy was performed. Breast on cut surface showed typical caseating tubercular granulation tissue, which was confirmed on histological examination (Fig. 2). She was given streptomycin, isoniazid and para-amino salicylic acid in standard dosages, on which she showed improvement.

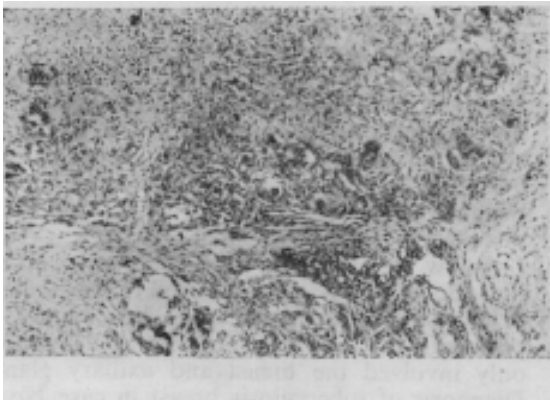


Fig. 2.

Photomicrograph showing widespread granulomatous lesion leaving only a few isolated breast ductules (center). H & E x 70.

Case Report 3 :

S.S., 22 years old, married lady presented two years back with pyrexia, dry cough, loss of appetite and marked weakness. She had no

children. Her mother was suffering from tuberculosis.

On examination, pulse rate was 110 per minute and blood pressure 116/78mm. of mercury. There were no abnormal signs in the chest. Liver and spleen were slightly enlarged. Other systems were normal.

Routine haemogram showed slight polymorphonuclear leucocytosis and erythrocyte sedimentation rate was 38 mm. in first hour (Wintrobe). Skiagram chest revealed fine miliary opacities in the both lung fields. She was diagnosed as a case of miliary tuberculosis and she was given streptomycin, isoniazid and para-amino salicylic acid daily in standard dosages with corticosteroids. She improved clinically and the miliary shadows cleared up. Corticosteroids were tapered off and streptomycin was withdrawn after three months. Treatment became irregular after six months and it was taken interruptedly during the succeeding year.

About April 1974, she developed low grade fever and other general toxæmic symptoms. She also developed two small nodules in the region of areola of left breast which later burst open and formed sinuses discharging a thin watery fluid. Examination of the fluid did not reveal tubercle bacilli or any other organisms. Skiagram chest showed complete resolution of shadows.

This lesion in breast was considered to be a complication of haematogenous tuberculosis. She was given ethambutol, prothionamide and isoniazid in standard dosages. She showed improvement on this therapy but sinuses did not heal completely and the discharge continued. After six months a local excision was performed. Histology of the tissue revealed tuberculous granulation tissue (Fig. 3). Chemotherapy was continued and since then she is perfectly well.

Case Report 4 :

B., aged 28 years, mother of five children presented in March 1975 with a lump in right breast along with multiple sinuses on the surface, loss of appetite and low grade pyrexia for ten months. There was history of cough haemoptysis and fever two years back when she was treated as a case of pulmonary tuberculosis with streptomycin and isoniazid which she took only for three months. Presently there were no chest complaints. She did not take any specific treatment, for her breast ailment.

On examination, there was a lump palpable in the lower part of right breast which was

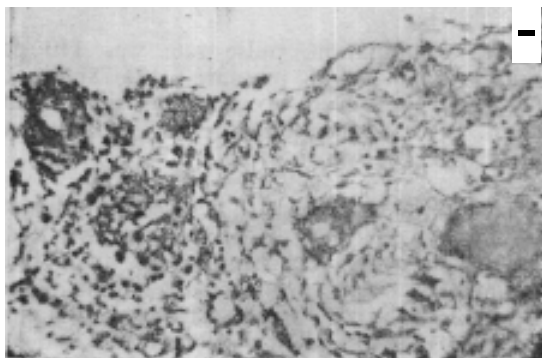


Fig. 3.

Photomicrograph showing a tubercle with giant cell (T). Disorganized breast ductules are seen on the left. H & E x 200.

4 x 5 cm. in size, firm, mobile and nontender. Nipple was slightly retracted. There were multiple sinuses present all along the lower border of the areola (Fig. 4). The left breast was normal. Right axillary lymph nodes were enlarged, firm and mobile. Respiratory and all other systems were normal.

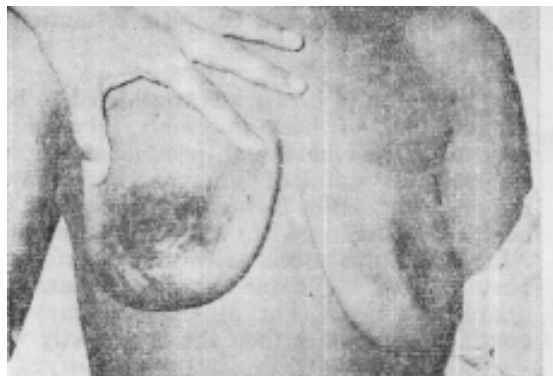


Fig. 4.

Showing multiple sinuses present all along the lower border of the areola.

Blood examination revealed haemoglobin 13.5 percent, erythrocyte sedimentation rate 28 mm. in first hour (Wintrobe) and white cell count 9,900 per cubic mm. with polymorphs 67 percent, lymphocytes 26 percent and eosinophils 7 percent. Previous skiagram chest of January 22, 1973 showed exudative lesion in the right upper and middle zones. Recent skiagram dated March 12, 1975 was normal. Biopsy from breast lesion revealed tuberculous granulation tissue.

A diagnosis of tuberculosis of right breast was established and she is being given streptomycin, ethambutol and isoniazid in standard dosages.

Discussion

Breast is not a common site for localization of tuberculosis. Incidence as reported in the Western literature is low, ranging from 0.06 to 1.6% (Dawson and Harvey, 1942; Carinci, 1956; Haagensen, 1956; Logino, 1962; Sandison and Walkar, 1962; Aureggi and Picardi, 1963).

Chaudhury (1957) is credited with the first report of breast tuberculosis from India. He reported 13 cases with an incidence of 3%. Isolated cases have been described from time to time, but detailed reports are few. Dharkar *et al.* (1968) reported 4 cases of breast tuberculosis out of 113 breast lesions in one year (3.5%). Dubc and Agarwal (1968) described 20 cases out of 445 breast lesions (4.5%) in 10 years. Pratap *et al.* (1971) have reported 23 cases out of 437 breast lesions (5.38%) in a 13 years period. We encountered 4 cases out of 110 breast lesions (3.63%) during one year.

Women in the younger age group i.e. 20-35 years are more often affected (Sandison and Walker, 1962; Aureggi and Picardi, 1963). One of our patients was a 45 years old lady and the remaining three belonged to the age group of 22-35 years. It is extremely rare in males.

Tuberculous mastitis may be seen as an apparently primary condition, where it is assumed to be of haemotogenous origin. But probably more instances are secondary to tuberculosis of ribs, sternum or lungs and may present as an inframmary cold abscess. In some cases passage from tracheo-bronchial or internal mammary lymph nodes and thence to breast has been postulated (Sandison and Walker, 1962). Loginow (1962) in his case could not succeed in detecting the primary location of tuberculosis in the body. Here in our cases Nos. 1 and 2 no primary site could be established as the process only involved the breast and axillary glands. Diagnosis of tuberculosis breast in case No. 1, was mainly clinical based on symptoms of tubercular toxæmia, findings of lump in right breast with discharging sinus, enlarged draining glands with multiple sinuses and a strongly positive mantoux test. She responded well to the antituberculous chemotherapy. Later diagnosis was confirmed by biopsy whereas in case No. 3 it was a part of generalised haemotogenous disease for which she did not take treatment regularly. Biopsy in these cases was not advisable because of active, progressive and untreated

disease. Wolf and Peak (1969) have also stressed on a clinical diagnosis in these cases. In both the cases excisional biopsy was not required for diagnosis but for therapeutic purposes. In case No. 4 it followed pulmonary tuberculosis which was inadequately treated two years ago.

Lesions are mostly unilateral with localization in supero-external segment (Aureggi and Picardi, 1968). Pain may be present and sometimes fistulae form. A clinical diagnosis has been stressed by Wolf and Peak (1969). A confirmed diagnosis is established histologically (Carinci, 1956; Logino, 1962; Aureggi and Picardi, 1963).

