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NEWS & NOTES * **ABSTRACT**

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DRUG RESISTANCE

The phenomenon of "drug tolerance" has been recognised from ancient times. When certain drugs like arsenic, opium, etc., are taken in small doses for long periods, it is found that as time goes on, more and more of them have to be taken to produce the desired effects. This means that tolerance to the drug increases as time goes on. More recently it has been observed that organism like the tubercle bacillus that invade the human body can also acquire the power of resisting drugs used against them. This is but natural, since adaptation to adverse surroundings is a necessity for survival of biological evolution.

When anti-tuberculosis drugs like streptomycin, para-amino Salicylic acid and Isonicotinic acid Hyderazid came into common use during the last 15 years followed by encouraging results of treating tuberculous patients and dramatic reduction in the tuberculosis death rates in many countries, hopes ran high that tubercle bacillus would soon be conquered. However, a study of the effect of the drug on patient has shown that the bacilli in the human body are not killed off by these drugs, but are mainly devitalized and rendered incapable of multiplying, giving a chance for the system to control the disease. At the same time it was found that the drugs also may stimulate the bacilli to bring out their defensive powers to resist them. Some fear that this phenomenon of drug resistance may become a major problem in the fight against tuberculosis and hence a subject of serious study and research throughout the world.

Clinicians have observed that in many cases, the effectiveness of the drugs gradually decreases during prolonged treatment. This is

supposed to be due to the gradual aquisition of drug resistance by the bacilli. In some cases it has been noted that the bacilli were already resistant to the drugs even before the treatment was started. This may be due to the fact that some bacilli have "primary assistance", that is, they have a natural resistance even before they are exposed to the drugs. In rare cases it may be even found that the patients are worse off with the drugs than without. This has been explained as due to the presence of "drug dependent" bacilli, that is, bacilli that thrive better in the presence of the drug, than in its absence. It has also been found that a combination of drugs prevents or delays the emergence of resistance. Considering these facts some advocate that before instituting drug treatment the bacilli are to be tested for resistance and whenever they are found not resistant, to hit them hard with a suitable combination of drugs so that they are given a knock-out blow before they get time to acquire resistance.

Bacteriologists have observed that tubercle bacilli exposed to the drugs, especially Isoniazid, for long periods of time, go into a state of "defensive hybernation"; change their habits and characteristics and become almost a different type of bacillus. They continue to live, but they may not multiply. They are visible under the microscope but fail to grow in cluture. They may disappear from the sputum of patients quickly, but the x-ray shadows of lesions may not clear up rapidly. In appearance they do not change much by exposure to the drugs, but they become less capable of causing active disease.

Clinicians and Bacteriologists are now collaborating in the study of this phenomenon in greater detail and trying to lay down international standards for the quick detection and exact measurement of drug resistance.

When more and more patients are treated with the drugs in the future, the drug resistant bacillary population may increase and these may infect healthy people, thereby it may pose an epidemic-logical problem in the future. This problem is referred to in the articles by Dr. P.K. Sen and Dr. S. Velu *et al* published elsewhere in this Journal. One saving factor is that the drug-resistant bacilli are usually less virulent than others. While drug resistance is a factor

to be reckoned with in the management of individual patients, it has so far not emerged as a serious epidemiological problem in any other countries of the world.

Field research to determine the extent of the prevalence of drug resistant bacilli in communities and fundamental research into the secrets of the biological mechanism of drug resistance as well as its repercussion on epidemiology of tuberculosis are now going on in many parts of the world.

T. J. Joseph

Domiciliary Treatment of Pulmonary Tuberculosis

(A study on 5,883 cases—reported in July, 1958, at the International Union Meeting)

By

P. K. SEN

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This paper is based on part of the data and conclusions of an investigation made by the author and presented by him at the Domiciliary & Ambulatory Committee meeting of the International Union Against Tuberculosis at Paris in July, 1958. The report was submitted to the Tuberculosis Association of India soon thereafter.

The study attempted to answer broadly the comprehensive question: "Is home or domiciliary treatment good or beneficial enough to justify its acceptance in the control programme of pulmonary tuberculosis in a country"? A direct answer to this question can only be given if in a community two comparable groups are investigated over a long period one having this treatment and the other none. Such an experiment is hardly possible and is probably unethical in the light of established values of chemotherapy. As this is impracticable, the answer should be sought in an indirect manner accepting the result of hospital treatment as the standard of adequacy and comparing the result of chemotherapy at the home and hospital.

In addition, it will be reasonable to assess the effect of factors in which the home differs from the hospital. Provided chemotherapy is adequate or comparable, then, any difference in the result of treatment between these two will mainly be due to such factors. Important factors in this respect are (a) movement of the patient, (b) social status indicating nutrition and general environment, and (c) supervision. In all these respects the hospital is likely to be much superior to the home specially for the groups of patients included in this study. Besides a comparative study of the results of treatment at the home and the hospital, an evaluation of the effects of these factors were attempted by comparing the results of treatment in different groups of domiciliarily treated cases with distinct differences in respect of these factors.

It may be well worth remembering that in assessing the justifiability mere finding of the comparative result with hospital treatment or evaluation of differing factors may not be quite adequate. Keeping patients at the homes may prove more dangerous for the contacts than isolating them at the hospitals. Regular self-administration of drugs may also be very much more difficult at the homes than in the hospitals. On the former issue the author has published a study on home contacts of the domiciliary cases in this journal in Vol. VI, No. 4 September, 1959. A comparative study of such contacts with contacts of hospital treated cases is necessary. This could not be made as he did not have sufficient material for the purpose. The author intends to present a study soon on the issue of the extent and nature of irregularities in self-administration of drugs at home.

MATERIAL, METHOD AND RESULT

Domiciliary Group:

Under the term "Domiciliary Treatment" were included those cases who had been treated at home and not known to have been hospitalised anytime. It also included cases who had different grades of ambulation from the very start of treatment, thus ambulatory cases as well as those who followed adequate rest regime had been included under the same heading: "domiciliary". In the vast majority of cases the treatment was meant chemotherapy by a combination of two drugs in which INH has always been used.

Random samples of 5,883 domiciliarily treated cases from different clinics in Calcutta (Chest Department, Medical College, Tuberculosis Clinic, Urban Health Centre, All India Institute of Hygiene & Public Health; Corporation Clinic, Kidderpore; Chest Clinic, Islamia Hospital; Tuberculosis Relief Association Clinic and Niramoy Clinic), private cases of the author and one clinic from a small town (Chinsurah) were collected. No case was accepted who had less than three months treatment or had major irregularity in chemotherapy.

These cases were re-assessed by very experienced and competent workers of different clinics and by the author and his colleagues in his department under a common schedule with clearly defined terminologies prepared by the author. To reduce many elements of errors and biases that may enter into a retrospective study of this type two workers sat together to assess most of the cases with clear direction that in cases of doubt the lower category in terms of improvement should be accepted. Smear tests only for sputum were accepted.

Hospital Group:

Similar procedures could not be adopted for the assessment of the hospital cases. Information gathered were under the terminologies used by individual hospitals (U.M.T. Sanatorium, Madanapalle, S. India; Lady Linlithgow Sanatorium, Kasauli; K.S. Ray T.B. Hospital and Bangur T.B. Hospital, West Bengal). They were neither alike for all hospitals nor the same as used for the clinic schedules. The author, therefore, took the liberty to rearrange the data from different hospitals in such a way that they may be roughly comparable to the clinic data. The author was aware that there might be some error in doing so but, at the same time, he felt that, by and large, the rearranged data were comparable. Information on 2,472 cases from different parts of India were collected in this respect.

COMPARATIVE RESULTS OF DOMICILIARY AND HOSPITAL TREATMENT

The results are summarised in tabular form with brief explanations whenever necessary.

Terminologies and definitions used to indicate the results of treatment were as follows:

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1. Worse— Extension of infiltration, and/or enlargement of the cavity, and/or new cavitation, and/or appearance of new lesion, and/or sputum reversion.

2. Stationary— The lesion and the cavitation and the sputum status remain almost the same.

3. Improved— Retrogression of infiltration, and/or diminution in the size of the cavity, and/or sputum conversion.

4. Quiescent— (a) Lesion must be stable showing adequate fibrosis and retrogression, and must not show evidence of cavitation in the ordinary P. A. view of the chest, (b) Three consecutive sputum tests must be negative for AFB by direct smear examination, (c) No tuberculous toxaemia and exercise tolerance normal.

TABLE I

A comparative study on the result of domiciliary and hospital treatment in respect of X'ray findings.

Groups	Results-X'ray findings					Total
	Worse	Stationary	Improved	Quiescent	Dead	
Domiciliary-Ambulatory	257 4.4%	857 14.6%	3,431 58.3%	1,338 22.7%	—	5,883
Hospital-at discharge	45	157	1,140	1,023	107	2,472
U.M.T. & Lady Linlithgow Sanatorium	0.02%	6.35%	46.11%	41.38%	6.14%	

TABLE II

A comparative study on the result of domiciliary and hospital treatment in respect of sputum test findings.

Groups	Result-in relation to sputum test				
	Total 2132		Total 3306	Total 3306	
	Converted +/-	Stationary +/+	Stationary -/-	Reverted -/+	Not known
Domiciliary-Ambulatory Percent reverted or remained stationary.	1,618 75.9%	514 24.1%	3,203 96.9%	103 3.1%	445
Hospital (K.S. Ray and Bangur) Percent reverted or remained stationary.	432 67.3%	210 32.7%	1,365 97.8%	31 2.27%	

Accepting the categories of "improved and quiescent" together as hospital terminology for the "quiescence" seemed somewhat more lenient, the result seemed to be slightly superior for the hospitals but the sputum conversion rate was slightly better for the domiciliary group. The latter may be also due to better sputum examination in hospital group. Considering the results as a whole, it may justifiably be concluded that the result of treatment at home is slightly inferior to that in a hospital.

EFFECTS OF FACTORS IN WHICH HOME DIFFERS FROM HOSPITAL ON THE RESULT OF TREATMENT.

Social status and supervision by Home Visitors.

It has been assumed that poorer classes of patients have poorer nutrition, inferior housing and environmental conditions. That this assumption is likely to be true will be evident to any body who had visited the Calcutta Bustees where the majority of the poorer classes lives.

Supervision at home by the Health Visitors and Doctors is also not uniform for all clinics. There had been regular home visitings for some of these cases, only casual visits for another section and none for the others.

To show the influence of these factors, the domiciliarily treated patients have been grouped according to their social status and extent of home visiting in the following way and the results of treatment of each such group in relation to X-ray and sputum test findings are shown in Tables III and IV.

Groups: -

Group 'A'— Upper and middle class. No home visits (City).
Group 'B'— Poor class. Regular home visits (City).
Group 'C'— Poor class. No home visit for majority. Casual home visits for a few (City).
Group 'D'— Lower middle class. No home visits (City).
Group 'E'— Poor and lower middle class. Casual or no home visit (small town: Chinsura).

TABLE III

Result of treatment in relation to X-ray findings according to social status and home supervision.

Groups	X'ra				TOTAL
	Worse	Stationary	Improved	Quiescent	
A.	2 0.39%	35 6.86%	351 68.82%	122 23.35%	510
B.	42 4.85%	190 21.96%	544 63%	89 10.29%	865
C.	136 4.4%	443 14.4%	1,663 54.2%	825 27%	3,067
D.	51 6.71%	60 7.30%	576 70.15%	134 16.32%	821
E.	26 4.2%	129 20.8%	297 47.9%	168 27.1%	620
TOTAL	257 4.4%	857 14.6%	3,431 58.3%	1,338 22.7%	5,883

T TBLE IV

Result of treatment in rèlation to sputum test findings according to social status and home supervision.

