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FIFTH FIVE YEAR PLAN FOR TUBERCULOSIS CONTROL

The fourth five year plan will end shortly and the fifth plan is already on the anvil. This is the proper time to take stock of the achievements and shortfalls of the current plan and the reasons thereof, while making recommendations for the fifth plan.

The main constituents of the national control programme, at present, are the "District Programme" and "BCG Vaccination". It was expected that by the end of the fourth plan, existing clinics in the headquarters of all administrative districts in the country would be upgraded and equipped to serve as district tuberculosis centres. Actually the programme has yet to be implemented in about 70 districts. If the speed of upgrading in the last few years is any guide for the future the target obviously cannot be achieved. It is, therefore, essential that the upgrading of district clinics should be considerably stepped up so that the programme is implemented in all districts as early as possible. It has also been seen that, usually, there is a very long time-lag between sanction of the upgrading and the actual implementation with full quota of staff and equipment. This time-lag must be reduced to not more than a few months at the utmost.

What is more disturbing is that even in those districts where the national programme has been implemented, the achievement is far short of the targets. This is mostly due to the weakness in the infra-structure. When the national programme was formulated, a certain stage of development of the infrastructure viz. the peripheral health institutions was taken for granted. Integration of anti tuberculosis measures with the general health services appears to be the only solution to the problem of tuberculosis in the rural areas but integration cannot be fruitful if the peripheral institutions are not adequately staffed and equipped. It is a well known fact that many peripheral institutions are short of the sanctioned medical and para-medical personnel. The number of microscopy centres in the districts in some states is too small and the expansion too slow. These lacunae have to be removed before targets can be achieved. Posting of a separate person for sputum examination and treatment organisation in every peripheral institution would be a good interim measure. After all, Malaria eradication programme is dependent on special personnel. Why not Tuberculosis programme too ?

Human factor is still another reason for shortfall. The medical and para-medical personnel are not convinced about the merit and feasibility of the programme and, therefore, are lukewarm in its implementation. To remove this difficulty, both medical and para-medical personnel must be involved in the

tuberculosis control programme during their training period and steps must be taken continuously to motivate those who had their training long time back. This last function belongs to the State Training and Demonstration Centres of which there is one each in at least 15 states. These centres which should have played a significant role in stepping up of the activities of the peripheral centres are unfortunately also not adequately staffed and equipped; and in some places where they are, this responsibility has not been given to them so far by the Directorate of Health Services in the states. The feeling one often gets is that the sense of urgency with which the programme should have been implemented at all levels is sadly lacking. Thus, the suprastructure also has to be strengthened simultaneously, mainly by proper training and motivation.

Position in regard to BCG vaccination leaves much to be desired. The target of at least one BCG team per administrative district has not yet been achieved with the result that the coverage is poor. Mobility of the BCG team in many districts is some times handicapped owing to diversion of the BCG vehicle for other purposes and during the period of this diversion, the BCG work comes to a standstill. It has to be stressed that unless and until the BCG coverage reaches about 70% or so of those eligible year after year, its impact on tuberculosis problem will not be significant. The planners must therefore see that number of BCG teams in the country should be increased as quickly as possible, BCG supply should be adequate, the supply line should be maintained regularly, P.O.L. provision should be adequate and the BCG vehicles must be kept in position and in running order.

Apart from these two main constituents of the national programme there are a few other matters which must receive the attention of the planners. The position in relation to "antituberculous drugs" is not altogether satisfactory. Some drugs, sometimes, run short in the market. Even if the existing production is enough for the needs of patients under treatment in the various institutions, the bottlenecks disturb the supply line; these have to be eliminated. With increasing diagnostic facilities at the peripheral institutions, the number of freshly diagnosed cases is bound to go up and, therefore, steps must be taken to expand the production of the standard anti-tuberculous drugs. Any difficulty in respect of import of intermediate products must be removed.

Even though it is not necessary to hospitalize every TB patient, yet in a country like ours, many patients do need "hospitalization" for socio-economic and other reasons. There are about 36,000 beds in the country for the treatment of tuberculous patients at present. These would not be far short of the minimum requirement if they are rationally and fully utilized. Many beds in the institutions run by voluntary organisations remain vacant. Instead of adding new beds in the existing hospitals/sanatoria or starting new institutions, the state and other agencies like the railways, ESI etc. should subsidize voluntary organisations to enable them to fill the vacant beds with free patients and thus utilize these to the fullest extent possible. And whenever and wherever new beds are sanctioned, these should preferably be located in general hospitals. This will be economical and will improve their utility also.

Stepping up of "community awareness" and to tap the vast resources in

"community participation" are essential for the control of any communicable disease, more so tuberculosis which has many social bearings. Efforts in this direction, commendable at some places have been inadequate at most others. A uniform, systematic and organised programme should be planned in co-operation with voluntary organisations in which Tuberculosis Association of India with its State Branches can play a significant role.

"Operational Research" not only helps in leading a programme in the right direction, but is financially helpful also by fixing priorities and eliminating duplications and redundancies. Nationally important problems should be singled out and studies on these should be undertaken. The Indian Council of Medical Research and the Tuberculosis Association of India may be given the responsibility for the conduct of such research.

A time bound plan of action is dependent on the prevailing conditions, needs and expectations. Partial implementation of a programme may not always be proportionately gainful. It may even create certain irrevocable and adverse conditions which may make subsequent programmes far more difficult. The planners may keep this in mind and make-up for the short-falls of the previous plans during the fifth plan period.

A CONCURRENT COMPARISON OF AN UNSUPERVISED DAILY ORAL REGIMEN OF THIA CETAZONE PLUS ISONIAZID AND A FULLY SUPERVISED TWICE-WEEKLY REGIMEN OF STREPTOMYCIN PLUS ISONIAZID IN THE DOMICILIARY TREATMENT OF PULMONARY TUBERCULOSIS-A CO-OPERATIVE INVESTIGATION

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Studies carried out at several centres have **shows** that a daily oral regimen of thiacetazone and INH is efficacious and not particularly **toxic** in the domiciliary treatment of pulmonary tuberculosis. It has the additional merit of being relatively inexpensive. However, being an unsupervised regimen, reliance has to be placed on self-administration of the drugs, a practice known to have serious limitations. In this context a fully supervised intermittent (twice-weekly) regimen of streptomycin and INH is a promising alternative as it permits a precise knowledge of and, therefore, greater control over the amount of chemotherapy actually administered and has been shown to be efficacious (Chemotherapy Centre Madras, 1964). This regimen, however, requires the co-operation of patients in attending the clinics regularly twice a week and a different type of organisation by the clinics. With a view to determine the relative merits of these two regimens (supervised intermittent streptomycin and INH and unsupervised daily thiacetazone and INH) the Tuberculosis Expert Group of the Indian Council of Medical Research decided in 1968 to organize a controlled clinical trial.

Method

Since ours is a vast country with considerable regional variations, it was decided to carry out the study simultaneously with a common protocol, from 4 to 8 centres so that the results obtained from the study may be representative of the entire country. The protocol was approved by the Tuberculosis Expert Group in November, 1968. Eight centres were originally selected but only six, namely Ajmer, Calcutta, Delhi, Lucknow, Nagpur and Patiala agreed to participate in the trial.

The trial was co-ordinated from the New Delhi Tuberculosis Centre and its laboratory was selected to function as a central laboratory for this trial. The participating centres were required to send sputum specimens in accordance with the protocol by air to the central laboratory for culture and sensitivity tests.

The following criteria were laid down for including patients in the trial :—

1. Two specimens of sputum positive by direct microscopy.
2. Age 15 years or more.
3. Not more than 2 weeks of previous anti-tuberculosis chemotherapy,
4. Patients should be living in the area covered by the domiciliary service of the clinic and likely to remain in the area for another year.

Patients who were in a moribund condition or had a massive pleural effusion, pregnancy or any complication e.g. diabetes which could lead to difficulty in the management of the patient from the out-patient department were to be excluded from the trial even if otherwise eligible.

The two treatment regimens were as follows :—

SHITH

Streptomycin 1 g. by intramuscular injection and isoniazid 400 mg orally in a single dose, six days a week for the first two weeks, followed by thiacetazone 100 mg orally and isoniazid 200 or 300 mg in a single dose daily, for the rest of the year.

SHISHTW

Streptomycin 1 g by intramuscular injection and isoniazid 400 mg orally in a single dose, six days a week for the first two weeks, followed by streptomycin 1 g plus isoniazid 600 or 700 mg orally in a single dose, both drugs given together twice-weekly, under supervision, for the rest of the year.

Pyridoxine in a dosage of 10 mg was administered with every dose of isoniazid in the first 2 weeks for the SH/TH patients and

throughout (he year for the SH/SHTW patients).

During the 2-52 weeks period, the dosages of the drugs were graded according to body-weight, as shown below :—

Weight (Kg.)	SH/TH regimen		SH/SHTW regimen	
	Thiacetazone (mg)	Isoniazid (mg)	Isoniazid (mg)	Streptomycin (mg)
Less than 40	100	200	600	1
40 or more	150	300	700	1

If, at a routine examination, a patient was found to have gained weight and moved into the higher weight category, the drug dosage was increased in accordance correspondingly with the above schedule. However the dosage was not reduced for any loss in weight.

For allocation of patients to the two regimens, each participating centre was provided with sealed envelopes by the statistician of the New Delhi TB Centre, each envelope containing a slip of paper stating the regimen to be used for the particular patient for whom the envelope was to be opened. Allocation was made by opening the next in the series of sealed envelopes.

Pre-treatment investigations included a conventional size P. A. skiagram of the chest, two specimens of sputum collected on different days, and examined by direct smear and culture. Sensitivity tests were carried out for INH and streptomycin.

During the course of treatment, two specimens of sputum were collected by the participating centres and sent to the central laboratory at 12,24,40,44,48 and 52 weeks for culture examination and sensitivity testing. If the patient had no sputum, cough was induced by tickling the throat by a swab and then asking the patient to clear his throat and the material thus spat out was examined in lieu of sputum. For patients who became un-cooperative and stopped treatment prematurely, attempt was to be made to collect two specimens of sputum at 44, 48 and 52 weeks. The participating centres, in addition, examined the sputum of all patients once a month.

Change in chemotherapy was permissible in

case of serious toxicity or serious intolerance that could not be controlled by temporary alteration of dose or administration of anti-histamines. If the patient showed serious clinical or radiographic deterioration at any time during the trial, withdrawal was permissible provided the sputum smear continued to be positive.

When a patient failed to attend on the appointed day in any of the two regimens, a home visit was made as early as possible, but not later than 3 days, by a health visitor for retrieval of the defaulter. If this failed to produce the desired result, two more visits were to be paid within two weeks and then a final attempt after 4 weeks, before the patient was labelled as "un-cooperative". For SH/TH patients two surprise home visits were to be paid during each four-week period at approximately fortnightly intervals to check the regularity of drug-taking by counting the stock of pills. Urine examination to check the ingestion of INH was not found possible.

Material

Intake into the study was started in May, 1969 and terminated on 31st March, 1971. During this period 525 patients in all were included in the trial (Table 1). Two hundred and seventy five of these were included in the SH/TH regimen and 250 in the SH/SHTW regimen. Subsequently it was found that the bacilli in the pre-treatment sputum of 69 patients, 38 in the SH/TH and 31 in the SH/SHTW regimen, were resistant to INH and/or streptomycin. These 69 patients have, therefore, been analysed separately and the remaining 456 (237 and 219 respectively) patients whose pre-treatment sputum showed bacilli sensitive to INH and streptomycin are included in the main analysis.

Each centre was expected to include about 100 patients in the study during the stipulated period. As can be seen from Table 1, three of the centres reached or almost reached this target and two others were not very far behind. In centre II however, the intake was rather slow and only 51 patients could be inducted into the study. The same table also shows the number of patients in the different centres whose pre-treatment sputum culture was found resistant to INH and/or streptomycin and who have, therefore, been excluded from the main analysis. The percentage of such patients varies from 8% to 19% in the different centres.

Table 2 gives the age and sex distribution of patients included in the main analysis. As

TABLE 1

Patients included in the study from various centres and those included in the main analysis

	All patients			Patients included in the main analysis		
	SH/TH	SH/SHTW	Total	SH/TH	SH/SHTW	Total
I	50	47	97	44	40	84
II	23	28	51	21	26	47
III	52	49	101	47	43	90
IV	47	33	80	35	30	65
V	39	35	74	34	29	63
VI	64	58	122	56	51	107
Total	275	250	525	237	219	456

TABLE 2

Age and sex distribution of patients included in the main analysis

	SH/TH		SH/SHTW		Total	
	No.	%	No.	%	No.	%
	15—24 years	86	36.3	79	36.1	165
25—34 years	54	22.8	59	26.9	113	24.8
35—44 years	55	23.2	45	20.5	100	21.9
45— years	42	17.7	36	16.4	78	17.1
Males	163	68.8	151	68.9	314	68.9
Total Females	74	31.2	68	31.1	142	31.1
Both sexes	237	100.0	219	100.0	456	100.0

stated earlier, patients below the age of 15 years were not eligible for inclusion in the study. The distribution of patients in the two treatment regimens with respect to age and sex is almost the same.

The extent of disease at start among patients in the two groups is shown in table 3. The two groups are fairly uniform in this res-

pect. One tenth of the cases were minimal and one fourth were far advanced with involvement of 4 and 5 zones.