Radical surgery is seldom necessary (Case, 1959). Local excision followed by chemotherapy is now-a-days regarded as the treatment of choice (Wolf and Peak, 1969), but in diffuse lesions a radical mastectomy may be required (Aureggi and Picardi, 1968). In two of our cases local excision was done after treating with antituberculosis drugs. Results were good in both the cases.

In case No. 2 a provisional diagnosis of carcinoma was made and radical mastectomy was performed which grossly and histologically showed caseous tuberculosis. Truni and Gazzano (1957) have also stressed that closed forms are easily taken for cancer. Sandison and Walker (1962) in one of their 8 cases of tuberculosis breast performed radical mastectomy thinking it to be carcinoma. In such cases, the possibility of a tuberculous lesion should be considered and diagnosis should be confirmed by biopsy examination before proceeding with mastectomy. This is specially significant in our country where the incidence of tuberculous mastitis does not appear to be as low as recorded in the Western countries (Dube and Agarwal, 1968).

Summary

Four cases of tuberculosis of breast are reported, underlining the fact that tuberculosis

of breast is not so rare in India as reported in Western literature. Relevant literature is briefly reviewed.

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PULMONARY TUBERCULOSIS AND LEUKEMIA

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Leukemoid reaction is known to occur in active tuberculosis and may cause confusion with leukemia (Wintrobe, 1967); sometimes leukemia may involve the lung and simulate pulmonary tuberculosis (Perry & Holmes Sellors, 1963). The tuberculous infection is often miliary. Andre *et al* (1961) have suggested this possibility of tubercle bacilli as a causative agent of leukemia. The occasional association of leukemia and tuberculosis has therefore aroused considerable interest. In the earlier studies of Susman (1993) and Wintrobe and Hasenbugh (1939) tuberculosis was found less frequently in leukemia patients than in the general population. The later studies of Parker *et al* (1932), Kirshbaum and Preuss (1943), Abbat & Lea (1957), Lowther (1959) and Horrow & Anderson (1965) revealed tuberculosis to be equally frequent in leukemic and non-leukemic patients. Coburn *et al* (1973) found active tuberculosis associated more frequently with haematological diseases as compared to other patients. They have given a review of literature and added the study of 130 cases of their own. With such divergent views in literature, we present here our findings of a review of the hospital records of tuberculosis and leukemia cases with special reference to co-existence of the two diseases.

Material and Methods

Clinical records of all cases of pulmonary tuberculosis and leukemia seen in the Outpatients' Department and Medical Wards of Jawaharlal Nehru Medical College Hospital, Aligarh during the year 1970-74 were reviewed. Tuberculosis was diagnosed on the basis of clinical features, chest X-rays, and sputum examination, and leukemia on the basis of clinical features and peripheral blood film examination.

Results

Total of 63,674 cases of pulmonary tuberculosis were seen in Tuberculosis outpatients section of the hospital. Of the 9,131 cases admitted in the Medical Wards, there were 1,200 (13.3%) cases of pulmonary tuberculosis, and 45 (0.49 %) cases of leukemia of whom 7 were acute leukemia, 3 chronic lymphatic leukemia, and 35 chronic myeloid leukemia. Among all the cases reviewed only one case was found in whom there was co-existent pulmonary

tuberculosis and leukemia (of the chronic myeloid type). This case is described in detail below. The prevalence of tuberculosis among all leukemia cases was therefore 2.2%, and among chronic myeloid leukemia 2.9%. There was no case of leukemoid reaction among the 64,874 cases of tuberculosis, and also there was no case of leukemic involvement of the lung detectable by chest X-ray among the 45 cases of leukemia.

Case Report:

S.S., 40 years old male farmer, was admitted on 16.12.72 with progressively increasing lump in left upper abdomen for 2 years and increasing weakness and fatigue for 11 years. In addition, he had cough with expectoration and evening rise of temperature for 4 months before admission. There was no history of haemoptysis or chest pain. He smoked 10-12 'bidis' per day for 25 years.

Physical examination disclosed pallor, but there was no icterus, cyanosis, clubbing of fingers, lymphadenopathy or pedal oedema. His temperature was 99° F pulse 100 per minute and regular, and blood pressure 126/78 mm Hg. There was bronchial breathing in left upper lung field and coarse and fine crepitations in both upper and left mid-lung fields, the spleen was enlarged to 18 cm and liver 2 cm below the costal margin. There was no free fluid in the abdomen, and examination of other systems revealed no abnormality. A roentgenogram of the chest showed a large cavity in the left upper zone and infiltration in left middle and right upper zones (Fig. 1). Sputum smear was positive (+ + +) for acid-fast bacilli and sputum culture grew mycobacterium tuberculosis. Examination of the peripheral blood revealed haemoglobin 6.5 gm%, and total leucocyte count 1,74,800/c mm. Differential leucocyte count showed 58% immature cells (myelocytes 31 %, metamyelocytes 18%, blast cells 9%). 40% polymorphs, and 2% lymphocytes, leucocyte alkaline phosphatase score by Kaplow (1955) technique was 3, 5, and 7 on three successive occasions. Fasting blood sugar, blood urea, serum bilirubin, serum alkaline phosphatase, serum glutamic oxalacetic and pyruvic transaminases were all normal.

The patient was treated with streptomycin

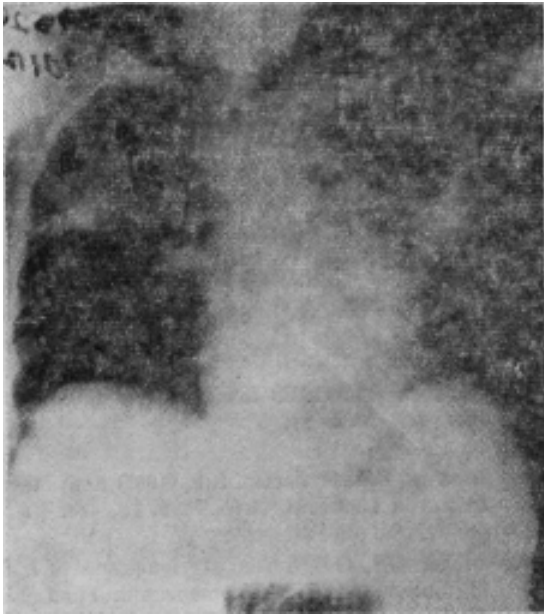


Fig. 1

0.75 gm intramuscularly, Isoniazid 300 mg and Thiacetazone 150 mg once daily for tuberculosis, and Busulfan 4 mg daily for leukemia. After two months' treatment, he was afebrile and chest systems had subsided. The chest X-ray showed marked clearing of infiltrate and decrease in cavity size, and sputum became negative for acid-fast bacilli. The spleen remained only just palpable under the left subcostal margin, and total leucocyte count dropped to 9,000/c mm with 70% polymorphs, 15% lymphocytes, 2% eosinophils and 13% immature cells (myelocytes and metamyelocytes) and haemoglobin concentration increased to 10 gm%. He was discharged with advice to continue streptomycin 0.75 gm. Isozone Forte 1 tablet and Busulfan 2 mg daily.

