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Editorial

LEPROSY CONTROL IN ETHIOPIA

In this number of *Leprosy Review,* we present a leading article by a highly experienced group of research workers on dapsone resistance in Ethiopia, and combine this with other contributions on the subject of leprosy and the health services, in a part of Africa which has been described (Schaller, 1972) as "unmatched among the tropical countries as far as abundance of pathology is concerned".

In addition to this abundance of pathology, the physical character of the country itself presents formidable problems, many of which are described in detail in a volume on Ethiopia in the remarkable Geomedical Monograph Series, published by Springer-Verlag, Berlin (1972), and from which we extract information on leprosy in this number by Professor K. F. Schaller, Director of the Ernst Rodenwald Institute in Koblenz and Chairman of the Medical Commission of ILEP. Ethiopia has a population of about 24 million, of whom only 2 million live in cities, most of the registered leprosy patients occupying the central, hilly areas (Cap and Mulatu, 1976). The number recorded as having been registered is in itself a matter of concern; in the *Weekly Epidemiological Record* of January 1979, WHO estimate 135,000 cases of leprosy for Ethiopia, of whom only 59,000 are registered. The lepromatous rate is given as 50%—an unusually high figure for Africa.

Clearly this means that well under half the estimated cases have been registered and that amongst the *un*registered (and therefore presumably untreated) cases, no fewer than 50% may be excreting bacilli into the environment, mainly—as numerous contributions to this and other journals in recent years have confirmed—from the nose and nasal mucus.

These sombre facts on the leprosy control situation in a large country where roads, communications, government and medical services have never been well developed, must now be considered in the context of several years' political chaos and bloodshed, as yet by no means resolved. Even when all the fighting is over, the course of events in some other African countries suggests that Ethiopia may take a long time to make a medical recovery, and it would be unrealistic to expect that leprosy will be given a high priority in this process. Elsewhere in this issue, Dr A. P. Oomen (Amsterdam) draws on his long experience of Ethiopia in reviewing some of the achievements—and the setbacks, of health manpower training.

In his account of this disease, published in 1972, Professor K. F. Schaller refers to "vast areas of Ethiopia where leprosy represents a major problem, with which the country will be confronted for many years to come". On top of all the difficulties he had in mind, we now have to face the increasingly well-documented fact of resistance to dapsone, for which Dr J. M. H. Pearson and

his colleagues present further evidence in the following pages. Although most of their patients were drawn from the Addis Ababa area, it is noteworthy that they include cases from elsewhere in the country, 28 of them being proved resistant by mouse foot-pad tests. Their conclusion that dapsone resistance is now "so widespread in Ethiopia as to threaten the practical possibility of leprosy control by chemotherapy alone", is, to say the least, disquieting. Taken with their previously published work on dapsone resistance in Malaysia, it surely points—as WHO have indeed already stressed—to the urgency of further investigating the whole matter, not only in Ethiopia, but in other countries of the world where dapsone has been used in low dosage, and irregularly, over a period of years. One thinks immediately of India, with its own estimate of 3.2 million cases of leprosy, as a country from which data on dapsone resistance, from large groups of treated and untreated patients, would be of the utmost value.

Meanwhile, we have to consider the most advantageous use of the drugs available, and in the Correspondence section of this number, Dr Harold Wheate, Director of Training at ALERT in Addis Ababa, stresses the importance of looking for dapsone resistance in the large pool of registered patients who have received dapsone, often inadequately and irregularly for many years, suggesting a suitable regimen of drug treatment for them. This is accompanied by a reply from Dr R. J. W. Rees in which he draws attention to the additional grim possibilities of resistance to rifampicin or thiosemicarbazone (thiacetazone) under certain circumstances in relapsed cases.

In view of these therapeutic difficulties in leprosy, together with the limited number of drugs available and the practical problems of distributing them regularly and for long enough to a significant percentage of those estimated to suffer from the disease, many will consider that the facts call for even further impetus towards the development of a vaccine. While this is in progress, it looks as if more information about dapsone resistance, scientifically based on mouse-foot-pad techniques, or perhaps on a radioactive assay, such as that described by Ambrose and his colleagues in 1978, must be obtained by other investigators from as many countries as possible. It will then be possible to assess with greater accuracy the relative importance of the two factors upon which the strategy—and the cost—of leprosy control probably depends most vitally—(1) the large numbers of patients estimated by WHO to be unregistered and therefore untreated (amongst which there are some countries with disturbingly high lepromatous rates), and (2) the extent of primary and secondary dapsone resistance in the world.

A. C. McDOUGALL

References

Ambrose, E. J., Khanolkar, S. R. and Chulawalla, R. G. (1978). A rapid test for bacillary resistance to dapsone. *Lepr. India* **50,** 131. (Reviewed in Abstracts of *Lepr. Rev.* **50** (1979) by Dr M. F. R. Waters.)

Cap, J. A. and Mulatu, B. (1976). La lèpre en Ethiopie; situation actuelle. *Med. Trop.* **36,** 11.

Schaller, K. F. (1972). *Leprosy in Ethiopia; a Geomedical Monograph,* pp. 114–116. Springer-Verlag, Berlin, Heidelberg, New York.

WHO (1979). Leprosy. *Wkly Epidem. Rec.* No. 3, 17.

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Dapsone-resistant Leprosy in Ethiopia

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During the 5 years 1973–1977, 254 patients suspected of developing dapsone-resistant leprosy were seen in the Addis Ababa area. They were drawn from a pool of about 1500 registered patients with lepromatous leprosy, giving an incidence of about 3% per annum (among patients at risk). Fifty-one were proved resistant by mouse foot-pad tests, and 57 more by clinical trial. The remainder, who continued in trial treatment, conformed to the clinical pattern of those proved to be dapsone resistant. Only 2 patients were proved to be sensitive to dapsone.

In addition, among 106 suspected cases from elsewhere in Ethiopia giving a "classical" history, 28 were proved resistant by mouse foot-pad tests, and only one was dapsone sensitive. Eleven out of 17 patients who relapsed having discontinued dapsone treatment were also found to have developed dapsone-resistant leprosy (7 by mouse foot-pad tests, and 4 more by clinical trial): 2 were sensitive to dapsone.

Mouse foot-pad testing for primary dapsone-resistant leprosy was performed in 29 patients. Fourteen lived in the Addis Ababa area; 5 of them were resistant. Fifteen came from elsewere in Ethiopia; 11 were resistant. Dapsone-resistant leprosy has become so widespread in Ethiopia as to threaten the practical possibility of leprosy control by chemotherapy alone.