There are some slight differences in the two groups in respect of the extent of initial cavities as can be seen from Table 4. The proportion of patients without any cavities was somewhat more in the SH/SHTW group and

TABLE 3

Extent of disease at start among patients included in the main analysis

	SH/TH		SH/SHTW		Total	
	No.	%	No.	%	No.	%
1 zone	19	8.1	24	11.1	43	9.5
2 or 3 zones	157	66.5	136	63.0	293	64.8
4 or 5 zones	60	25.4	56	25.9	116	25.7
Total	236	100.0	216*	100.0	452*	100.0

*Initial x-rays of 4 patients (one in the SH/H-I group and three in the SH/SKTW group) were not available

TABLE 4

Extent of cavitation at start among patients included in the main analysis

	SH/TH		SH/SHTW		Total	
	No.	%	No.	%	No.	%
No cavity	12	5.1	30	13.9	42	9.3
Single cavity	107	45.3	88	40.7	195	43.1
Multiple cavities-unilateral	62	26.3	40	18.5	102	22.6
Multiple cavities-bilateral	55	23.3	58	26.9	113	25.0
Total	236*	100.0	216*	100.0	452*	100.0

*Initial x-rays of 4 patients (one in the SH/TH group and three in the SH/SHTW group) were not available

patients with a single or multiple unilateral cavities were relatively more numerous in the SH/TH group. The differences on the whole are, however, not so marked as to warrant standardisation of the results presented in the following tables. Among cavitory cases, size of cavities was not significantly different in patients in the two regimens.

Results

All patients did not complete the stipulated treatment for 52 weeks and Table 5 shows the stages at which 165 (36.2%) patients discon-

tinued the treatment. This percentage was significantly more in the SH/TH group (40.1%) than in the SH/SHTW group (32.0%). ($X^2=7.62$ for 1 d.f. $P<0.01$). The percentage of patients dropping out of the study did not only vary with the regimens but also in the various centres, the range being 15.4% to as many as 64.7%.

The maximum loss of patients (16.7%) occurred in the first 12 weeks of treatment. This means that at least in some centres, either due regard was not paid to the residential qualifications or that wrong statement made

TABLE 5

Patients prematurely stopping treatment during successive periods upto 52 weeks

Patients prematurely stopping treatment							
	Patients included in the main analysis	0—12 weeks	13—24 weeks	25—49 weeks	41—52 weeks	0-52 weeks	
SH/TH	No.	237	43	14	22	16	95
	%	100.0	18.1	5.9	9.3	6.8	40.1
SH/SHTW	No.	219	33	13	17	7	70
	%	100.0	15.1	5.9	7.8	3.2	32.0
Total	No.	456	76	27	39	23	165
	%	100.0	16.7	5.9	8.6	5.0	36.2

by the patient about their likely stay was not verified by the clinic's home visiting staff.

Table 6 shows that premature stoppage of treatment was almost entirely due to a large number of patients leaving the area or ceasing to co-operate. This is a reflection of the existing state of facilities available at these centres. Centre IV for example had only one

part-time health visitor for defaulter action and no sub-centres for injections in its extensive area to facilitate supervised treatment. Centre V on the other hand had all the facilities but due to certain administrative problems, beyond its control, its achievement in respect of regularity and loss of patients was rather poor. In centres III and VI, where the facilities were adequate, loss was very low.

TABLE 6

Reasons for premature stoppage of treatment under protocol before 52 weeks

Patients prematurely stopping treatment							
	Patients included in main analysis	Left area	Drug toxicity	Non-co- operation	Death due to non-TB causes	Total	
SH/TH	No.	237	47	2	44	2	95
	%	100.0	19.8	0.8	18.6	0.8	40.1
SH/SHTW	No.	219	23	4	42	1	70
	%	100.0	10.5	1.8	19.2	0.4	32.0
Total	No.	456	70	6	86	3	165
	%	100.0	15.4	1.3	18.8	0.6	36.2

The fact that a large number of patients leave the area prematurely also needs comment. The protocol stated clearly that only patients who belong to the domiciliary treatment area and who were likely to stay on for at least one year were to be included in the study. The fact that as many as 1/6th patients were lost because they left the area within 52 weeks suggests that either this provision was not adhered to as strictly as it should have been in some centres or quite a number of patients were forced to move out because of socio-economic difficulties.

An extremely low loss due to drug toxicity is noteworthy specially in the SH/TH group. An earlier ICMR co-operative trial (Pamra, 1971) had shown that thiacetazone toxicity was of the order of 4.1% as against only 0.8% in the present study.

One case in SH/TH regimen died in a street accident after completing 48 weeks' treatment and another in the same regimen died of acute gastro-enteritis after completing 20 weeks. In the SH/SHTW regimen there was only one death unconnected with tuberculosis, after 24 weeks treatment. Patient was admitted as an emergency in a general hospital and died soon afterwards and the cause remained unascertained.

Fifteen cases had to be withdrawn from the study due to worsening in the SH/TH regimen and 10 in the SH/SHTW regimen. They were all sputum positive at the time of withdrawal

from the study and have been counted as failures.

There were 12 deaths in all from tuberculosis which in Table 6 are shown as having completed treatment. Five of these deaths were in SH/TH group and 7 in the SH/SHTW group. Three of the deaths in the SH/TH group occurred within 8 weeks and the remaining two between 36th and 40th week. In the SH/SHTW group, 3 deaths occurred within the first 8 weeks and one each of the remaining four in the 10th, 12th, 15th and 24th weeks.

The extent of regularity* in drug collection/administration is shown in Table 7. The regularity pattern in different centres was more or less the same as in the loss of patients shown in the earlier table, the range of patients taking treatment with a regularity of 80% or more being 66% to 96%. The overall regularity was somewhat more in SH/TH than in SH/SHTW regimen, irrespective of the length of treatment ($\chi^2 = 5.64$ for 1 d.f. $P < 0.02$). It has to be remembered that in the SH/TH regimen patients were required to attend the centres only 25 times during 52 weeks whereas in the SH/SHTW regimen, 112 visits had to be paid to the main centre or the subsidiary injection centre for treatment. The opportunities for default were obviously greater in the latter regimen and more home visiting was therefore required. It has been calculated that the actual home visits for defaulters in the SH/TH regimen were 3.61 per patient and 4.35 in the SH/SHTW regimen. Since the number of

TABLE 7
Extent of regularity in drug collection / administration during 52 weeks' treatment

		Patients included in main analysis	Patients with over 95% regularity	Patients with over 90% regularity	Patients with over 80% regularity	Patients with less than 80% regularity
SH/TH	No.	237	113	179	213	24
	%	100.0	47.7	75.5	89.9	10.1
SH/SHTW	No.	219	96	143	180	39
	%	100.0	43.8	65.3	82.2	17.8
Total	No.	456	209	322	393	63
	%	100.0	45.8	70.6	86.2	13.8

Patients who took drugs with a regularity of 80% or more have been deemed as regular and the rest irregular.

TABLE 8 Results of bacteriological examination at end of 52 weeks

	Patients included in the mam analysis	Patients completing 52 weeks' treatment	Patients whose bact. results are available at 52 weeks	Patients with sputum negative by Direct Smear	Patients with sputum negative by Culture	Patients resistant to INH and/or SM at 52 weeks
SH/TH	237	142	142 100.0%	117 82.4%	111 78.2%	8
SH/SHTW	219	149	147 100.0%	123 83.7%	121 82.3%	8
Total	456	291	289 100.0%	240 83.0%	232 80.3%	16

patients dropping out of the study at various stages was not uniform in the two regimens, the results have been standardised for varying lengths of treatment and the calculated standardised rate is 3.40 visits per patient in the SH/TH regimen and 4.65 visits in the SH/SHTW regimen. In other words, the supervised drug regimen required 37% more home visiting than the SH/SHTW regimen. Routine visits paid in the SH/TH regimen for pill counting have not been taken into consideration for this purpose.

The results of bacteriological examination at the end of 52 weeks are shown in Table 8. One hundred and forty two patients in the SH/TH regimen completed 52 weeks' treatment and out of these sputum was negative by direct smear in 82.4% and by culture in 78.2%. In the SH/SHTW regimen, the bacteriological results were available only in 147 out of 149 who completed 52 weeks' treatment and 83.7% were negative by direct smear and 82.3% by culture. The differences in the conversion rate by culture are not statistically significant ($X^2=0.78$ for 1 d.f. $P>0.30$).

If a patient is considered as converted only if all cultures at 44, 48 and 52 weeks were negative, the number comes down from 111 to 102 in SH/TH regimen and from 121 to 112 in the SH/SHTW regimen. For calculation of conversion rates, deaths and worsening have been counted as 'completed 52 weeks' treatment but failed to convert'.

Since the number of patients who were irregular and yet completed 52 weeks' treatment is rather small (11 in the SH/TH and 14 in the SH/SHTW regimen) comparison of sputum conversion results among regular and irregular patients is not worthwhile. If however, irregular patients were not taken into consideration, the 'conversion by culture' rates

would have been 81.7% in SH/TH and 84.2% in the SH/SHTW regimen, a difference which again is not significant. Sputum conversion rates were also calculated in respect of various degrees of regularity. It was found that whether the regularity was 95% and above or 90% and above or 80% and above, the results remained practically the same.

Sputum conversion rates in the two regimens were also compared separately for cavitory and non-cavitory cases but the differences failed to attain statistical significance in both regimens.

The overall sputum conversion rates in different centres are not shown separately but they follow more or less the same trends as standards of regularity obtained in the various centres, the rate of conversion varying from 56.2% to 100%.

Table 8 shows that of the 31 patients who remained unconverted at the end of 52 weeks in SH/TH regimen, 8 showed bacilli resistant to INH and/or streptomycin. In the SH/SHTW regimen, 8 patients out of 26 unconverted were excreting bacilli resistant to streptomycin and/or INH.

As for acquired resistance (Table 9), there were 18 patients in SH/TH regimen and 24 in SH/SHTW regimen in whom the bacilli at the time of starting treatment were sensitive but who showed bacilli resistant to INH and/or streptomycin some time or other during the course of treatment. Nine of the 18 in SH/TH regimen and 16 out of 24 in the SH/SHTW regimen were however converted before the end of treatment. In the SH/TH regimen, 7 were resistant to INH alone and 2 of these were converted, 5 were resistant to streptomycin only and all were converted and 6 were resistant to both streptomycin and INH and only 2 of these were converted. In the SH/SHTW regimen, 4 were

TABLE 9

Emergence of acquired bacillary resistance during treatment in the two regimens and final bacteriological results in such patients

	Drug regimens								
	SH/TH			SH/SHTW			Total]		
	Total conversion	Sputum		Total conversion	Sputum		Total conversion	Sputum	
Resistant to INH only	7	2	28.6%	4	4	100.0%	11	9	54.5%
Resistant to SM only	5	5	100.0%	1	1	100.0%	6	6	100.0%
Resistant to SM and INH	6	2	33.3%	19	11	57.9%	25	13	52.0%
Total	18	9	50.0%	24	16	66.7%	42	25	59.5%

resistant to INH and all were converted, 1 was resistant to streptomycin and was converted, 18 were resistant 10 both INK and streptomycin and 11 of these were converted.

It has been mentioned earlier (Table 5) that 95 patients in SH/TH and 70 in SH/SHTW regimen did not complete 52 weeks' treatment. However, 34 out of 87 whose bacteriological status at the stage of dropping out was known had already been converted in SH/TH regimen and 26 out of 72 in SH/SHTW regimen when they discontinued treatment. Sputum of none of them could be examined thereafter inspite of efforts to do so at 44, 48 and 52 weeks, as required per protocol.

Table 10 shows the toxic reactions observed during the trial. Eighteen patients in SH/TH and 14 in the SH/SHTW regimen showed some toxic reactions. Of these, treatment had to be discontinued in the case of 2 patients in SH/TH and 4 patients in SH/SHTW regimen. One case of jaundice was noticed in each of the two regimens. Anorexia, nausea, diarrhoea and abdominal discomfort occurred in 4 patients in SH/TH and in 1 patient in SH/SHTW regimen. Giddiness and rash were noticed in equal number in both regimens. Two patients in SH/TH regimen complained of emotional and mental dis-equilibrium. The toxic reactions were almost evenly divided during the first and second quarter of treatment in both regimens and were comparatively few thereafter.

Table 11 shows the results of treatment amongst 69 patients who were excreting bacilli initially resistant to INH and/or streptomycin and whose results are not included in the previous tables. Out of these 69, only 40 patients, 20 in each of the two regimens, completed 52 weeks' treatment, and out of these 20, 12 in each regimen were converted at the end of 52 weeks. Of the 12 that were converted in SH/TH regimen, 2 were resistant to INH, 7 to streptomycin and 3 to both INH and streptomycin. In the SH/SHTW regimen, 8 of the 12 who were converted had bacilli resistant to streptomycin and 4 to both INH and streptomycin. The conversion rate in these patients is significantly ($P < 0.02$) lower than amongst those who were initially sensitive.

Discussion

The main objective of this study was not merely to determine the intrinsic superiority of one regimen over the other but to determine whether there is any difference in the results actually obtained with the two regimens in a domiciliary set up.