Discussion

The occurrence of co-existent leukemia and tuberculosis was found to be very infrequent among the cases seen in our hospital. Compared to the general hospital incidence of 13.3%, the incidence of tuberculosis among leukemia cases was only 2.2%. This was very similar to the results of a post mortem survey by Susman (1903) who found 41 cases of leukemia of whom only one (i.e. 2.4%) had tuberculosis, in contrast to 877 cases of tuberculosis (i.e. 12.2%) among the 7,200 necropsies reviewed. The rarity of co-existence of these two diseases was also testified by Wintrobe & Hasenbugh (1939) who found

no case of tuberculosis among 86 cases of leukemia. On the other hand, Parker *et al* (1932) found tuberculosis in 10% of 81 cases of leukemia which was the same as the general hospital incidence of tuberculosis, and Kirshbaum & Preuss (1943) found tuberculosis in 13% of 128 cases of leukemia which was also similar to the incidence of tuberculosis among their non-leukemic patients. Abbat & Lea (1957) and Morrow & Anderson (1965) also found tuberculosis to occur about equally frequently in leukemia and in the population generally. Lowther (1959) found that during 27 years (1925-52) there were 16 (6.4%) cases of active tuberculosis out of 266 patients with leukemia who came to autopsy. Oswald (1963) during a 31 years survey found tuberculosis in 8.7% of his 242 cases. Muller (1943) found 12.8% of 86 patients with leukemia had active tuberculosis. O'Brien (1954) reviewed 66 cases of non-reactive tuberculosis and found 13 patients (19.7%) having leukemia. It was suggested that blood changes were due to either depression of cell mediated immunity in leukemia which permits activation of a latent tuberculosis infection, or fresh opportunistic infection, and loss of immunity due to antileukemic therapy. Susman (1903) found that when leukemia and tuberculosis co-existed, it was 2.5 times more frequent with lymphatic than with myeloid leukemia. But Lowther (1959) and Morrow & Anderson (1965) found it about twice as frequently with chronic myeloid leukemia as with other types of leukemia. The only case of co-existent tuberculosis and leukemia found in this study was that of chronic myeloid leukemia. But the number of cases of other types of leukemia were too small to give any idea of the incidence of tuberculosis in them.

Among the 63,674 cases of tuberculosis reviewed in this study, only one case of leukemia was found. This argues against the suggestion of Andre *et al* (1961) that tubercle bacilli may be a causative agent of leukemia, because if it was so, more cases of leukemia should have been expected amongst the tuberculosis cases. We therefore agree with Morrow & Anderson (1965) who concluded that there is no evidence to support the concept that tuberculosis is involved in the genesis of myeloproliferative disorders.

Leukemic involvement of the lung may cause pulmonary parenchymal infiltration, miliary or submiliary nodulations, reticulations, cavitation, pleural effusion, or hilar adenopathy (Perry & Holmes-Sellers, 1963). In acute leukemia, although autopsy may show lung involvement in as many as 25% cases, radiologically detectable abnormalities are rare (Nathan & Sanders, 1955). Among the chronic leukemias, lung involvement is much more frequent in the

lymphatic than in the myeloid type. Vieta & Graver (1941) found radiologically detectable pulmonary involvement in 25% of chronic lymphatic leukemia cases but in only 8% of chronic myeloid leukemia. In the present study there were 45 cases of leukemia of whom only seven were acute leukemia and three chronic lymphatic leukemia. The remaining 35 cases were of chronic myeloid leukemia, and radiologically detectable lung involvement by leukemia was not found in any of them.

Leukemoid reaction can occur in association with many infections, but most frequently with tuberculosis (Wintrobe, 1961). The incidence of leukemoid reaction in tuberculosis is not known, but it usually occurs in miliary tuberculosis (Wintrobe, 1967). Among the 63,674 cases of tuberculosis reviewed, there were only three cases of miliary tuberculosis, leukemoid reaction was not found in any case.

It thus appears that while co-existence of leukemia and pulmonary tuberculosis is rare in our patients, the incidence of leukemoid reaction in tuberculosis or of leukemic involvement of the lung is equally rare or perhaps even rarer. This study reinforces the view of Shohet & Blum (1968) that efforts must be made to establish the diagnosis of both the diseases when a patient presents with elevated immature leucocyte count and X-ray picture suggestive of tuberculosis, rather than considering one disease as an explanation for both lesions. This is important for planning correct line of treatment. The case presented here demonstrates that both diseases respond well to specific therapy for the two diseases given simultaneously.

Summary

Clinical records of 64,874 cases of pulmonary tuberculosis and 45 cases of leukemia were reviewed. Only one case was found to have co-existent pulmonary tuberculosis and chronic myeloid leukemia. Diagnosis of tuberculosis was established by positive sputum culture, and of the leukemia by peripheral blood smear findings and low leucocyte alkaline phosphatase scores. Both diseases responded well to specific therapy for both diseases given simultaneously. Leukemoid reaction was not found in any case of tuberculosis, and leukemic infiltration of the lung was not detected in any case of leukemia. The importance of establishing the diagnosis of both diseases by specific laboratory studies in such cases is emphasised.

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PARKINSONIAN SYMPTOMS IN TUBERCULAR MENINGITIS

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Parkinsonism is a clinical syndrome which results from damage to the globus pallidus and substantia nigra. It is a progressive disease of insidious onset and slow course, usually occurring in second half of life. It is characterised by (1) Akinesia, bradykinesia and mask like face, monotonous speech, stopping posture and shuffling gait, (2) Rigidity usually 'cog wheel' type, but some time lead pipe type may be seen, (3) Tremors rhythmic, fine to coarse tremors are seen which are present at rest but inhibited by voluntary movements.

The commonest type is idiopathic paralytic agitans. Post-encephalitic, drug induced (Phenothiazine group), poisoning with carbon monoxide, manganese and arteriosclerotic types are other common varieties. Tuberculous meningitis is known to produce a wide variety of neurological complication like epileptic fits, hemiplegia, cranial nerve palsies, parnlegia, mental changes, deafness, hydrocephalus. But Parkinsonism, as a complication of tuberculous meningitis, is extremely rare in the literature. We report here three cases because of its rarity.

Case No. 1:

S, aged 16 years admitted in March 1968 with a history of vomiting for 6 days, headache for 4 days and weakness on the right side of body for 2 days. No history of fever or cough.

Examination revealed a young girl, moderately built, pulse 90/mt. regular, temperature 100°F and blood pressure 100/70 mm. Hg. She was irritable with positive signs of meningeal irritation. Examination of the motor system showed mild right-sided weakness and typical parkinsonian tremors with cog wheel rigidity of both lower limbs. The signs were more obvious on the right side. All the tendon reflexes were brisk and planters were extensor. Fundi were normal, pupils on both sides equal in size and reacting to light. There were signs of cavity on the left apex and crepitations in the same area.

On investigations, her haemoglobin was 9

gin%, total leucocyte count 9,000 cmm. Erythrocyte sedimentation rate 60 mm 1st hour (Westergren's). Sputum for A.F.B. was positive. Skiagram of the chest showed small cavity in the left upper zone. X-ray skull was normal. Left carotid angiogram showed narrowing of the left middle cerebral artery just distal to its origin (Fig. 1).



Fig. 1

On lumbar puncture the C.S.F. pressure was raised to 270 mm. and it contained 150 cells/cmm, all lymphocytes. The proteins were 160 mg%, sugar 20 mg% and chloride 590mg%. The smear did not show any A.F.B. She was put on streptomycin 1gm. daily, I. N.H. 600 mg. and 12 gms. of PAS with 60 mg of prednisolone.

The above treatment was continued. She used to walk with short steps. After six weeks of treatment her CSF almost returned to normal, hemipresis completely recovered and parkinsonian

symptoms also showed improvement. But the Parkinsonian symptoms completely regressed after four months. After this the patient did not come for follow up, so could not be followed further. Again, she was admitted to hospital after 10 months for a similar episode. She was again put on antitubercular treatment with prednisolone and she completely recovered within four weeks (Patient had stopped the antitubercular treatment at home). She was regularly followed up for one and half year and had complete recovery.

Case No. 2 :

G, aged 24 years, admitted on 22.10.71 with the chief complaints of vomiting off and on for 9 months, headache for 1 week, no history of pyrexia or cough.

Examination revealed a young lady, moderately anaemic, pulse 80/minute regular, temperature normal and BP 120/80 mm. Hg. She was irritated with positive signs of meningeal irritation. During her stay in the hospital after two weeks she developed right-sided hemiplegia with motor aphasia. Pupils were equal, reacting to light. Fundi were normal. She developed mask-like face, typical Parkinsonian tremors with cog wheel rigidity of both upper and lower limbs. There was no apparent sensory deficit. All the tendon reflexes on the right side were brisk with bilateral planter extensors.

On investigation, her hemoglobin was 10 gm%. total leucocyte count 15,700/cmm. Erythrocyte sedimentation rate 36 mm first hour (Westergren's). Skiagram of the chest and skull were normal. Left carotid angiogram revealed complete block of the left middle cerebral artery at its origin (Fig. II).