Introduction

Dapsone has been used for over 30 years to treat leprosy, and remains by far the most suitable and widely used drug for field therapy. The widespread emergence of dapsone-resistant strains of *Mycobacterium leprae* would require

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major changes in the practice of leprosy control. It is important, therefore, to obtain data on dapsone resistance in a form that can be utilized for planning leprosy control programmes. This essentially means accurate determination of the prevalence (and if possible incidence) of resistant cases in a defined area.

This paper represents such a study. The Medical Research Council Leprosy Project in the Addis Ababa Leprosy Hospital was initiated in January 1973. From then until its closure in August 1978 the Project had a special interest in dapsone-resistant leprosy, and was fortunate to have assistance from colleagues both inside and outside the hospital, who referred all suspected cases to the Project for assessment. This paper, therefore, includes information on all patients who were suspected of developing dapsone-resistant leprosy and who attended the Addis Ababa Leprosy Hospital for investigation and treatment during the 5 year period 1973–1977. However, particular emphasis is given to the findings among patients registered for treatment in the Addis Ababa area, where closer surveillance was possible and ensured that every patient suspected of developing dapsone-resistant leprosy was studied by the MRC Project, and enabled accurate prevalence and incidence figures to be obtained.

The first reports of proven dapsone-resistant leprosy came from studies in an inpatient institution (Pettit and Rees, 1964). The figure given for prevalence was probably correct at that time, though many new cases have subsequently been diagnosed (Pearson *et al.*, 1975), but the size of the problem which might develop in the future was seriously underestimated. In Ethiopia, preliminary reports have indicated both that the prevalence of acquired resistance may be significantly greater than had been observed elsewhere, and also that primary dapsone resistance may be not uncommon (Pearson *et al.*, 1976, 1977). These preliminary findings are confirmed and amplified in this paper. If dapsone-resistant leprosy is a half, or even a quarter as frequent elsewhere as it is in Ethiopia, the practicability of leprosy control by chemotherapy alone must be considered as seriously in doubt.

Materials and Methods

The patients included in this study may be considered as comprising two major groups:

PATIENTS LIVING IN THE ADDIS ABABA AREA

Prior to their referral to the MRC Project, these patients were all routinely treated on an outpatient basis, using oral dapsone, unless they developed some complication requiring hospitalization. Most attended a clinic (either in the Addis Ababa Leprosy Hospital or a city Municipal Clinic) once a month; at this visit they were seen by a paramedical worker, and their treatment issued. Every 6 months, however, they attended the "Review Clinic" in the hospital, where they were seen by a doctor, and treatment for the next 6 months prescribed. Most of the Addis Ababa patients included in this study were referred for assessment from the Review Clinic.

PATIENTS FROM ELSEWHERE IN ETHIOPIA

These patients attended clinics in country towns or market villages, and seldom or never saw a doctor. Those included in this study were either referred to the Addis Ababa Leprosy Hospital by the worker in charge of the clinic, or in some cases referred themselves because they were not satisfied with their progress.

Patients from Addis Ababa were usually seen within a few months of developing symptoms or signs suggestive of dapsone resistance, whereas patients from outside Addis Ababa tended to have more advanced disease by the time they reached the hospital. Once there was suspicion of dapsone-resistant leprosy, however, all patients reaching the hospital were referred to the MRC Project for assessment and management. This report therefore includes all suspected cases of dapsone-resistant leprosy from the Addis Ababa area, but only random cases from the rest of Ethiopia.

Most patients gave the "classical" history of dapsone resistance; that is, initial improvement followed by deterioration despite continued treatment. However, a number of patients were studied who had relapsed because their treatment had been discontinued. Other atypical suspected cases included patients with reactions developing much later than usual in the course of treatment; and patients who, without definite relapse, appeared to show less improvement than would be expected from the duration of treatment.

Many patients had received dapsone in low or irregular dosage. Therefore the majority were started on a period of trial treatment with dapsone in high dosage. Assessments, which were undertaken at the start of the trial and every 6–12 months thereafter, included clinical drawings, skin smears from the most active looking lesions, and biopsies (which, however, were often omitted if the clinical progress and skin smear results were satisfactory).

Patients were not routinely admitted to hospital for treatment; supervision, therefore, amounted in practice to encouragement of the patient to take treatment regularly. This was accomplished in 3 ways:

(1) Increased doctor/patient contact. Addis Ababa patients were seen every 1–2 months by a doctor, usually one of the MRC team.
(2) Health education. The patient was made aware of his problem, the need for the tests was explained, and the fact that we needed his help to establish the correct treatment for him was emphasized.
(3) Alternative presentations of dapsone. Patients who lived close enough to the hospital to attend for weekly injections were offered this treatment. Most other patients received a sugar coated tablet containing dapsone 100 mg: this "new treatment" was supplied directly by the doctor when he saw the patient, and was not available through the hospital pharmacy. Its use appeared to encourage regular clinic attendance and probably also regular daily treatment.

The period of trial treatment was terminated when it was clear that the patient's disease was failing to improve; these patients were considered to have shown clinical proof of dapsone-resistant leprosy. Some patients, however, did not have a period of trial treatment with dapsone, but were changed at once to non-sulphone drugs. Indications for immediate change of treatment included:

(1) Severe complications, particularly ocular involvement. It was obviously not ethical to risk the patient's eyesight for the sake of clinical proof of drug resistance.
(2) Advanced disease, together with a strong (subjective) impression that the patient was truthful and had been taking dapsone regularly.
(3) Social conditions, particularly the presence of young children in the patient's home.
(4) Patients living in remote areas, who would be unable to return for assessment for a year or so.

These patients were, however, given some priority for mouse foot-pad tests, so that, if the patient proved to have dapsone-sensitive bacilli, he could be changed back to dapsone treatment when the results of the tests became available.

In addition to these investigations of acquired dapsone-resistant leprosy, a programme was undertaken to assess, by mouse foot-pad tests, the prevalence of primary dapsone-resistant leprosy. Patients studied included both residents of Addis Ababa and persons living elsewhere in Ethiopia in areas where anti-leprosy treatment had been readily available for at least 10 years.

Mouse foot-pad tests were performed using routine methods (Rees, 1967) both in the Addis Ababa Leprosy Hospital (by J.M.H.P.) and in the National Institute for Medical Research, London (by R.J.W.R.). Mice were fed dapsone in the diet from the day of inoculation, and occasional duplicate tests were undertaken to confirm that results from the two laboratories were in agreement.