Irregularity and premature stopping of treatment in a self-administered regimen is well-known and has been attributed to forgetfulness, laziness or indifference on the part of the patients who, as a result of some treatment, have become symptom-free (Fox, 1962). It has also been assumed that in a self-administered regimen, collection of drugs need not always

TABLE 10
Nature and degree of toxic reactions and intolerance in the two regimens

Degree of toxicity ¹	Drug regimens	Total patients complaining of toxic symptoms	Nature of toxicity				
			Mucocutaneous	Gastrointestinal	Giddiness/tinnitus	Jaundice	Miscellaneous
First degree	SH/TH	5	—	1	2	—	2
	SH/SHTW	4	1	—	1	—	2
Second degree	SH/TH	11	6	1	2	1	1
	SH/SHTW	6	4	1	2**	—	—
Third degree	SH/TH	2	—	2	2**	—	—
	SH/SHTW	4	—	—	3	1	—
Total	SH/TH	18	6	4	6	1	3
	SH/SHTW	14	5	1	6	1	2
Grand total		32	11	5**	12**	2	5

*First degree = No interruption in treatment

Second degree = Temporary interruption

Third degree = Withdrawal from study

** One case in SH/SHTW and two cases in SH/TH regimen had both giddiness and abdominal symptoms,

TABLE 11

Results of treatment among patients whose pre-treatment cultures were resistant to INH and/or streptomycin

	Patients initially resistant to INH and/or SM	Patients not assessed at 52 weeks				Patients assessed at 52 weeks	Patients with sputum negative by culture
		Left area	Non-cooperation	Removed due to toxicity	Non TB deaths		
SH/TH	38	9	8	—	1	20* 100.0%	12 60.0%
SH/SHTW	31	2	7	2	—	20* 100.0%	12 60.0%
Total	69	11	15	2	1	40 100.0%	24 60.0%

• Includes 2 deaths (Td)

reflect faithfully the consumption of drugs and there is no entirely dependable criterion of measuring this 'concealed' irregularity (Fox, 1958). Intermittent therapy was, therefore, advocated since in such a regimen, the question of 'concealed' irregularity does not arise at all.

This trial has shown that the supervised regimen is not significantly superior to the unsupervised oral regimen, whether the results are analysed in terms of sputum conversion among patients who completed the treatment as per protocol regularly or dropped out prematurely or were irregular. An important controlled trial with intermittent regimen of streptomycin and high doses of INK have also shown that the results achieved with this regimen are no superior to the results obtained from the standard oral self-administered regimens using PAS or thiacetazone as a companion drug with INH (Tuberculosis Chemotherapy Centre 1964, Bignall 1970, Polansky 1970 etc.). The point naturally arises that if a drug regimen without any 'concealed' irregularity gives just the same results as another one in which 'concealed' irregularity is likely (the extent of which cannot be ascertained accurately), then why should the former be considered as superior to the latter in a community programme?

In a developing country with high prevalence of disease, the cost of treatment cannot be altogether divorced from the merits and demerits of various regimens. The cost of drugs required for one year's treatment in the intermittent supervised regimen is considerably greater than the cost in the INH/thiacetazone regimen. If the cost of arranging over 100 injections per patient per year and the much larger number of home visits are also taken into consideration, the overall expenditure incurred in the former regimen is nearly three or four times that in the latter.

Apart from the cost, organisational problems such as arranging injections for a large number of patients from various sub-centres near their residence also constitutes a formidable problem. Devi (1972) after a similar trial in Singapore also came to the conclusion that any advantage which supervised treatment may have is too small to justify its introduction as a routine therapy.

In conclusion, if the cost of drugs and organisational difficulties are also taken into consideration, the unsupervised regimen becomes distinctly superior to the supervised regimen in situations where resources are limited and the number of patients to be treated is very large.

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REFERENCES

1. Bignall, J.R. (1970); *Bull. Int. Un. Tuberc.*, **43**, 253.
2. Den, S. (1972); *Bull. Int. Un. Tuberc.*, **47**, 15.
3. Fox, W. (1962); *Bull. Int. Un. Tuberc.*, **32**, 307.
4. Fox, W. (1968); *J. Am. Rev. Resp. Dis.*, **97**, 767.
5. Pamra, S.P. (1971); *Ind. J. Med. Res.*, **59**, 683.
6. Poiansky, F. (1970); *Bull. Int. Un. Tuberc.*, **43**, 295.
7. Tuberculosis Chemotherapy Centre (1964); *Bull. W. ff. O.*, **31**, 247.

EFFICACY OF THREE NON-SUPERVISED CHEMOTHERAPEUTIC REGIMENS IN TUBERCULAR LYMPHADENOPATHY

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(From T.B, Demonstration And Training Centre, Agra)

Introduction

Daily or intermittent chemotherapy with or without initial intensive chemotherapy in patients with pulmonary tuberculosis has been shown to be highly efficacious by several workers (1, 2, 3, 4, 5, 6, 7.)

In any chest clinic or out-patient department, the number of patients presenting with tubercular sinuses and glands in the neck is formidable. The workers find it difficult to decide as to which type of chemotherapy would be suitable and whether early recourse to surgery would be desirable or not. As a matter of fact, till recently, surgeons used to take out the large glands and give medical treatment for a month or two thereafter. The patients improved but some of them returned with still larger glands or sinuses or disease in other parts of the body. The present study was undertaken with a view to evolve an efficacious, and cheap chemotherapeutic regimen and to find out the indication of surgical intervention in the treatment of tubercular lymphadenopathy.

Material and Methods

Selection of Patients : The study concerns one hundred eighty ambulatory patients presenting with hemiphral lymphadenitis satisfying the following criteria of selection.

1. Age five years and above.
2. Size of tuberculin (one TU RTXXIU with tween 80) Reaction 20 mm or above.
3. Size of the largest gland at least 3 cm.
4. Domiciliary stability—belonging to Agra District only.
5. Willingness to accept the prescribed treatment.

Treatment

Patients satisfying the above criteria of selection were randomly allocated to the three undermentioned non-supervised regimens on a domiciliary basis.

1. THSH₂/SH₂ Initial 8 weeks

Isoniazid 7 mg/kg, thiace-tazone 3.5 mg/kg in a single dose once daily after evening meal. Additional isoniazid 7 mgm/kg and streptomycin 40 mgm/kg at the same time, bi-weekly.

44 weeks

Isoniazid 14 mgm/kg and streptomycin 40 mgm/kg at the same time after evening meals bi-weekly.

2. SH₂

52 weeks

Isoniazid 14 mgm/kg and streptomycin 40 mgm/kg at the same time after evening meals, bi-weekly.

3. TH

52 weeks

Isoniazid 7 mgni/kg and thiacetazone 3.5 mgm/kg in a single oral dose after evening meals once daily.

Pretreatment Investigations

1. Intradermal tuberculin test with TU RTXXIlin 0.1 ml. phosphate bufler containing 0.005 per cent tween 80 on the volar aspects of the left forearm and reading was done between 72 to 96 hours.
2. Skiagram chest (70 mm film).
3. Sputum examination by direct microscopy and culture in patients having radiological lesions.
- S. Tracing of source of infection.

General Management

Duration of the existence of glands and history of previous antitubercular chemothe-

rapy were recorded before the initiation of treatment. Size and number of glands in each patient was recorded initially and then at the end of 2, 6 and 12 months. Grading of glands according to their sizes was done as given below.

1. Massive - 3 cm or more
2. Lemon — 2—2.9 cm
3. Almond — 1—1.9 cm
— Less than 1 cm.

All the patients were placed on domiciliary chemotherapy. Before the drugs were given, patients were educated several times in self administration of drugs. Drugs were issued for a month at a time. On each visit investigations as required were done and drugs were issued after re-education.

Investigations during treatment

1. Skiagram chest (70 mm) at 6 and 12 month.
2. Other investigations if necessary.

Patients in the analysis

One hundred eighty patients were admitted to the study. One patient (TH series) who got the largest gland removed by surgical intervention had to be excluded from the analysis. Thus there remained 179 patients (60-THSH-/SH², 60-SH² and 59-TH) in the analysis.

Condition on admission

Patients were similar in the three series in respect of sex, age, tuberculin reaction, size of the largest gland initially, total size of the initial massive glands, consistency of glands and duration of existence of glands.

Results

TABLE 1

Mean size of the largest gland at various stages of treatment in three regimens

Months after start of chemotherapy	THSH ₂ /SH ₃ patients		SH ₂ patients		TH patients	
	No.	Mean size of the largest gland (cm.)	No.	Mean size of the largest gland (cm.)	No.	Mean size of the largest gland (cm.)
0	60	4.5	60	4.8	59	4.9
2	56	2.9	56	2.5	54	3.1
6	44	2.1	51	2.2	46	1.7
12	34	1.2	38	1.7	34	1.2

TABLE 2

Clearance of glands at 12 months treatment by duration of glands at the time of intake

Duration of glands in months	Total patients		No of patients in whom glands were cleared	
	No.	%	No.	%
< 12 months >	52	24	24	46%
12 months	54	1	14	26%
Total	106	38		36%

TABLE 3

Distribution of the patients according to clearance of glands at 12 months by the total size of the initial massive glands

Total size of the initial massive glands	No. of patients in whom the glands		
	Cleared	Not cleared	Total
3.0 to 7.0 cm. more than 7.0 cm.	29 (45%) 9 (21%)	35 (55%) 33 (79%)	64 42
Total	38	68	106

TABLE 4

Favourable response at 6 and 12 months in three regimens

	THSH ₂ /SH ₂ Patients		SH ₂ Patients		TH Patients	
	No.	%	No.	%	No.	%
<i>at 6 months</i>						
Number of patients	44	100	51	100	46	100
(1) Marked imp.	29	66	30	59	32	70
(2) Moderate imp.	14	32	20	39	13	28
(3) Improvement all grades	43	98	50	98	45	98
<i>at 12 months</i>						
Number of patients	34	100	38	100	34	100
(1) Marked imp.	28	82	30	79	31	91
(2) Moderate imp.	6	18	8	21	3	9
(3) Improvement all grades	34	100	38	100	34	100

TABLE 5

Comparison of the three regimens at the end of 12 months

	THSH ₂ /SH ₂ Patients		SH ₂ Patients		TH Patients	
	No.	%	No.	%	No.	%
Favourable response	34	100	38	100	34	100
Clearance of glands	16	47	8	21	14	41
Residual massive glands	2	6	6	16	3	9
Healing of sinuses	16/16	100	18/18	100	14/15	93
Non-cooperation	26/60	43	20/58	34	25/59	41
Scope of surgery	2		6		3	
Cost (in Rs.) per year	82		78		30	

Conclusions

- (i) Ratio of male and female patients was 2:7 (78% females and 22% males). Males predominated only upto 10 years of age and thereafter females suffered much more than males.
- (ii) Size of the largest glands as well as duration of existence of gland at the start of chemotherapy does not seem to influence the efficacy of the regimens.
- (iii) Duration of existence of glands affected the clearance of glands ($P < 0.05$). Residual gland or glands of pea size or less was defined as clearance (table 2)
- (iv) Clearance of glands was 45% in patients in whom the total size of the initial massive glands was 3.0 to 7.0 cm and 21% in patients in whom the total size of the initial massive glands was more than 7.0 cm. The difference was statistically significant ($P < 0.05$). Hence the total size of the initial massive glands affected their clearance (table 3).
- (v) All the three chemotherapeutic regimens used, were equally efficacious, acceptable and well tolerated. As such any one of the regimens may be chosen depending on the situation. However, a regimen comprising of streptomycin seems to be more effective for early healing of discharging sinuses. As in most of the cases healing of the sinuses occurred within first 2 months of the chemotherapy. (77% in THSH₂./SH₂, 65% in SH₂, and 53% in TH Regimen).
- (vi) An induration of 20 mm or more to 1 TURT-XXm with tween 80 along with atleast one gland measuring 3 cm or more in persons presenting with lymphadenopathy provides a rather satisfactory screening criterion for the diagnosis of tubercular lymphadenitis.
- (vii) Scope of surgical enucleation of the gland seems to be rather limited. It may be considered
 - (i) If the size of the largest gland at the start of treatment is 8.0 cm or more;
 - (ii) If the size of the residual gland is about 3.0 cm at the end of 12 months prescribed chemotherapy.

REFERENCES

1. Tuberculosis Chemotherapy Centre, Madras.: Intermittent treatment of pulmonary tuberculosis. A concurrent comparison of twice-weekly isoniazid plus streptomycin and daily isoniazid plus p-amino-salicylic acid in domiciliary treatment, *Lancet*, (1963), 1, 1078.
2. Tuberculosis Chemotherapy Centre, Madras : A concurrent comparison of intermittent (twice-weekly) isoniazid plus streptomycin and daily isoniazid plus PAS in the domiciliary treatment of pulmonary tuberculosis. *Bull. Wld. Hlth. Orgn.*, (1964),31,247.
3. Tuberculosis Chemotherapy Centre, Madras : Isoniazid plus thiacetazone compared with two regimens of isoniazid plus PAS in the domiciliary treatment of pulmonary tuberculosis in South Indian patients. *Bull. wrld Hlth. Orgn.*, (1966) (1964), 34, 194.
4. Dawson, J.J.Y., Dcvadatta, S., Wallace Fox, Radhakrishna, S., Ramakrishnan, C. V., Somasundaram, P. R., Stotl, H., Tripathy, S. P. and Velu, S.: A 5-year study of patients with pulmonary tuberculosis in a concurrent comparison of home and sanatorium treatment for one year with isoniazid plus PAS. *Bull. Wrld. Hlth. Orgn.* (1966), 34, 533.
5. The East African and British Medical Research Council.: Isoniazid with Thiacetazone (Thioacetazone) in the Treatment of Pulmonary Tuberculosis in East Africa-Third Investigation : The Effect of an Initial Streptomycin Supplement. *Tubercle*, (1966). 47, J, 1.
6. The East African and British Medical Research Council.: Isoniazid with thiacetazone (Thioacetazone) in the treatment of pulmonary tuberculosis in East Africa; Second report of fifth investigations. *Tubercle* (1970), 51, 4, 4.
7. M. L. Mehrotra, D. C. Pande, K. L. Grovsr & K. p. Gautam.: Comparison of various Drug Regimens in Domiciliary Chemotherapy. *Ame. Kcv. Rbsp. Dls.*, (1970). 102,607.