On lumbar puncture, the cerebrospinal fluid pressure was 350 mm. and the cobweb formed. It contained 450 cells/cmm. all lymphocytes. The proteins were 144 mg. %, sugar 194 mg% and chloride 610 mg%. The smear did not show any acid fast bacilli but on culture A.F.B. was grown. She was put on streptomycin 1 gin. daily, 600 mgs. I.N.H. and 15 gms. of PAS with 60 mg. of prednisolone. She was given physiotherapy and speech therapy.

Six weeks after the treatment patient started showing improvement. Her power in right lower limb improved almost to normal but power in the upper limb improved only 3/5. The rigidity, tremors of the hands improved, pill-rolling movements also improved. She was discharged from the hospital after four months, on antitubercular treatment only. She was regularly

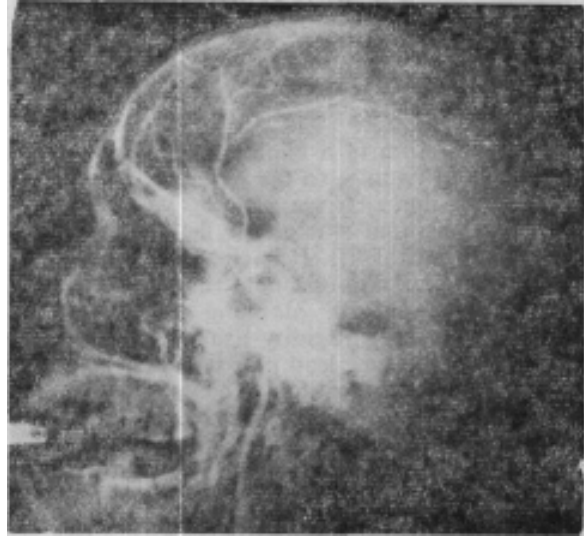


Fig. 2

followed up for two years. Within one year of treatment she showed remarkable improvement in hemiplegia & Parkinsonian symptoms completely disappeared, but aphasia was only partially cured.

Case No. 3 :

A, aged 14 years, Hindu female was admitted in June 1973 with history of fever for 5 days, generalised fits for 1 day, unconsciousness for 1 day. Five months earlier patient had tubercular osteomyelitis of medial and of left clavicle. She was taking antitubercular treatment irregularly.

Examination revealed emaciated young girl with mask like face, dehydrated. Cervical lymph glands enlarged about 1 inch by 1 inch, firm and matted. Pulse 120/mt. regular, good in volume. Blood pressure 110/70 mm., temperature 103°F. She was very irritable, did not like to be examined and lied curled up in bed. Neck rigidity and kernings signs were positive. The fundi were normal. There was left-sided upper motor neuron type of hemiplegia. The tendon reflexes were exaggerated and planters were extensor. The pupils were equal and reacting to light. Respiratory and cardiovascular systems did not reveal any abnormality.

Investigations

Her haemoglobin was 8 gm. %, total leucocyte



Fig. 3

count 6,000/cmm. Erythrocyte sedimentation rate was 65 mm in the first hour (Westergren's), X-ray skull showed a punched out area in the left parietal bone 1 cm by 1 cm, X-ray chest was normal. Pneumoencephalogram was normal. Right carotid angiogram showed block at the origin of right middle cerebral artery but good collateral circulation.

On lumbar puncture the cerebrospinal fluid pressure was 250 mm. and cobweb formed. It contained 50 cells/cmm all lymphocytes. The proteins were 100 mg%. The smear did not show acid fast bacilli. Culture revealed acid fast bacilli.

She was put on streptomycin 1 gm daily, 600 mgs I.N.H. and 10 gms of PAS with 40 mg of prednisolone per day. Patient started to improve clinically, temperature settled down, she became cooperative, her hemiplegia completely recovered within two weeks time. But during this phase she developed excessive sweating salivation, cog wheel rigidity in the limbs. The upper limbs demonstrated typical pill-rolling Parkinsonian tremors. She walked with short steps with a tendency to fall forward. Neck

rigidity & kernings sign also disappeared completely in four weeks time.

The above treatment was continued and within 6 weeks of this, CSF returned to normal with 4 lymphocytes per cmm and 40 mg% proteins. Although the Parkinsonian features improved but still patient complained of stiffness and tremors. She was discharged from the hospital and has been followed up further for one and a half year. Her Parkinsonian symptoms had completely improved within six months. Corticosteroid were tailed off after three months. Patient still gets epileptic fits off and on.

Comments

These three cases were detected during routine cerebral angiography in cases of tuberculous meningitis. The clinical features of Parkinsonism were noted in these cases during the course of the disease. Aetiological relationship is further strengthened by the fact that the clinical features of Parkinsonism vanished almost completely with anti-tubercular therapy.

In all the three cases there was no history of phinothiazine group of drugs being used in the past. They were all young and did not show any other disease known to be associated with Parkinsonism.

In all these cases the cerebral angiography revealed narrowing and blocking of middle cerebral artery respectively. Probably this was due to tuberculous arteritis. Same type of arteritis might have occurred in the striate branches of the middle cerebral artery and perforating branches of the anterior cerebral artery which supply the globus pallidus, thus causing vascular insufficiency or vascular occlusion to the globus pallidus. It is well known that multifocal cerebral softening due to vascular occlusion is the basis of Parkinsonism due to cerebral arteriosclerosis.

It is thus presumed that Parkinsonian features in tuberculous meningitis were probably due to tubercular arteritis causing ischemia of globus pallidus.

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TUBERCULOUS OSTEOMYELITIS OF ZYGOMATIC BONE

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Involvement of skull bones in tuberculosis is uncommon. Whenever present, it usually occurs within the vault in young people. Tuberculous involvement of mastoid process of malar bone is extremely rare (Wright and Handfield-Jones, 1957). Recently we have encountered a case of tuberculous osteomyelitis of zygomatic bone which is being presented because of its rarity.

Case Records

A boy aged 10 years was admitted with complaints of discharging sinus over left cheek for last 8 months and swelling over left side of neck for last 4 months. Eight months ago patient developed a painful swelling over left cheek which burst a fortnight later. The swelling subsequently subsided, leaving a pus discharging sinus which was persisting since then. Four months ago the patient also developed swelling on the left side of neck which increased in size for initial 2 months but later its course became stationary. There was no history of tuberculosis in the family.

The clinical examination revealed that the child was undernourished and anemic. Pulse, respiration and temperature were normal. Local examination revealed a swelling over left cheek bone in the centre of which a pus discharging sinus was present. Swelling was about 2.5 cm in diameter and was situated slightly below and lateral to left eye. Surface was smooth and the margins were diffuse. There was no change in the colour of the skin except slight pigmentation around the sinus. Local temperature was not raised. The swelling was tender and bony hard in consistency; the skin over it was free except in the vicinity of the sinus. Mouth of the sinus was about 5 mm in diameter; granulation tissue were sprouting out of it and yellowish pus discharge was present. It was fixed to the bone underneath. A probe could be passed posteriorly for about 1.5 cm. The cervical lymph nodes on the left side were enlarged and matted and measured 8 x 5 in size. There was no tenderness and local temperature was not raised. Skin over the glands was free.

Investigations

The haematological examination revealed a

haemoglobin content of 9.5 g percent, total leucocyte count 6,800/cu mm with a differential as polymorphs 51 percent and lymphocytes 49 percent. The corrected erythrocyte sedimentation rate for first hour was 36 mm (Wintrobe). Urine and stool examination revealed nothing abnormal. The Mantoux test was positive. X-ray of the skull (occipito-mental view) showed rarefaction and destruction of left zygomatic bone (Fig 1). X-ray chest (P.A. view) showed almond size radio-opaque shadow in right hilum with increased broncho-vascular markings on right side.



Fig. 1.