Because of limited facilities, only a proportion of patients were tested, some at the start of a clinical trial, others when it finished. In some cases, bacilli were screened against a full range of concentration of dapsone in the mouse diet (0.01%, 0.001% and 0.0001%); but often only one or two concentrations were used (0.01% gives blood levels of dapsone in the mouse in the same range as those in man taking 100 mg daily, and 0.0001% inhibits multiplication of normal sensitive strains of *M. leprae*).

Results and Comments

"CLASSICAL" PRESENTATION OF DAPSONE RESISTANCE

(1) *Patients in the Addis Ababa area*

The numbers of patients in the Addis Ababa area with clinical suspicion of dapsone-resistant leprosy seen year by year are shown in Table 1: most of them (220 out of 254) presented with the "classical" history. The number of registered patients with lepromatous leprosy in the Addis Ababa area has been stable at about 1500 for some years; the incidence of suspected cases during this period was therefore about 3% per annum.

Of the 220 patients with a classical history, 41 (19%) were advised to discontinue treatment with dapsone at once, and start new treatment: 22 were shown by mouse foot-pad tests to be dapsone resistant. The remaining 179 patients continued to take dapsone for a period of trial treatment. These

TABLE 1
Number of patients from the Addis Ababa area with suspected dapsone-resistant leprosy seen during the period 1973–77

Year	"Classical" history	Atypical presentation	Total
1973	46	3	49
1974	47	9	56
1975	41	7	48
1976	47	8	55
1977	39	7	46
Total	220	34	254

patients were able to attend the hospital clinic for follow-up regularly, and only 5 have been lost (4 by default and 1 by known death). Thus the results of the period of trial treatment for 174 patients are available for analysis.

Seventy-seven patients were female, 97 male: this is not significantly different to the male/female proportion of lepromatous patients under treatment in Addis Ababa. They had received treatment for 2–21 years prior to showing clinical evidence of dapsone resistance (Fig. 1).

Biopsy classification was as follows:

LL, LLp, LLs, LI—130 cases, BL—24 cases, BB—4 cases,

Not available—16 cases.

The frequency distribution of the values for averaged Bacterial Index (BI), Morphological Index (MI), and biopsy index and classification were similar for male and female patients.

The initial BI was reported as negative in 2 patients; their biopsies, however, showed "BL active" and "LL resolving" respectively. In the remaining 172 cases the BI was positive, ranging from 0.5 to 6.0 (average 3.5). The MI was

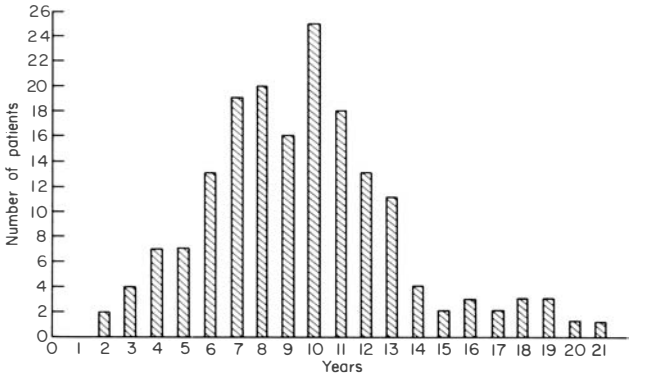

Fig. 1. Time in years from start of treatment with dapsone to emergence of suspected dapsone resistance in 174 patients with lepromatous leprosy.

TABLE 2
Overall results of period of trial treatment of 174 patients with "classical" history of dapsone-resistant leprosy

Outcome of trial treatment	Number of patients
Clinically resistant, confirmed by mouse foot-pad tests	25
Clinically resistant, not confirmed by mouse foot-pad tests	57
Continue in trial, foot-pad tests show dapsone resistance	4
Continue in trial, foot-pad tests show dapsone sensitivity	2
Continue in trial, foot-pad test results not available	86

raised (i.e. solid staining morphologically normal bacilli were observed in the skin smears) in all but 33 cases. Of these 33, the biopsy was reported as showing histological activity in 23 cases: it was regressional in 4 (including 2 with ENL) and was not available for the remaining 6 cases. Thus, there was evidence of active leprosy, uncontrolled by treatment, in all but 10 cases in the series.

Entry to the trial was spread over 5 years, and patients were assessed every 6–12 months during the trial. Thus, when the trial was reviewed early in 1978, some patients had been studied for a few months only, but some had been followed for as long as 5 years. The overall results at that time are shown in Table 2, and the clinical status of the trial patients at their last assessment in Table 3. About half the patients (86 out of 174) had already been shown (clinically or by mouse foot-pad tests) to harbour dapsone-resistant strains of *M. leprae,* and a further 12 were not doing well clinically. Only 2 were proved by foot-pad tests to be fully sensitive to dapsone. An interesting feature was that as many as 25 patients who started trial treatment in 1973 and 1974 were still doing well.

This prolonged response was related to the treatment the patients had received before they entered the trial. They may be divided into two groups:

"Weekly dosage" group (44 patients).

TABLE 3
Clinical status of 174 trial patients at final

Start of trial (year)	Duration of follow-up (years)	Number of patients in trial		
		Total	Improved	Worse
1973	4–5	25	11	14
1974	3–4	33	14	19
1975	2–3	40	17	23
1976	1–2	42	20	22
1977	0–1	34	18	16
Total		174	80	94*

* Eighty-two of these patients had been removed from the trial and started on treatment with non-sulphone drugs.

These had received weekly dosage of dapsone (usually 200 or 300 mg) before the trial (or were changed to daily dosage 6 months or less before the start of the trial).

"Daily dosage" group (130 patients).

These had received dapsone in daily dosage (usually 100 mg) for more than 6 months prior to the start of the trial.

Of the 25 patients who were doing well when assessed after 3 or more years of trial treatment, 17 were in the weekly dosage group; the other 8, though included in the daily dosage group, had been changed from weekly to daily dosage only 12–15 months before the start of the study. These two groups of patients can be divided into cohorts according to the number of months they were studied. During each period a patient might show clinical deterioration (usually with removal from the trial); improvement and continue in the trial; or improvement but be "lost" from the trial because he was last assessed during this period. This analysis is summarized in Table 4, confirming that the weekly dosage group of patients improved for much longer than did the daily dosage group.

Although most patients in the trial were treated with dapsone 100 mg daily (oral) 24 received dapsone by injection (375 mg weekly, suspended in 1.5 ml hydnocarpus oil). Despite the lower dosage of dapsone, they did no worse than the rest of the patients. The hydnocarpus oil is unlikely to have been therapeutically active, as the recommended dosage is at least 15 ml weekly (Cochrane, 1959).

