

PREVALENCE OF DRUG RESISTANCE IN PATIENTS WITH
PULMONARY TUBERCULOSIS PRESENTING FOR THE
FIRST TIME WITH SYMPTOMS AT CHEST CLINICS
IN INDIA*.

Part II.

FINDINGS IN URBAN CLINICS AMONG ALL PATIENTS,
WITH OR WITHOUT HISTORY OF PREVIOUS
CHEMOTHERAPY.

(Indian Council of Medical Research.)

[Received for publication, October 26, 1968.]

INTRODUCTION.

A previous report (Indian Council of Medical Research First Drug Resistance Investigation, 1968) presented the results of a co-operative investigation on the prevalence of drug resistance in patients with pulmonary tuberculosis, presenting for the first time with symptoms at chest clinics in India and giving no history of previous antituberculosis chemotherapy. However, the information obtained from that investigation is of rather limited value because, in most clinics, fairly large proportions of patients reporting for the first time do so with a history of previous treatment. This is because antituberculosis chemotherapy is offered not only by chest clinics, but also by general hospitals and private practitioners. In these circumstances, information on the prevalence of drug resistance among *all* patients, irrespective of the history of previous antituberculosis chemotherapy, will be of great value, not only to the clinicians-in-charge of the chest clinics but also to those responsible for formulating general policies of treatment in the country. The second drug resistance investigation was undertaken

*This investigation was executed through a special sub-committee of the Indian Council of Medical Research consisting of Drs. N.L. Bordia (Chairman), B.K. Sikand, P.K. Sen and M.D. Deshmukh, Dr. P.R.J. Gangadharam, Senior Research Officer, Tuberculosis Chemotherapy Centre, Madras, was seconded to look after the work of the Central Laboratory as well as to co-ordinate the work of all the participating centres.

The following doctors participated from the various Centres : Dr. J.L. Bhatia (Amritsar), Dr. R. Susaimary (Bangalore), Dr. M.D. Deshmukh (Bombay), Dr. N.N. Sen (Calcutta), Dr. B.K. Sikand (Delhi), Dr. D. Umapathy Rao (Hyderabad), Dr. M.A. Hamid (Madras), Dr. P.A. Deshmukh (Nagpur) and Dr. J.P. Karan (Patna).

The Central Laboratory was situated in the premises of the Tuberculosis Chemotherapy Centre, Madras, and was afforded all the necessary facilities by the Director of the Centre (Dr. N.K. Menon) and the Head of the Laboratory (Dr. S.P. Tripathy).

The analyses were undertaken and the report prepared by Dr. P.R.J. Gangadharam, assisted by Miss V. Devaki (Research Assistant), and Mr. K. Mohan and Mr. A.S.L. Narayana (Statistical Assistants). The report should be referred to as the Indian Council of Medical Research Second Drug Resistance Investigation. Reprints can be obtained from the Director, Tuberculosis Chemotherapy Centre, Chetput, Madras-31.

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by the Indian Council of Medical Research to obtain this information, and the findings are presented below.

PLAN AND CONDUCT OF THE INVESTIGATION.

Participating Centres.— The same 9 Centres which participated in the first investigation participated in the present investigation. These Centres were situated at :

1. Amritsar (R.B. Sir Gujjarmal Kesardevi Tuberculosis Sanatorium),
2. Bangalore (Lady Willingdon Tuberculosis Demonstration and Training Centre),
3. Bombay (Tuberculosis Clinic, J. J. Group of Hospitals),
4. Calcutta (K. S. Ray Tuberculosis Hospital),
5. Delhi (New Delhi Tuberculosis Centre),
6. Hyderabad (Institute of Diseases of Chest and Tuberculosis),
7. Madras (Government Tuberculosis Demonstration and Training Centre),
8. Nagpur (Tuberculosis Control and Training Centre), and
9. Patna (Tuberculosis Demonstration and Training Centre).

Criteria for eligibility of patients.— A patient was eligible for admission to the investigation if he/she

- (a) was aged 12 years or more,
- (b) had resided in the area served by the clinic the previous year and was expected to do so for another year,
- (c) was attending the clinic for the first time and because of chest symptoms (patients detected by mass miniature radiography were not eligible), and
- (d) had radiographic evidence suggestive of tuberculosis (however, patients with evidence of only minimal disease, calcification, pleural thickening, hilar gland enlargement or fibrotic foci were not eligible).