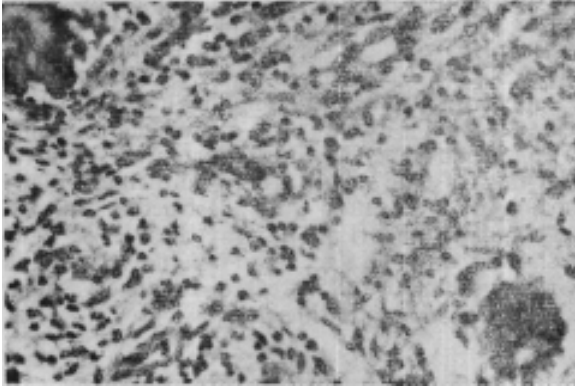
X-ray skull (occipito-mental view) showing rarefaction and destruction of left zygomatic bone.

Surgery

Curettage was done under general anaesthesia. At operation the zygomatic bone was found necrosed and replaced by granulation tissue which was curetted and sent for Histopathological examination. A cervical lymphnode was also removed for histological examination.

Histopathology

The histological features of the curetted material were that of tuberculous osteomyelitis (fig. 2) and the cervical lymph node showed tuberculous lymphadenitis.



Photomicrograph showing **histopathological** features of tuberculous osteomyelitis. (H & E x 100).

Treatment and Follow-up

The patient was given antitubercular treatment consisting of streptomycin 0.75 g IM1 and I.N.H. 300 mg daily. He was discharged on 15th post-operative day, the sinus had healed by that time. The patient was advised to continue anti-tubercular treatment at home. A six month follow-up showed no palpable lymphnode in the neck and no recurrence of sinus.

Discussion

Tuberculosis of bone with rare exceptions is always secondary to an established focus of tuberculosis elsewhere in the body (Sharrard, 1971). Two types of bony tuberculosis are

recognized (Chaduley, 1968) (i) tuberculous osteitis : which starts as blood borne infection lodging in the cancellous bone and (ii) periosteal tuberculosis : which commonly affects the flat bone e.g. the sternum, skull or ribs, commences in the deeper layers of the periosteum which becomes oedematous and is soon separated from the underlying bone by granulation tissue, caseation and cold abscess formation follow, the superficial structures becoming progressively adherent and invaded while the bone itself is eroded. Finally the skin is involved and the abscess discharges on the surface and secondary infection may follow.

The present case appears to be of periosteal tuberculosis. The primary focus appeared to be present in the lung which secondarily infected the zygomatic bone. The invasion of cervical lymphnodes by tuberculous process in this case appears to be a result of lymphatic extension.

The patient showed complete cure after curettage followed by anti-tubercular treatment. This is in agreement with the observations of Mukhopadhya and Mishra (1957), who have reported uniform success with radical curettage in bony tuberculous sinuses.

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NEWS & NOTES

31ST NATIONAL CONFERENCE

The 31st National Conference on TB & Chest Diseases was held in Lucknow from 15th to 19th November, 1976. Dr. Tahir Mirza of Kashmir was the President. The Conference was inaugurated by Dr. M. Channa Reddy, Governor of Uttar Pradesh. Over 300 delegates attended it. Important papers presented at the Conference as also summaries of other papers will be published in the April 1977 issue of the Journal which will be brought out as the 'Conference Number'.

32ND NATIONAL CONFERENCE

The 32nd National Conference on TB & Chest Diseases will be held in Trivandrum, Kerala, in November/December, 1977. Subjects selected for the Conference are: (1) National TB Control Programme—including the role of TB Associations and other voluntary organisations in the working of the programme, (2) BCG vaccination—its present position, efficacy and operational aspects, (3) Epidemiology of TB in India, (4) Chemotherapy, including short-term regimens, (5) Hypersensitivity diseases of the lung, (6) Direct smear Microscopy for case-finding and follow-up, (7) Training Programme (8) Urban TB Control Programme, (9) Immunology of Tuberculosis, (10) Tuberculosis in Industry and assorted papers. Those who wish to present papers may inform the Secretary-General, Tuberculosis Association of India, together with an abstract of the paper latest by 31.3.1977.

HEALTH VISITORS' COURSE

The 1977-78 TB Health Visitors' Course will commence in July, 1977. The course will be of nine months duration, of which five months will be spent in New Delhi TB Centre, two weeks in a rural health Centre, two weeks for examination and three months internship (including two weeks in a rural centre in Pataudi, District Gurgaon). The minimum qualification for admission to this course is Higher Secondary/Pre-University with Science or Hygiene and Physiology in matriculation. Application for admission to this course should reach the Secretary-General, TB Association of India, 3, Red Cross Road, New Delhi by 30th April, 1977.

CHANCHAL SINGH MEMORIAL AWARD —1977

The Tuberculosis Association of India will award a cash prize of Rs. 500/- to a TB Specialist

preferably below 45 years of age, for an original article not exceeding 30 double-spaced foolscap typed pages (approximately 6,000 words) excluding charts and diagrams on a subject relating to tuberculosis. Papers may be sent in quadruplicate, to reach the office of the TAI before 31st August, 1977.

REFRESHER COURSES

A Refresher Course in Tuberculosis for general practitioners was organised by the New Delhi TB Centre from 1st to 6th November, 1976. Dr. M.S. Chadha, Chairman of the Centre and Vice-Chairman of the Tuberculosis Association of India, inaugurated the course. Seventeen doctors from nine States and Union Territory of Delhi attended the course. There were four doctors from Uttar Pradesh, two each from Punjab, Bihar, Kerala and Delhi and one each from Haryana, Himachal Pradesh, Orissa, Maharashtra and Tamil Nadu. The candidates who came from outside Delhi were paid rupees one hundred each, towards out of pocket expenses.

The TB Association of Agra organised a refresher course from 7th to 12th February, 1977 for the benefit of doctors from Agra and neighbourhood.

PROF. DADDI

Professor G. Daddi, former Director of the Forlanini Institute, Rome, Italy gave a lecture on "Recent Advances in Chemotherapy of Tuberculosis" in the Conference Hall of the Association on 19.1.1977. The lecture was largely attended by TB workers and chest specialists in Delhi.

EASTERN REGION CONFERENCE

The Eleventh Conference of the Eastern Region of the International Union Against Tuberculosis will be held in Colombo in 1979 under the joint auspices of the Sri Lanka National Association for the Prevention of Tuberculosis and the Eastern Region of the International Union Against Tuberculosis.

IUAT CONFERENCE

The 24th World Conference on Tuberculosis and its allied meetings under the auspices of the I.U.A.T. will be held in Brussels in 1978. This conference will be known as "World Conference" of the Union. Prof. Gyselen of Belgium is the President of this Conference.

RAJAJI TB SANATORIUM

Rajaji TB Sanatorium in Tiruchirapalli, one of the oldest TB institutions in the country, has been taken over by the Government of Tamil Nadu on 5th January, 1977.

SHRI AMRUT MODY ANNUAL AWARDS

Shri Amrut Mody Research Foundation invites nominations from scientists and research workers for their two annual awards of Rs. 10,000/- each, one in the field of "Special branches of Medicines" and the other in the field of "Pharmacy and Pharmaceutics". Details can be had from the Secretary, Amrut Mody Research Foundation, Unichem Bhavan, S.V. Road, Jogeswari, Bombay.

ADVANCES IN INTERNAL MEDICINE

The Medical Research Centre of Bombay Hospital Trust will be organising a International Conference on Advances in Internal Medicine in Bombay at Birla Matushri Sabhagar from 8th to 11th January, 1978. Details can be had from the Organising Secretary, Medical Research Centre of Bombay Hospital Trust, Sir Vithaldas Thackersey Marg, Bombay-400 020.

OBITUARY

Lt.-Col. Jaswant Singh, former Director General of Health Services and Chairman of the Tuberculosis Association of India, passed away in New Delhi on 13th February, 1977. As Chairman of the Association from September 1957 to February 1960, he guided the activities of the Association with cool judgement and wide experience in public health matters. We offer our sincere condolences to the bereaved family.

Lt.-Col. V. Srinivasan, former Director General of Health Services and Chairman of the Tuberculosis Association of India, passed away recently in Madras. He was Chairman of the Association from 1960 to 1962 and guided the activities of the Association efficiently. We offer our sincere condolences to the bereaved family.

Dr. S.K. Shome, a TB specialist of Delhi, passed away after a brief illness on 26th November, 1976. Dr. Shome was the Assistant Director (Microbiology), National Institute of Communicable Diseases, Delhi, and a very enthusiastic TB worker. The TB Association of India conveys its deepest condolence to the members of the bereaved family.