Groups	Sputum					Total
	+/-	+/+	-/-	-/+	Not known	
A.	192 80.0%	48 20.0%	248 100%	0	22 4031%	510
B.	292 72.5%	109 27.5%	424 96.3%	16 3.7%	24 2.8%	865
C.	567 74.0%	199 26%	1,886 96.7%	61 3.3%	354 11.5%	3,067
D.	334 86.4%	64 13.6%	386 96.2%	15 3.8%	22 2.9%	821
E.	233 71.2%	94 28.8%	259 95.1%	11 4.9%	23 3.7%	620
Total	1,618 75.8%	514 24.2%	3,203 96.8%	103 3.2%	445 7.5%	5,883

No appreciable difference in the result of treatment is evident whatever might be the social status, that is, nutritional and environmental conditions, and also the nature of home supervision except in Group B. In order to ascertain the reason for this and for the presence of any other bias the groups were checked against the duration of chemotherapy, the nature of initial disease and sputum status on diagnosis. No significant difference in the duration of chemotherapy could be detected for any group. There was, however, appreciable differences in the nature of lesions in terms of presence or absence of cavitation and, to some extent, in sputum status. These differences are shown in Table V. The whole of group 'D' and part of group 'C' had been eliminated as these had miniature films only.

TABLE V

Distribution of Cavitary and Sputum Positive Cases.

GROUPS	TOTAL	CAVITY	POSITIVE SPUTUM
Group A.	510	253 49.6%	240 47.1%
Group B.	865	576 66.5%	401 46.3%
Group C.	1451	487 33.5%	387 24.3%
Group E.	620	372 57.3%	34 1 53.8%

It may therefore be accepted that the nature of the lesions, specially cavitations had noteworthy influence on the result of treatment whereas special status, home environment and supervision did not show any appreciable effect on this result.

Movement and Work

Rest followed by graduated movement is still an accepted measure in the treatment of tuberculosis. In the hospital such a regime can be well controlled but not so at home. Home treatment will, therefore, generally differ from that of hospital in this regard. An attempt has, therefore, been made to evaluate the effect of movement and work on the result of treatment.

One thousand seventy-five patients were separately investigated in this regard. Each patient was closely interrogated in respect of their movement and work from the start of treatment. The patients were classified under the following heads according to this information.

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W_1—Those who had generally followed the medical advice of initial rest and thereafter graduated movement.

W_2—Those who moved about somewhat against medical advice but did not do usual work.

W_3—Those who continued to do his usual work not involving manual labour against medical advice.

W_4—Those who continued to do work involving manual labour against medical advice.

Table VI shows the result of treatment in relation to such "movement and work".

TABLE VI

Work and Result of Treatment

Working status	Worse	Stationary	Improved	Quiescent	Total
W_1 (Rest etc.)	14 6.78%	47 22.27%	123 49.42%	23 11.11%	207
W_2 (Casual)	16 3.65%	102 23.29%	287 65.53%	33 7.53%	438
W3 (Light)	10 3.66%	62 22.71%	167 61.17%	34 12.46%	273
W4 (Heavy)	6 3.82%	38 24.2%	102 64.97%	11 7.00	151
Total	46 4.27%	249 23.17%	679 63.17%	99 9.20%	1,075

It will be noted that there is no appreciable difference in the result of treatment between these groups.

Large random samples from each group were then tested with regard to the duration of chemotherapy, initial extent of the lesions and cavitations and sputum status in search of possible important biases. The following tables summarise the findings—

TABLE VII

Analysis of cases according to sputum status at the start of treatment

Working status	Total No.	Sputum Status Positive
W_1 Rest etc.	118	40 33.9%
W_2 Casual	301	143 47.5%
W_3 Light	203	108 53.2%
W_4 Heavy	114	61 53.5%

TABLE VIII

Analysis of cases according to the extent of the lesions and cavitations at the start of treatment

Working Status	Total	Nature of lesion			Cavity Present
		I	II	III	
W_1 Rest etc.	128	66 51.56%	18 14.06%	44 34.38%	65 50.78%
W_2 Casual	317	76 23.97%	50 15.77%	191 60,26%	112 57.41%
W_3 Light	214	35 16.35%	44 20.50%	135 36.91%	130 60.74%
W_4 Heavy	130	36 27.69%	11 8.46%	83 63.85%	82 63.075

Classification of extent of lesions:

I. When the total area involved is not more than the area of one zone roughly.

II. When the total area involved is more than one, but not more than two zones.

III. When the total area involved is more than two zones.

TABLE IX

Analysis of cases in relation to duration of treatment.

Working status	Total	3-6 months	7-9 months	10-12 months	more than 12 months
W_1 Rest etc	128	36 28.12%	22 17.18%	15 11.71%	55 42.99%
W_4 Casual	317	106 33.43%	81 25.55%	45 14.19%	85 26.83%
W_3 Light	214	66 30.84%	38 17.75%	42 19.62%,	68 31.79%
W_4 Heavy	130	37 28.48%	30 23.07%	29 22.30%	34 26.15%

Study of these tables show that there is no appreciable bias in these important factors. So, it may be justifiable to conclude that "movement and work", even from the very start of treatment, did have no appreciable influence on the immediate result of the treatment.

COMMENTS

This study should be regarded as a preliminary and rough one. The author is aware that in a retrospective study of this type from clinic records there could be many deficiencies and results obtained may not be as reliable as in a well controlled study. Important deficiency in this study was in the hospital group where the duration of chemotherapy could not be ascertained. Advantages are, however, its inexpensiveness and assessment of the result of a service under normal field conditions.

Another important deficiency in a study like this is uniform assessment of cases and proper recording. The author believes that both could be somewhat minimised, as in this case, by accepting a large number of patients and assessing them under a common schedule by many well qualified workers. By this process the biases, if any, may tend to be neutralised.

It may be noted that in some places differences in percentages seemed significant statistically but two good statisticians opined that, in a study like this, much differences may justifiably be noted as "no appreciable difference". So this notation had been recorded.

From experiences gained by this study, the author is convinced that there is a definite scope for co-operative studies on this subject which can be planned ahead and executed in a manner that most valuable light can be thrown on our field conditions and these, in their turn, may help greatly in the proper conduct of the domiciliary service.

SUMMARY AND CONCLUSIONS

Five thousand eight hundred eighty three cases were accepted for this study. Records were randomly collected from 8 clinics and were reassessed under a common schedule with defined terminologies. The clinic cases could be differentiated, on the basis of the population they serve, into different social groups and also according to the home visiting service available to them.

A group of 1,075 clinic cases, not necessarily included in the above group, were specially investigated in the light of "movement and work" they persued from the start of treatment.

All cases known to have been hospitalised and/or had less than 3 months chemotherapy and/or had major irregularities in chemotherapy were excluded from the study.

Informations on 2,472 cases were collected from 4 good hospitals/sanatoria. The data were rearranged, as far as possible, for a comparative study with the clinic group of cases.

In comparative studies among the clinic groups some important factors through which biases and consequently errors might occur were checked.

The findings were summarised in tabular form and analysis seemed to show that:

1. The result of treatment at the hospital was only slightly superior to domiciliary treatment.

2. The differences in (a) social status (implying good to poor nutrition and environment) (b) extent of home visits (from no visits to good supervision) and (c) extent of movement and work from the start of treatment (from rest to manual work) had no appreciable influence on the result of treatment.

3. Character of the disease, specially presence of cavitation, seemed to have significant harmful effect on the result of treatment.

Reasonable deductions made from these findings were:—

1. Like many other bacterial diseases, control of the bacillary population is of prime importance in tuberculous disease also. And further, the anti-tuberculous drugs seem to achieve this to such an extent that all other measures and conditions are relegated to an unimportant position in the cure of the disease.

2. Drug action and ultimate healing was in someway related to structural changes.

3. If these preliminary findings are even roughly true, then, the question is not where we treat but when we diagnose and how best we treat (chemotherapy) barring a group needing additional care for major surgery and emergencies. Only in this context the question of home or hospital treatment arises. Conduct of proper chemotherapy should, therefore, be a must in domiciliary service and to this end our main efforts should be channelled.

4. Some of the findings of this investigation were, therefore, somewhat revolutionary and deserves to be further studied.

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The Results of Treatment with Streptomycin Plus Pyrazinamide in Patients with Active Pulmonary Tuberculosis Despite Prolonged Treatment with Isoniazid Plus PAS

By

S. VELU, R. H. ANDREWS, S. DEVADATTA, WALLACE FOX,

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There have been a number of reports on the use of pyrazinamide in combination with other drugs in the treatment of pulmonary tuberculosis. It has been used in combination with isoniazid (Donnerberg et al., 1957; United States Public Health Service, 1959a), with cycloserine (Schwartz & Moyer, 1957; Toguri & Atwell, 1958) and with viomycin (Pfeutze & Pyle, 1957) in the treatment of patients who had failed to attain quiescence with previous antitubercu4osis chemotherapy. It has also been used successfully in the treatment of newly-diagnosed disease in combination with isoniazid, with daily and bi-weekly streptomycin and with PAS (Muschenheim et al., 1954; Allison, 1959; Tucker & Matthews, 1959; United States Public Health Service, 1959b). A major disadvantage of pyrazinamide, however, is the occurrence of hepatic toxicity, which sometimes results in jaundice or death, especially since liver function tests do not always give adequate warning of impending hepatic damage (American Trudeau Society, 1957 ; Potter & Chang, 1955 ; Spengos & Cuizon, 1958 ; United States Public Health Service, 1959a). In a controlled study, the United States Public Health Service (1959a) reported hepatic toxicity of between 2% and 3% in a 12 week period with daily dosages of 25 or 40 mg of pyrazinamide per kg body weight. In a 24 week period the toxicity increased to 6.6% with the larger dose but remained unaltered with the 25 mg dose. Joint pains, elevation of the serum uric acid and frank clinical gout have also been reported (Yaeger et al., 1952 ; Cullen et al., 1956).

This report presents the findings during a year or more of observation of 20 South Indian patients who, after an initial course of isoniazid plus PAS, were treated with streptomycin plus pyrazinamide for active pulmonary tuberculosis. The combination of streptomycin plus pyrazinamide was chosen, first, because of its likely therapeutic effectiveness, since all the patients had streptomycin-sensitive strains of bacilli, secondly, because it presented an opportunity to study *supervised* drug administration in domiciliary patients in a community in which the self-administration of antituberculosis drugs could not be depended on (Fox, 1958 ; Tuberculosis Chemotherapy Centre, 1959, 1960 ; Velu et al., 1960). The patients were either unsuitable for or unwilling to undergo surgery.

Up to 30 January 1959, 22 patients were admitted to treatment with the combination of streptomycin plus pyrazinamide; 2 have been excluded because

*The Centre is under the joint auspices of the Indian Council of Medical Research, the Madras Government, the World Health Organisation and the British Medical Research Council.

their treatment was interrupted early in its course ; 1 patient developed an amoebic hepatitis with an abscess which ruptured into the lung 6 weeks after the start of the new regimen and it was considered inadvisable to continue pyrazinamide ; the other patient absconded from Madras in the second month of treatment as he was wanted by the police. All the 20 cases were excreting tubercle bacilli when the streptomycin plus pyrazinamide regimen was started. In 16 the disease had previously failed to attain a quiescent state on the standard combination of isoniazid plus sodium-para-aminosalicylate (the daily dose of isoniazid ranged from 150 to 200 mg and the daily dose of PAS (sodium salt) from 7.5 to 10 g, according to the patient's body weight) given in this Centre for periods varying from 9 to 25 months. The remaining 4, after achieving quiescence, had relapsed bacteriologically with radiographic spreads of the disease. Of the 20 patients, 17 had had a recent radiographic deterioration, 2 had had a clearcut clinical deterioration associated with an haemoptysis and the remaining patient still had a positive sputum after 2 years of treatment with isoniazid plus PAS. Thus, all the 20 cases were treatment failures of a standard combined chemotherapy. When the original treatment began, 14 had sensitive organisms to both isoniazid and PAS, 4 had isoniazid-resistant organisms, and 2 (who received their treatment in the first pilot study in the Centre) had no sensitivity results at that time.

It was the intention in the study reported here to treat every patient with streptomycin plus pyrazinamide for a minimum of a year and, provided the patient would cooperate, for a period of up to 2 years. If, however, the sputum remained persistently positive after 6 months of treatment the case was reviewed. Because of the possibility of toxicity, treatment with the combination was stopped if it was considered, in the light of the radiographic and bacteriological response (including the streptomycin sensitivity test results), that there was no reasonable likelihood that further improvement would result from continuing the regimen.

The treatment regimen

The standard regimen was streptomycin sulphate 1 g daily (i. e. 24 to 32 mg per kg body weight) in a single intramuscular injection on 6 days a week, plus pyrazinamide 1 to 1.5 g daily (30 to 40 mg per kg body weight) in 1 dose. The pyrazinamide was given 6 days a week under direct supervision in the clinic and 1 dose was given to be taken at home on Sundays.