TABLE 4

Number of patients still improving clinically after different periods of trial treatment

Years of treatment in the trial	Proportion of patients improving clinically	
	Previous treatment	
	Daily dapsone	Weekly dapsone
1	63/130 (44%)	38/44 (86%)
2	24/63 (38%)	27/38 (71%)
3	8/24 (33%)	18/27 (67%)
4	1/7 (14%)	6/18 (33%)
5	0/1 (0%)	6/6 (100%)*

* Four of these patients have mouse foot-pad proof of dapsone-resistant leprosy (see Table 7).

TABLE 5
Results of mouse foot-pad tests for dapsone resistance in 93 patients

Degree of resistance	Number of patients tested		
	Trial patients	Other patients	Total
Resists dapsone 0.01% in mouse diet	9	11	20
Resists dapsone 0.001% in mouse diet	2	3	5
Resists dapsone 0.0001% in mouse diet	3	12	15
Resistant, not fully titrated	15	33	48
Sensitive to dapsone	2	3	5
Total number of patients treated	31	62	93

The results of mouse foot-pad tests are shown in Table 5, both for this group of trial patients and for all Ethiopians tested in the period 1973–77. Of 93 patients tested, only 5 proved to be dapsone sensitive. The history and clinical features of the whole group conformed to the pattern of the trial cases: it is therefore likely that, despite their initial response to dapsone, the majority of the 92 patients continuing in the trial would prove to be resistant on further follow-up. Indeed, 4 of them showed mouse foot-pad proof of dapsone-resistant leprosy, though they had improved for 2.5 years or more (see Table 6).

(2) *Patients treated outside Addis Ababa*

One hundred and six patients were included in this group, all with lepromatous leprosy. The results of mouse foot-pad tests on 29 (27%) of these patients are shown in Table 7; only one patient proved to be dapsone sensitive.

Fifty-six patients were advised to continue dapsone treatment for a trial period. The results of this trial at review early in 1978 were:

Those continuing in trial—15, changed treatment—20 and defaulted—21.

These results are hard to interpret precisely. The trial was unsupervised, and the abnormal conditions in the countryside which resulted from the political situation during this period often made "defaulting" inevitable. However, 97%

TABLE 6
Duration of response to treatment in 4 patients with dapsone-resistant leprosy proven by mouse foot-pad tests

Case no.	Level of resistance*	Trial treatment (weekly, w; daily, d)	Duration of response (months)
1	0.0001%	Inj. dapsone 375 mg/w	30
2	0.0001%	Inj. dapsone 375 mg/w	37
3	0.001%	Inj. dapsone 375 mg/w	49
4	0.01%	Tab. dapsone 100 mg/d	53

* Percentage of dapsone in diet that inhibited growth of *M. leprae* in the mouse foot-pad.

TABLE 7
Results of mouse foot-pad tests on 106 patients with "classical" dapsone-resistant leprosy from outside Addis Ababa

Clinical management	Number of patients			
	Resistant	Sensitive	Not tested	Total
Changed treatment at once	16	1	33	50
Started on trial treatment with dapsone	12	0	44	56
Total	28	1	77	106

(28 out of 29) of the mouse foot-pad tests showed dapsone-resistant strains of *M. leprae*. This indicates that most of the patients in this group were infected with dapsone-resistant organisms.

ATYPICAL PRESENTATIONS OF SUSPECTED DAPSONE-RESISTANT LEPROSY

Fifty-eight patients were studied, 34 from Addis Ababa and 24 from elsewhere in Ethiopia. Thirteen patients, however, defaulted, and are excluded from this analysis. The 45 patients may be grouped thus:

"Relapse cases" (new lesions developing after stopping treatment)—17, "solitary leproma of the eye"—4, "late reversal reaction"—8, "late ENL reaction"—4 and "slow improvement"—12.

(1) *Relapse cases*

Seventeen lepromatous patients (13 of whom lived in the Addis Ababa area) were studied. All had received dapsone for periods of 2–16 years (average 8 years), and had then stopped treatment for 1–5 years. All 17 had a positive BI (average 4.1): in 14 the MI was positive, and 2 of the remaining 3 cases showed histological activity. Eleven were classified BL, LI or LL, one Indeterminate (though the BI was 2.2) and one was not biopsied.

All these patients were advised to take dapsone for a period of trial treatment. The outcome of this trial is shown in Table 8. Eleven patients showed evidence (clinical, mouse foot-pad, or both) of dapsone-resistant

TABLE 8
Outcome of trial treatment and results of mouse foot-pad tests in 17 relapse cases

Outcome	Number of patients
Dapsone resistant (mouse foot-pad tests)	7
Dapsone sensitive (mouse foot-pad tests) and removed from trial	2
Deteriorated clinically during trial treatment (mouse foot-pad tests not performed)	4
Improving under trial treatment (mouse foot-pad tests not performed)	4

TABLE 9

Clinical findings in patients developing reversal reaction later than usual in the course of dapsone treatment

Case no.	Findings prior to reaction: Classification (clinical)	Treatment (years)	BI	Findings at onset of reaction: BI	MI	Biopsy	Findings following reaction: Steroid treatment	Duration (years)	BI	MI	Biopsy
1	L	13	0	2.3	0	BT	None	1.5	3.5	4	BL*
2	L	7	1.7	1.8	0	BT	None	1.5	2.6	1	LL
3	L	13	NA†	3.3	0	BB	None	3	1.8	0	L/ENL
4	L	4	0	3.5	0	BB/BT	None	3	0.5	POS	Indet.
5	L	8	0	2.7	1	BT/BB	None	3	0.7	0	NA
6	L	7	0	1.2	0	BL-BT	None	2.5	0.6	0	NA
7	BL	4	0	NA	NA	BB-BT	Given	1	0	—	Indet.
8	BL	4	0	3.8	1	BB	None	2	1.8	0	NA

*Foot-pad tests showed dapsone resistance at 0.001% dapsone in the mouse diet (but sensitive at 0.01%). After 2.5 years continued monotherapy with dapsone the disease was clinically quiescent, BI = 0, Biopsy = Indeterminate.

† NA = Not available.

POS = Positive, figure not available.

leprosy; and of the 4 patients improving under trial treatment who did not have mouse foot-pad tests performed, 3 were followed up for a year or less.