* * *

NEWS FROM STATES

Andhra Pradesh

The Andhra Pradesh Association organised a Symposium on National TB Control Programme in Hyderabad on 4th December, 1976. Inaugurating the Symposium Sri K. Rajamallu, Minister for Health, said that diagnostic and treatment facilities should be available to the rural masses and all sections of the community should be involved in the TB Control Programme. Dr. S.N. Mathur, Director of Medical & Health Services, referred to the false propaganda against BCG and asked responsible persons to counter it. Papers were presented by Drs. O.A. Sharma, Srinivasa Rao, Mrs. V. Chittiseshu, Raja Rao, Narasimham and Shri B. Narasiah. Dr. D.R. Nagpaul, the Moderator, stated that the Peripheral Health Institutions have failed to deliver goods and the reasons for this were (1) the doctor has not applied his mind to the control of diseases, (2) nobody in PHI's is assigned with special responsibilities for the work and (3) DTO is not given proper administrative set up. He suggested that a multipurpose worker be appointed in the Peripheral Health Institutions to look after TB work.

Dr. Nagpaul delivered the Benjamin Memorial Oration in Hyderabad on 4-12-1976 on the subject "Some new concepts on Tuberculosis as a disease and case-finding". Dr. S.N. Mathur, Director of Medical and Health Services and President of Academy of Medical Sciences (Andhra Pradesh) presided. Shri K. Rajamallu, Hon'ble Minister for Health and Chairman of the State Association, presented a Gold Medal to Nagpaul.

The 14th Annual Meeting of the Andhra Pradesh Association was held on 11th December, 1976 at Nellore. Dr. Umopathy Rao presented the annual report and the accounts. The General body adopted the revised Memorandum, Rules & bye-laws of the Association. The 12th Conference of Secretaries of District Associations and Seal Sale organisations was also held on 12th December.

The VIth Andhra Pradesh TB & Chest Diseases Workers Conference was held in Nellore on 11th and 12th December, 1976. Shri Anam Venkata Reddy, Minister for Mine & Irrigation, inaugurated the conference and

unveiled a portrait of the well known Philanthropist, Shri Tikkavarapu Kami Reddy. Dr. D. Umamathy Rao in his presidential address mentioned that there were about 4 to 5 lakhs radiologically and one lakh bacteriologically positive cases in the State. Papers were presented by Drs. C. Srinivasa Rao, O.A. Sarma and D. Lakshmanchar. Dr. K.V. Krishnaswami of Madras Medical College and Chest Institute, delivered the guest lecture on Chemotherapy of TB with charts and slides on the findings.

Dr. Krishnaswami chaired the symposium on Chemotherapy of TB. Papers presented included "Role of Placental extract in treatment of cavitary diseases" (Dr. Mrs. M. Sundaramma) "Streptomycin toxicity in the initial management of pulmonary TB" (Dr. S. Brahmananda Rao), "Treatment regimen of Tuberculosis" (Dr. O.A. Sarma). There was also a panel discussion on Chemotherapy. The Conference was attended by about 200 doctors from the Primary Health Centres and Government Taluk dispensaries.

Gujarat

The Gujarat Association organised their fifth Gujarat State TB Workers' Conference at Jamnagar on 28th November, 1976. The Conference was inaugurated by Dr. H.I. Zala, former Director, Haffkin Institute, Bombay. Dr. A.P. Shukla, Chairman of the Executive Committee, Gujarat TB Association, presided. Shri K.P. Shah, President, Jamnagar District TB Association, welcomed the guests and delegates. Among those who participated in the discussions at the Scientific session included Dr. D.R. Nagpaul, former Director, National TB Institute, Bangalore. About 150 delegates from all over Gujarat participated in the Conference.

Karnataka

The Sixth Karnataka State Conference on TB & Chest Diseases was held at Manipal Medical College and Hospitals, South Kanara on 3rd and 4th December, 1976. Shri T.A. Pai, Union Minister for Industries, inaugurated the Conference and Shri B.P. Mouria, Minister for State for Industrial Development formally launched the Seal Sale Campaign. Papers by specialists from Manipal and Mangalore Medical Colleges were presented. Dr. K.V. Krishnaswami who was the guest lecturer gave a talk on TB Control programme and the modern views on treatment of TB. The Conference of Secretaries decided to hold the next State TB Conference at Mercer, Porgy, during the first week of May, 1977.

The Karnataka Association had been organising several anti-TB camps. During the past three

years it has been conducting Shibirs in slum areas in both rural and urban towns of Bangalore in cooperation with the Lions, Rotary and Jaycees Clubs, Church authorities, educational and banking institutions, village panchayats, municipalities and philanthropic persons. It has so far conducted about 160 Shibirs at Bangalore (39), Chickmagalur (27), Hassan (18), Bellary (17), Chitradurga (17), Tumkur (10), South Kanara (9), Kolar (5), Mysore (4), Shimoga (3) and Coorg (9). The Shibirs brought a large number of non-school going children under BCG vaccination and resistant cases which were diagnosed and brought under treatment. A special feature of these camps had been that the couples who were eligible for Family Planning were registered and sterilised. At the suggestion of Shri Uma Shankar Dikshit, Governor of Karnataka, the Association understood house to house survey of poor people in the slum areas of Blackpally and Bharathinagar and covered 2,340 houses. At the Shibir held at Mulki on 26.12.1976, Dr. Mulki stated that in the South Kanara District there are about 1 \ lakhs of beedi workers among whom there may be a large number of TB cases and he pleaded for setting up a TB Hospital for the district.

The Centenary celebration of shibirs was conducted by the Karnataka Association in Bangalore on 16.10.1976. Shri Uma Shankar Dikshit, Governor of Karnataka, inaugurated it and Shri H.M. Channabasappa, Minister for Health, presided. The Honorary Secretary of the Association presented a report on Shibirs. On this occasion the Health Minister distributed Shawls, Certificate of merit and Cash awards to Honorary Secretaries, Health Officers and others in appreciation of their contribution to the success of Shibirs and training programme of para-medical personnel.

During 1976, 40,000 new-born babies were vaccinated at the Lady Willingdon TB Centre at the request of the Association. The Association has also decided to raise funds for constructing a 200-bedded open air sanatorium near Bangalore for the benefit of poor patients.

Madhya Pradesh

The Madhya Pradesh Association has acquired a plot of land measuring 10,000 sq. ft. allotted by the Government on Idgah Hills for the construction of "Kshaya Bhavan". The Lease Deed is under preparation and the plan for the construction of the Bhavan is in progress. A sub-committee has been appointed to make recommendations.

NEWS AND NOTES

Maharashtra

The XVth Maharashtra State TB & Chest Diseases Conference will be held in Bombay from 11th to 13th March, 1977. Besides the Scientific Sessions, there will be an anti-TB Shibir in a neighbouring rural area and also the concluding session for the benefit of rural medical practitioners.

It may be recalled that Maharashtra State Anti-TB Association which took the lead in organising Shibir have so far held 88 anti-TB camps mostly in rural areas and numerous smaller drives. During 1976 the Association held 15 full-scale anti-TB shibirs and 50 TB & BCG vaccination drives resulting in a total output of 5,746 symptomatics examined, 2,737 screened, 458 X-ray positives, 121 sputum positives and 12,013 BCG vaccination. Among these notable ones are those at Barsi (Dist. Sholapur), Chirner (Dist. Kolaba), Wadala—Bombay, Mhokave (Dist. Kolhapur), Nandgaon (Dist. Nasik).

Pondicherry

The TB Association of Pondicherry has been giving special training to para-medical workers attached to the peripheral medical institutions to administer BCG vaccination to all new born infants and school-going children. It is also giving special training to multi-purpose workers in TB

Control with emphasis on home visits. It also organised Seminar-cum-Refresher Courses for medical officers, nursing staff and para-medical personnel.

Tripura

The TB Association of Tripura is planning to construct a Rehabilitation Home for drug defaulting TB patients and has appealed to the State Government to make available a plot of land for the purpose.