In 7 patients it became necessary to reduce the daily dosage of streptomycin to 15 mg per kg because of the development of giddiness.

The majority of the patients were treated entirely under ambulatory domiciliary conditions, but 4 patients spent part of the period in sanatorium, during which time they received streptomycin on all 7 days of the week.

Routine examinations

The patients were examined clinically and radiographically at monthly intervals. At each month 2 overnight sputum specimens were examined by smear and culture and a pair of laryngeal swabs by culture. A streptomycin sensitivity test was performed on a positive culture at each month, when 1 was available. The bacteriological techniques have been described elsewhere (Tuberculosis Chemotherapy Centre, 1959). The urine was examined for bilirubin twice a week using a simple test (Sobotka et al., 1953) if the result was positive, a simple spectroscopic examination for urobilin was performed (Harrison, 1957).

There are few centres in India that have access to liver function tests ; if the present study was to have any bearing on the current tuberculosis problem in India it

was therefore essential to know whether pyrazinamide could be used without undue risk in the absence of such tests. For this reason, no special tests of liver function were undertaken in this study.

Condition at the start of treatment with streptomycin plus pyrazinamide

The patients' ages ranged from 18 to 51. Three were under 20 years, 9 were aged 20 to 29 years, 5 were aged 30 to 39 years and 3 were older. Fourteen were males and 6 were females.

The majority of the patients had advanced disease. Thus, on postero-anterior radiography, 16 had moderate or extensive cavitation and only 2 had no evidence of cavitation. All except 1 patient had 3 or more lung zones involved in disease, 12 having 5 or 6 lung-zone involvement. The positivity of the sputum was graded on the basis of smear and culture examination of a single overnight collection specimen. The specimens in all 20 patients were positive, 18 on both smear and culture and 2 only on culture ; 14 had 3-plus (heavy) or 2-plus (moderate) positive smears. All, as already mentioned, had streptomycin-sensitive strains of bacilli.

RESULTS

Cooperation of the patients

The cooperation of the patients in accepting treatment was remarkably good. It was necessary to give some patients limited financial assistance, as explained in an earlier report (Tuberculosis Chemotherapy Centre, 1959). Most of the patients were given money for fares since they had to attend the clinic 6 days a week for many months and travel up to 5 miles each way under tropical conditions. In all, 17 patients received an average of Rs. 5.84 a month for fares, or an average of Rs. 4.96 per month for the whole series of 20. Even so, patients occasionally failed to attend for their injection, but no patient had an interruption of chemotherapy of more than a few days at any time.

Treatment changes during the year

Seven patients had their treatment changed in the second 6 months, 6 in the eighth month and 1 in the tenth month. In only 1 of these patients was there evidence of radiographic deterioration. The others had their treatment changed because the sputum was positive and it was considered they would not improve further either radiographically or bacteriologically.

Radiographic changes

In the first 6 months, 17 of the 20 patients showed radiographic improvement; in 9 of these patients it was classified as moderate or considerable by an independent assessor (Dr. Raj Narain). Two patients showed no change and 1 patient had deteriorated radiographically. Considering the 13 patients who continued on the streptomycin-pyrazinamide regimen for a full year, 9 showed radiographic improvement over the period, 2 no change and 2 had deteriorated.

Bacterial content of the sputum

The average number of culture examinations was 2.7 per month, the range being 1.8 to 3.8 per month.

There was a rapid and striking fall in the bacterial content of the sputum in the early months (Table 1); at 2 months only 1 of the 20 patients yielded a positive culture. By 3 months the position had changed and 7 patients yielded positive cultures. Again, at 6 months, 7 patients yielded positive cultures, 5 specimens being

TABLE 1

Presence of Tubercle Bacilli in Multiple Specimens taken at Monthly Intervals

Months after start of chemotherapy	Number of patients with treatment changed	Total patients on initially prescribed regimen with culture examination	Patients with at least 1 positive culture			Patients with all cultures negative*	
			Smear positive	All smears negative	On laryngeal swab only	No.	% of the 20 patients admitted to study
0	0	20	18	2	0	0	0
1	0	19	4	3	0	12	60
2	0	20	0	1	0	19	95
3	0	20	1	5	1	13	65
4	0	20	3	4	1	12	60
5	0	20	5	3	1	11	55
6	0	20	5	2	0	13	65
7	0	20	6	1	2	11	55
8	6	14	2	1	1	10	50
9	6	14	0	1	2	11	55
10	7	13	9	0	0	10	50
11	7	13	2	1	0	10	50
12	7	13	1	2	0	10	50

* Even if the smear was positive

TABLE 2

Bacteriological Status at 12 Months According to the Condition on Admission to Study

Condition on admission to study		Total patients	Bacteriological status at 12 months	
			Quiescent	Active, relapsed or treatment changed
Extent of Cavitation	Extensive	4	3	1
	Moderate	12	3	9
	Slight	2	2	0
	Nil	2	2	0
Number of lung zones involved in disease	6	7	3	4
	5	5	3	2
	4	4	3	1
	3or2	4	1	3
Bacterial content of sputum on smear examination	3-plus	7	4	3
	2-plus	7	4	3
	1-plus	4	0	4
	Negative	2	2	0

positive on smear examination also. By 9 months 6 patients had had their treatment changed because of bacteriological relapse and, of the remaining 14, 3 yielded positive cultures. The position was essentially unchanged at 12 months.

Sensitivity test results

(a) *Streptomycin sensitivity tests :* At 1 month 1 of 6 strains was streptomycin-resistant. At 2 months the only positive culture from the 20 patients was resistant. Both at 3 and at 6 months 6 of 7 cultures were streptomycin-resistant. From 7 months onwards all the positive cultures were resistant.

In all, 10 patients yielded streptomycin-resistant strains, 1 for the first time at 1 month, 1 first at 2 months, 4 at 3 months, 2 at 4 months, 1 at 7 months and 1 at 8 months. In 7 of 8 patients in whom the first resistant strain was obtained at 3 months or later, this strain was also the first positive bacteriological finding following 1 or more months of culture negativity. Thus, in this group of patients, there was a very clear “fall and rise” phenomenon, i.e. a fall in the bacterial content of the sputum followed by a rise in its content associated with the emergence of streptomycin-resistant organisms. In each of the 10 patients with streptomycin resistance at any time during the year, the first resistant strain (resistance ratio of 8 or more) which emerged was highly resistant, that is, had a resistance ratio of 100 or more.

(b) *Pyrazinamide sensitivity tests:* . Considerable difficulty was experienced in the Centre’s laboratory with the standardisation of pyrazinamide sensitivity tests and reliable results are not available for these patients, either before or during treatment.

Assessment of the bacteriological status at one year

At 1 year, 10 of the 20 patients had bacteriologically quiescent disease, 7 having been bacteriologically negative from the first month onwards and 3 from the second month. Two patients, after periods of culture negativity of 3 and 7 months, respectively, had relapsed to bacteriological positivity. One patient had bacteriologically active disease throughout the year. The remaining 7 patients had had their treatment changed, because they were consistently bacteriologically positive and were considered unlikely to derive further benefit. (One had also had a radiographic deterioration when treatment was changed.)

Prognostic value of the clinical features at the start of treatment with streptomycin plus pyrazinamide

The bacteriological status at 12 months is set out in Table 2 in relation to the radiographic features and the bacterial content of the sputum at the start of treatment. Bacteriological quiescence was attained in 3 of the 4 patients with extensive cavitation and in 3 of the 12 patients with moderate cavitation. Six of the 12 patients with 5 or 6 lung zones involved in disease attained quiescence. Four of the 7 patients with a 3-plus bacterial content of the sputum on smear examination attained quiescence and so did 4 of 7 with a 2-plus bacterial content. It may be concluded that patients with extensive disease and large bacterial populations were capable of attaining quiescence. A striking feature was the ability of the combination to sterilise major cavitated lesions even though the cavities remained open. Two cases are illustrated in figures 1 to 4. Of the 4 patients who had had isoniazid-resistant strains when treatment with isoniazid plus PAS was begun, 2 had quiescent disease after a year of treatment with streptomycin plus pyrazinamide.

Drug toxicify

(a) *Streptomycin:* In all, 9 patients complained of giddiness. This responded to anti-histamine drugs in 2, but in 7 patients the dosage of streptomycin was reduced to 15

mg per kg body weight for the rest of the period of treatment. Some patients complained of pain at the site of the injections, but in no case was treatment interrupted because of this.

(b) *Pyrazinamide:* No patient developed symptoms or signs suggestive of liver toxicity. A weak positive finding for bilirubin in the urine was reported in 6 patients. In this Centre such a finding was not uncommon in tuberculous patients under investigation prior to treatment and, since the spectroscopic test for urobilin was negative, these results were ignored. Five patients had transient joint pains in the early months which responded to symptomatic treatment.

Continuation of treatment with streptomycin plus pyrazinamide for a second year

In 13 patients treatment was continued into the second year. Of these, 3 had active disease at 1 year; the combination was stopped for these 3 patients after 17, 16 and 14 months, respectively, since it was considered that they would derive no benefit from further treatment. In 2 of these patients a radiographic spread had occurred during treatment with the combination.

The remaining 10 patients had quiescent disease at 1 year and have remained quiescent. Treatment was discontinued in 1 patient after the completion of 26 months and in 3 patients after the completion of 2 years. One patient stopped the treatment of his own accord after 15 months. In 1 patient the treatment was stopped after 13 months because of persisting giddiness; this patient, a male aged 48, provided the only example of serious toxicity to the combination encountered in the whole series. Four more patients are still receiving treatment and have so far completed 23, 20,17 and 15 months, respectively.

DISCUSSION

The United States Public Health Service (1959b) has reported that streptomycin plus pyrazinamide daily is a valuable combination in the treatment of fresh cases of pulmonary tuberculosis. The present study reports the use of this combination in 20 patients, all of whom had previously failed to respond to prolonged treatment with the combination of isoniazid plus PAS and were unsuitable or unwilling for surgery. It has shown that streptomycin plus pyrazinamide has a place in the treatment of such cases, for 10 patients attained bacteriological quiescence at the end of a year. The results are not as good as those reported by the United States Public Health Service (1959b) but are favourable in comparison with the general experience of the retreatment of failure cases with new combinations of drugs. Of the 10 patients whose disease became quiescent 8 had been previously treated *at home* with isoniazid plus PAS. A study already reported from this Centre (Tuberculosis Chemotherapy Centre, 1959) has shown that bacteriological quiescence can be attained in a high proportion of patients treated at home. The present report demonstrates that patients who have failed to respond to the combination of isoniazid plus PAS may subsequently still attain quiescence with streptomycin plus pyrazinamide (the results of domiciliary chemotherapy with isoniazid plus PAS can thus be improved upon). It may be argued that better overall results could be obtained by treating from the outset *all* patients with streptomycin, isoniazid and PAS daily for several months and only then continuing with 2-drug therapy. On the other hand, it is much more simple under domiciliary conditions to organise a service on the basis of the administration of an oral combination and then to treat with streptomycin plus pyrazinamide the comparatively small proportion of patients who fail to respond.

A striking feature of the study was the rapid sputum conversion in the 10 patients who attained quiescence; 7 had converted by 1 month and the remaining 3 by 2 months. It is, therefore, easy to differentiate between patients who are responding successfully and those who are not, for the latter usually show a clearcut "fall and rise" phenomenon of the bacterial content of the sputum (Mitchison, 1950; Joiner et al., 1952; Coates et al., 1953; Wallace et al., 1954) in the early months, associated with the emergence of highly streptomycin-resistant organisms. The prolonged treatment of patients who are not likely to show substantial benefit from the combination can therefore be avoided.

Although treatment with the combination in this series was long-term (4 patients with quiescent disease having so far completed 2 years of uninterrupted treatment) and although the patients were drawn from a malnourished section of the community (Tuberculosis Chemotherapy Centre, 1959) there was no clinical evidence of hepatic damage. It has proved possible to use pyrazinamide in a daily dosage of 30 to 40 mg per kg body weight, in the absence of liver function tests, without complications, so that the findings have relevance to Indian conditions, for special laboratory facilities are at present not generally available here. (A further considerable series of patients is under treatment with the combination and hepatic toxicity has so far not been encountered in them either.)