(2) *Solitary leproma of the eye*

Lepromata of the eye were noted in about 5% of patients with suspected dapsone-resistant leprosy. There were, however, 4 patients in whom an ocular leproma was the sole evidence of active leprosy. The BI was positive (0.5–2.7) in all 4 cases, though the MI was 0, and clinically the disease appeared to be quiescent in the skin. Following treatment with clofazimine (together with treatment of iridocyclitis if present) vision was preserved in 3 cases; the fourth was already blind. In one patient (together with another in whom skin nodules were also present), the superficial part of the leproma of the eye was removed surgically, and used as a source of bacilli for mouse foot-pad inoculation. Both cases proved to be dapsone resistant.

(3) *Reversal reaction occurring later than usual in the course of treatment*

We have studied 8 patients in this category; all of them had previously been classified as lepromatous, and had been treated for 4 or more years. The BI had been reported negative in 6 cases. They all presented with the appearance of new lesions which, both clinically and histologically, were in the borderline range.

Although the appearance of BB or BT lesions in a previously lepromatous patient must be categorized as reactional, only one patient showed sufficiently active lesions and neuritis to warrant the use of corticosteroids. The remainder were treated with dapsone in full dosage. The results of this trial are shown in Table 9. In 2 patients (cases 1 and 2) the BI rose and the classification downgraded to lepromatous; in one of them mouse foot-pad tests showed dapsone resistance. In a third (case 3) the BI fell, but the appearance of ENL lesions indicated that downgrading had occurred. It is likely that these 3 patients were dapsone resistant. In addition, case 4, though apparently improving, still showed occasional solid staining bacilli in skin smears when last assessed.

In the remaining 4 patients the lesions resolved, the BI fell, and the disease became quiescent once more (one of these patients received steroid treatment for his reaction). It would be tempting to consider them as dapsone sensitive. However, the patient with proved dapsone resistance responded well to dapsone monotherapy (after initially downgrading from BT to BL); 4 years after the appearance of his lesions he was clinically quiescent, BI = 0, and histologically Indeterminate. Much longer follow-up would therefore be required to say confidently that these 4 patients were dapsone sensitive.

(4) *ENL reactions occurring later than usual in the course of treatment*

Four patients were studied in whom an attack of ENL was the first indication of possible recrudescence of disease. Three patients had been found smear negative during the year preceding the reaction; the fourth (case 1) had

TABLE 10
Clinical data of 4 patients developing erythema nodosum leprosum (ENL) later than usual during treatment

Case no.	Prior to onset of ENL: Treatment (years)	Smear results BI	Smear results MI	At time of ENL: Smear results BI	Smear results MI	Duration of ENL (months)	Treatment	Outcome
1	10	3.0	0	3.3	0	6	Dapsone	Improved at 4 years
2	6	0	—	0.7	0	3	Dapsone	Improved at 2 years
3	6	0	—	5.4	3.0	2	Clofazimine	Improved at 2 years
4	8	0	—	0	—	1	Dapsone	Improved at 1 year

shown a slowly rising BI for the previous 2 years, but his disease looked inactive.

The clinical findings of this group of patients are shown in Table 10. Mouse foot-pad tests were not performed in any of them (and would indeed only have been possible in case 3). Case 3 received clofazimine because of severe ENL: the combination of ENL and a raised MI makes it likely that he was dapsone resistant. The other 3 patients showed no evidence of resistance after 1–4 years follow-up.

(5) *Apparent slow improvement under treatment with dapsone*

Twelve lepromatous patients were studied in whom an apparent slow improvement had led to suspicion of resistance. They said they had "never really improved", but in most cases the clinical records were inadequate to confirm this statement. The period of treatment ranged from 1 to 14 years.

The BI was positive in all cases, but the MI raised only in 6 (Table 11). Mouse foot-pad tests were set up in 2 patients; one of them was fully sensitive, the other showed high grade DDS resistance. An additional patient relapsed under trial conditions. The remaining 9 were doing satisfactorily, when followed up for periods of 3–25 months.

PRIMARY DAPSONE-RESISTANT LEPROSY

Mouse foot-pad tests were undertaken in 29 patients with previously untreated lepromatous leprosy. They had lived for many years in Addis Ababa or other areas of Ethiopia where dapsone treatment had been regularly available for 10 or more years, but were otherwise unselected. More than half (16 out of 29) of them showed primary dapsone-resistant leprosy (Table 12) indicating that some years previously, when these patients were infected, about half the infectious index cases were already suffering from sulphone-resistant

TABLE 11

Clinical data of 12 patients apparently responding slowly to treatment with dapsone and outcome following trial treatment

Case no.	Previous treatment (years)	At start of trial			Mouse foot-pad tests	Trial of treatment (months)	Outcome on follow-up
		BI	MI	Biopsy			
1	2	3.2	2.0	*NA	Fully resistant	9	Deteriorated, changed treatment
2	10	4.7	0.5	NA	NA	17	Deteriorated, changed treatment
3	1	4.1	6.0	LL	Fully sensitive	12	Improving
4	2	5.0	1.0	Ls	NA	23	Improving
5	10	3.5	4.0	LI	NA	3	Improving
6	5	3.7	4.0	BL	NA	3	Improving
7	3	4.0	0	BL	NA	25	Improving
8	11	0.8	0	LL	NA	12	Improving
9	4	1.7	0	NA	NA	12	Improving
10	14	1.3	0	Idt	NA	8	Improving
11	2	5.3	0	Lp	NA	4	Improving
12	2	3.7	0	NA	NA	3	Improving

*NA = Not available.

TABLE 12
Results of mouse foot-pad tests on 29 previously untreated patients with lepromatous leprosy tested for primary dapsone-resistant leprosy

Result of foot-pad test	Number of patients	
	Living in Addis Ababa	Living elsewhere
Sensitive	9	4
Resists 0.0001% dapsone in diet	2	4
Resists 0.001% dapsone in diet	1	3
Resists 0.01% dapsone in diet	0	1
Resistant, not fully titrated	2	3

leprosy. The proportion of primary resistance among patients living outside Addis Ababa was at least as high as that found in Addis Ababa itself.

Discussion

GENERAL

A number of conclusions can be drawn from this study.

(1) In the Addis Ababa area the incidence of new cases of suspected dapsone-resistant leprosy is about 3% per year of registered lepromatous cases, and the great majority of these are truly resistant.
(2) Most patients referred from outside Addis Ababa with suspected acquired dapsone resistance have also proved to be resistant when it has been possible to carry out tests adequately.
(3) The proportion of patients with primary dapsone-resistant leprosy is no less in centres outside Addis Ababa than it is among patients living in the Addis Ababa area.