ASSESSMENT OF RATE OF INACTIVATION OF ISONIAZID BY THE SULPHADIMIDINE ACETYLATION TEST

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Introduction

The rate at which inactivation of isoniazid takes place is genetically determined and varies from race to race and from individual to individual but is constant in the same individual. The rate of inactivation depends on the rate of its acetylation (Evans and White 1964; Peter Miller & Brown 1965). Based on the rate of inactivation of isoniazid, individuals can be broadly classified as slow or rapid inactivators (Knight, Selin & Harris 1959; Evans, Manley & Mckusick 1960; Jenne 1960; Sunahara, Urano & Ogawa 1961). With the advent of intermittent chemotherapy regimens, the isoniazid inactivation rate has assumed special significance. Increasing the interval between two doses to one week seems to adversely affect the response in rapid inactivators (TCC 1970). Both isoniazid and sulphadimidine are acetylated in the liver by similar enzymatic processes (Evans and White 1964) and the rate of acetylation of isoniazid closely parallels that of sulphadimidine (Evans and White 1964). The acetylation of sulphadimidine (sulfamethazine) has been found to be under the same genetic control as isoniazid (Evans 1965, Evans and White 1964).

Material and Methods

105 patients, of whom 73 were men and 32 women, were included in this study. Subjects who had (i) history of asthma or eczema (ii) major gastro-intestinal surgery (iii) a history of adverse reaction to any drug or (iv) any other serious organic disease were excluded from the study. Antituberculous drugs were withheld for at least 2 days prior to the test. Prior to administering the drug, a urine specimen from each patient-subject was tested for aromatic amines and other interfering substances by modified Bratten and Marshall method (Varley 1962). Subjects were given on an empty stomach powdered sulphadimidine tablets with a glass of water at 7.00 a.m. in the following doses :- (Ellard, 1971)

500 mg for subjects upto 51 kg
750 mg for subjects between 51 and 83 kg
1000 mg for subjects over 83 kg

After 5 hours the urine was voided and discarded. The subjects were then given a

glass of water. At 6 hours urine and a sample of blood were collected.

Free sulphadimidine and total hydrolysable sulphadimidine (free sulphadimidine plus acetylated sulpha) were determined in urine and plasma in the following way.

Urine

The urine samples were diluted 20 fold with 4.5% Trichloroacetic acid. Free sulphadimidine was then determined in a 2 ml aliquot by adding 0.2 ml of 0.1% aqueous sodium nitrite (freshly prepared daily). Shaking well and keeping for 3 minutes 0.2 ml of 0.5% of aqueous ammonium sulphamate was added. After a further 2 minutes 1 ml of 0.05% I-N-Naphthyl ethylene diamine dihydrochloride was added and kept for 10 minutes after which the optical density was measured at 540 (A)

The total sulphadimidine was determined by pipetting a 0.5ml of diluted urine in a graduated centrifuge tube and adding 1.5 ml of 2 N HCl and heating for one hour at 100°C. After cooling the volume was made up to 2 ml with water and total sulphadimidine was determined as above (B). The percentage sulphadimidine acetylated was determined by the formula.

$$\frac{(4B-A)}{(4B)} \times 100$$

Plasma

1 ml of plasma is pipetted into a centrifuge tube together with 2 ml of water and 1 ml of 20% Trichloroacetic acid. After shaking gently the precipitated plasma proteins are removed by centrifugation and the supernatant taken off with a pipette. Free sulphadimidine is determined as above on 1 ml of this supernatant with 1 ml of 5% Trichloroacetic acid added (C). Total sulphadimidine is determined by pipetting another 1ml aliquot of the supernatant into a graduated centrifuge tube together with 1 ml of 2 N HCl and heating at 100°C for one hour. After cooling and diluting to 2 ml with water, sulphadimidine was determined as above (D). The percentage of acetylated sulph-

adimidine is determined by the formula.

$$\frac{D-C}{D} \times 100$$

For ten randomly selected subjects the per cent of sulphadimidine acetylated in the urine and plasma were measured to check on the accuracy of the procedures.

For the first 50 subjects the sulphadimidine acetylation test in the urine was repeated after an interval of one week. The variation in the results was within 1%.

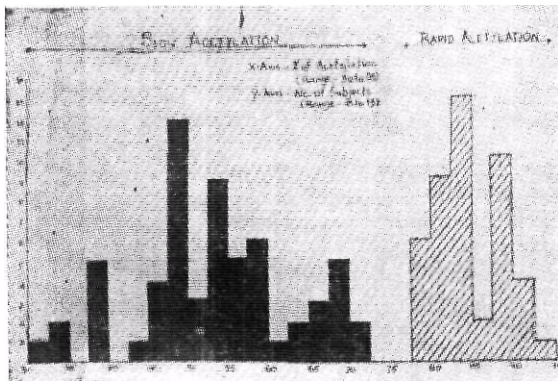
For 28 of these subjects the ratio of acetylisoniazid to isoniazid in urine was estimated at the Tuberculosis Chemotherapy Centre, Madras. There was cent per cent correlation with the results obtained by the sulphadimidine acetylation test in urine on all these patients.

Classification

Subjects are classified as slow acetylators if they have 78% or less of the drug acetylated in the urine at 5-6 hours, or 41% or less of the drug acetylated in the plasma at 6 hours (Ellard 1971). Thus, by measuring the per cent of sulphamethazine acetylated in the urine and plasma one has a check on the accuracy of the procedures, and discrepant results would indicate that the analysis ought to be redone.

Distribution of Cases

	Rapid inactivator	Slow inactivators	Total
Men	33	40	73
Women	12	20	32
Total	45(43%)	60(57%)	105



The homogeneity of the subject is confirmed by comparing the mean of a random sample from among the subjects to the mean of the 2 groups.

Discussion

Most of the previous classification methods have been based on serum isoniazid determinations after oral, intravenous or intramuscular doses of the drug. These have the disadvantages of requiring blood samples plus the instability of isoniazid in serum coupled with the technically more difficult analytical methods required for its determination. The sulphadimidine test described above is a simple test, requiring only a colorimeter or visible range spectrophotometer. The results could be made available the same day. Both sulphamethazine and acetyl-sulphamethazine are stable in urine or plasma at room temperature, although a crystal of thymol may be added to the samples as a preservative to prevent bacterial contamination. Though Evans (1969) observed that the percentage of acetylated sulphadimidine in serum appeared to be a better phenotypic discriminant than the same constituent in urine, Rao et al (1970) found that urine sulphadimidine test is preferable to the blood test since in their study, the urine test was slightly more efficient than the blood test in discriminating between slow and rapid inactivators of isoniazid.

The method used by us for determining the acetylator phenotype in man uses a small dose of sulphadimidine which is practically free from side effects.

Summary

Sulphadimidine acetylation test was carried out on 105 subjects for classification as rapid and slow inactivators. The test is simple, easy to perform and the results could be made available the same day. The patients may be classified as slow inactivators if the preparation of acetylated sulphadimidine is 78% or less in urine at 5-6 hours and 41% or less in plasma at 6 hours. Among the subjects tested 57% were slow inactivators of isoniazid and 43% rapid inactivators of isoniazid.

REFERENCES

Ellard, G.A. (1971) personal communication.
 Evans D.A.P (1965) *Annals of the New York Academy of Sciences* 123, 178.
 Evans D.A.P (1969) *Journal of Medical Genetics* 6, 405.
 Evans D.A.P, Manley K.A, and McKusick V.A (1960) *British Medical Journal* 2, 485.
 Evans D.A.P and White T.A (1964) *Journal of Laboratory and Clinical Medicine* 63, 394.

- Jenne J.W (1960) *American Review of Respiratory Diseases* 81, 1.
- Jenne J.W (1961) *American Review of Respiratory Diseases* 83, 906-
- Knight R.A, Selin M.J and Harris H.W (1959) *In transactions of the Eighteenth Conference on the Chemotherapy of Tuberculosis* p. 52 Veterans Administration, Washington.
- Peters J.H, Miller K.S and Brown P (1965) *Journal of Pharmacology and Experimental Therapeutics* 150, 298.
- Rao, K..V.N, Mitchison, D.A, Nair K..G.K, Prema K, Tripathy S.P *British Medical Journal* 1970, 3, 497.
- Sunahara S, Urano M and Ogawa M (1961) *Science* 134,1530.
- Tuberculosis Chemotherapy Centre, Madras (1970) *Bulletin of the world Health Organization*
- Varley H (1962) *Practical Clinical Biochemistry*, 3rd Edn. p. 634 Heinemann, London

IMPACT OF TUBERCULOSIS CONTROL PROGRAMME IN A RURAL AREA

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(From All-India Institute of Hygiene and Public Health, Calcutta.)

National Tuberculosis Sample Survey made during 1955-58 provides a rough basis for the prevalence of the disease in the urban, semi-urban and rural areas. There had been no comprehensive or co-operative study thereafter, specially for rural areas, to find the effect of our Tuberculosis Control Programme. According to our knowledge, there is only one study by Fridodt Molier on this subject in South Indian rural areas. The present study in a rural area of West Bengal in the practice field of All-India Institute of Hygiene and Public Health, Calcutta, possibly provides some indication in this direction in relation to the programme followed so far.

The area under study is not like other rural areas. The community in this area is utilised for training of public health workers of different categories. For this reason the community is better motivated in health education and receives better medical care than that generally obtained by rural population. Private medical practitioners are also met more frequently and they cooperate well with the programme. Almost always they refer suspected cases to the clinic for X-ray, laboratory investigations and for treatment also.

Because of these reasons the findings of all rural areas. But the information will certainly be of value for expecting certain results under certain conditions and these conditions can be obtained everywhere if x-ray facilities are made available in the neighbourhood by ordinary units in mobile vans.

Material and Methods

This is a retrospective study utilising the data from the records of Singur Chest Clinic which is entrusted with the responsibility of tuberculosis control at Singur Community Development Block under Hooghly District of West Bengal.

Place and people

According to 1961 census the area of operation is 57 sq. mile having 101 villages and 1,28,574 population. It is 34 km away from Calcutta with which it is linked by both rail and road. The people in general are poor, 67% of them are illiterate, 65% are

engaged in agriculture, 80% of the people live in mudbuilt houses with inadequate lighting and ventilation, and 50% of the households have only one living room.

MAP OF SINGUR

R.H.U.&T.C. □
HEALTH SCHOOL ▲
RAILWAY |||||
ROAD -----

General health scrvms

Singur people enjoy well-organised community health services since 1939 due to collaboration between the state government, central government, international health agencies and the local people. At present there are 8 health centres and 100 indoor beds to cater to the basic health needs of the community. The 'Health School' is a training centre for nurses-midwives and also has intensive programmes for maternity and child welfare, family planning and applied nutrition. The "Rural Health Unit and Training Centre" is the practice field for medical and para medical students of under-graduate and post-graduate courses of All-India Institute of Hygiene and Public Health, Calcutta. It has specialised sections of Environmental Sanitation. Public Health Laboratory, Family

Planning, Maternity and Child Welfare, Health Education and Chest Clinic. These training centres and its students actively participate in strengthening the routine health services of the area.

Private practice

In the area there are about 12 qualified private practitioners of modern specific medicine and 36 unqualified practitioners. All of them cooperate in the public health programme including tuberculosis control.

Tuberculosis services

7. *Case finding* : The medical officers of all the health centres and training centres in the Block and the local private practitioners refer all patients suspected of tuberculosis to the chest clinic. They are investigated clinically, radiologically and by sputum microscopy. The relevant information is recorded in the tuberculosis master register by the Public Health Nurse.

The household contacts of index cases are examined by miniature radiography and tuberculin test but the coverage has not been satisfactory.

2. *Treatment and follow-up* : Domiciliary chemotherapy is given by standard combination of INH and PAS or Thiacetazone with or without Streptomycin for an average of 18 months. Drugs are distributed from 7 Health Centres in different parts of the area so that drug collection becomes easier. The medical officers of the Health Centres cooperate by sending the patients every three months for review in the chest clinic.

3. *Home supervision* : Visits are paid by a Public Health Nurse or a Lady Health Visitor in 3 health centres of the area for supervision of chemotherapy and for imparting health education. All are polyvalent health workers. Home supervision does not exist in other 4 health centres.