Finally, the study has demonstrated that it is possible to persuade Indian patients to cooperate for periods of 1 to 2 years in ambulatory daily *supervised* drug administration, which includes streptomycin injections, given especially favorable clinic facilities for the supervision of the patients and the administration of the treatment. In view of the difficulties encountered with the long-term *self-administration* of oral medicaments (WHO Expert Committee on Rheumatic Diseases, 1957; Fox, 1958; Tuberculosis Chemotherapy Centre, 1959; 1960; Velu et al., 1960), this observation raises the possibility that, if effective *intermittent* antituberculosis regimens become available, the organisation of entirely supervised drug-administration might be developed in mass campaigns against tuberculosis, as has been done in the field of leprosy (Laurel et al., 1956; Ross Innes, Personal communication, 1958).

Information on a further series of patients receiving the combination is accumulating and will be reported later.

SUMMARY

(1) Twenty patients with chronic pulmonary tuberculosis and organisms sensitive to streptomycin were treated with daily streptomycin plus pyrazinamide, the majority attending a clinic daily for the therapy; all had previously been treated with isoniazid plus PAS.

(2) Treatment was stopped in 7 patients after 8 to 10 months because the disease was still active.

(3) Of the 20 patients 13 completed a year's treatment, and 10 attained bacteriological quiescence.

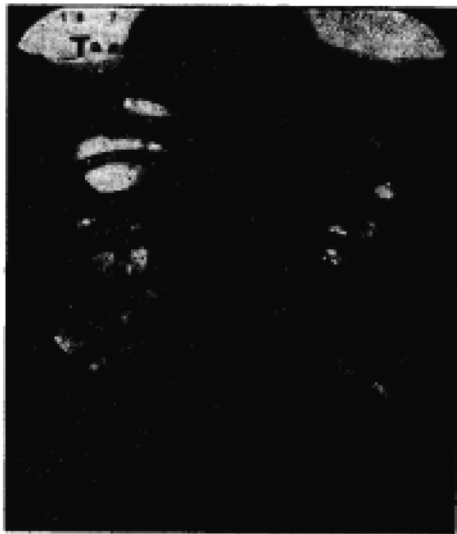
(4) Sputum conversion was very rapid in the patients who attained bacteriological quiescence.

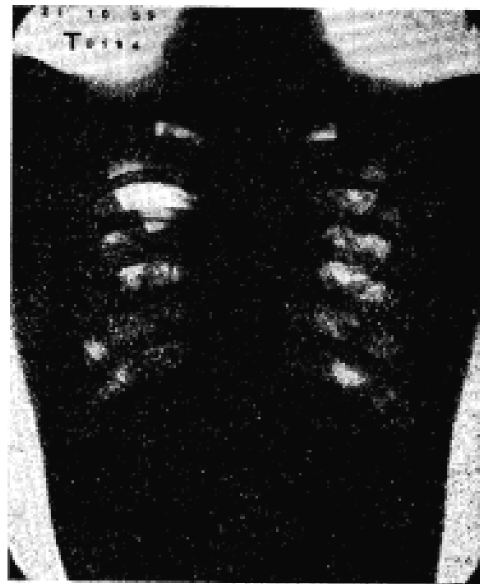
(5) A clearcut "fall and rise" phenomenon associated with a high level of streptomycin resistance was present in the patients whose response was unsatisfactory.

(6) Toxicity was not a problem with either drug.

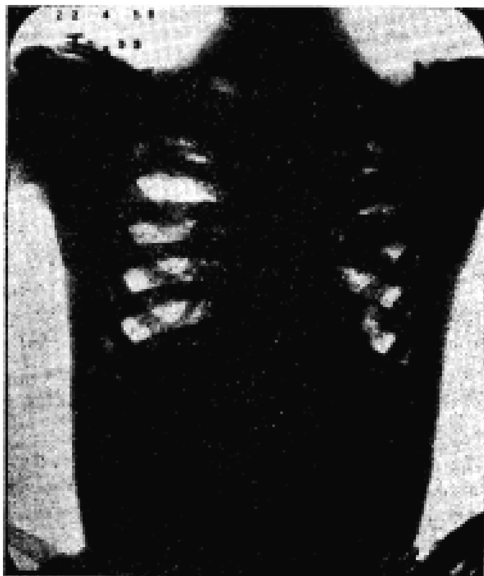
(7) It is possible in India, given especially favorable clinic facilities, to ad minister long-term daily streptomycin and pyrazinamide under ambulatory conditions.

Case No. T.0194—Male, aged 18 years





Case No. T.0653— Male, aged 34 years



ILLUSTRATIVE CASES

Case No. T.0194—Male, aged 18 years

This patient had extensive bilateral pulmonary tuberculosis which responded initially to the combination of isoniazid plus PAS. In the twelfth month, due to a slowly deteriorating lesion (see figure 1), treatment with daily streptomycin plus pyrazinamide was commenced. Within a month the sputum became negative and remained so thereafter. Treatment was stopped after 26 months on the combination (see figure 2). During this period 73 consecutive negative cultures were obtained. The patient travelled 10 miles daily for treatment and, in the last 6 months, was in full-time employment.

Comment: This case illustrates the rapid disappearance of tubercle bacilli from the sputum and the maintenance of bacteriological negativity, despite persisting extensive residual cavitation after 26 months of treatment with the combination of streptomycin plus pyrazinamide.

Case No. T.0653—Male, aged 34 years

This patient had extensive bilateral pulmonary tuberculosis which responded initially to the combination of isoniazid plus PAS. In the seventeenth month the patient had an haemoptysis and the radiograph at this stage showed a deteriorating lesion (see figure 3). Treatment with daily streptomycin plus pyrazinamide was commenced in sanatorium. Within 2 months the sputum became negative and remained so thereafter. The patient was discharged from sanatorium after 9 months and has so far completed 23 months on the regimen (see figure 4). All the 57 cultures since the second month Wave been negative. The patient has been back in full-time employment for the last 13 months.

Comment: This case also illustrates the rapid disappearance of tubercle bacilli from the sputum and persisting bacteriological negativity, despite extensive residual cavitation after 23 months of treatment with the combination of streptomycin plus pyrazinamide.

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Respiratory Functions After Pneumonectomy

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At present Pneumonectomy is being widely used in the treatment of Pulmonary Tuberculosis where we come across a destroyed lung or where stenosis of the main bronchus is present and is considered a safe procedure both as far as the post-operative mortality and the ability of the patients to bear the strains of high degree of physical activity is concerned. Experimental studies on the physiological effects of removal of one of a pair of vitality important organ as the lung is have been studied by Bremer (1937) on cats and Longaere *et al* (1937) on dogs. The physiological studies in man will be of great practical value for assessing individual cases and chiefly in helping to decide which are the most favourable conditions for the maintenance of higher degree of functional efficiency in the remaining lung after pneumonectomy. This has been attempted by few workers only.

Me Ilroy & Bates (1956) reported that after Pneumonectomy the Vital Capacity is reduced to half the normal predicted values. Hirdes & Bosch (1955) post-pneumonectomy in 38 patients reported an increase in Vital Capacity & M.B. C. with the course of time. Cournand and Berry (1942) and Cournand & Austrian (1950) reported development of emphysema after pneumonectomy. However, Hirdes & Bosch (1955) found a downward tendency in the values for Residual Volume, an observation which is in opposition to the widely held thought that after pneumonectomy emphysema develops in the course of time. This shows that the ventilatory reserves become larger, a fact that is favourable for working conditions.

MATERIAL AND METHODS

The material for study was selected from cases admitted to K.T.B. Clinic & Hospital. A detailed examination of the Pulmonary Functions was done in each case considered suitable for Pneumonectomy. The following tests were performed one week prior to the operation and repeated about two months after the operation when the patient had fully recovered:

1. Vital Capacity (V.C.)
2. Inspiratory Reserve Volume (I.R.V.)
3. Expiratory Reserve Volume (E.R.V.)
4. Residual Volume (R.V.)
5. Functional Residual Volume (F.R.V.)
6. Total Lung Capacity (T.L.C.)
7. Maximum Breathing Capacity (M.B.C.)
8. Breathing Reserve in Percentage of M.B.C. (B.R. %)
9. Exercise Tolerance Index. (E.T.I.)

All the patients were given respiratory exercises in the preoperative as well as postoperative period. Before recording the values preoperatively the patients were already acquainted with the use of spirometer several times.

Some of the gradings and classifications used in the assessment of cases in the Pulmonary Function Test Laboratory are as follows:

1. Grading of dyspnoea

The patients are asked to step up and down a height of 20 cms, thirty times in one minute. The reaction of the patient is noted during the period of recovery limited to 5 minutes.

Less than 2 min. of recovery period....... No dyspnoea
Upto. 2 min .... + dyspnoea
From 2 — 5 min .... ++ dyspnoea
More than 5 min .... + + + dyspnoea

2. Grading of ratio R.V./T.L.C. X *100*

Since the normal figures for this ratio in our Laboratory range from 25% to 35% we have found the following as a convenient classification.

Normal..25—35%
Slight Emphysema ....36—40%
Moderate Emphysema............................41—50%
Advanced Emphysema ....51—60%
Far Advanced Emphysema .... Over 60%

3. Unilateral Volumetric Measurements

The accepted normal values for the function contributed by the right lung are 55 % and for the left 45 % of the calculated normal value for both lungs. In the absence of facilities for unilateral volumetric measurements Hirdes & Bosch (1955) rated these values as 100 % for the remaining lung and compared the changes in lung volume observed after pneumonectomy.

We have also followed this method with some modifications as in our laboratory we have found lower values for the different lung volumes in normal healthy adults as compared with the European normal figures. Since the various prediction formulae are based on European standards we did not think it proper to calculate the normal values from these formulae. We therefore examined fifty healthy persons and calculated the average normal values for a healthy adult and then calculated the values for right lung (55 %) and left lung (45 %) separately. The values obtained for each were as follows:

Side	Vital Capacity in cc's	Residual Vol. in cc's	Functional R.V. in cc's	'Total lung' capacity in cc's	Ratio R.V. T.L.C. x 100
Right Lung	2200	825	1375	3025	27%
Left Lung	1800	685	1135	2485	27%

4. Radiological Classification

The cases were classified according to the recommendations of Indian Tuberculosis Association (1940) into three stages depending on the extent of parenchymal involvement.

5. Exercise Tolerance Index

It was performed as described by Mutthuswami (1954).

A pneumonectomy was performed in the following group of cases:

1. Tuberculous cavitation (destroyed lung)...6 cases (60%)
2. Unexpanded Lung after Tuberculous Empyema... 2 cases (20%)
3. In the present series we were provided with an unusual opportunity to study two cases (20 %) with Stage II disease in which originally a Lobectomy was planned but due to accidental nick in the Pulmonary artery on the operation table a Pneumonectomy had to be performed.

Out of the ten cases studied, 6 cases (60 %) were females and 4 cases (40 %) were males. The female patients belonged to age group 20-28 years (mean 24 yrs.), and the male patients belonged to age group 25 years to 32 yrs.(mean 28 yrs.). Two cases (20%) belonged to Stage II disease while the rest to Stage III disease (80%).

In six cases a left sided Pneumonectomy was performed and in the remaining four a right sided Pneumonectomy was performed.

RESULTS

This study comprise of ten cases in whom a Pneumonectomy was performed. In none of the cases supplementary collapse measures were undertaken for the reduction of dead space.

The data regarding functional changes noticed is given in the accompanying table. An analysis of the data reveals the following results:

Vital Capacity

It was reduced in all the cases. The maximum reduction noticed was 28 % (range being from 3% to 28%) and the average reduction being 9.7%.

In two cases with Stage II disease in which originally a Lobectomy was planned but due to accidental nick in the Pulmonary Artery a Pneumonectomy had to be performed, demonstrated a reduction of 28% and 15% respectively.

In six cases with a destroyed lung the maximum postoperative reduction noticed was 12% (range being from 7% to 12%) and the average reduction being 8%.

In the remaining two cases with unexpanded lung postoperative reduction noticed was 3% and 4% respectively.

Analysis of the values found postoperatively in terms of the normal values for one lung the figures ranged between 92% to 117%.