West Bengal

The Bengal TB Association is operating a Mobile Chest Clinic and Laboratory in the slum and industrial areas of Calcutta to detect and treat TB cases. The Mobile Clinic which functions on Sundays also covers places 75 miles away from Calcutta. Men, women and children are examined clinically (Sputum tests also) and probable cases are referred to the Association for X-ray facilities. It also organised the Annual Flag Day on 7th August, 1976 and collected Rs. 20,563.17. Dr. Prasanta Kumar Ghosh Oration was held on 21st December, 1976 under the presidentship of Surgeon-Commodor Dr. J.C. Mookerjee, Principal & Superintendent, N.R. Sarkar Medical College & Hospital. The speaker, Dr. Panchanan Saha, read a paper on "Clinic-based impression on TB".

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ABSTRACTS

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Abst. No. 1

A controlled trial of daily and intermittent Rifampicin plus Ethambutol in the retreatment of patients with Pulmonary Tuberculosis: results upto 30 months.

Hong Kong Tuberculosis Treatment Service} Brompton Hospital!British Medical Research Council. Tubercle: 1957, 56, 179.

575 Chinese patients, smear positive, isoniazid resistant pulmonary tuberculosis were allocated at random to regimens of rifampicin plus ethambutol daily (ER7), twice weekly (ER2), once weekly (ER1) or daily for 2 months and then once weekly (ER7 ER1), or to standard retreatment regimen of daily ethionamide plus pyrazinamide plus cycloserine (EtZc). The ER-7 patients were allocated to 12 to 18 months of chemotherapy, and the remainder to 18 months.

Assessed at 18 months, a favourable response was achieved in 87 percent of 91 (ER7 patients), 79 percent of 84 (ER2 patients), 81 percent of 53 (ER1 patient) 87 percent of 62 (ER7 ER1 patients) and in 88 percent of 68 (EtZc patients), 93 percent of 59 (EtZc patients).

Assessed at 18 and 30 months the ER7 regimens was as effective as the control EtZc regimen and 18 months of chemotherapy on ER7 regimens conferred no benefit over 12 months. No patient on either regimen relapsed after 18 months.

Adverse reactions were uncommon on the daily rifampicin regimen but relatively common on the intermittent and control regimen.

H.B.D.

The Influence of Age and Sex on the incidence of 'Flu' Syndrome and Rifampicin-dependant Antibodies in patients on intermittent Rifampicin for tuberculosis.

Hong Kong Tuberculosis Treatment Service/British Med. Res. Council. Tubercle: 1957, 56, 775.

The 'Flu' syndrome was commoner in women than in men but the difference was not statistically significant. In men its frequency was

($P < 0.001$) and severity ($P < 0.005$) increased with age.

Rifampicin dependent antibodies occurred with similar frequency in men and women, but in men these incidence increased significantly with age ($P < 0.005$).

The incidence and severity of adverse reactions on daily rifampicin and control regimen was not influenced by age or sex.

H.B.D.

The ABO and Rhesus blood groups in patients with Pulmonary Tuberculosis.

Viskum, K. Tubercle (1957), 56, 239.

99 percent of 554 patients of pulmonary tuberculosis were typed according ABO and rhesus system.

The bacillary patients showed an excess of group O and AB and deficit of A and B as compared to the general population. The deviation was highly significant statistically for groups O and A.

The ABO and rhesus distribution of abacillary patients did not differ significantly from the expected pattern.

During a follow up period of 2-5 years after the initial diagnosis, 104 bacillary patients died, the ABO pattern among the survivors was now close to the normal; this resulted from a high number of deaths from tuberculosis among patients of group O and a low number among those belonging to group O and a low number among those belonging to group A. More rhesus negative patients died from tuberculosis than rhesus positive.

H.B.D.

Microbiology of Cutaneous Tuberculosis

Sharma R.C., Singh, Ratan and Bhalia, V.N. Tubercle, (1957), 56, 342.

Mycobacteria were isolated in 12 out of 51

different cases of cutaneous tuberculosis; of these 9 were identified as *M. tuberculosis* and 3 as anonymous mycobacteria.

Acquired resistance to one or more than one drug; (streptomycin, isoniazid, PAS and thiacetazone) was observed in 3 out of 9 strains of *M. tuberculosis*. All the anonymous strains were resistant to all drugs except ethionamide and ethambutol.

H.B.D.

Studies of Serial Plasma Isoniazid Concentrations with different doses of a slow-release preparation of Isoniazid.

Sanna, Raghupati C., Kailasam, S., Mitchison, D.A., Nair, N.G.K., Radhakrishna, S., and Tripathy, S.P., Tubercle (1975), 56, 314.

The study about suitability of a slow-release matrix preparation of isoniazid for use in once weekly chemotherapy by serial plasma isoniazid concentration upto 6 hours following doses of 15, 30, 45 and 60 mgm/Kg body weight in rapid inactivators and upto 10 hours following doses of 15, 30, 45 and 60 mgm//Kg body weight in rapid inactivators showed that isoniazid levels were sustained and peak concentration (per unit dose) was considerably lower than with ordinary isoniazid. It was estimated that a matrix isoniazid dose of 35 mgm/Kg in slow inactivators and 50 mgm/Kg. in rapid inactivators would produce a peak similar to that attained with a non-toxic dose of ordinary isoniazid 15 mgm/Kg. in slow inactivators.

In another investigation matrix isoniazid 40 mgm/Kgm in rapid inactivators produced a coverage (with 0.2 ug/ml) and exposure similar to those attained in slow inactivators with a highly effective dose of ordinary isoniazid 15 mgm/Kg while 30 mg/Kg gave substantially lower values.

Large increase in plasma isoniazid concentration was observed in rapid inactivators with increase in matrix isoniazid dose.

In slow inactivators both doses of matrix isoniazid 30 and 40 mgm/Kg. resulted in coverage and exposure that were substantially higher than those obtained with ordinary isoniazid 15 mgm/Kg.

H.B.D.

Tuberculosis in Tanzania : A National Sampling Survey of Drug Resistance and other factors.

An East African and British Med. Research Council Cooperative investigation. Tubercle (1957), 56, 269.

In a random sample of 1,884 patients, 87.4% had pulmonary tuberculosis, 2.5% had pulmonary and extra pulmonary tuberculosis and 10.1 % had extra pulmonary tuberculosis. Of the 256 extra pulmonary tuberculous lesions in 237 patients, 58 % were lymph nodes, 26 % bone and joint and 12% pleural, pericardial or peritoneal.

Of 1,694 patients with pulmonary tuberculosis with or without extra pulmonary tuberculosis, 96.3% gave no history of previous chemotherapy and 3.6% a definite history.

Direct smear was positive in 675 (50 per cent) in 1,338 patients and 694 (55 percent) of 1,257 cultures.

Of the 636 patients with no history of previous chemotherapy and sensitivity test results, 9 percent had a strain resistant to isoniazid and/or streptomycin. The total prevalence of resistance to isoniazid was 6% and to streptomycin 4%.

Of the 1,278 patients, radiologically examined showed that 86 per cent had pulmonary pathology.

Of the 1,171 patients, having lung lesion, gross extensive or moderate disease was present in 73 per cent and cavitation in 66 percent. The type of disease was assessed as acute in 36%, mixed acute in 40%, mixed in 19 percent and chronic in 5%.

There was no evidence of association between drug resistance and the extent or type of disease or presence of cavitation.

H.B.D.

Pulmonary Tuberculosis in Scotland. A National Sample Survey and Follow up (1968-70). The characteristics of the cases notified in 1968.

Heffeman, Joh F: Nume. Andrew. J, Peto, Jullian and Fox, Wallace, Tubercle (1975), 56,253.

The estimated notification rate for the total population was 33.3 per 100,000. The highest rate for males was 89.8 for those aged 55 or more and for females 29.5 for those age 25 to 54. The rates for bacteriologically confirmed cases were 51.6 and 16.0 respectively for these two groups. Active disease was reported in 50% of chest

radiographs. Nearly half the patients were referred by general practitioners and 20% were hospital inpatients when diagnosed. Contacts and mass radiography services produced many fewer cases and proportion of infectious cases in these groups was low.

H.B.D.