Procedures followed by the participating Centres.— At each of the 9 Centres, a specimen of sputum was collected (in a sterile universal container) from about 175 to 250 patients, under the direct supervision of the clinic staff, and despatched by air to the Central Laboratory at Madras ; if there was any delay in despatching, the specimen was stored in an ice-box or a refrigerator, whenever this was practicable.

In order that the Central Laboratory may not be overloaded with specimens, each participating Centre was asked to restrict the number of specimens to 25 *per week*. It was emphasized that these specimens were to be collected from the first 25 eligible patients who attended the clinic in that week.

At the time of the first attendance at the Centre, each patient was specifically questioned as to whether he had received any antituberculosis drugs previously ; this was done by the physician-in-charge and also, whenever possible, by other members

of the staff. About 3 to 4 weeks later, a second interrogation was undertaken, with no knowledge of the sensitivity test results.

Investigations undertaken by the Central Laboratory.—The following investigations were undertaken :

(1) Direct smear examination using fluorescence microscopy (Holst, Mitchison and Radhakrishna, 1959), positive results being graded as 3-plus (heavy), 2-plus (moderate) or 1-plus (scanty).

(2) Culture examination for tubercle bacilli, employing the technique described by the Tuberculosis Chemotherapy Centre, Madras (1959). Growth typical of *Mycobacterium tuberculosis* was recorded as 3-plus (confluent), 2-plus (innumerable discrete colonies), 1-plus (100-20 colonies) or the actual number of colonies, if less than 20.

(3) Tests for sensitivity to isoniazid, streptomycin, PAS and thioacetazone*, using the procedures described earlier (Indian Council of Medical Research First Drug Resistance Investigation, *loc. cit.*), but with the concentrations of drugs set out below :

<i>Drug</i>	<i>Drug concentration (µg.ml.)</i>	
<i>Test strain</i>	<i>H37Rv</i>	
Isoniazid	0.2, 1, 5, 50	0.025, 0.05, 0.1, 0.2, 1
Streptomycin	4, 8, 16, 32, 64	1, 2, 4, 8
Sodium PAS dihydrate	0.5, 1, 2, 4, 8, 16	0.125, 0.25, 0.5, 1, 2
Thioacetazone	0.25, 0.5, 1, 2, 4, 8	0.25, 0.5, 1, 2, 4, 8

For isoniazid, streptomycin and thioacetazone, an approximately 4 mg./ml. suspension of the culture was employed, while a 1 : 10 dilution was employed in the case of PAS for reasons given by Selkon *et al.* (1960). A standard (approximately 3 mm.) loopful of the appropriate suspension was inoculated on to the Lowenstein-Jensen slopes containing the drug concentrations set out above, as well as on to a drug-free slope as control. The standard sensitive strain of *Mycobacterium tuberculosis*, H37Rv, was also set up with each batch of tests. The results of all the tests were read at the end of 4 weeks of incubation at 37°C. The results of isoniazid and thioacetazone sensitivity tests were expressed as MICs—that is, the minimum concentrations of the drugs inhibiting growth (defined as 20 colonies or more), while those of streptomycin and PAS were expressed as resistance ratios—that is, the MICs of the test strains divided by the corresponding MICs of H37Rv. If the MIC of isoniazid was 1 µg./ml. or the resistance ratio for streptomycin or PAS was 4, the test was repeated.

Definitions of drug resistance.—The definitions of resistance employed were the same as in the first drug resistance investigation, namely :

Isoniazid.—MIC of 5 or more, or 1 followed by 1 or more in the retest.

* Thioacetazone is the recommended international non-proprietary name (see World Health Organization, 1962) for 4'-formylacetanilide thiosemicarbazone (thioacetazone, TB1-698).

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Streptomycin.— Resistance ratio of 8 or more, or 4 followed by 4 or more in the retest.