FUNCTIONAL CHANGES IN THE REMAINING LUNG AFTER PNEUMONECTOMY

Case	Name	Sex	Stage Dis-case	Special remarks about Lung Lesion	Side of Pnru-monec-tomy	VITAL CAPACITY		Preoperative		
						calculated average normal value for one lung	of pre-opera-tive value (%)	I.R.V. in cc's		
1	2	3	4	5	6	7	8	9	10	11
1.	B.D.	F	III	Unexpanded left lung after empyema.	Left	+ 6%	- 3%	1483	494	3
2.	G.S.	M	III	Destroyed lung left side	Left	+ 2%	- 7%	1494	498	3
3.	R.J.	F	III	Unexpanded left lung after empyema.	Left	+ 4%	- 4%	1475	492	2.9
4.	S.K.	F	II	Fibrocavernous with infiltration left upper zone.	Left	+9%	-28%	1952	650	3
5.	R.K.	M	III	Destroyed lung left side	Left	- 6%	-12%	1445	500	2.8
6.	C.B.	F	II	Infiltration with a cavity left upper zone.	Left	+ 17%	-15%	1947	649	3
7.	C.K.	F	III	Destroyed lung right side.	Right	- 8%	- 4%	1600	546	2.8
8.	K.P.G	M	Ill	Destroyed lung side.	Right	+2%	- 8%	1854	600	3
9.	K.K.	F	Ill	Destroyed lung right	Right	+ 4%	- 6%	1850	618	2.9
10.	O.K.	M	III	Destroyed lung right side	Right	+ 2%	-10%	1870	630	2.9

Maximum Breathing Capacity

Out of the ten cases it was reduced in eight, while no change was observed in the remaining two cases. The maximum reduction noticed was 30 % (range being from 7 % to 30%) and the average reduction being 10%.

In two cases with Stage II disease the postoperative reduction noticed was maximum (being 30% and 25% respectively). While in the two cases with unexpandiable lung, postoperatively no change in M.B.C. was noticed.

Residual Volume

It was reduced in all the cases studied. The maximum reduction noticed was 39% (range being from 25% to 39%) and the average reduction being 32%.

Analysis of the data found postoperatively in terms of the normal values for one lung, our cases demonstrated an increase of the Residual Volume in all the cases. The maximum increase was 33 % (range being from 1.2% to 33 %) and the average rise being 12.6%. The two cases with stage II disease had a rise of 1.2% and 2.5% respectively, which is small and negligible.

Functional Residual Volume

It was reduced in all cases studied. The maximum reduction noticed was *2S°/* (range being from 18% to 28%) and the average reduction being 22%.

Table—*(Contd.)*

Post Operative			Functional Residual Vol.		Residual Volume		Total Lung Capacity		R.V/T.L.C.X 100	
I.R.V. in cc's	E.R. V. cc's	Ratio	Change in terms of pre-operative value	Change in terms of calculated average normal values for one lung	Change in terms of pre-operative value	Change in terms of calculated average normal value for one lung	Change in terms of pre-operative value (%)	Change in terms of post-operative value (%)	Preoperative (%)	Post-Operative (%)
12	13	14	15	16	17	18	19	20	21	22
1420	496	2.7	-21%	+ 11%	-30%	+ 12%	-15%	+ 8%	36	29
1344	500	2.6	-25%	+ 14%	-35%	+ 15%	-22%	+ 6%	38	30
1375	503	2.7	-20%	+ 8%	-30%	+ 6%	-16%	+ 5%	35	28
1480	493		-21%	+ 14%	-25%	+ 1-2%	-22%	+ 12%	28	29
1219	480	2.5	-28%	+ 15%	-37%	+22%	-30%	+ 2%	41	33
1580	527	3	-20%	+ 12%	-28%	+25%	-19%	+ 15%	27	27
1520	534	2.9	-20%	+ 18%	-37%	+33%	-24%	+ 4%	45	35
1665	579	2.8	-28%	+ 5%	-39%	+ 5%	-25%	+ 3%	37	28
1700	598	2.8	-22%	+ 11%	-30%	+ 13%	-18%	+ 7%	35	29
1600	644	2.4	-18%	+ 16%	-28%	+ 16%	-20%	+ 6%	35	30

Analysis of the postoperative data in terms of the normal values for one lung our cases demonstrated a rise in F.R.V. in all the cases. The maximum rise was 18% (range being from 4% to 18%) and the average rise being 12%.

Total Lung Capacity

It was reduced in all the cases. The maximum reduction noticed was 30% (range being from 15% to 30%) and the average reduction being 21 %.

Analysis of the data found postoperatively in terms of the calculated normal values for one lung, our cases demonstrated an increase in T.L.C. The maximum rise was 15 % (range being from 2 % to 15 %) and the average rise being 6.8 %. This much of rise in T.L.C. is of no significance.

Ratio R.V./T.L.C. X 100

Preoperatively a normal ratio was found in 5 cases, evidence of slight emphysema in 3 and moderate in 2 cases. None of the cases had evidence of severe Emphysema.

Postoperatively a normal ratio was found in all the cases. Thus evidence of Emphysema (as suggested by this ratio) was not found in any case postpneumonectomy, in the remaining lung.

Table—*(Contd.)*

Change in Maximum	Exercise tolerance index			Breathing Reserve %			Dyspnoea	
breathing capacity in terms of Pre-operative Value. (%)	Preoper -ative	Post-operative	Change	Preopera-tive	Post-operative	Change	Preopera tive	Post-Operative
23	24	25	26	27	28	29	30	31
No Change	78	80	+ 2	*W*	79	—	Normal	Normal
-7.6%	60	69	+ 9	74.5	73.6	— 0.9	+ +	+
No Change	72	65	-7	88.5	78.0	-10.5	Normal	+
-30%	98	98	*0*	88.6	82.5	- 6.1	Normal	Normal
-6.6%	80	68	-12	80.3	77.2	- 3.1	Normal	+
-25%	95	92	- 3	85.0	82.0	-3	Normal	Normal,
-7.6%	65	65	o	78.5	72.0	- 6.5	+	+ +
-10%	75	70	_ 5	81.9	80.2	- 1.7	Normal	Normal
-10%	68	69	+ 1	72.6	75.0	+ 2.4	+	+
-8%	55	50	- 5	74.1	65.2	- 8.9	+	+ +

Ratio I.R.V./E.R.V.

Me Ilroy & Bates (1956) describe slight reduction in this ratio as representing Over inflation and from moderate to severe reduction as evidence of Emphysema. Analysing our preoperative data in these terms, a normal ratio was found in 8 cases, and evidence of over inflation in two cases only.

Postoperatively a normal ratio was found only in 3 cases while the remaining 7 cases showed a slight reduction. Thus postoperatively most of our cases had evidence of over inflation only but none of them showed evidence of Emphysema in the remaining lung, as judged by the standards of Me Ilroy & Bates.

Breathing Reserve/M.B.C. X 100

Postoperatively a reduction in B.R. % was noticed in 8 cases. The maximum reduction noticed was 10.5% (range being from 0.9% to 10.5%) and the average reduction being 5.1%.

One case showed an increase of +2.4 % and another did not show any change in B.R.%.

Preoperatively as well as postoperatively cases which had no dyspnoea on exercise the B.R. % was 79 % or over. Below 79 % dyspnoea was present on exercise. Between 73 % to 79 % ' +dyspnoea' and below 73 % ' + +dyspnoea' was noticed. In none of the

cases '+++dyspnoea' on exercise was present in our cases either preoperatively or post-operatively.

Exercise Tolerance Index

Postoperatively 2 cases did not show any change and in three cases it increased, the values being +9, +2 and +1 respectively. In the remaining 5 cases it showed a reduction. The maximum reduction was—12 (range being from —3 to —12) and the average reduction being —6.4.

Preoperatively as well as postoperatively no dyspnoea was noticed on exercise when the values were above 70, while dyspnoea was invariably present when figure was below 70.

Clinical and Radiological Follow up

Postoperatively dyspnoea was seen on exercise in 6 cases. Out of these four cases had it already preoperatively. In case No. 2 ' + +dyspnoea" seen preoperatively lessened to '+' postoperatively. In cases No. 7 and 10 '+dyspnoea' seen preoperatively increased to '++' postoperatively. In case No. 7 postoperatively there was presence of Bronchitis while case No. 10 had a late postoperative recovery. He developed a huge serosanguinous effusion after Pneumonectomy which necessitated several aspirations. In the remaining cases No. 3, 5 & 9 only '+dyspnoea' was noticed postoperatively. The cases 3, 5 did not demonstrate any dyspnoea preoperatively. This can only be explained by assuming that in the remaining lung the ventilation for a given amount of exercise is doubled and the mean inspiratory resistance to the greater flow of air through the bronchial tree of the remaining lung is increased.

None of the cases postoperatively developed any evidence of Bronchopleural Fistula.

Radiologically evidence of emphysema was found in case No. 4, 6 and 10. In others the remaining lung did not show any appreciable change as compared to the preoperative state.

DISCUSSION

I. Ventilatory Functions

There occured a reduction in ventilatory functions in all cases postpneumonectomy. An average reduction of 9.7 % in Vital Capacity and 10 % in M.B.C. was observed. Such a small reduction in Ventilatory functions after Pneumonectomy suggests that most of the function was being contributed by the normal lung.

Two cases with Stage II disease demonstrated the maximum reduction in Ventilatory Functions—(V.C.—28% &—15%, M.B.C.—30% and—25%) while in other cases with Stage III disease the average reduction noticed was only —7%. This clearly demonstrates that if a destroyed or completely unexpanded lung is going to be removed a minimal reduction in Ventilatory Functions should be anticipated.

II. Development of Emphysema after Pneumonectomy

When the preoperative values were compared with the calculated normal values for one lung, the cases demonstrated a raised residual volume without any change in the T.L.C. This shows the patient's inability to or unwillingness on his part to perform a deep expiration. This is supported by finding similar values of E.R.V. preoperativley

as well as postoperatively which suggests breathing at a higher level postoperatively. A higher level of breathing without an increase in T.L.C. does not suggest emphysema.

Since we have been able to demonstrate an unwillingness on the part of the patient to perform deep expiration, it is expected that with the course of time this inhibition would disappear and the Ventilatory reserve would increase. Hirdes et al (1955) have reported increase in ventilatory reserves with the course of time after following cases of Pneumonectomy for a period of two years.

The presence of raised Functional residual volume without any change in T.L.C. only suggests Overinflation of the remaining lung. This is further supported by the presence of only slight reduction in T.R.V./E.R.V. ratio.

III. Role of Thoracoplasty after Pneumonectomy

In follow up our cases did not demonstrate the development of Emphysema, bronchopleural fistula or any other complication which is supposed to be prevented by supplementary collapse measures after Pneumonectomy. Similar reports have come from Earland (1953), Nuboer (1953) and Hirdes & Bosch (1950).

In none of the cases in present series a thoracoplasty was done so it is not possible to judge its value. But on one hand the report of Workers like Gaensler and Strieder (1951) and Mathey et al (1952) that thoracoplasty after Pneumonectomy accomplishes just opposite of the desired results, and on the other the finding in present series, that the patients are doing well without Thoracoplasty there is sufficient indirect evidence to conclude that the value of thoracoplasty is doubtful.

It is further supported by the fact that most of our cases had B.R. near about 80% of M.B.C. and Cournand & Berry (1948) have reported that when the B.R. is less than 85% of M.B.C. the possible advantages to be gained by Thoracoplasty must be weighed against the chances that a further reduction in Pulmonary Functions in the Post-operative period may reduce the patient to a permanently incapacitated individual, dyspnoeic on slightest exertion.

IV. Invalidism Following Pneumonectomy

Cournand & Berry (1942) reported that whatever dyspnoea there was seemed to be most closely related to a diminution in B.R. We therefore made an attempt to correlate dyspnoea with B.R. % and Exercise tolerance index.

We found a close association in between three:

B.R. between	80—85%	
E.T.I above	70	+Dyspnoea not noticed.
B.R. between	80—85%	
E.T.I below	70	Dyspnoea present.
B.R. between	80%	
E.T.I below	70	Dyspnoea present.

Thus in marginal cases the dyspnoea appears to be related to the data for E.T.I. If it was above 70 no dyspnoea, while if it was below 70 dyspnoea on exertion was noticed. Thus E.T.I can be taken as a reliable test for determining the postoperative invalidism.