It is therefore certain that dapsone-resistant leprosy is widespread throughout Ethiopia. A high prevalence of such cases is serious in itself: each patient demands considerable outlay of resources for diagnosis and long term treatment. But the more serious aspect of the problem is that these cases can become epidemiologically significant; that is, they become the index cases for a significant number of patients with primary dapsone-resistant leprosy. It is hard to define the point at which this occurs: a consensus might settle for about 5% primary resistance as a figure which, if exceeded, would be epidemiologically alarming. It is certain, however, that our figure of about 50% of primary dapsone-resistant leprosy indicates a major defeat for the policy of attempting to control leprosy by chemotherapy with dapsone alone.

The degree of dapsone resistance shown by a strain of *M. leprae* depends chiefly on the dosage of dapsone the patient is receiving. Low dosage permits low grade resistant bacilli to multiply, but high dosage prevents all but high grade resistant mutants from multiplying. Thus weekly and often low dosage of dapsone was employed in Ethiopia till about 1975; therefore the majority of patients with primary dapsone-resistant leprosy identified prior to 1978 show low grade resistance. It may be anticipated that the daily and usually higher

total dosage employed from about 1975 on will ensure that in future a larger proportion of strains of *M. leprae* will show high grade dapsone resistance.

"CLASSICAL" DAPSONE RESISTANCE

This remains the most common presentation of suspected acquired dapsone resistance, accounting for 83% of all cases in this series. The results of this out-patient study differ in several ways from those reported from hospitalized patients with "classical" histories (Pearson *et al.*, 1975).

(1) Our patients developed resistance more rapidly (2–20 years, peak at 7–11 years),
(2) Our patients responded for longer under trial treatment with dapsone (at least 15% for 3 years or more),
(3) Some 5% of our patients proved to be dapsone sensitive on mouse foot-pad tests.

These differences are most probably related to the uncertainties of both history and therapy during out-patient treatment. In addition, patients developing resistance very rapidly may well have been suffering from low grade primary dapsone-resistant leprosy.

When patients have previously received irregular (or weekly) treatment, they are likely to experience a prolonged remission on regular monotherapy with dapsone. Such patients are not proved sensitive even if still improving under reasonably supervised treatment after 2 or 3 years. This indicates that they usually have low grade dapsone resistance, and that dapsone in full dosage often remains efficacious. There would be a good case for treating such patients with dual therapy (dapsone plus a second drug) for a year or two when they are first seen: such a regimen, followed by dapsone monotherapy, might often prove curative.

RELAPSE PATIENTS

One of the unexpected findings of this trial was that out of 17 relapse patients tested, 11 showed clinical or foot-pad proof of dapsone resistance. If these results are confirmed by studies elsewhere, it will indicate that all relapse cases should receive dual or triple therapy for a year or two when they restart treatment, in the hope that continued monotherapy with dapsone thereafter may be curative.

LEPROMATA OF THE EYE

The eye is an unusual site to find nodules in previously untreated leprosy. It is, however, a fairly common site in patients with acquired dapsone-resistant leprosy. Patients with this complication often develop severe and prolonged iridocyclitis; they should, therefore, be changed to treatment with another drug combination as soon as the leproma is observed, rather than undergoing a period of trial treatment with dapsone.

The nodules are usually on the lateral aspect of the corneoscleral junction, and encroach on the cornea only very slowly. The superficial part of the nodule can readily be sliced off under local anaesthetic. It is full of bacilli,

which can be used for mouse foot-pad inoculation. If there are no nodules elsewhere on the body, this is the only reliable way to prove dapsone resistance.

REVERSAL REACTION OF LATE ONSET

Most patients who develop reversal reaction do so within a year or two of first starting treatment: to develop reaction at a much later stage must lead to suspicion that the reaction has been triggered by bacillary multiplication and may therefore indicate the emergence of dapsone resistance.

Of the 8 patients we studied who developed reversal reaction after 4 or more years of treatment, 3 seem fairly likely to prove resistant, and in a fourth case there is foot-pad proof of resistance despite a prolonged remission under trial treatment with dapsone. Only one patient, however, developed reaction severe enough to warrant corticosteroid therapy: the others, though previously (and correctly) classified as lepromatous, presented with lesions that were clinically and histologically in the borderline range. This may be the same process that occurs during the development of lepromatous leprosy prior to treatment. Patients with lepromatous leprosy will often give a history of initially localized lesions which, from the description, appear to have been in the borderline range; they describe subsequent spread of the disease, which downgrades to lepromatous, with or without accompanying reactions. Three of the 8 patients in this group showed downgrading without overt reaction: it would be instructive to follow the clinical progress of the remainder. Patients in this category could well prove to be of unusual immunological interest.

Downgrading and upgrading within the BL/LL range have also been observed in a number of female patients with probable dapsone-resistant leprosy in association with pregnancy. This phenomenon will be reported fully elsewhere.

ENL OF LATE ONSET

In the patients we studied this appeared to be of little or no value as evidence of the emergence of dapsone-resistant leprosy. Moreover, the MI in such patients is usually zero, so mouse foot-pads will seldom be successful: proof of resistance must be by clinical trial. However, the combination of ENL and a persistently raised MI is likely to indicate dapsone resistance.

APPARENT SLOW IMPROVEMENT UNDER TREATMENT WITH DAPSONE

It is hard to interpret these findings, though case 1 seems to be a case of primary dapsone-resistant leprosy, and case 2 of acquired resistance. Much longer periods of follow-up would be needed to assess whether or not the remaining patients were in an early stage of incubation of dapsone-resistant leprosy, or whether they were merely irregular tablet takers.

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References

Cochrane, R. G. (1959). In *Leprosy in Theory and Practice*, 1st edit., p. 208. John Wright & Sons, Bristol.

Pearson, J. M. H., Rees, R. J. W. and Waters, M. F. R. (1975). Sulphone resistance in leprosy: a review of one hundred proven clinical cases. *Lancet* **2,** 69.

Pearson, J. M. H., Ross, W. F. and Rees, R. J. W. (1976). DDS resistance in Ethiopia—a progress report. *Int. J. Lepr.* **44,** 140.

Pearson, J. M. H., Haile, G. S. and Rees, R. J. W. (1977). Primary dapsone resistant leprosy. *Lepr. Rev.* **48,** 129.

Pettit, J. H. S. and Rees, R. J. W. (1964). Sulphone resistance in leprosy: an experimental and clinical study. *Lancet* **2,** 673.

Rees, R. J. W. (1976). Drug resistance of *Mycobacterium leprae*, particularly to DDS. *Int. J. Lepr.* **35,** 625.