PAS and thioacetazone.— As in the first drug resistance investigation and for the same reasons, no formal definitions of resistance have been employed, the findings being presented in the form of distributions.

- (4) A series of identification tests for *Mycobacterium tuberculosis*, namely :
- (a) niacin production-test as described by Medveczky (1960),
 - (b) qualitative test for catalase activity as described by Selkon and Mitchison (1959),
 - (c) growth on Lowenstein-Jensen medium after incubation at 25°C. for 4 weeks, and
 - (d) pigmentation and morphology of growth after incubation at 37°C. for 4 weeks, in the dark and in the light.

Intake of specimens.— The intake of specimens commenced in June 1965 and concluded in April 1967, the period of intake for the individual Centres varying from 2 to 15 months. In all, 1890 specimens were obtained from the same number of patients and despatched to the Central Laboratory from the 9 Centres. Of these, 28 (1.5 per cent) have not been considered further in this report—1 because the specimen was obtained from a patient who had attended the clinic earlier, 7 because they were from patients who were less than 12 years of age, and 20 because the bottles had broken or the sputum had leaked out during transit. The remaining 1,862 specimens are considered in the analyses.

RESULTS.

Sex and age.— Of the 1862 patients, 1177 (63 per cent) were males, the proportions in the individual Centres ranging from 52 per cent in Amritsar to 74 per cent in Delhi. The age distributions for the males and the females are presented in Table I, separately and jointly for the 9 Centres.

Smear and culture results.— The results of direct smear and culture examination of the sputum specimens are set out in Table II. In all, 67 per cent of the specimens yielded a positive smear, the proportions in the individual centres varying from 37 per cent in Calcutta to 85 per cent in Amritsar. The proportions of specimens which yielded a positive culture ranged from 35 per cent in Calcutta to 84 per cent in Hyderabad, the mean for the 9 Centres being 66 per cent.

There were 154 (8 per cent) specimens which yielded a smear-positive culture-negative result, the proportions in individual centres ranging from 1 per cent in Hyderabad to 23 per cent in Patna.

Contamination of the culture occurred in 144 (8 per cent) of the specimens, the proportions ranging from 2 per cent in Madras to 13 per cent in Bombay. It occurred in 9 per cent of 612 smear-negative specimens as compared with 7 per cent of 1,249 smear-positive specimens, fairly similar findings.

TABLE I.

Distribution of patients according to sex and age.

Centre.	MALES :					FEMALES :				
	Total.	Percentage of patients :				Total.	Percentage of patients :			
		Less than 25 years.	25-34 years.	35-44 years.	45 years or more.		Less than 25 years.	25-34 years.	35-44 years.	45 years or more.
Amritsar	103	18	34	20	27	95	32	35	15	18
Bangalore	117	32	30	16	21	82	35	40	16	9
Bombay	179	35	25	20	20	67	34	34	24	7
Calcutta	159	23	21	28	28	89	33	35	16	17
Delhi	147	20	34	19	27	52	38	37	15	10
Hyderabad	115	17	32	23	29	82	20	55	16	10
Madras	137	18	29	23	31	63	30	43	14	13
Nagpur	127	27	32	16	25	73	36	38	19	7
Patna	93	27	25	24	24	82	56	26	10	9
All Centres	1177	24	29	21	25	685	35	38	16	11

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TABLE II.

Results of direct smear and culture examination of sputum specimens.

Centre.	Total number of specimens.	PERCENTAGE OF SPECIMENS WITH A :			
		Positive smear.	Positive culture.	Positive smear but negative culture	Contaminated culture.
Amritsar	197*	85	77	6	8
Bangalore	199	74	80	4	7
Bombay	246	72	70	7	13
Calcutta	248	37	35	8	6
Delhi	199	63	68	9	4
Hyderat	197	79	84	1	7
Madras	200	62	61	14	2
Nagpur	200	66	71	6	12
Patna	175	71	49	23	10
All Centres	1861	67	66	8	8

*Excluding one specimen with no smear result.

Sensitivity test results.— Of the total of 1,862 specimens, 1,220 yielded a positive culture, but 14 of these were found to contain atypical mycobacteria. Of the remaining 1,206 cultures, all of which were identified as *Mycobacterium tuberculosis*, 98.1 per cent had a sensitivity test result for isoniazid, 98.1 per cent for streptomycin, 97.5 per cent for PAS and 97.3 per cent for thioacetazone.