Status of B.C.G. Vaccination in Children under Five Years of age in a Rural Area—A Scar Survey.

Singh, K.P., Gulati, P.V. Ind. Jour. Fed. Vol. XIII. 9, 1976.

A scar survey done in a rural area in Goa to determine B.C.G. coverage under five years age showed that 41.2 per cent of 2,343 children had received B.C.G. vaccination.

In 0-1 year group, 30.5 percent children were vaccinated. The vaccination status improved with age. There is no difference in vaccination status of male and female children.

H.B.D.

Tuberculin Hypersensitivity before and after B.C.G. Vaccination in Indian children of an Urban Community—A Pilot Study.

Mohanty, LC., Saha, K., and Gupta, S. Ind. Fed., Vol. XIII. No. 8, 1976.

Tuberculin test done in 214 B.C.G. vaccinated children between age varying from 1 month to 13 years using 10 Tu and 100 Tu showed 100% conversion taking 6 mm. as positive. Among non-immunized children, 80-86% were non-reactors in first two years of life. 40% are spontaneously sensitized by ten years of age.

H.B.D.

Rapid Differentiation of Meningitis by N.B.T. Test.

Praharaj, K.C., Nath Sharma, K.C., Rao, E. Raghvendra. Ind. Fed. Vol. XIII, No. 9, 1976.

Nitroblue Tetra Zolium (N.B.T.) test was done in 12 patients of pyogenic meningitis, 16 patients of tuberculous meningitis and 25 healthy children as control. The mean percentage and absolute count of N.B.T. positive cells in healthy controls were 8.2 ± 21.6 and 214 ± 142.0 respectively, whereas in pyogenic meningitis, these were 35.75 ± 17 and $36,535 \pm 2,537$ respectively. The results of pyogenic meningitis differed significantly as compared to healthy

controls. ($P < 0.001$). The mean percentage and absolute count of N.B.T. - - positive cells in tuberculous meningitis were 7 i 4.97 and 453.15 ± 218.4 and they did not differ significantly as compared to healthy controls. To differentiate pyogenic meningitis from tuberculous meningitis N.B.T. test seem to be useful adjunct to other laboratory investigations.

H.B.D.

A study to assess the Intradermal, Triangular Needle and Bifurcated Needle Techniques in the administration of B.C.G. in newborns.

Allan, W.G.L. Tubercle. (1957), 56, 139.

B.C.G. was administered to 3,297 new born babies in Hong Kong using intradermal simple triangular needle and bifurcated needle techniques.

Tuberculin testing at 3 months showed similar mean reactions for the intradermal and simple triangular needle methods namely 9.74 m.m. and 9.87 m.m. with 9.94 m.m. for triangular needle method when B.C.G. strength was doubled using the bifurcated needle, the mean reactions were significantly lower, 8.69 m.m., 9.01 m.m. with double strength B.C.G. and 8.92 m.m. with puncture through a skin drop.

It is concluded that the bifurcated needle is not satisfactory method of administering B.C.G. to new born even if the concentration of B.C.G. is increased.

H.B.D.

Controlled Trial of 6 and 9 Months Regimen of Daily and Intermittent Streptomycin plus Isoniazid plus Pyrazinamide for Pulmonary Tuberculosis in Hong Kong.

Hong kong Tuberculosis Treatment Services! British Medical Research Council. Tubercle (1975), 56, 81.

A comparison between 6 and 9 months regimens of streptomycin, isoniazid and pyrazinamide given daily, three times a week or twice a week in the treatment of newly diagnosed, smear positive, pulmonary tuberculosis in Chinese patients showed that five (4 percent) of 126 patients with drug sensitive strains had unfavourable bacteriological status compared with only two (1 percent) of 141 on thrice weekly regimen and none of 137 patients on daily regimen of the total of 211 patients treated for 9 months, only one of 74 on the twice weekly regimen relapsed between 6 and 9 months.

The bacteriological relapse rate after six months of chemotherapy was 13 per cent on the daily, 16 per cent on the thrice weekly and 18 per cent on the twice weekly regimen. After nine months chemotherapy, it was three percent, four percent and four per cent respectively. All 33 relapses were with strains sensitive to isoniazid and streptomycin and 76 per cent of them occurred in the first three months.

H.B.D.

The influence of Age and Sex on the incidence of the Flu Syndrome and Rifampicin Dependant antibodies in patients on Intermittent Rifampicin for Tuberculosis.

Hong Kong Tuberculosis Treatment Service!British Medical Research Council, Tubercle (1975), 56, 175.

Chinese adults were retreated with regimens containing rifampicin daily, twice weekly, once weekly or daily for two months and then once weekly, or with control regimen of ethionamide, pyrazinamide and cycloserin.

'Flu' syndrome was more common with intermittent rifampicin in women than men, but difference was not statistically significant. In men, its frequency ($P < 0.001$) and severity ($P < 0.005$) increased with age. Rifampicin dependant antibodies occurred with similar frequency in women and men, but in men their incidence increased significantly with age ($P < 0.005$) on the daily rifampicin regimen and on the control regimen, the incidence and severity of adverse reaction were not influenced by age or sex.

H.B.D.

Beclomethasone Dipropionate Aerosol and Oropharyngeal Candidiasis.

Willey, R.F., Milne, L.J.R., Crompton, O.K. and Grant, I.W.B. Brit. J. Dis. Chest (1976) 70, 32.

45 % prevalence of oropharyngeal thrust was observed in a survey of 400 consecutive patients. The prevalence of this complication was not related to sex, age, duration of treatment with beclomethasone or concurrent treatment with prednisolone.

Yeasts were isolated from throat swabs in about 60% of all patients and in 48 % of normal controls. Although a diagnosis of oropharyngeal thrush was recorded, when presence of characteristic lesions in the pharynx was associated with a

positive culture, there were a number of patients and controls without thrush, who harboured yeasts in the throat. One in three patients with thrush complained of sore throat or hoarseness, but one in few patients without thrush had similar symptoms.

These findings suggest that although treatment with beclomethasone dipropionate aerosol can cause oropharyngeal thrush, this condition is not an inevitable result of colonization of the oropharynx by yeast, nor is it necessarily associated with symptoms.

H.B.D.

Tuberculosis of the Cervical Lymph Nodes : A Clinical, Pathological and Bacteriological Study.

Huhti. E., Paloheimo. Soili., and Sutinen. S: Tubercle. (1975), 56, 27.

Of the 59 consecutive patients with cervical lymph node, Mycobacteria were isolated from 41 (69%) specimens. Of these 40 were M. tuberculosis and one M avian M intracellular complex. All strains were sensitive to streptomycin, isoniazid and PAS.

No mycobacteria were isolated from the biopsy specimens of the 10 patients, who had received anti-tuberculosis drug therapy. Mycobacteria were isolated equally from caseating and non-caseating specimens.

In 10 specimens acid fast bacilli could be demonstrated by staining but attempts at isolation were unsuccessful. None of these 10 patients had been treated with anti-tuberculosis drugs previously. Histological examination of the specimens from which a growth of a typical mycobacteria had been obtained failed to show any distinctive features.

H.B.D.

A comparative study of daily followed by twice or once weekly Regimens of Ethambutol and Rifampicin in retreatment of patients with Pulmonary Tuberculosis.

A Cooperative Tuberculosis Chemotherapy Study in Poland. Tubercle (1975), 56, 1.

A comparison was made at one year of once and twice weekly supervised intermittent regimen of rifampicin 1200 mgm plus ethambutol 50 mgm/Kgm body weight under out patient conditions after an initial phase of rifampicin 600 mgm

ABSTRACTS

and ethambutol 25mgm/ Kgm daily for 12 weeks in 247 patients allocated at random.

201 patients completed one year's treatment

After daily phase of 12 week's treatment, 82 percent were negative on smear and 85 percent on culture . In the continuation phase 98 percent in once weekly (E_1R_1) as well as twice weekly

(E_2R_2) regimen were negative on culture at 28 weeks. The corresponding proportion at weeks was 97 per cent.

At 12 months 96 percent of 101 ER/ E_1R_1 and 96 percent of 100 ER/ E_2R_2 who completed one year's treatment were culture negative.

H.B.D