Lepr. Rev. (1979) **50**, 201–211

The Reliability of Self-administration of Dapsone by Leprosy Patients in Burma

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A study of urinary dapsone/creatinine (D/C) concentration ratios has been performed on 852 leprosy patients in the Rangoon and Mandalay regions of Burma. The results show that, by comparison with in-patients who are assumed to be compliant with their therapy, hospital out-patients and urban and rural clinic patients had overall compliance rates of only 74% and 24% respectively. In each group, substantial numbers of patients were identified who had taken no dapsone (DDS) tablets whatsoever.

The findings are in line with similar studies performed in other countries and they indicate an urgent need to reassess the existing programme of treatment supervision particularly in the urban and rural clinic environments.

Introduction

Compliance with DDS therapy may be monitored by a quantitative test in which DDS and its diazotizable metabolites, and creatinine concentrations, are determined on single urine samples (Ellard *et al.*, 1974*a*). The DDS/creatinine (D/C) concentration ratios measured on urine samples from patients receiving

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supervised administration of DDS are compared with the urinary D/C concentration ratios determined from patients who are relied upon to self-administer their DDS. An estimation may then be made of the percentage of prescribed DDS therapy taken by the unsupervised patients (Ellard *et al.*, 1974*b*).

Compliance with DDS therapy has been studied in populations of leprosy patients in Africa, (Ellard *et al.*, 1974*b*; Low and Pearson, 1974; Huikeshoven *et al.*, 1976) and India (Balakrishnan, 1977; Naik and Ganapati, 1977). The results show disappointingly low levels of compliance among out-patients.

This paper assesses, in a similar manner to previous authors, compliance with DDS therapy by leprosy patients in two regions of Burma—Mandalay and Rangoon. The degree of supervision with therapy varies between groups of patients in these areas. A small proportion of patients who are resident in leprosy hospitals receive full supervision of their medication, while other patients regularly attend out-patient clinics but are relied upon to administer their own medication. The majority of the Burmese patients studied live in rural areas and receive treatment through a system of drug distribution by leprosy health workers. The successful mass treatment of leprosy is therefore largely dependent on the regularity of patients to self-administer their medication and on the system of drug distribution. Some of the present findings have been the subject of a previous report (Kin Ma Gyi *et al.*, 1978) and are reassessed together with further findings obtained in different parts of Burma, which are published for the first time.

Methods

PATIENTS

All leprosy patients were on a 6 days/week regimen of either 12.5 mg, 25 mg, 50 mg, 75 mg or 100 mg DDS with the exception of one patient taking 200 mg. Urine samples were collected from a total of 852 patients in Mandalay and Rangoon. The patients consisted of the following groups:

(a) Leprosy hospital patients: in Mandalay residents receiving either 100 mg or 50 mg DDS, and in Htauk Kyant, Rangoon, residents receiving 50 mg DDS, each provided a urine sample 24 h after ingestion of DDS therapy. Hereinafter these patients are referred to as IN-PATIENTS.

(b) Hospital out-patients: urine samples were collected from patients at their weekly visit to the Special Skin Clinic at Mandalay General Hospital and these patients were prescribed either 12.5 mg, 25 mg, 50 mg or 100 mg DDS. Urine samples were provided also by patients attending their weekly visit to the Htauk-Kyant out-patient clinic in Rangoon and those patients attending Rangoon General Hospital out-patient clinic. The Rangoon out-patients were prescribed 50 mg DDS. Hereinafter these patients are referred to as OUT-PATIENTS.

(c) Urban and rural clinic patients: in Mandalay, urine samples were provided by patients prescribed either 25 mg, 50 mg, 75 mg or 100 mg DDS. These patients live in the townships of Madaya, Patheingyi and Amarapura and Maymyo Town. In Rangoon, urine samples were provided by patients from

Htauk Kyant village, prescribed 50 mg DDS, and patients from Taik Kyi village and the Hmawbi and Hlegu areas, all prescribed 100 mg DDS. Leprosy workers collected urine samples from the urban and rural clinic patients at surprise visits by the worker to each village or town. Hereinafter these patients are referred to as URBAN AND RURAL CLINIC PATIENTS.

Areas from which patient urine samples were obtained are identified by map references, indicated in Fig. 1.

All urine samples from the Rangoon patients were collected and preserved in 0.5 volumes of 2N HCl. Urine samples from the Mandalay patients were not acidified but were refrigerated until determinations could be carried out. Ten volunteers from the staff of the Htauk Kyant Leprosarium, Rangoon, provided urine samples for control determinations.

CREATININE AND DDS DETERMINATIONS

Creatinine was determined by the alkaline picrate method (Ellard *et al.*, 1974*a*). DDS, as total diazotizable compounds, was determined by modifications of the Bratton and Marshall (1939) procedure. In Rangoon, the modification carried out was as described by Ellard *et al.* (1974*a*); in Mandalay, as recently described by Hagan and Smith (1979).

EXCLUSION OF DATA

D/C concentration ratios of 53 patients were excluded from this study, leaving 799 out of the original 852 results. The reason for such exclusion was that these samples had unusually high D/C concentration ratios. Some had creatinine levels of zero, suggesting that the samples were not urine at all. Others, with measurable creatinine concentrations, had grossly high DDS concentrations, indicating either that the samples were contaminated or that the patients were taking sulphonamides or other drugs which yield the same colour in the analysis. The upper limits for acceptable D/C concentration ratios, 150 μg/mg for patients on DDS 100 mg/day, 120 μg/mg for those on DDS 50 mg/day, were set slightly higher than the upper limits observed by Low and Pearson (1974) in a study of fully compliant patients.

A further 76 results were not included in the calculation of group compliance rates (Tables 1, 2 and 3) either because the numbers were too small for valid estimates to be made or because no appropriate supervised group of patients was available for comparison. The excluded data consisted of 14 results from Mandalay General Hospital and 22, 18, 14 and 8 from Madaya, Patheingui, Amarapura and Maymyo townships, respectively.

CALCULATION AND STATISTICAL EVALUATION

Estimates of the proportions of DDS doses taken by different groups of patients (compliance rates) were derived as described by Ellard *et al.* (1974*a*). Individual urine samples found to have D/C concentration ratios of < 6.8 μg/mg, the highest figure obtained in control urine samples from volunteers not taking DDS, were classified as negative. Patients providing such samples were judged to be totally non-compliant.