Isoniazid and streptomycin.— Table III presents the findings of isoniazid and streptomycin sensitivity tests for the 9 Centres. Considering all the Centres together, the prevalence was 9.1 per cent for isoniazid *alone* and 7.0 per cent for streptomycin

TABLE III.

Findings of isoniazid and streptomycin sensitivity tests.

Centre.	Number of cultures with H or S sensitivity test results.	PERCENTAGE OF CULTURES RESISTANT TO :					
		H only.	S only.	H and S.	H.	S.	H or S or both.
Amritsar	148	9	7	17	26	24	33
Bangalore	156	11	7	5	16	12	23
Bombay	167	4	10	25	29	35	39
Calcutta	81	11	5	58	69	63	74
Delhi	132	14	7	11	26	18	33
Hyderabad	166	8	4	16	23	19	27
Madras	118	8	5	10	18	15	23
Nagpur	134	10	2	7	16	13	22
Patna	81	9	15	6	15	21	30
All Centres	1183	9.1	7.0	15.8	25.0	22.9	32.0

H = isoniazid ; S = streptomycin.

alone, the prevalence in individual Centres ranging from 4 per cent in Bombay to 14 per cent in Delhi for isoniazid alone, and from 4 per cent in Hyderabad to 15 per cent in Patna for streptomycin alone. Resistance to both isoniazid and streptomycin was observed in 15.8 per cent of the cultures ; excluding Calcutta which had a very high proportion of 58 per cent, the range was 5 per cent (in Bangalore) to 25 per cent (in Bombay).

The *total* resistance to isoniazid was 25.0 per cent and the *total* resistance to streptomycin was 22.9 per cent. Considering the individual Centres, the prevalence of total isoniazid resistance ranged from 15 per cent in Patna to 69 per cent in Calcutta, while the prevalence of total resistance to streptomycin ranged from 12 per cent in Bangalore to 63 per cent in Calcutta.

Finally, 32.0 per cent of the patients had resistance to at least one drug ; the prevalence in individual Centres varied considerably. In Table IV, the 9 Centres are arranged in the ascending order of this proportion and, in the next column, the proportion of patients with a history of previous chemotherapy (of 10 days or more) is presented. It can be seen that, in general, Centres with a high prevalence had a high proportion of previously treated patients. Indeed, regression analysis of the data showed that over 90 per cent of the variation between the Centres in the proportion resistant could be accounted for by differences in the proportion of previously treated patients.

TABLE IV.

Prevalence of resistance in the nine centres related to the percentage of patients with a history of previous chemotherapy.

Centre.	PERCENTAGE OF PATIENTS WITH :	
	Resistance to H or S or both.	10 or more days of previous chemotherapy.
Nagpur	22	20
Madras	23	13
Bangalore	23	6
Hyderabad	27	10
Patna	30	30
Delhi	33	29
Amritsar	33	37
Bombay	39	44
Calcutta	74	90
All Centres	32.0	28.1

Prevalence of resistance related to duration of previous chemotherapy.— There was very clear evidence that longer durations of previous chemotherapy were associated with a higher prevalence of resistance (Table V). Thus, of 851 patients *who had received no chemotherapy previously* (apart from 2 who had received 4 days of chemotherapy), 22 per cent had resistance to streptomycin or isoniazid or to both drugs,

the corresponding proportions being 26, 33, 42, 52, 67, and 76 per cent in patients who had received chemotherapy from 10 days to a month, 1-2 months, 2-3 months, 3-6 months, 6-12 months and 12 months or more, respectively. The trend in these percentages is highly significant ($P < 0.00001$).

TABLE V.

Prevalence of resistance related to duration of previous chemotherapy.

Duration of chemotherapy.	Number of patients.	RESISTANCE TO H OR S OR BOTH:	
		Number.	Per cent.
<i>Nil*</i>	851	185	22
10 days–	46	12	26
1 month–	27	9	33
2 months–	24	10	42
3 months–	46	24	52
6 months–	54	36	67
12 months or more	135	103	76
All patients	1183	379	32.0

* Including 2 patients who had 4 days of previous chemotherapy ; neither of these had resistance. to either drug.