We have found an average reduction of 5% in B.R. and 6.4 in E.T.I, postpneumonectomy. In view of the findings if pneumonectomy is performed in a patient with preoperative B.R. of less than 85 % of M.B.C. and E.T.I, of less than 77 there is danger of making the patient a respiratory cripple.

CONCLUSIONS

There occurs a reduction in Ventilatory functions after Pneumonectomy. The cases did not demonstrate any evidence of Emphysema two months after Pneumonectomy. Based on the indirect evidence the role of thoracoplasty after Pneumonectomy appears doubtful. The study suggests that if a Pneumonectomy is performed in patient with a preoperative B.R. of less than 85% of M.B.C. and E.T.I, less than 77 there is danger of making the patient a respiratory cripple.

SUMMARY

Ten cases have been studied to assess the effect of Pneumonectomy on Ventilatory Functions of the Lung, to assess the role of Thoracoplasty after Pneumonectomy. An attempt has been made to evaluate the minimal Ventilatory reserve when a pneumonectomy can be safely performed without making the patient a respiratory cripple. This is a preliminary report of the whole project in which the cases will be followed for a period of 5 years.

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Graded Activities and the Development of Work Tolerance Through Occupational Therapy Activities

By

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Many of you will recall or have read of the detailed programmes worked out in the old days for patients suffering from tuberculosis. I say "old days" because with increased use of surgery, the use of chemotherapy and domiciliary treatment, comparatively little of the old detailed routine has remained. There is some of it in the hospitals and sanatoria but most of the detail has been dispensed with. You will recall elaborate charts of advancement of the patient from 10 minutes sitting up, one bathroom privilege, one time to wash his face, than a bath given to him in the bath-room and finally giving one to himself. Along with this he progressed from being fed (in severe cases) to self feeding, first in bed. then in a chair and finally to going to a dining room on the ward or to the hospital dining-room. I need not further elaborate the details. As Occupational Therapy was recognised as an useful adjunct, it was brought into the same approach and when I did my clinical training at the Hermann M. Biggs Memorial Hospital, Ithaca N. Y. and later spent some time at the Mt. Morris Tuberculosis Sanatorium, also in New York State, we integrated the Occupational Therapy with the progress programme. Occupational Therapy was first allowed once or twice a day for ten to fifteen minutes only, and no activity project could be left with the patient. We planned our progress down the ward, bed by bed or room by room, on a time basis, and also had tags for the beds as to the Grade of the patient. After a week or two, the time might be increased to 15 or 20 minutes and on up to a half hour or more. Along with this increase in time came variety of the activity. At first we could give only such activities as required the use of the hands up to the wrist. When these activities were allowed for half an hour and depending on the total condition of the patient as observed by the physician, the patient could be given an activity requiring use of the forearm and elbow, and finally the use of the whole arm with certain precautions. The patient was also allowed more and more time out of bed and finally to come to the Occupational Therapy Workshop where again he was graded from sitting to standing and by time.

You will have noted that I have called this the "progress programme" and this has been done deliberately although it was not called by this term in the Sanatorium, simply the Patient's Graded Privileges. I have called them "progress" because both to the physician and staff and to the patients these were definite signs or measures of his progress. There were many differences between the patients in the rate at which they advanced from Grade to Grade and sometimes a patient who became too despondent would be given a light up-grading just for psychological reasons and it was frequently an important and useful event in his total thinking and behaviour. Equally if a patient became too pleased with himself, too over-confident and would over-do, not follow routine and so on, he could be dropped back a grade and thus warned and it was a mild form of "punishment" or control which often proved highly effective.

There were several other important factors in this type of treatment as we could also measure his dexterity, his interests, hand and eye coordination and adaptability

to new activity projects. The Occupational Therapist would try to relate them to his previous occupation or job and could give the physician, Social Service Department, and Vocational Guidance Adviser important information. If the patient was allowed to take a correspondence course or have a teacher for school studies, this was also related to the knowledge accumulating about him and the time involved fitted into his total programme and amount of activity.

Another part of the work of the Occupational Therapist was to develop work tolerance, particularly when it was decided as to whether he could go back to his former job or must seek a new type of work more suitable to his health. This was done by up-grading for time, posture, weight of work materials and any other elements of his future work. A work situation as close as possible to that which he would be having was arranged for him. Signs of fatigue were closely watched for, and noted for report, as well as stopping the activity immediately.

This is now pretty much a thing of the past and I can imagine some of you saving what a waste of time it was on record keeping, too much detail and so on but I can assure you that once the basis was worked out and simple forms for checking set up it was not a great burden either to the doctor or other staff and the Occupational Therapist also learned to plan, keep projects ready and have a routine arranged so as to meet the situation without strain. Now what about today in the Tuberculosis Institutions day clinics, and the domiciliary treatment programmes! In the hospitals and sanatorias whether the patient is for operation or for bed rest treatment with his chemotherapy, I believe the same approach can and should be used, even though in a modified form-I believe that psychologically a little light activity even for the sputum positive cases using only the hands and for a short period would do a great deal for the patients. I, believe that along with it they could be given at least part of a relaxation programme and that there would be real value in this. I also advocate that the preoperative cases have a modified programme which would orientate them to the post-operative exercises and activities which would give them “hope” and interest and faith in their improvement After surgery it is most important to start a graded programme at once so that the patient’s thinking is positive and related to reality.

For those outside the institutions but attending a clinic, I would like to see an attached Modified Sheltered Workshop where they could begin for as short a time as an hour a day to do some actual productive work. The time and the work should be related to their condition, amount and type of travel to the Workshop, etc. and could be increased and up-graded from time to time. The activities or work available in the Modified Sheltered Workshop should be of some variety. For instance there would be some types of general office routine which a clerk would have to do, folding papers and inserting into envelopes, addressing envelopes by hand, typing of addresses, assembling sets of literature or parts of a brochure, filing and all such related work. Another type of work could be pre-book binding in terms of making such things as writing-pads, covering files, making binders, etc. Assembly jobs such as safety pin bunching, radio or electrical assembly work could be taken up and other light work which could be secured from local companies. It is really surprising how much of this is available if one looks for it. There could be sections for heavier work and work requiring standing. To this Modified Sheltered Workshop there should be attached an Employment Officer whose duty it would be to work with the physician-in-charge and relate the man to his former work and have him taken back when ready for it unless it was of a nature which had been declared as countra-indicated. The Employment Officer would also find out suitable employment as is done in the Pilot Project for the Employment of the Disabled now going on in Bombay. This would develop job opportunities perhaps with the same company or organisation with which the patient had worked before but in a different department or in other companies. You will yourselves be able to think of other possibilities. The objection may be raised that people will be reluctant to employ ex-tubercu-

losis patients but just as propaganda must be done for the employment of the physically disabled, blind and deaf, in a similar manner it must be done for our ex-patients.

I have called them *Modified* Sheltered Workshops because they are a transition situation and not intended as a permanent place of work. The objective is to prepare them for open employment and then have them go to it, either their former job or a new one. These Sheltered Workshops should have rest facilities but it would be better to let the patient go home after his work period, a short rest, and perhaps a cup of tea or milk. Once he can put in more than a half days work, then he would have his lunch, either brought from home or purchased at the Canteen attached, perhaps a longer lunch period than normal for a few weeks but always the aim is toward a regular work situation.

The foregoing covers the general approach to the problem. Naturally I believe that a qualified Occupational Therapist is a necessary member of the staff of such an institution as he is trained in graded activities, assessment, and study of the various occupations. What other staff would be required would depend on the size of the venture, types of work provided and so on. What about the expenses for running this Modified Sheltered Workshop and payment of the patient workers! In the first few years the workshop would have to be subsidised as it would have to compete in the open market for sale of products or for work. The workers should be paid first some minimum daily or half day wage which would cover the normal transportation charges with something over for their tea or milk. This should not be done as “charity” for any longer than can be helped. The total for the day should cover transportation, tea or milk, and a light lunch cost (these should not be GIVEN to the worker). As soon as possible the worker should be put on production piece work but there may have to have a limit of production set by patient to avoid tension and pressures. It has been found at the Sheltered Workshop for the Physically Handicapped in Bombay that after the first few got into piece work after a daily wage of Rs. 1.50 the others came into it without much difficulty.

From the Hospital or Sanatorium, the patient may come under the Clinic and its Modified Sheltered Workshop and his records should be forwarded for information and guidance, particularly the Occupational Therapy Report. There remains the problem of those under Domiciliary Treatment, a situation to be somehow met, no matter how unsatisfactory. In the Home Treatment Programme also we must think of the development of work tolerance, graded activities, skill and preparation for work. They also should be considered for admission to the Modified Sheltered Workshop if one is available. Before that a Mobile Occupational Therapy Department which is used in the United States for rural work with the physically disabled such as polio children, should be developed to meet the needs. Equipment could be loaned and material supplied at cost. The principles are the same but done in the home situation.

So far I have only suggested some possible activities which could be used in the grading and development of work tolerance. According to material presented by me in a Special Tuberculosis Issue of the Indian Journal of Occupational Therapy of Dec. 1956 and of May 1959 based on American studies of Energy Cost of Self-Care and Work Activities we can consider various activities in terms of increase of the basic metabolic rate, (available at The Amerind, 15th Road, Khar, Bombay 21) Other related material was presented by Dr. K.K. Datey, Cardiologist, in a paper “Common Cardiac Condition and Recent Advances in Their Management” at the Annual Conference of the All India Occupational Therapists’ Association held in Bombay in June 1958 and printed in the May 1959 issue of the Indian Journal of Occupational Therapy. This material presents the Oxygen Requirements of Activities in Daily Living and various Occupations, based on per cent of resting rate. Certainly oxygen requirements for an occupation should be related to the lung capacity and is particularly pertinent for post

resection cases. Dr. Datey gives the Oxygen Requirements for Desk-work at 100%, Mechanics 225%, Welders 250% and Carpenters 350%. Other material is also available from time to time and should be studied in relation to the rehabilitation procedures for the ex-tuberculosis patient.

I have undertaken to give a picture of the usefulness of Graded Activities and their relation to the development of Work Tolerance as is and can be done by an Occupational Therapist. I have also suggested that a Modified Sheltered Workshop should be set up to meet the needs of the ex-tuberculosis patient in preparation for his eventual open employment.

Bronchial Adenoma With Mitral Heart Disease

By

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M.D., a 30 year old multiparous woman, first attended the Kingsway Chest Centre, outpatient department of this hospital, in March, 1957, complaining of cough, moderate expectoration, and occasional bouts of fever. The illness had started in August, 1956 with low-grade fever following upon cough and cola. Fever had gradually subsided on its own in three months time, but, a few days later, she started having pain and swelling in both ankles, involving the knees and wrists soon after, necessitating recumbency in bed. 15 injections of Irgapyrine (Phenyle Butazone—Amidopyrine) relieved the pain fully. The cough persisted. About two weeks of freedom from pain were followed by a recurrence, this time with fever. A week of Irgapyrine and Penicillin brought down the pain and fever, but the cough still persisted; X-Ray skiagram of the chest was taken, and she was given 1 Gm. Streptomycin daily followed by 10 days of Strepto-Penicillin. (In 1946, she had suffered from fever, cough and expectoration, and had been diagnosed as tuberculous, and treated as such for 3 months—exact treatment was not known, but it is presumed no chemotherapy was used.) Examination revealed a rather pale, obese young woman, having mildly clubbed nails, no positive findings being elicited in any system, including the respiratory and cardiovascular. The P. A. film, taken some two months previously showed an oval, uniformly dense, shadow in the left lower zone. adjacent to the cardiac silhoutte, cardiac contours normal.

After this first visit, the patient disappeared, and was next seen when she was admitted to the non-tuberculous section of the hospital in August, 1958, having been referred by another clinic. During this time, she had taken varied treatments, and had felt reasonably free of symptoms, apart from the persistent cough; till March 1958. She had also started getting breathless on moderately severe exertion. In March 1958, she had an abortion, the bleeding going on for 2 months, and leading again to low fever. Cough continued, and she started getting frequent haemoptysis, a teaspoon to half an ounce, causing her to seek medical aid, leading to this admission.