4. *B.C.G. vaccination* : No mass vaccination programme has been practised upto 1971. Only tuberculin negative contacts of index cases have been vaccinated by B.C.G.

5. *Consultation service* : A consultant tuberculosis specialist is attached to the All-India Institute of Hygiene and Public Health for guidance in T.B. control. Patients requiring surgical treatment and the drug failure

cases are referred to the chest department of Calcutta hospitals.

Besides these routine services, educational programmes are organised in the community and among the doctors to intensify case detection.

Method for evaluation of the effect of the programme

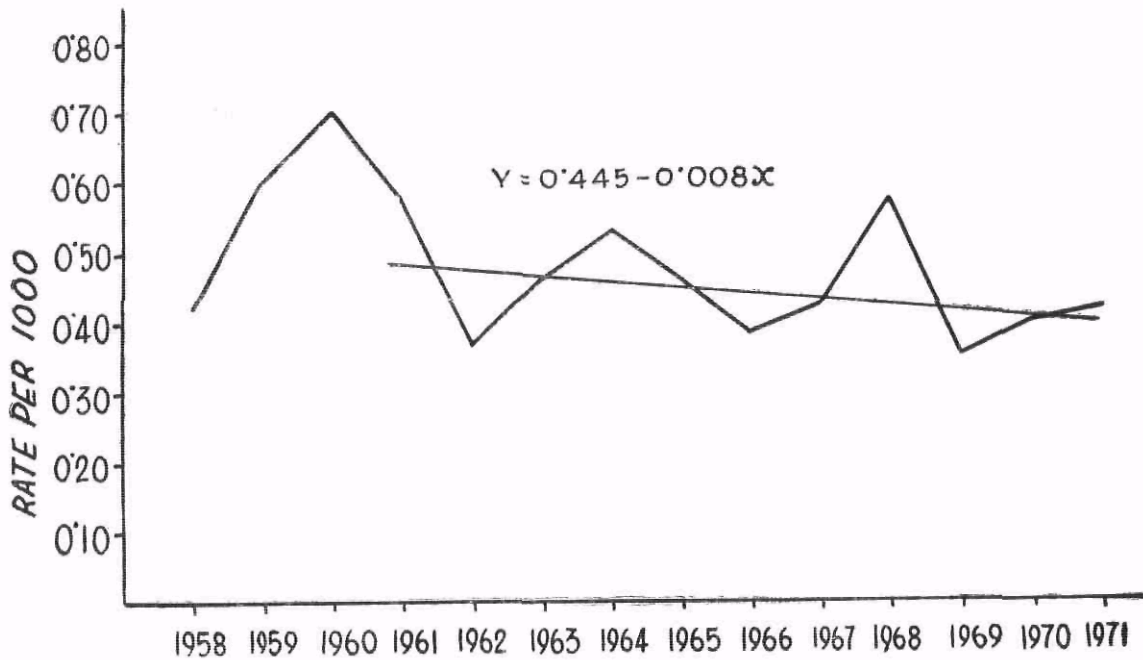
The annual total pool of bacillary excretors is regarded as the best index of tuberculosis in a community and the comparative study of the data from year to year may indicate the impact of the control programme over a number of years. These data have been collected carefully from the clinic records and are presented in table No. 1 and No. 2. It can be pertinently questioned that many cases in the community may remain in the unknown pool and therefore, data so collected may be quite inadequate for the purpose. The authors have checked this important question and they regard that practically all symptomatic cases in the community have been recorded in the clinic register.

During the years 1968, 1969, 1970 and 1971, an investigation was made in 4 villages of the area, each having about 1,000 population. For one village 82% of the population were covered by MMR and thereafter large x-ray and sputum tests were made wherever any pathology in M.M.R. was detected. In absence of mobile M.M.R. van, other 3 villages were thoroughly combed by clinical examination and all chest symptomatics and/or otherwise suspected persons were similarly x-rayed and sputum tested. To our surprise it was revealed that the cases detected in this survey were already diagnosed and registered in the clinic. This fact encourages us to regard the number of all newly diagnosed cases annually as the incidence of the disease and the total of old and new cases as the prevalence rates. This also encourages us to accept our figures of annual total pool of bacillary excretore as practically correct.

Accepting these contentions, the impact of the control programme, yearly for a period of 14 years, has been evaluated by comparing the total pool of bacillary excretors and the number of new sputum positive cases for the period of 1958 to 1971. The rates have been calculated per 1,000 mid-year estimated population. A tuberculous patient showing acid fast bacilli in the sputum smear at any time during a calendar year has been taken as a bacillary excretor for that year. New sputum positive

DIAGRAM-I

TREND OF BACILLARY EXCRETORS, SINGUR, 1958-1971



cases refer, however, to this status only at the initial stage of diagnosis.

Findings

TABLE I
Yearly pool of bacillary excretors,
Singur, 1958-71

Years	No. of cases	Rate per 1,000 population
1958	51	.42
1959	75	.60
1960	92	.72
1961	74	.57
1962	48	.36
1963	64	.46
1964	73	.52
1965	65	.45
1966	56	.38
1967	64	.42
1968	83	.57
1969	55	.35
1970	65	.40
1971	70	.42

increasing rate of the total pool of infectious cases till 1960. From 1960 to 1962 there has been a fall and after that till 1971 the rate remains somewhat stationary with slight fluctuations except in 1968. The trend line between 1961 and 1971 as calculated by least square method shows slight downward inclination. The data therefore show that the control programme was initially effective to diminish the pool but was later on not effective enough for further control of tuberculosis in the community.

The data on newly diagnosed sputum positive cases, possibly the incidence, as shown in Table 2 and Diagram 2 are similar in character to the total pool of bacillary excretors.

Discussion

This is a retrospective study from the well kept records of the rural health services of an important teaching institute like All-India Institute of Hygiene and Public Health, Calcutta. Although no complete survey has

Table I and the Diagram I show an

TABLE 2
sputum positive cases, Singur, 1958-1971

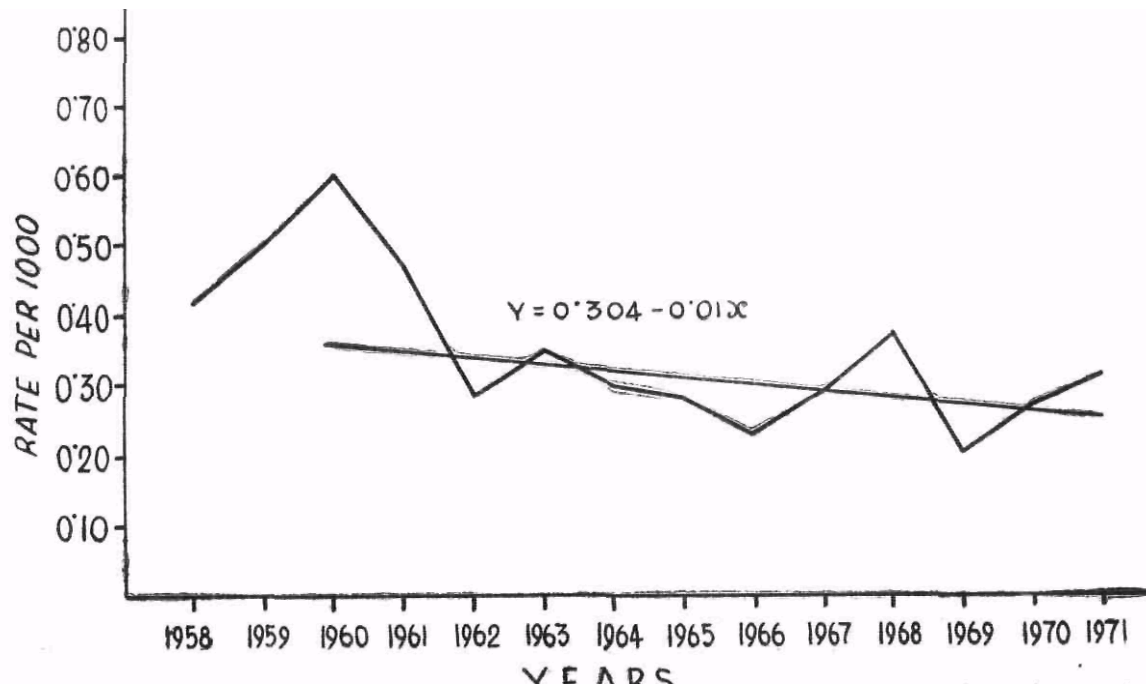
Year	No. of cases	Rate per 1,000 population
1958	51	.42
1959	62	.50
1960	75	.60
1961	59	.47
1962	38	.28
1963	50	.35
1964	41	.30
1965	43	.28
1966	36	.23
1967	43	.28
1968	57	.37
1969	29	.20
1970	43	.27
1971	51	.31

been made of the population of the area it is reasonably assumed as explained under the "method of evaluation of the effect of the control programme" that practically all tuberculosis cases have been recorded in the clinic register. For this reason the study may well represent the effect of an anti-T.B. programme currently in practice there or in other words the trend of tuberculosis in the community under such a programme.

The initial sharp rise in both the curves may be due to several reasons. There might have been a rapid draw of tuberculosis cases in the chest clinic from the unknown pool due to introduction of intensive control programme. It is also not unlikely that the disease had a rising tide in absence of a definite control programme. Whatever may be the cause of this rise, the disease definitely came down in 4th year and maintained a slightly downward trend over the next 10 years. The slope however was found not significant statisti-

DIAGRAM-2

TREND OF NEW SPUTUM POSITIVE CASES, SINGUR, 1958-1971



cally at 5% significance level. Therefore it can be said that a programme consisting of : (i) case finding by examination of chest symptomatics and (ii) domiciliary chemotherapy, had definite effect in controlling the rising tide of tuberculosis but did not have noteworthy impact in diminishing the disease thereafter. In view of these findings it is concluded that the existing T.B. control programme in question needs modification to get better and quicker result.

The fluctuations seen in the curves over 11 years are not great except one rise in 1968. Searching for causes of such fluctuations it was detected that during the previous year there had been a severe scarcity of food in the area for which gruel kitchen (Langar Khana) had to be opened by the Government. This may be the reason for upward fluctuation in question.

Summary

This retrospective study of the trend of tuberculosis in a rural area with a definite control programme over a period of 14 years, shows that it was effective for diminishing the total pool of infectious cases and the yearly

incidence of the disease. It was, however, not effective enough for quick control of the disease thereafter.

ACKNOWLEDGEMENTS

The authors are thankful to Professor **A.K. Banerjee**, Director, All-India Institute of Hygiene and Public Health, Calcutta, for permission to use the chest clinic data of the Rural Health Unit and Training Centre, Singur and to publish it. The authors also acknowledge the statistical help of Mr. A.K. Sen, Assistant Professor of Statistics and the valuable comments of Dr. A.L. Saha, Associate Professor of Epidemiology, All-India Institute of Hygiene and Public Health, Calcutta.

REFERENCES

3. I.C.M.R., New Delhi, *Tuberculosis in India, A Sample Survey 1955-58*.
2. **Frimodt-Moller, J.**, *Bulletin W.H.O.* 22, 1960.
3. **Census of India, 1961, District Census Hand Book, Hooghly, West Bengal.**

RESULTS OF TUBERCULIN TESTING IN AN APPARENTLY REALTY KASHMIRI POPULATION GROUP

S. N. DHAR, S. P. MISRA AND ABDUL RAUF
(From Government Medical College, Srinagar.)

Various Surveys of prevalence of tuberculous infection have been done in different parts of India and in this paper we intend to report results of our study of tuberculin testing from Kashmir valley, a region which differs from rest of India in its social, cultural and climatic conditions. This study is first of its kind from this part of the country.

Material and Methods

The state of Jammu and Kashmir consists of 3 regions viz. Jammu, Kashmir, and Ladakh. This study has been done on pure Kashmiri stock living in the valley of Kashmir. Subjects for the study came from rural and urban population groups. They were selected by random method to eliminate bias completely. The entire population was stratified and from every stratum (which was mohalla) households were selected by the systematic sampling method. The subjects were of both sexes within 5 and 25 years age group. The persons selected were apparently healthy and presented no symptoms pertaining to any disease. Persons having clear or even doubtful B.C.G. scars were excluded.

The city of Srinagar was divided into various zones and zones 1, 2, 4, 8, 10, and 11 were included in the study. All the houses in these zones were numbered and the survey was conducted in every 20th house.

All the persons normally resident in the house at the time of interview were tuberculin tested. This represented urban population. For the rural population groups, help of the Chittaranjan Mobile Teaching Cum Service

Hospital was taken. During a two-year period the latter was located at four places, viz; Shopian, Achabal, Ganderbal, and Tangmarg. One more village in District Baramulla was included to make it fairly representative of the entire valley. Same method of sampling as was employed in urban population was applied.

Tuberculin test was given on the volar aspect of the left forearm with due precautions, 0.1 ml. of 1 TU of PPD RT-23 was injected intradermally so as to produce a wheal of not less than 5 mm. Results were read after 72 hours, measuring accurately the transverse and longitudinal diameter of the induration in centimeters. The mean size of the induration was noted down.

Results

A total of 1711 subjects were studied. There were 1129 males and 582 females. The number of tuberculin positives was 709 and number showing less than 10 mm. of induration was 1002 (Tables I and II(a)).

It is evident from Tables II(b) and II(c) that age specific rates of tuberculin positivity are significantly different in males, but not in females.