Prevalence of resistance related to sex and age of the patients.— The prevalence of resistance was not associated with either the sex or the age of the patients. Thus, 31.7 per cent of 754 males had resistance to streptomycin or isoniazid or both drugs, as compared with 32.4 per cent of 429 females. The prevalence was 31, 35, 30 and 31 per cent in patients aged less than 25 years, 25-34 years, 35-44 years and 45 years or more, respectively. Similar conclusions were reached on relating separately the prevalence of streptomycin resistance and that of isoniazid resistance to the sex and age of the patients.

PAS.— The results of PAS sensitivity tests are set out in the form of distributions in Table VI. Considering all the 9 Centres, 9.7 per cent had a resistance ratio (RR) of 8 or more, 7.1 per cent an RR of 4 and the remaining 83.2 per cent an RR of 2 or less. The proportion with an RR of 8 or more was particularly high in Calcutta (36 per cent), and ranged from 2 per cent to 11 per cent in the other Centres.

Thioacetazone.— The findings of thioacetazone sensitivity tests are set out in Table VII in the form of distributions. Considering all the 9 Centres, 55.4 per cent had an MIC of 1 µg./ml. or less, 20.0 per cent had an MIC of 2 µg./ml., and 24.6 per cent had an MIC of 4 µg./ml. or more. In the individual Centres, the proportion with a low MIC (1 µg./ml. or less) ranged from 38 per cent in Madras and to 71 per cent in Patna.

Findings in patients with no history of previous chemotherapy.— Among the patients in this investigation who had no history of previous chemotherapy, 15.5 per cent had an isoniazid-resistant culture and 13.8 per cent a streptomycin-resistant culture ; the corresponding proportions in an earlier investigation (Indian Council of Medical Research First Drug “Resistance Investigation, *loc. cit.*), were similar, namely, 14.5

TABLE VI.

Findings of PAS sensitivity tests.

Centre.	Number of cultures tested.	PERCENTAGE OF CULTURES WITH A RESISTANCE RATIO OF:		
		2 or less.	4	8 or more.
Amritsar	148	87	5	8
Bangalore	155	85	8	7
Bombay	164	82	7	10
Calcutta	81	54	10	36
Delhi	128	87	5	9
Hyderabad	166	80	11	8
Madras	118	86	7	7
Nagpur	133	93	5	2
Patna	80	84	5	11
All Centres	1175	83.2	7.1	9.7

TABLE VII.

Findings of thioacetazone sensitivity tests.

Centre.	Number of cultures tested.	PERCENTAGE OF CULTURES WITH AN MIC ($\mu\text{g./ml.}$) OF :		
		1 or less.	2	4 or more.
Amritsar	146	62	18	20
Bangalore	154	49	29	22
Bombay	165	55	21	24
Calcutta	80	45	16	39
Delhi	132	61	19	20
Hyderabad	165	55	15	30
Madras	118	38	28	34
Nagpur	134	63	19	19
Patna	80	71	10	19
All Centres	1174	55.4	20.0	24.6

and 11.8 per cent, respectively (Table VIII). The findings in the individual centres are also fairly similar with the exception of Patna where the prevalence of isoniazid resistance was 5 per cent of 57 in this investigation and 18 per cent of 130 in the earlier investigation, a significant difference ($P=0.04$).

The findings in this investigation also confirm the existence of large differences between the Centres in the susceptibility to thioacetazone of strains from untreated patients (last two columns of Table VIII) ; in particular, strains from Madras patients were less susceptible, the geometric mean of the MICs being $2.10 \mu\text{g./ml.}$ in the present investigation and $2.38 \mu\text{g./ml.}$ in the earlier investigation.

TABLE VIII.

Findings in patients with no history of previous chemotherapy.