Examination on admission revealed the following, apart from features noted 17 months earlier :—

Temperature 99° to 100° F; Pulse range 80 to 90 P.M.; respirations 20 P.M.; breath sound poor over both lungs, scattered rales both sides with occasional rhonchi; apex beat in the 5th left space, a presystolic murmur localised in the Mitral area, followed by a short and loud first heart sound; B. P. 130/90.

Laboratory reports at this time were as follows:—

Sputum negative for A. F. B. by repeated cultures on *Ziehl-Nneilson slopes.* Blood; WBC normal; ESR 17 mm. 1st hour Westergren, Hb. 9.5 Gm.%, RBC 3.5 millions/cmm., PCV 32%, MCV 94 /* *H,* MCHC 31.2%

Urine (non-catheter specimen) showed a trace of albumen and a few pus cells. Stools normal, Mantoux positive (O.T. 1/1000). Histoplasmin negative.

Skiagrams of the chest showed a lobulated dense opacity in the left lower lung field, just adjacent to the cardiac shadow, with a translucency in its upper part. Lateral projection revealed the opacity to lie in the area of the lingula, with a well-defined ring shadow in it (see fig. 1), cardiac contours normal. RAO with barium swallow showed no enlargement of the left atrium.

Bronchoscopy did not reveal any abnormality in the visible tracheobronchial tree. ECG showed Pmitrale with a PR interval of 16 seconds.

Patient was submitted to surgery in December, 1958, a Lingulectomy being performed. On cutting the lingular bronchus, it was seen to be almost completely occluded by a tumour, found on section to be an adenoma of cylinderomatous type, the neoplasm having almost entirely replaced

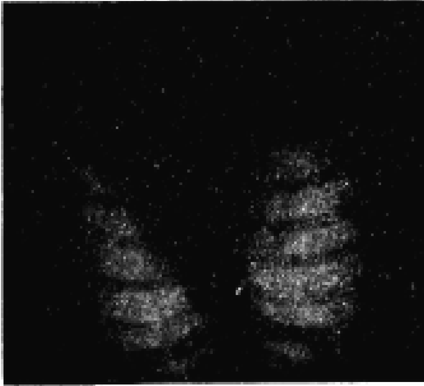


FIG. 1

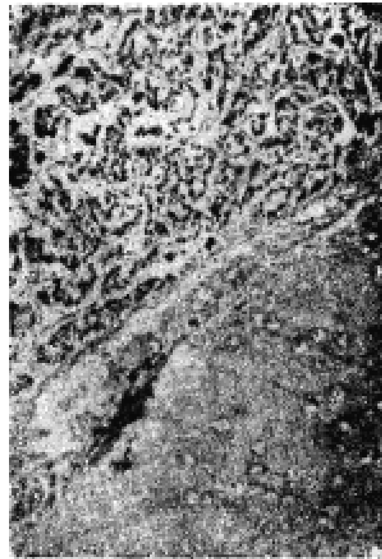


FIG. 3

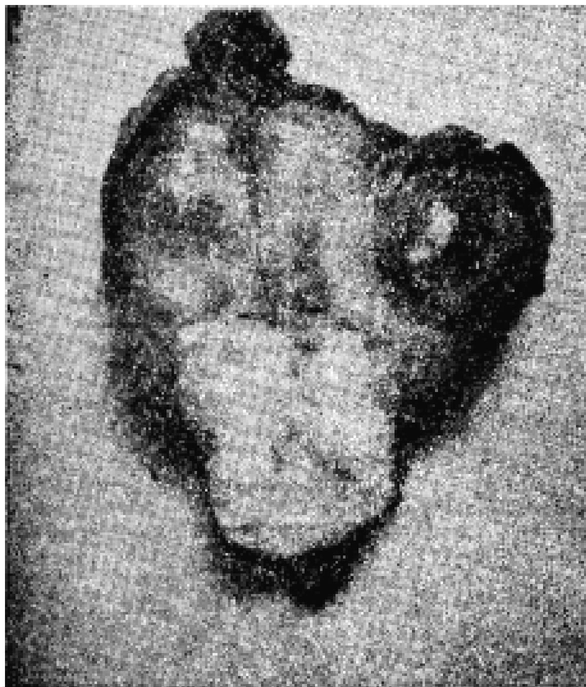


FIG. 2

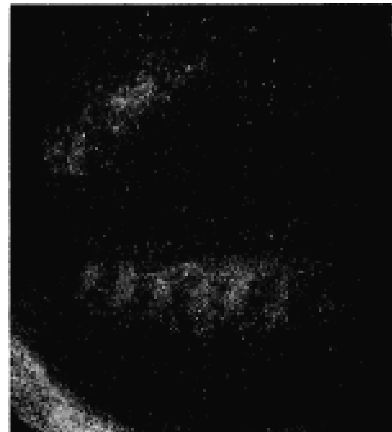


FIG. 4

the normal bronchial structures, small islands of cartilage only being seen. The mass in its entirety also showed two cystic, fluctuating masses, distal to the tumour, which were seen to be continuous with branches of the lingular bronchus, and showed a thin, fibrous wall, devoid of any identifiable histological patterns giving a clue to its origin. However, in view of the naked eye appearances, the Pathologist had no hesitation in considering them to represent dilated bronchi, as a result of blockage caused by the growth.

The patient was discharged on the 13. 2. 59, post-operative progress being uneventful.

Follow-up

The patient has now been watched for almost a year after resection. Shortly after discharge, there was a minor episode of cough with expectoration which cleared off on a few days of Penicillin. She has also twice had small haemoptysis. ECG taken in April, 1959 showed a counter clockwise rotation as compared to her per-discharge graph, and a prolongation of PR to .22 sec. The heart now showed a definite exaggeration of its right border, and the barium-filled oesophagus was now distinctly displaced backwards, (fig. IV) Before these investigations had been evaluated, she started having pain in the precordium, and an acute rheumatic episode was diagnosed. Her dyspnoea also had increased considerably, so that level walking was now uncomfortable. She was prescribed salicylates, but did not take them, and at check-up in August, had developed a grade II mitral systolic murmur also, and dyspnoea too had increased. She now started taking salicylates in full dosage, and when last seen in the first week of December, 1959, was better symptomatically.

Comment

This case has been presented because of several interesting features. Firstly, the fortuitous combination of two conditons, either of which could have given rise to most of the clinical features. There was a fairly late onset of rheumatic fever in this woman, and its development into clinically significant cardiac involvement is noteworthy. As, at the time of admission, it was not known that one of us had seen this patient previously—(this was discovered at follow-up only), the mitral stenosis was taken as incidental, and active cardiac rheumatism was not considered likely, and as is seen from the report, was discovered only at follow-up The diagnosis of the lung condition was in doubt till the specimen was removed. The pathological appearances distal to the tumour, again, are worthy of note.

It may be mentioned that at the first examination, the idea of the articular manifestation, (as related by patient), being a typical pulmonary osteoarthropathy, had certainly been toyed with.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. P.U. Rao, Resident Superintendent, S.J. T.B. Hospital, Delhi, for his helpful suggestions in the course of the treatment etc. of this patient, and for permission to report the case. The pathological work was carried out at V.P. Chest Institute by Dr. H.D. Tandon, and the authors are indebted to him for the report. Dr. J.S. Karanwal, former Thoracic Surgeon of the hospital, performed the resection, and this opportunity is taken to thank him.

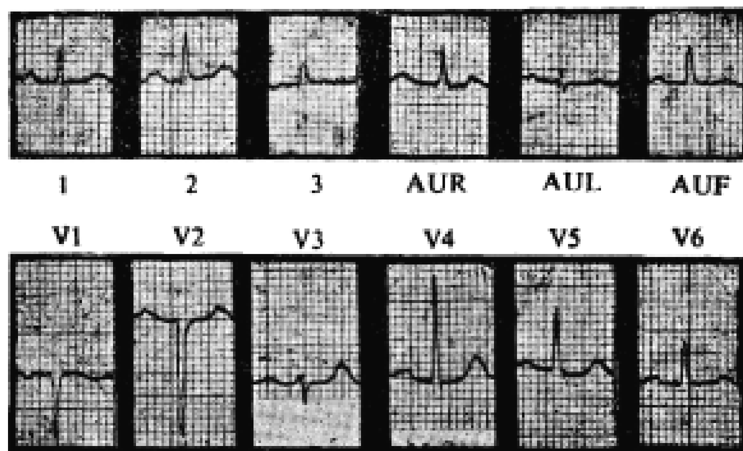
LEGENDS

FIG. I. P.A. and Lateral skiagrams on admission, (see text)

FIG. II. ECG—pre-operative, and in April, 1949. (see text)

FIG. III. (a) Naked eye appearances in resected specimen—longitudinal section, almost actual size. The tumour is seen at the bottom of the picture. Above is seen one of the saccular dilatations described in the text, (b) High Power view of the solid tumour—note the cartilage tissue in the lower right corner of the field. The rest of the field is taken up by cells in acinar arrangement.

FIG. IV. P.A. and R.A.O. views of the heart, after a Barium swallow, taken in April, 1959. (see text)



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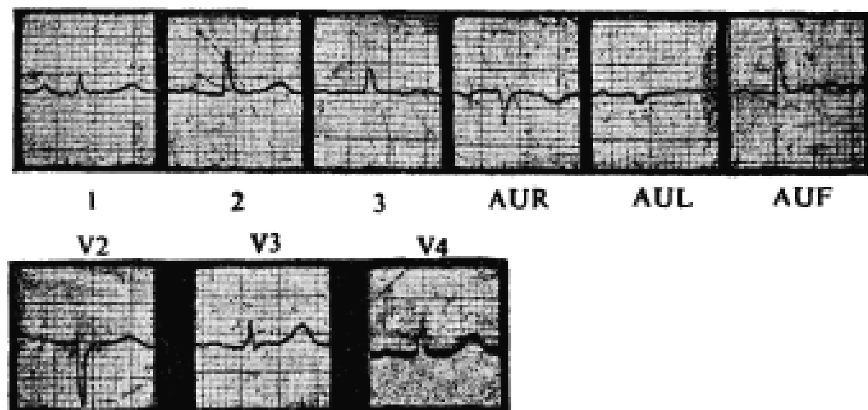

18.3.59

NEWS & NOTES

Meeting of the Eastern Regional Committee

The second regular meeting of the Eastern Regional Committee of the International Union Against Tuberculosis met in Sydney, Australia on the 19th & 20th May, 1960. The meeting was inaugurated by Sir Kenneth Street and the sessions were presided over by Dr. P. V. Benjamin, President of the Committee.

The Committee unanimously approved the report and the statement of accounts for the period October, 1958 to April, 1960 presented by Shri B.M. Cariappa, its Secretary and Treasurer. It recommended that every country in the Eastern Region be requested to establish strong and effective National TB Associations in order to assist their governments in the Campaign against Tuberculosis. It has also suggested that delegates from member countries be invited to attend the annual TB Workers' Conference in India.

The Committee re-elected Dr. Benjamin as its President and Shri B.M. Cariappa as its Secretary and Treasurer for a further period of two years. It also decided to continue its headquarters in New Delhi for another term of two years.

XVI International Tuberculosis Conference, Toronto

The International Union Against Tuberculosis has announced that the XVI International Tuberculosis Conference will be held in Toronto, Canada, September 10th-14th, 1961 under the presidency of Dr. G.J. Wherrett.

Among other things, an interesting scientific programme as well as visits to hospitals and clinics have been arranged. Tours in the city of Toronto and surroundings will provide opportunities to observe various aspects of Canadian life. There will be a full day trip to Niagara Falls and pre-and-post convention tours in Canada and the United States. Special arrangements for travel with reduced fares for chartered aircraft, will be made through national travel agents.

Full details of the Conference can be obtained from the General Secretary, Dr. C.W.L. Jeans, 265 Elgin Street, Ottawa, Canada, or Dr. W. Gellner, Executive Director, International Union Against Tuberculosis, 15 Pomereu Street, Paris 16, France.

XVII TB Workers' Conference

The Seventeenth Conference of Tuberculosis and Chest Diseases Workers in India is likely to be held early in 1961 in Cuttack, Orissa. The highlight of the Conference will be a symposium on the problems of "Drug Resistance". Papers on Clinical behaviour of Abacillary Pulmonary Tuberculosis, Allergic conditions of the lungs, Evolution of Primary Tuberculosis, Tuberculin testing in 0-4 years age group, Rehabilitation needs of the patients, B.C.G. Vaccination of the new born in Andhra Pradesh and Surgery of Pulmonary suppurations will be presented at the Conference.