Subjects showing an induration of 15 mm. or more were examined for clinical and radiological evidence of tuberculosis. Out of the 37 cases, 12 had healed and 25 active disease.

Two of the cases showing fibrocaceous type of tuberculosis were found positive for A.F.B.

TABLE I

Shows the tuberculin status of 1,711 subject by sex

Sex	Tuberculin Negative	Percentage	Tuberculin Positive	Percentage	Total
Males	696	61.6%	433	38.4%	1129
Females	306	52.6%	276	47.4%	582
Total	1002	58.6%	709	41.4%	1711

TABLE II (a)

Shows the tuberculin status of 1711 subjects by age

Age group	Total	Tuberculin Negative	Percentage	Tuberculin Positive	Percentage
6-9 years	142	98	69.09%	44	30.91%
10-13 „	267	173	64.80%	94	35.20%
14-17 „	344	216	62.50%	128	37.50%
18-21 „	445	241	54.16%	204	45.84%
22-25 „	513	274	53.42%	239	46.58%
Total	1711	1002	58.61%	709	41.41%

TABLE 11 (b)

Shows the age-specific tuberculin positivity rates of 1,129 male subjects

Age Group	Total No. of subjects tested	Tuberculin Negative	Tuberculin Positive
6-9 years	105	77	28
10-13 „	192	131	61
14-17 „	247	165	82
18-21 „	275	153	122
22-25 „	310	170	140
Total	1129	696	433
		61.65%	38.35%

TABLE II (c)

Shows the age-specific tuberculin positivity rates of 582 female subjects

Age group	Total No. of subjects tested	Tuberculin Negative	Tuberculin Positive
6-9 years	37	21	16
10-13 „	75	42	33
14-17 „	97	51	46
18-21 „	170	88	82
22-25 „	203	104	99
Total	582	306	276
		53.62%	46.28%

III

Shows the subjects found tuberculous (infective and active)

Sex	Calcified spots	Percentage	Active tuberculous cases	Percentage	Total
Males	7	.41%	14	.82%	21
Females	5	.29%	11	.64%	16
					1.23%
					.93%

on sputum swears. None of those showing calcified spots on chest radiographs indicated any evidence of active disease.

Discussion

Tuberculin testing of a large number of individuals in a population is supposed to provide fairly accurate information regarding the prevalence of infection in a given community. However, in spite of its high degree of sensitivity and specificity, problems arise in the interpretation of the test in areas where non-specific sensitivity due to prevalence of atypical mycobacterial infections is widespread. We in this state had no guide-lines for the criteria of positivity under the local milieu. The definition of a positive reaction has varied from time to time and place to place. Thus most of the earlier workers, and MRC (1959) had rather arbitrarily considered a reaction size of 5 m.m. or more to indicate infection. Sikand, Raj Narain and Mathur, during their three surveys (1952 to 1958) among Delhi police recruits, had taken a reaction of 6 m.m. after 72 hours of the test with 5 TU of PPD, as positive. On the results of Madanapalle survey (1950-1955) wherein 5 TU of PPD was used Fridmot Mofler noted that no disease active or probably active was seen among the many with small reactions of 9 m.m. or less, even among those with 5-9 m.m. Later, Raj Narain et al (1963) recommended, for epidemiological studies, reactions of 10 m.m. or larger size for estimating infection rates. Edwards and Edwards (1965) stated that 12 m.m. and larger reactions to 5 TU of PPD was indicative of tuberculous infection. Cornstock and Palmer (1966) estimated 'population truly infected' by doubling the number of those with 15 m.m. or more of induration. Again Raj Narain (1968) from a controlled study in Bangalore using 1 TU of PPD RT-23 concluded that for a meaningful classification of those actually infected with "tubercle bacilli, only an induration of 15 m.m. or more

may be regarded as evidence of infection. Considering all these factors we have taken an induration of 10 m.m. and more to 1 TU of PPD RT-23 after 72 hours as the criteria of positivity. The same criterion was adopted by Pamra et al (1970) in their survey of household contacts. Further, in view of Raj Narain's Bangalore study, all individuals registering a reaction of 14 m.m. and above were subjected to detailed clinical radiological examination, since it was in this group of individuals that we expected to find cases of tuberculosis. We did not include individuals above 25 years of age for the reasons that the well known phenomenon of waning allergy occurs in the aged, and the boosting of allergy of non-specific infections among elderly persons, would have vitiated the results in a preliminary study like this.

In our study of 1,711 individuals 709 subjects reacted positively, i.e. 41.45% of our subjects upto the age of 25 years were infected with mycobacterium tuberculosis. By the age of 9 years, nearly 1/3rd of Kashmiri population in the 6-25 years age group was found infected. The prevalence of infection was seen to rise steadily with age (table No. 2) as has been the case in other studies. Raj Narain (1963) though this rise 22-25 years age group was less than 1%.

A break-up of the prevalence figures for the two sexes again shows the phenomenon of increasing infection with age, with the difference that whereas 43.24% of girls by 9 years were found infected, only 26.66% of boys upto this age revealed positivity. The over-all prevalence was also higher among the females. Probably a wider study could have clarified the position.

To know the prevalence of pulmonary tuberculosis in the valley it should have been our endeavour to undertake X-Ray and sputum examination of all the infected subjects dis-

covered during this study, but it was not practicable under the limitations of our circumstances. We, therefore, investigated only those who reacted with an induration of 15 m.m. and more.

Clinical and radiological evidence of active tuberculosis was found in 25 of the 709 tuberculin positive subjects i.e. in 1.46% of reactors. Calcified spots, highly suggestive of inactive tuberculosis, were noted on radiographs of 12 subjects. Thus evidence of active and inactive tuberculosis was obtained in 2.16%, a figure, by and large, agreeing with other Indian studies, Raj Narain (1964) found 2.5%, Fridmodt-Moller (1955) 1.2% to 2.5% and Sohan Singh reported 1.3% to 2.5% at Patiala Conference in 1970. The figure might have become marginally higher if all the tuber-f cases were infected. The overall prevalence of bacillary cases in our study was 0.28%. Since we encountered only 25 active cases this meant that 8% had bacteriologically confirmed disease on smear examination alone. Our figures for bacillary cases are on the low side as compared to the figure of 0.4% of the National sample survey (1955-58), and the range of 0.23% to 3.41% of the Tumkur Survey (1963). This may be due to the fact that cases in higher age groups were excluded from our study and also that sputum smears alone without cultures were depended upon.

Summary

This study was undertaken to find out prevalence of tuberculous infection among apparently healthy Kashmiri subjects belonging to 6-25 years age group. An induration of 10 m.m. and larger to ITU of PPD-RT-23, read at 72 hours was taken as positive.

The results of tuberculin test have been analysed and discussed with respect to prevalence related to sex and age groups. Subjects showing a reaction size of 35 m.m. and larger were investigated to find out cases of healed (inactive) and active disease. The prevalence of infection and of disease appears to be in broad agreement with studies undertaken elsewhere.

REFERENCES

- Edwards and Edwards. *American Review of Tuberculosis* (Supplement) 81-, 1960.
- J. Fridmodt Moller, Jacob and R. Parthasarathy. Observations on the protective effect of B.C.G. vaccination in a South Indian population, *Bull. Wkl. Hlth. Org.* 30,545-574, 1964.
- Pamra, S.P. and others. Disease among household contacts of pulmonary tuberculous patients. Paper read at 25th National conference on T.B. and Chest Diseases. Patiala. Jan 1970.
- Raj Narain Problems in defining a case of pulmonary tuberculosis in prevalence surveys. *Bull. Wld. Hlth. Org.*, 39/5,701-729., 1968.
- Raj Narain, S.S. N'air, P. Chandershakher and G. Ramanathan Rao. Problems connected with estimating the incidence of tuberculosis infection. *Bull. Wld. Hlth. Org.*, 34., 605-622., 1966.
- Raj Narain, A. Geser, M.V. Jambunaihan & M. Subramaniam. Tuberculosis prevalence survey in Tumkar district. *Ind. J. Tuberc.* No. 3, 85-116.. June 1963.
- Sikand, B.K. and others. Incidence of T.B. as found judged by resurveys. *Ind. J. Tuberc.* 6., No. 3.,73-83., 1959.
- Sohan Singh. Proceedings of the 25th National Conference on tuberculosis and chest diseases. Patiala, Jan 1970.

TOLERANCE TO SODIUM PAS ADMINISTERED INTRAVENOUSLY

B.K. KHANNA.

(From K.G. Medical College, Lucknow)

The study was undertaken to evaluate the tolerance to high doses of sodium PAS administered by intravenous route for sixteen weeks in patients suffering from pulmonary tuberculosis.

Material and Methods

In all, 48 patients suffering from pulmonary tuberculosis were selected for the study. All of them had been grossly treated with various combinations of anti-tuberculosis drugs prior to their inclusion in the study.

PAS was administered as sodium salt ("Aminacyl" Wander) in the dosage of 25 gm of the salt dissolved in 500 cc of normal saline. The drip was run rapidly so as to last for 45 minutes to 90 minutes. 25 gms of the salt, as claimed by manufacturers, contained 19 gms of active PAS. The drip was administered on alternate days.

Sodium PAS (hereinafter written as PAS) drip was administered in combination with second line drugs e.g. ethionamide, pyrazinamide, cycloserine and ethambutol in conventional doses.

Result

I. Acceptability of I.V. PAS Therapy.

The therapy was very poorly accepted by the patient.

	No. of cases
At the initiation of Therapy	48
Completed 4 weeks of therapy	34 (70%)
Completed 8 weeks of therapy	9(19%)
Completed 12 weeks of therapy	4 (9%)
Completed 16 weeks of therapy	1 (2%)

2. Reasons for rejection:

Total No. of cases	47
(i) Pain and thrombophlebitis	36 (74%)
(ii) Failure to find veins for further drip	8(18%)
(iii) Repeated pyrogen reaction	15 (32%)
(iv) Diarrhoea and vomiting after I.V. drip	6(13%)

(Phlebothrombosis or Thrombophlebitis was recorded in all the cases, though complained of by only 36 cases).

Discussion

Administration of PAS by intravenous route was considered to be worthy of trial on several counts:

1. Resistance to PAS by the TB develops least commonly of all the primary group of anti-tuberculosis drugs. Therefore, it could be of practical utility, as an adjunct, in the management of grossly treated cases.

2. Results of drug sensitivity studies on PAS (for TB) are still not as reliable as those of streptomycin and INH. This might imply that many organisms labelled as resistant to PAS, in vitro could still, in vivo, be sensitive to PAS.

3. Administration of PAS in such high doses by intravenous route could lead to peak serum levels which necessarily would have greater bacteriostatic effect on TB than when the same drug is administered by mouth.

4. Dearth and erratic availability of acceptable drugs for the treatment of drug resistant cases of pulmonary tuberculosis.

5. This form of therapy is practicable in hospital practice.

6. The cost of treatment, per drip, in the hospital would work out to around Rs. 2.50.

The study revealed two important observations. First, this form of PAS therapy is very poorly tolerated by the patients. Besides the problems of venothrombosis, pain at the site of drip, and pyrogen reactions it was difficult to locate a new vein every time the drip had to be administered. Secondly, six patients had recurrent diarrhoea and vomiting (without associated pyrogen reaction) following the drip. It is possible that these symptoms following systemic PAS therapy, could be due to excretion of the drug in G.I. Tract and therefore could still be a consequence of local irritation. However, for want of suitable facilities, this aspect of the problem could not be confirmed.

Phlebothrombosis or thrombophlebitis has another aspect which must be seriously considered. Fragments of blood clots from thrombosed veins could be a future source of pulmonary embolism. How frequently that would happen has not been studied by us. However, production of a source of pulmonary embolism, which by itself may be a lethal complication, by parenteral administration of a drug, which is weakly tuberculostatic, may not be very desirable.

The only redeeming feature of the study was rapid defervescence and improvement (clinically and bacteriologically) noted in cases who continued to accept this form of therapy. In 5 instances, the fever had not responded to a combination of 2 or 3 second line drugs till I.V. PAS was also added to the regimen. The defervescence, once recorded, persisted even after I.V. PAS therapy had to be stopped. The improvement noted after this therapy could be due to any of the first three factors recorded above (vide supra). However, since the drug

was used only as an adjunct to second line drugs and not as a definitive treatment by itself, the results of therapy have not been discussed in this paper.

In conclusion, PAS administered by I.V. drip is, though clinically useful, poorly tolerated by patients, and hence cannot be recommended for routine use even in drug resistant cases. It may lead to phlebothrombosis which at least hypothetically can lead to pulmonary embolism.

Summary

PAS was administered as an adjunct by rapid I.V. drip in 48 patients suffering from pulmonary tuberculosis in conjunction with 2 or 3 second line drugs. The drug leads to phlebothrombosis at the site of drip associated with considerable pain locally. It is poorly accepted by the patients. Because of these problems, this form of therapy can not be recommended for use even in hospitalised cases.