Centre*.	PERCENTAGE OF CULTURES RESISTANT TO ISONIAZID.		PERCENTAGE OF CULTURES RESISTANT TO STREPTOMYCIN.		GEOMETRIC MEAN OF MIC OF THIOACETAZONE ($\mu\text{g./ml.}$)	
	Present report.	Earlier report†.	Present report.	Earlier report†.	Present report.	Earlier report†.
Amritsar	16	14	12	13	1.38	0.89
Bangalore	14	11	10	8	1.55	1.39
Bombay	17	20	21	19	1.52	1.31
Delhi	19	13	15	9	1.24	0.91
	21	15	15	10	1.71	1.09
Hyderabad	15	13	14	12	2.10	2.38
Nagpur	11	11	9	10	1.19	1.03
Patna	5	18	16	14	1.31	1.01
All Centres	155	14.5	13.8	11.8	1.49	1.21

*Excluding Calcutta since, in the present investigation, only 8 of the positive cultures were from untreated patients.

† Indian Council of Medical Research First Drug Resistance Investigation (*loc. cit.*).

DISCUSSION.

This report gives information on the prevalence of drug resistance in tuberculous patients reporting for the *first* time with symptoms at 9 chest clinics in India. The investigation is based on all patients—that is, regardless of whether or not they had received chemotherapy previously from any other source, and the findings therefore give some indication of the problems involved in evolving suitable chemotherapeutic regimens for routine use at chest clinics in the country.

Considering all the Centres, 25.0 per cent of the patients had resistance to isoniazid and 22.9 per cent to streptomycin, including 15.8 per cent with resistance to both the drugs. In other words, 32.0 per cent of the patients had resistance to one or both of these very potent drugs. These findings are broadly similar to those reported from Hong Kong (Hong Kong/British Medical Research Council Drug Resistance Survey, 1964), where 33 per cent of the patients had isoniazid resistance and 23 per cent had streptomycin resistance.

In the present investigation, the prevalence of resistance was not associated with either the sex or the age of the patients. However, it was, as may be expected, closely correlated with the duration of previous chemotherapy; thus, the prevalence of resistance (to either or both drugs) was 22 per cent in patients who had no history of previous chemotherapy and 26, 33, 42, 52, 67 and 76 per cent in patients who had received chemotherapy for 10 days to a month, 1-2 months, 2-3 months, 3-6 months, 6-12 months and 12 months or more, respectively.

Considering next the findings in individual Centres, the prevalence of resistance (to one or both drugs) varied considerably, the proportion being 22 per cent in Nagpur, 23 per cent in both Madras and Bangalore, 27 per cent in Hyderabad, 30 per cent in

Patna, 33 per cent in both Delhi and Amritsar, 39 per cent in Bombay and 74 per cent in Calcutta. However, further analyses showed that over 90 per cent of the variation between the Centres could be explained by differences between them in the proportion of patients with a history of previous chemotherapy.

Among the patients with *no history of previous chemotherapy*, the prevalence of isoniazid resistance was 155 per cent in the present investigation as compared with 14.5 per cent in an earlier investigation (Table VIII) ; the corresponding proportions for streptomycin resistance were 13.8 per cent and 11.8 per cent respectively. The similarity of these figures is gratifying, and enhances the confidence that can be placed on the findings of the earlier investigation. Finally, the results of the present investigation confirm that there are large differences between the Centres in the susceptibility to thioacetazone of strains from untreated patients and, in particular, that strains from Madras patients are less susceptible than those from the other Centres.

As in the earlier investigation, the co-operation obtained from the participating Centres was of a high order, a finding which is encouraging for the conduct of future bacteriological investigations in India on a cooperative basis.

SUMMARY.

1. A co-operative investigation was undertaken to estimate the prevalence of drug resistance in tuberculous patients reporting for the first time, with or without a history of previous chemotherapy, at 9 urban chest clinics in different parts of India.
2. At each Centre, one specimen of sputum was collected from each of about 175-250 patients and despatched by air to a Central Laboratory at Madras.
3. The prevalence of resistance, based on about 1,200 positive cultures from the 9 Centres, was 25.0 per cent to isoniazid and 22.9 per cent to streptomycin, *including* 15.8 per cent to both the drugs.
4. The prevalence was very high in Calcutta, namely, 69 per cent to isoniazid and 63 per cent to streptomycin, but so also was the proportion of patients with a history of previous chemotherapy, namely 90 per cent. At the other Centres, the prevalence of isoniazid resistance ranged from 15 per cent to 29 per cent, and streptomycin resistance from 12 per cent to 35 per cent.