Dr. J. Frimodt-Moller, Director, Madanapalle TB Research Unit, Madanapalle (Andhra Pradesh) will preside over the conference.

Fight TB Fund, Hyderabad

The Central Committee of the TB Association of Andhra Pradesh in its meeting of 14th May, 1960 under the Chairmanship of Shri P.V.G. Raju, Minister for Health and Medical affairs reviewed with concern the downward trend in TB Seal Sale Campaign and decided to intensify the ensuing campaign by making it as broad based as possible by associating with it workers ranging from business to political community and consequently to educate and enthuse the public on this mighty national health problem. A fuller report of the results achieved in this conference will be published in the September issue of the Journal.

The Indian Journal of Tuberculosis

ABSTRACTS

Vol. VII **June, 1960** **Abst. No. 3**

A SINGLE TUBERCULIN TEST FOR EPIDEMIOLOGICAL USE : A COMPARISON OF THE MANTOUX AND HEAP TESTS.

A report to the Research Committee of the British Tuberculosis Association by their Tuberculin Sub-Committee.

Intracutaneous (Mantoux 5 T.u.) and multiple puncture (Heaf) using the same batch of PPD tuberculin were made at the same time on opposite arms of 3640 individuals.

The reactions were read three, seven and ten days later. Those with negative reactions to the intracutaneous 5 T.u. tests at three and seven day reading were retested with 100 T.u., the reaction being read three days later. 6 mm or more induration was considered as a positive reaction.

The intracutaneous 5 T.u. test showed that 45.5 percent of population were positive after three days, 45.6 percent after seven days and 24.1 percent after ten days; while the multiple puncture test the corresponding positives were 74.3 percent, 78.0 percent and 78.3 percent.

The intracutaneous 5 T.u. test followed if negative by 100 T.u. showed 78.5 percent of the population to be positive after three days, thus the multiple puncture test read at seven days gave results closely similar to those of the two stage intracutaneous test read at three days.

For epidemiological use the multiple puncture test will in most circumstances be preferred to intracutaneous test with 5 T.u. because of its greatest sensitivity and ease of performance and reading.

(Tuber, Loud. (1959) 40, 317.)

Occult Carcinoma of the Bronchus: A Study of 15 cases of Insitu or early invasive Bronchogenic Carcinoma.

Cytologic examination gave positive results in 73 percent cases and bronchoscopy biopsy was positive in 46 percent.

Treatment in these early lesions is associated with highly favourable results.

(Woolner, Lewis B; Anderson, Howard A; and Bernatz, Philip E: Dis. Chest, Vol XXXVll, No. 3, March, 1960.

Pleural fluid Glucose with Special Reference to its Concentration in Rheumatoid Pleurisy with Effusion.

In 54 out of 57 pleural fluids examined for glucose concentration in cases of malignant lesion, conjestive heart failure, pulmonary infarction and miscellaneous inflammatory and traumatic conditions, the glucose level was 60 mgms. per 100 m. 1. of fluid.

In 6 cases of Rheumatoid arthritis with rheumatoid pleurisy with effusion, the pleural fluid glucose concentration varied from less than 5 mgms to 17 mgms per 100 m. 1.

In Tuberculosis there is also low concentration of glucose in pleural fluid. Estimation of the concentration of glucose in pleural fluid was of only slight value in the differential diagnosis of the disease causing pleurisy effusion.

(Can-, *David T; Power, Marschelle, H: Dis. Chest, Vol XXXVll, No. 3, March, 1960.)*

Primary Pulmonary Histocytosis X

Primary Pulmonary histocytosis X is a disease of unknown etiology. It is more common in men than women and is associated with interstitial histocytic infiltration and obstruction of lung parenchyma.

Symptoms, Physical signs and Laboratory data are rather non-specific.

Roentgenogramms of the chest show diffuse reticulonodular pulmonary fibroses associated with small cystic areas. If it is associated with spontaneous pneumothorax, diabetes inspidous, the possibility of primary pulmonary Histocytosis X should be borne in mind. The diagnosis can only be confirmed by biopsy.

The clinical course of disease is variable, hence the prognosis is guarded. The disease runs a mild course with tendency to remission. It may lead to pulmonary fibroses, Cor Pulmonale and Conjestive Cardiac failure.

Treatment with Cortisone is the treatment of choice.

(Nadeau. Pierre, J; Ellis F; Harrison, Edgar J; and Fontana, Robert, S: Dis. Chest, Vol XXXVll, No. 3, March, 1960.)

Bacteriologic Studies of the Sputum in Patients with Chronic Bronchitis and Bronchiectasis.

Bacteriologic studies of the sputum were made at monthly intervals on eighty-nine patients with chronic bronchitis or bronchiectasis, who were treated from three to thirty-one months with tetracyclin, penicillin, an Oleandomycin-penicillin mixture or sucrose placibo tablets.

Hemophilus influenza staphylococcus aureus and pneumococcus were considered to be the most important pathogens. Tetracyclin or Oleandomycin penicillin therapy caused a significant diminution in the frequency with which these micro-organism were cultured from sputum.

Tetracyclin was more effective in decreasing the H. influenza.

There was increase in the Proteus in Oleandomycin penicillin group and pseudomonos in the tetracyclin group. In none of the patients did these micro-organisms appear consistently in the sputum after therapy.

No therapeutic regimes produced any significant shift in resistance to any of the microbials used in the study on the part of the staphylococii isolated from any of the treatment groups except that tetracycl in resistant strains implanted more frequently in the sputum of the patients treated with that antimicrobial than tetracyclin susceptible strains.

Seasonal incidence regarding H. influenza was noticed being more frequent in colder months.

(Dowling, Harry F, Mellody, Margaret; Lepper, Mar H; and Jackson, George, G: Amer. Rev. Resp. Dis., Vol 81, No. 3, March, 1960.)

Pulmonary Ventilatory Function in Military recruits During Health and Acute Viral Respiratory Disease, including Pneumonia.

Pulmonary Ventilatory function tests of maximal breathing Capacity, Vital Capacity and one second and three second Vital Capacity performed serially at 2 to 3 weeks intervals for eleven weeks in a group of 60 Air Force recruits showed a more marked decrease of Vital Capacity in those patients with pulmonary infiltration during the time of their illness while there was significant decrease in vital capacity on one occasion in the group without respiratory disease.

(Stone Hill, Robert B; Schallet, Norbert; Young, William, Y: SaltZman, Herbert; and Homer, Harold, B: Amer. Rev. Resp. Diseases; Vol. 81; No. 3; March, 1960.)

Tropical Eosinophilia.

Pathological changes in the lung, liver and lymph nodes of typical cases of tropical pulmonary eosinophilia revealed the presence of microfilaria in the centre of the nodules.

These microfilaria demonstrated has been identified as W. Bancroft; type.

Direct invasion by these organisms is the cause of the lesion.

Cases have been reported with involvement of lymph node and liver without lung involvement.

(Webb, J.K.G; Job, C. K; Gault, E. W: Lancet, No. 7219, Vol. 1, April 16, 1960.)

TREATMENT OF TUBERCULOSIS IN CHILDREN

A Statement by the Committee on Tuberculosis and Respiratory diseases in childern.

USE OF DRUGS

Isoniazid:- should be a part of every regimen for treatment of active tuberculosis in doses as high as 30 mgm per Kg. daily, though the usual dosage recommended is 15 mgm per Kg.

A.S.O.:- Para Aminosalycilc acid is the most common used second drug when a combination of regimen is employed in dosage of 200 mgm per Kg. daily. Salts such as of sodium potassium or calcium should have a higher dosage of 300 mgm per Kg. In general children have better tolerance of all forms of P.A.S. than do adults.

Streptomycin:- is only used under special conditions. The drug is undesirable because it must be given intramuscularly and because it is Toxic especially to eight nerve. The usual dosage is 20 mgm per Kg. daily.

Dihydrostreptomycin should not be used since it has selective and irreversible toxicity for the auditory division of the eight nerve and audiometeric studies may be impossible in the very young. Viomycin, Cycloserine and Pyrazinamide have no place in childrens tuberculosis.

Triple Drug Therapy:- is not recommended because of the possibility of increased toxicity. It is reserved only for very serious forms of disease.

Corticosteriods:- are given in 1 mgm Kgm. dose in very sick cases and are specially indicated in pleurisy, meningitis and endothoracic primary complex.

Duration of Therapy:- The usual duration of therapy varies from 3 2 months to 24 depending on the extent and severity of disease when streptomycin is used in triple therapy. It should be discontinued one month after satisfactory clinical response.

TYPE OF DISEASE

Endothoracic Primary Tuberculous Complex:- Enlarged tracheo-bronchial lymphnodes and diseases due to bronchial obstruction and/or bronchogenic spread are the most common forms of endothoracic tuberculosis in children.

Drug therapy consisting of Isoniazid and P.A.S. should be continued for a minimum of one year.

Fresh Pulmonary infiltration responds quickly to drug therapy. Large mediastinal nodes and segmental involvement usually show slow changes when endomural granuloma is the cause of obstruction. Bronchoscopic removal of the granuloma may hasten the re-aeration of the segment involved.

In young children with intense dysponea caused by tuberculous bronchitis and tuberculous medias tinal nodes, marked relief may be obtained very quickly through the addition of Corticosteriods.

Tuberculous Meningitis:- Triple drug therapy with daily streptomycin, high dosage of Isoniazid and Corticosteriods are recommended. Isoniazid and P.A.S. should be continued for a minimum of one year and even longer, although streptomycin should be discontinued.

Miliary Tuberculosis:- Triple drug therapy with high doses of Isoniazid and daily streptomycin is recommended.

The Cortiosteriods may be used to assist in releaving extreme dysponea associated with miliary disease. Isoniazid and P.A.S. should be continued for at least a year.

Extra Thoracic Tuberculosis:- All superficial and accessible abscesses caused by tubercle bacilli should be drained as freely and as readily as abscess caused by other organs.

Local excision of tuberculous tissue is safe with a cover of effective antitubercular Chemotherapy.

Renal Tuberculosis:- Triple Drug Therapy is recommended for about a period of two years. *Superficial Lymph adenopathy:-* Drug therapy with Isoniazid and P.A.S. along with drainage and excision, if required should be continued for about one year.

Tonsillectomy and adenoidectomy is not done routinely.

Tuberculosis of Bones and Joints:- In addition to drug therapy, local excision and drainage are recommended; for the non-weight bearing joints, prolonged immobilization is necessary.

P.A.S. and Isoniazid for eighteen to twenty-four months should be given.

Serious Effusion:- Diagnostic aspiration is advised in all cases. Some recommend complete withdrawl of fluid.

The use of Corticosteroids in addition to drugs is recommended for prevention of pleural thickening and adhesions particularly pericardial adhesions.

Pulmonary Tuberculosis of Adult type in Children:- The general principles regarding cavity closure and sputum conversion apply here as in adult tuberculous.

Thoracoplasty should be avoided although surgery is indicated.

So-called Prophylactic treatment of the Tuberculosis converter with no manifest disease:- If tuberculin conversion is known to have occurred within one year prior to the time of examination. It is the opinion of majority that all children upto 14 years should be placed on treatment using either one or two drugs, one of which should be Isoniazid. This should be continued for one year or longer. Isolation and bed rest are not necessary.

When the date of conversion of the tuberculin is unknown and patient has no signs and symptoms it is thought, for maximal safety all patients less than 36 months should be treated for at least one year.

The longer the initial tuberculin reaction the greater the risk of child's developing active tuberculous disease.

Both recent converters and those whose conversion date is unknown should remain under careful observation for many years and should be closely followed in the event of intercurrent infection as the patient approaches age of puberty. An tuberculin positive child who is receiving steroid treatment for another disease should receive concurrent antituberculous treatment.

A child with a positive tuberculin reaction should receive antituberculous therapy for at least four weeks in the event of an attack of measles.

Tuberculin Testing:- All children at the age of six to eight months should be tested with 5 T.U. of P.P.D.S. If negative, the child should be tested at least once a year.

In case of suspected exposure the test should be administered as soon as possible. If negative it should be repeated every four weeks.

(Amer. Rev. Resp. Dis. Vol. 81. No. 3, March. 1960.)