CASE REPORTS

TUBERCULOSIS AND LEPROSY

M.S. AGNIHQTRI, S. RASTOGI AND R.C. AGARWAL

(From K.G. Medical College, Lucknow)

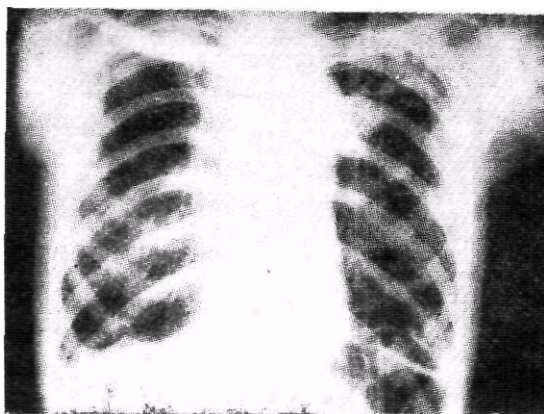
Both leprosy and tuberculosis are caused by bacilli of Mycobacterium family. B.C.G. has demonstrated protection against tuberculosis and leprosy (Souza Campos, 1953). The antigenic similarity between Mycobacterium tuberculosis and Mycobacterium leprae was clinically demonstrated by the fact that B.C.G. vaccination leads to lepramin conversion also (Brown, 1966). Only few reports of simultaneous occurrence of tuberculosis and leprosy clinically are available in literature (Gajwani 1968; Gupta, 1971).

The present article reports three cases of tuberculosis and leprosy attending Kasturba T.B. Clinic and Hospital, Lucknow.

Case Reports

Case 1

M.M., 65 years old, farmer, resident of Basti, was admitted in Kasturba T.B. Clinic and Hospital, Lucknow with the complaints of cough with expectoration, fever and marked weakness for last one year. On physical examination, he was an old man of average build, without dyspnoea and clubbing. Systemic examination apart from presence of crepitation over both apices, revealed anaesthetic, hypopigmented patches over elbow and thigh. His ulnar nerve was thickened. X-ray chest showed bilateral pulmonary tuberculosis, acid-fast bacilli were detected in sputum and biopsy from anaesthetic patch showed evidence of tuberculoid leprosy.

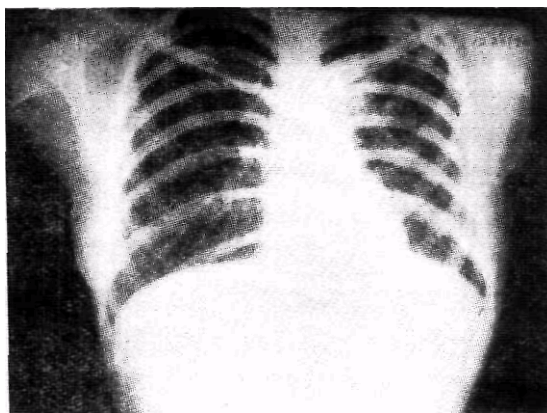


Case 2

D.S. 18 years, Male resident of Lakhimpur, farmer, was seen in Kasturba Clinic and Hospital, Lucknow in November 1969 because of cough with expectoration and weight loss for one month and had haemoptysis 7 days back. On general examination, he was a young man of average built, not dyspnoic, no clubbing or cyanosis. On systemic examination revealed harsh vesicular breathing with crepitation at left infra-clavicular region, multiple depigmented anaesthetic spots on the upper and dorsal part of forearms and thickened ulnar nerves. X-ray chest showed evidence of pulmonary tuberculosis, acid fast bacilli were detected in sputum smear and skin biopsy from affected area confirmed the diagnosis of tuberculoid leprosy.

Case 3

S.K., aged 30 years, female married housewife, resident of Allahabad, was seen in skin outpatient department for depigmented, anaesthetic patches present over face fore arms and elbows for two months and dry cough for one month. Physical examination revealed signs of unilateral lung disease, multiple hypopigmented patches with thickened ulnar and greater auricular nerves. X-ray chest showed evidence of pulmonary tuberculosis with acid fast bacilli in sputum examination. Skin biopsy from affected area confirmed the diagnosis of leprosy.



Discussion

In our cases the diagnosis of leprosy was based on clinical manifestation like anaesthetic depigmented patches, thickened nerves and

TUBERCULOSIS AND LEPROSY

demonstration of acid fast bacilli in skin biopsy. The diagnosis of associated tuberculosis was made on characteristic radiological lesions and sputum smear examination. In two cases diagnosis of leprosy could be suspected only in the wards after thorough examination whereas third case was referred to us from skin out-patient department where she was being treated for leprosy. Our patients presented with tuberculoid type of leprosy, which is against the view of Relvich (1954) that association of tuberculoid form of leprosy with tuberculosis was uncommon. But Gajwani et al. 1968 and Gupta et al. 1971 also reported association of tuberculoid type of leprosy with tuberculosis. As tuberculoid leprosy is characterised by gradually developing anaesthetic hypopigmented patches on skin and thickened nerves, it does not force a patient to seek medical attention for a long time. Only one female patient reported to skin out-patient department first; that too, probably because of cosmetic reasons. Therefore a careful search for any evidence of early leprosy is advisable in tuberculosis hospitals, as both tuberculosis and leprosy are related to over-crowding and poverty.

B.C.G. could prevent development of leprosy also (Chaussinand 1948; Rees 1966). Lowe et. al. (1956) has noted lepramin conversion after J.J.C.G. vaccination which denotes only antigenic similarity between Mycobac-

terium tuberculosis and Mycobacterium leprae. The present observations of three reported cases demonstrate clinical relationship between tuberculosis and leprosy.

Summary

Three cases of tuberculosis and leprosy are reported. The clinical importance of association between tuberculosis and leprosy have been emphasised.

REFERENCES

1. Brown, J.A.K. and Slono, M.M. (1966) *Brit. Med. J.* 7.
2. Chaussinand, F. (1948; *Int. J. Up.* 16 : 431.
3. Gajwani, B.W., Verma, B.S. Marwaha, R.K.. and Pande, R.S. (1968). *J. Ass. Phy. Ind.* 16 : 563.
4. Gupta.MC. and Prasad, M. (1971) *Ind. J. Med. Sci.* 25 : 183-185.
5. Lowe, J. and Mdadzean, J. A. (1956) *Leprosy Rev.* 27 : 140.
6. Rees, R.J.W. (1966) *J. Leprosy.* 34 : 186.
7. Souza Compos, N. (1953) *Int. J. Leprosy*, 21; 603,

NEWS & NOTES

NEW PRESIDENT OK E R C.

Dr. M.S. Chadha, Vice-Chairman of the Tuberculosis Association of India, has been nominated as the President of the Eastern Region of the International Union Against Tuberculosis. The 9th Conference of the Eastern Region will be held in New Delhi in 1974. The Conference will be held jointly with the 29th National Conference on Tuberculosis and Chest Diseases in Delhi in November 1974.

CHEST AND HEART ASSOCIATION FELLOWSHIP

Shri P.N. Raman, Administrative Officer, Tuberculosis Association of India and Mrs. M. Paul, the Chief Public Health Nurse, New Delhi TB Centre who were awarded the Chest and Heart Association Fellowships have returned after spending about two months in the U.K. and a week in the continent. While in the U.K. Shri Raman studied the administrative set up and working of the Chest and Heart Association, London, and its affiliates. Mrs. Paul studied the TB Control Programme and the Training Programme of Public Health Nurses and other para-medical personnel especially in the field of Tuberculosis. They attended the Conference of Surrey and South West London Care Committees and also the Conference on Management of Asthma organised by the Chest and Heart Association. They visited the Scottish Branch of the Chest and Heart Association in Edinburgh and a number of TB Institutions in London, Edinburgh, Cardiff, Manchester, Birmingham, Wolverhampton, etc. In the Continent they spent a few days in the offices of the International Union Against Tuberculosis and the French National TB Association in Paris and the Carlo-Forlanini Institute in Rome studying the working of these organisations. Mrs. Paul visited Copenhagen and studied the working of the Central Dispensary and the Danish Index.

TWENTY-EIGHTH NATIONAL CONFERENCE

The Twenty-eighth National Conference on Tuberculosis and Chest Diseases will be held for four days from 25th to 28th November, 1973 in Bhopal. Subjects to be discussed at the Conference include District TB Control Programme, Chemotherapy, Community Participation in Tuberculosis Control, BCG, Relapse after medical and surgical treatment of pulmonary tuberculosis, Tuberculosis Meningitis, Fungus

Diseases of the Chest, Bronchogenic Carcinoma, and Air Pollution.

Those who wish to register as delegates to this Conference may kindly write to: Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110001, at an early date.

HEALTH VISITORS' COURSE

The 1973-74 TB Health Visitors¹ Course commenced in the New Delhi TB Centre on 2nd July, 1973. Ten candidates have joined.

TB SEAL CAMPAIGN

The 24th TB Seal Sale Campaign will commence as usual on 2nd October, the Mahatma Gandhi's birthday and terminate on 26th January, 1974, the Republic Day. The new Seal design carries the 'Butterfly' motif.

SHIBIRS—MAHARASHTRA

The Maharashtra State Anti-TB Association organised three Shibirs during May and June 1973 at Kankavli, Malvan (Dist. Ratnagin) and, Pali (Dist. Colaba). The 46th and 47th Shibirs held at Kankavli and Malvan were organised by the Konkan Medical Aid Society. In all 247 persons were examined of which 200 were screened, 54 cases of tuberculosis were found and given oral anti-TB drugs on the spot. 4,400 children were given BCG vaccination in nearly 30 village centres in Kankavli and Malvan. The 49th Shibir at Pali was organised in collaboration with Gram Panchayat Samiti of Pali Sudhagad and assisted by local doctors and social workers. In all 298 persons were examined of which 146 were screened. BCG vaccination was given to 2,198 persons and the 48 cases diagnosed as TB were given oral anti-TB drugs on the spot. The District TB Clinic at Alibag was entrusted with further treatment and follow up.

SHIBIR PUNJAB

The TB Association of Punjab has launched a medical campaign under the name of 'Medical Manthan' which was organised in Ropar District from 18th to 30th June, 1973. The Campaign included 50 multi purpose teams consisting of 100 experienced men and women doctors and 600 para-medical men from all over the State. The Para-medical personnel made door to door calls and enquired about people's ailments. The doctors prepared

family folders and experts carried out various tests. Serious cases requiring x-rays, BCG were given slips for expert treatment. The campaign covers Health Education, Prevention, Diagnosis, Treatment and Reference.

SEMINAR IN TAMIL NADU

The District TE Association, Coimbatore organised a Seminar on Tuberculosis at Coimbatore on 14th and 15th July, 1973 under the auspices of the Tamil Nadu TB Association for the benefit of medical practitioners. Thiru K. Aubazhagan, Minister of Health, inaugurated the Seminar, which was presided over by Dr. K.V. Krishnaswami. Subjects included in the Seminar were Epidemiology in Tuberculosis, BCG, Role of Cortico Steroids in TB, Gastro-entriology, TB in Genito Urinary system, Childhood Tuberculosis, TB in nervous system, Tuberculosis of bones, joints and skins and Control Programme of TB in Tamil Nadu.

The District TB Associations of Salem, North Arcot and Trichi have decided to conduct Seminars in their Districts also.

REFRESHER COURSE IN ANDHRA PRADESH

The TB Association of Krishna District, Machilipatnam, organised a TB Refresher Course on 22nd July, 1973 under the auspices of the TB Association of Andhra Pradesh. Dr. K. Ramesh Pai, Director of Medical and Health Services, Hyderabad, inaugurated the course. A team of TB specialists from Hyderabad conducted the Refresher Course.

TB SEMINAR IN KERALA

The TB Association of Kerala organised a two-day Seminar on Tuberculosis on 14th and 15th July, 1973. The Chief Minister of Kerala inaugurated the Seminar.

AWARDS BY THE ACADEMY OF MEDICAL SCIENCES

The Indian Academy of Medical Sciences will award the following Medals during the year 1973-74 :

1. "Dr. Misra Memorial Gold Medal" for the best unpublished work in any field of biomedical by a younger (below 35 years) biomedical scientist. Other selected scientists may be awarded certificates of merit.

2. "Sir Shriram Gold Medal" for the best published paper during the preceding three years on any Basic Medical Science subject (Anatomy, Physiology and Biochemistry including their sub-specialities). The work should have been done in India by any biomedical scientists *of any age*.

Further information may be obtained on a self addressed stamped envelope from the Executive Director, Indian Academy of Medical Sciences, C-II/16, Ansari Nagar, New Delhi-16.

MEMBERSHIP EXAMINATION

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ABSTRACTS

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Correlation between INH inactivation and therapeutic result in skin tuberculosis (Lups Vulparis)

L. Forstrom, M.J. Manila & H. Tiitinen. Annals of Clinical Research (Finland) ; 1972, 4, 165.

Lupus vulgaris was used for assessing the extent to which the INH inactivation rate of the patient influences the therapeutic response to INH. Since the rate of acetylation of INH resembles that of sulphadimidine, the study is based on latter rate. The study suggests a correlation between the rate of acetylation and clinical response to INH treatment in patients with lupus vulgaris treated for a relatively short period.

S.P.P.

The Value and possibility of applying a new method for collecting the sputum in anti-tuberculous dispensaries

A. ZOI, Viorica Bogdanescu, N. Evian, Maza Draga, Oigo Butnaru. Romanian Medical Review ; 1972 16 (2), 55.

The efficiency of various methods of collecting sputum in an out-patient department from the point of view of recovery of tubercle bacilli from these has been studied. Spontaneously expectorated sputum by the patient has been found to give positive results most frequently. In patients who are expectorating sputum, laryngeal swab examination gives poorer results than examination of the spontaneously expectorated sputum. Taking a laryngeal swab in addition to the expectorated sputum does not improve the percentage of positive results. In patients who are not producing any sputum, inducing cough by laryngeal swab and examining the material expectorated after induced cough gives better results than culturing the laryngeal swab.