Besides the Officers-in-charge, several other staff members of the participating Centres contributed to the success of this investigation. Competent technical assistance was rendered by the technicians of the Central Laboratory. Mr. P.R. Somasundaram gave valuable advice regarding the analyses of the material and the preparation of the report.

REFERENCES.

- HOLST, E., MITCHISON, D.A., and RADHA-KRISHNA, S. (1959) Examination of smears for tubercle bacilli by fluorescence microscopy. *Ind. Jour. Med. Res.*, **47**, 495.

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- HONG KONG/BRITISH MEDICAL RESEARCH COUNCIL DRUG RESISTANCE SURVEY (1964) Drug-resistance in patients with pulmonary tuberculosis presenting at chest clinics in Hong Kong. *Tubercle, Lond.*, **45**, 77.
- INDIAN COUNCIL OF MEDICAL RESEARCH (1968) Prevalence of drug resistance in patients with pulmonary tuberculosis presenting for the first time with symptoms at chest clinics in India. I. Findings in urban clinics among patients giving no history of previous chemotherapy. *Ind. Jour. Med. Res.* **56**, 1617.
- MEDVECZKY, E. (1960) ... A micromethod for the routine differentiation of human tubercle bacilli from other mycobacteria in primary cultures. *Amer. Rev. Resp. Dis.*, **81**, 757.
- SELKON, J.B., and MITCHSON, D.A. (1959) Atypical mycobacteria and drug resistant tubercle bacilli isolated during a survey of untreated patients with pulmonary tuberculosis. *Tubercle, Lond.*, **40**, 141.
- SELKON, J.B., SUBBAIAH, T.V., BHATIA, A.L., RADHAKRISHNA, S., and MITCHISON, D.A. (1960) A comparison of the sensitivity to p-aminosalicylic acid of tubercle bacilli from South Indian and British patients. *Bull. Wld. Hlth. Org.*, **23**, 599.
- TUBERCULOSIS CHEMOTHERAPY CENTRE, MADRAS (1959) Concurrent comparison of home and sanatorium treatment of pulmonary tuberculosis in South India. *Ibid.*, **21**, 51.
- WORLD HEALTH ORGANIZATION (1962) ... Cumulative list of proposed international non-proprietary names for pharmaceutical preparations, Geneva, 46.

APPENDIX.

Towards the end of the investigation reported in the preceding pages, the Indian Council of Medical Research decided to obtain similar information from 7 more Centres, namely, (1) V.M. Hospital, Agartala (Dr. B.C. Arora succeeded by Dr. N. Debbarma), (2) Tuberculosis Demonstration and Training Centre, Agra (Dr. M.L. Mehrotra), (3) K.N. State Tuberculosis Demonstration and Training Centre, Ajmer (Dr. P.N. Sharma), (4) District Tuberculosis Centre, Aurangabad (Dr. S.A. Jaleel), (5) Tuberculosis Control Centre, Panaji (Dr. M.R. de Menezes Mesquita), (6) Tuberculosis Clinic, Pondicherry (Dr. K.V. Ramanujam), and (7) District Tuberculosis Centre, Quilon (Dr. P. Srinivasan).

In the event, however, the numbers of sputum specimens obtained from Pondicherry and Quilon were too few, as was the number of positive cultures from Aurangabad. Consequently, the findings of isoniazid and streptomycin sensitivity tests are presented below, together with the proportions of patients with a history of previous chemotherapy, for the remaining 4 Centres only—namely, Agartala, Agra, Ajmer and Panaji.

Centre.	Number of patients with sensitivity test results.	PERCENTAGE OF PATIENTS WITH RESISTANCE TO :			Percentage of patients with a history of previous chemotherapy.
		Isoniazid.	Streptomycin.	One or both drugs.	
Agartala	143	10	20	23	11
Agra	120	48	45	58	42
Ajmer	86	12	17	22	10
Panaji	133	21	18	27	8