S.P.P.

Tuberculosis risk in persons with fibrotic lesions

L.B. Edwards, B. Doster, V.T. Livesay and S.H. Ferebee. Bull. Int. Un. against Tuberculosis; 1972, 47, 151.

Three groups of population with lesions radiologically compatible with tuberculosis but not considered active were followed for 5 to 20 years. None of these persons were treated. In all three groups, two factors emerged as prominently associated with risk of disease. One is length of time that a lesion has been present and stable and the other is the tuberculin reaction. The newly identified lesions appeared to be associated with a much higher risk of developing active disease than those which had been followed for some time. An inactive lesion in a tuberculin reactor is associated with a much higher risk of active tuberculosis than when it is present in a non-reactor.

S.P.P.

Tuberculosis risk in persons with fibrotic lesions

V.H. Springett. Bull. Int. Un. against Tuberculosis; 1972,47, 157.

Seven hundred tuberculin positive persons in the age groups 16 to 45 years, clinically well and at work, with a small radiological lesion which had been stable for one year earlier and at least 8 laryngeal swab cultures were negative during this period were followed up for a minimum period of 5 years. One hundred and fifteen or 17% of the 698 patients whose follow up was complete showed evidence of active disease radiologically and/or bacteriologically. In one half the evidence was only radiological. The percentage of women showing evidence of activity was 18% as compared to 15% in men. While in some age groups the percentage is closely similar in the two sexes, there is no age group with a higher rate of breakdown in females than in males. The evidence of re-activation was found in 7-5% in the first year, 4% in the second year,

3.2% in the third year and 2.3% in the fourth year of follow up.

S.P.P.

Tuberculosis risk in persons with fibrotic lesions

D. Dankova. Bull. Int. Un. against Tuberculosis; 1972, 47, 145.

One thousand eight hundred and ninety one persons with fibrotic lesions per 100,000 population in Kolin district of Czechoslovakia were followed up. In 10 years time their number rose to 3,800 per 100,000. In both sexes the number of such cases was small in the below 35 years age group. In the age group 45 years and above the proportion rose considerably more in men than in women. 0.9% amongst men and 0.7% in women developed active disease annually in 1962 and 1963. From 1964 onwards the rates were 0.5% and 0.4% respectively per year. The risk of developing tuberculosis did not vary with age. 48% of all new cases arose from the large group of persons with normal x-ray previously whereas the small group of 5% of the total with fibrotic lesions accounted for 1/3rd of all cases. It has been calculated that in men aged 25 to 44 years the risk of developing active disease was 28 times higher and in women aged 25 to 64 years, it was 20 times higher than the rest of the population. On the other hand, in men above 45 years and in women above 65 years, bacillary tuberculosis occurred 8 times more frequently than in the rest of the population.

S.P.P.

Tuberculosis risk in persons with fibrotic x-ray lesions

P. Steinbuck. Bull. Int. Un. against Tuberculosis; 1972, 47, 135.

Three thousand three hundred and one persons with fibrotic pulmonary lesions in the lungs discovered during mass surveys were followed up from 1961 to 1970. Three hundred and fifty three of these had treatment for pulmonary tuberculosis previously and the remaining 2,944 had never been diagnosed and treated as tuberculous. The latter group constituted 3.8% of the entire survey population (males 4.6%, females 3.3%). On the average, the latter group were older than the former group of those with residual lesions following previous treatment. The annual morbidity risk of persons with fibrotic lesions was 0.95% for males in the first 5 years and 9.78% in the subsequent 5 years. The corresponding rates

for females were 0.53% and 0.51%. The age specific rate increased considerably in males from 45th year of life onwards. In females, increased risk was seen only after the age of 60 years. While risk has a slight tendency to become lower during the second five year period in the age groups under 60 years, it remains high in age groups older than 60 years both in males and females. The risk of disease for persons in this group was found to be about 16 times higher than that of the remaining population without such lesions. 42.7% of all new cases came from the small group of persons with fibrotic lesions whereas the much larger segment of the population without these lesions contributed only 57.3% of all new cases. This proportion will continue to increase with regressing infection rates. The relatively high risk of tuberculosis justifies a very close supervision of persons with fibrotic lesions in countries with a regressing tuberculosis problem.

S.P.P.

The discharge of patients with inactive tuberculosis.

J. Edsall. Amer. Rev. Resp. Dis.; 1972, 105, 1018.

One hundred and forty five patients with reactivation of old healed disease in New York have been reviewed. In 57 patients fresh symptoms led to the identification of relapse. Relapse was detected during routine follow up in 51 patients and in the remaining 33 for various other circumstances such as routine chest film, investigation during hospital admission for other diseases etc. Since routine follow up of all arrested cases adds considerably to the work load of a clinic, factors present in 51 patients (35% of all relapses) were analysed. In 25 of these chemotherapy had been poor or irregular or of questionable adequacy. Alcoholism was present in 19 patients; lack of co-operation during treatment in 10 and diabetes in 6 other patients the bacilli had become resistant to standard drugs during initial treatment. Other factors with lesser prevalence were old age, pregnancy, cirrhosis, psychiatric disorders, bronchiectasis, gastrectomy hepatitis etc. In only 3 of the patients none of the above factors were present. The authors conclude that provided chemotherapy has been taken adequately and other adverse factors are absent routine follow up of all arrested cases is uneconomical.

S.P.P.

Annual risks of tuberculous infection in 14 countries derived from the results of tuberculin surveys in 1948-1952

Ian Sutherland, K. Styblo, M. Sampalik & MA. Bleiker. Selected Papers. Volume 14. Royal Netherlands Tuberculosis Association; 1971, 14, 75.

The results of extensive tuberculin surveys in 14 countries of Europe and North Africa from 1948 to 1952 have been analysed to provide information on the risk of fresh tuberculous infection in those countries. In Austria, Czechoslovakia, Greece and **Israel** there was a substantial decrease in the risk amounting to at **least** 7.5% annually. In Ecuador, Palestine, Poland, Tangier city and Yugoslavia the decrease was somewhere between 2.5% and 7.5% annually. There was no firm evidence of a change in the risk of infection during this period in Algeria, Egypt, Morocco, Syria and Tunisia.

S.P.P.

Present risk of developing active tuberculosis in Saskatchewan according to previous tuberculin and x-ray status

G.D. Barnett. S. Grzybowski and K. Styblo. Selected Papers. Volume 14; Royal Netherlands Tuberculosis Association; 1971, 14, 51.

Out of a total population of about 947,000 in **1964** in Saskatchewan, province of Canada, 759,000 (80%) had a negative tuberculin test. Among the positive reactors about 171,000 had a normal chest x-ray, a little less than 11,000 had fibrotic lesions in the lung and about 6,000 were ex-patients. The lowest risk of contracting tuberculosis viz 2.6 bacillary cases per **100,000** annually was seen in the tuberculin negative population. The rate did not vary appreciably in different age groups.

The groups of positive tuberculin reactors with a negative x-ray chest (18% of the total population) contributed fresh bacillary cases at the rate of about 15 per 100,000 tuberculin positives. The rate amongst the young adults aged 15 to 29 years was 24 per 100,000; 9 to 15 per 100,000 amongst those aged 30 to 59 years and 19 per 100,000 among people more than 60 years old.

The group with fibrotic lesions (1% of the population) showed a very high risk of developing bacillary disease (about 145 per 100,000 per year).

S.P.P.

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Identification of sources of infection.

J. Meijer, G.D. Barnett, A. Kubik & K. Styblo. Selected papers Volume 14, Royal Netherlands Tuberculosis Association; 1971, 14, 5.

Passive case-finding i.e. search for tuberculosis among patients who seek advice at a general or specialized health institution because of symptoms accounted for 45% to 66% of the fresh sputum smear positive cases discovered in Canada, Czechoslovakia and the Netherlands in the period 1956 to 1969. -Active case-finding i.e. search in the special risk groups such as contacts, symptomatics, and persons with inactive lesions by chest clinic surveillance team accounted for 10% to 12% of the new cases. The number of cases discovered by mass miniature radiography unit in unselected community indiscriminately was much lower. Since chemotherapy has changed profoundly the prognosis of even advanced cases, the value of mass miniature radiography in detecting so called early cases carries only marginal advantage. The same may be said about repeating successive x-ray survey every two to three years for case-finding purposes. Efficient diagnostic services for those who attend voluntarily because of symptoms and selective case-finding in high risk groups will pay much bigger dividends than routine mass miniature radiography of unselected healthy population.

S.P.P.

The role of BCG vaccination in the prevention of tuberculosis in the United States.

N. Paneth and F.E. Speizer. Amer. Rev. Resp. Dis.; 1972, 105, 1019.

A formula has been devised to calculate the justification or otherwise for BCG vaccination in USA on a cost-benefit basis. In incidence of tuberculosis greater than 7 per 100,000 per year in a population under 10 years of age justifies BCG vaccination of the new borns. Urban population in USA under the age of 10 years have rates of tuberculosis that are 3 to 5 times this, suggesting that high risk groups can be identified and vaccinated soon after birth. The cost of such a programme is considerably **less** than other forms of tuberculosis control including chemoprophylaxis.

S.P.P.

Roentgenologic Aspects of BCG-Osteomyelitis.

U. Erikson et al. Radiology; 1971, 101, 575.

Radiological findings in one case of culture-

Verified and 4 cases of unverified but suspected BCG Osteomyelitis are reported. Radiological characteristics are not specific and are comparable to those caused by the virulent human type of bacillus. The possibility of this condition should however be considered when an osteolytic process is seen in a child vaccinated less than 3 years previously. The lesions may be multiple.

S.P.P.

Generalized BCG tuberculosis with fatal course in two sisters

S. Sicevic. Acta Paediat, Scand. ; 1972, 61, 178.

Two cases with fatal generalized disease following BCG vaccination are reported. Clinical picture was dominated by signs of malignant scrofulosis. Autopsy in one case showed thymic dysplasia and hypoplasia of the peripheral lymphoid tissue. In the second case, biopsy specimens of a lymph node and the rectal mucosa showed poorly developed lymphoid tissue. Both cases had epithelioid granulomas in many organs but no typical tubercle structure was detected. Numerous acid fast bacilli indistinguishable from BCG were isolated from the lesions. In view of the clinical observations and immunologic investigations, the deficiency in the two cases has been termed as hereditary partial deficiency of cellular immunity.

S.P.P.

An evaluation of the long-term national BCG programme in Turkey.

H. Acan. Bull. Int. Un. Tub.; 1971, 46, 65.

Seventy five percent of the eligible population could be covered ordinarily but in the mass campaign the percentage went up to more than 90. Post-vaccination conversion rate is of the order of nearly 90% and post-vaccination complications i.e. adenitis 1.02%.

Mortality from tuberculosis was 262 per 100,000 in 1945. It had come down to 30 in 1968 after the mass campaign. The infection rate in children below the age of 6 years was 13% in 1953-59 and it came down to 3.8% in 1968-69. The prevalence of bacillary cases of pulmonary tuberculosis was 0.66% in 1962 but it came down to 0.17% in 1970. The prevalence of active tuberculosis was 0.3% in the BCG vaccinated and 3% in the un-vaccinated.

S.P.P.

Prevention of tuberculosis in the African context.

L. Azzouz. Bull. Int. Un. Tuberc.; 1971, Supplement, 45

Three hundred and twenty eight cases of infantile tuberculosis admitted to a hospital in Tunisia during 1952 and 1953 have been compared with 478 cases of infantile tuberculosis admitted in the same hospital from 1965 to 1969. Meningitis and miliary tuberculosis which constituted 37% of the total cases in the earlier period, constituted 1.7% only in 1965-69 period. Serous effusions and pleurisy accounted for 12% and 2.51% in the two periods respectively. Tuberculosis of adult type remained more or less constant at 18% and 20.50% in the two periods. The authors attribute this to crash BCG vaccination programme in Tunisia after 1953.

S.P.P.

Prevention of tuberculosis in the African context.

L. Mokhtari. Bull. Int. Un. Tuberc.; 1971, Supplement, 64.

The complications and undesirable effects of BCG vaccination during the mass vaccination campaign were very few. They consisted essentially of adenitis, the incidence of which was 3.88% in infants up to 1 year old at the time of vaccination; 0.47% in children aged 1 to 4 years; 0.09% in children aged 5 to 9 years and 0.02% in children 10 to 14 years old.

S.P.P.

A comparative evaluation of tuberculosis epidemiology between some villages of Yozgat Province (Turkey) where case-finding and treatment programmes have been applied and those where they have not been applied.

S. Akkaynek Bull. Int. Un. Tuberc.; 1971, 46, 82.

The prevalence of active tuberculosis based on a sample of nearly 10,000 persons was 2.18% in 1965-66 and 1.16% in 1970. Bacillary cases were 0.4% in 1965-66 and 0.18% in 1970. The prevalence of active disease in vaccinated individuals was 0.32% as against 2.0% in the non-vaccinated population.

S.P.P.