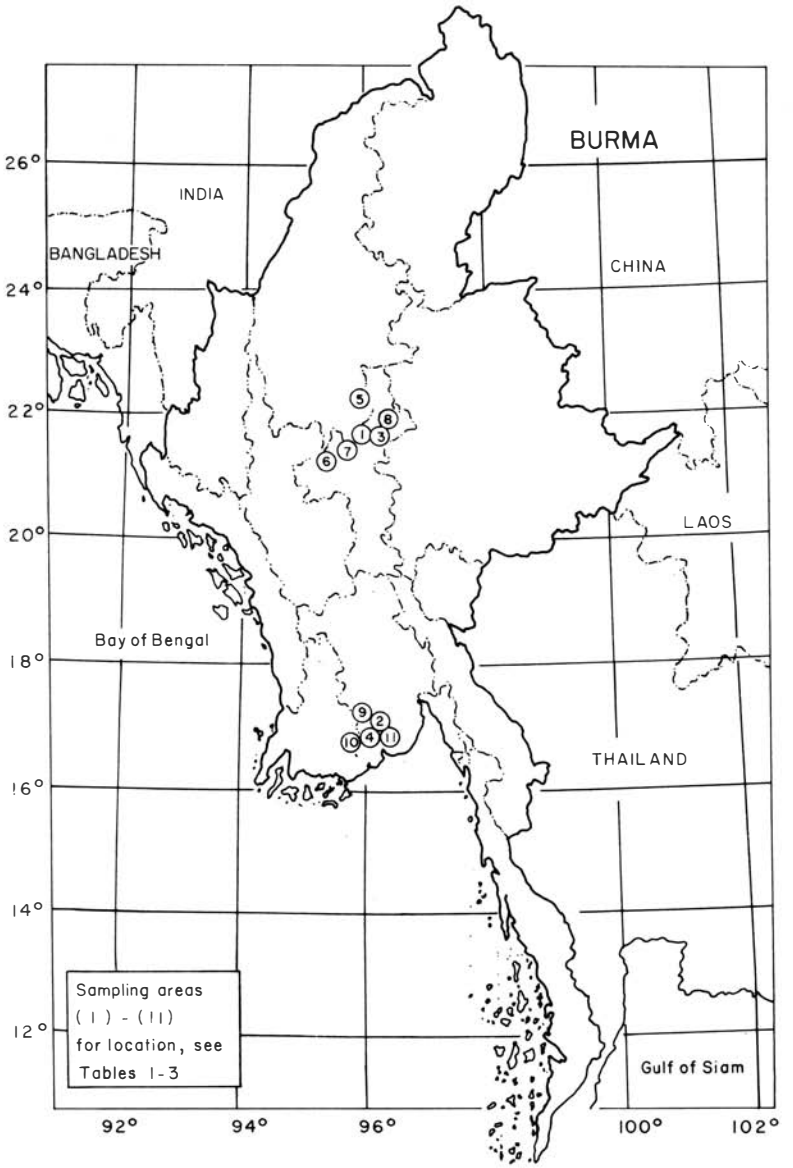

Fig. 1.

Comparisons between compliance and total non-compliance rates were effected by analysis of variance using a standard technique of nested data classification (Snedecor and Cochran, 1967).

Results

Group means (± S.E.M.) and ranges of individual D/C concentration ratios for in-patients, out-patients and urban and rural clinic patients are presented in Tables 1, 2 and 3 respectively. These tables also provide group estimates of percentages of DDS doses taken, together with sub-totals (by daily dosage) and weighted estimates of percentages of DDS doses taken (compliance rates) by each patient source (in-patients, out-patients, urban and rural clinic patients).

The results indicate that by comparison with in-patients (assumed compliance rates 100%), out-patients and urban and rural clinic patients showed 74% and 24% compliance respectively. This difference was statistically highly significant ($P < 0.001$), but no significant difference was found in compliance rates between regions (Rangoon v. Mandalay) nor between dosages (25, 50 or 100 mg/day) [Table 5(a)].

Estimates of the percentage of urine samples negative for DDS are given in Table 4. Seven per cent of in-patients, 24% of out-patients and 56% of urban and rural clinic patients had negative urines. The differences were statistically highly significant [Table 5(b)].

Group estimates of the percentage of DDS doses not taken (calculated from Tables 2 and 3) and the percentage of urines negative for DDS (calculated from Table 4), are illustrated in Fig. 2.

Discussion

This study has assessed the compliance with a 6 days/week DDS regimen in Burmese out-patients, by comparing the mean D/C concentration ratios of patients fully compliant with DDS therapy with the values obtained from the out-patients. Fifty-three D/C concentration ratios (6.2%) were excluded from the assessment because these ratios were unusually high. Several factors may have contributed to these high ratios:

(i) Simultaneous ingestion of sulphonamide therapy which may or may not have been officially prescribed. A similar problem was encountered by Ellard *et al.* (1974*a*), who were able to test suspect urine samples for interfering sulphonamides. Other drugs, notably the diuretics frusemide, hydrochlorothiazide, bendrofluazide and also diazepam and its metabolite desmethyldiazepam have also been found to interfere with the DDS assay in our laboratory. No interference was shown by rifampicin and its metabolites, clofazimine, erythromycin, indomethacin, clindamycin and its metabolite N-demethylclindamycin, or pyrazinamide, when tested in the assay procedure.

(ii) Patients ingesting more than the prescribed dose of DDS. It is conceivable that patient compliance was directly affected by the knowledge that they were to attend clinics (and temporary excess tablet consumption could result from this). The objective of this investigation was, however, kept hidden from patients, so the compliance study *per se* was unlikely to have influenced the results.

This study has shown substantial failure to comply with medication among some patients, most obviously those managed in urban and rural clinics. The

TABLE 1

Mean D/C concentration ratios and estimates of percentage of prescribed DDS doses taken by each population: IN-PATIENTS AND CONTROLS

Origin of samples (map ref.)	No. of subjects	Prescribed DDS dosage (mg/day)	D/C concentration ratio* Mean ± S.E.M.	Range	Estimated % of doses taken
Leprosy Hospital, Mandalay (1)	67	100	47.0 ± 4.5	5.0–150.5	100
Leprosy Hospital, Mandalay	15	50	38.3 ± 7.5	7.5–111.1	
Htauk Kyant hospital (2)	56	50	29.1 ± 2.8	4.0– 89.5	
(sub-total	71	50	31.2 ± 2.8		100)
(estimated	—	25	25.1		100)
ALL PATIENTS	138	25–100			100
VOLUNTEERS, no medication	10	0	3.6 ± 0.4	2.0– 6.8	

* µg DDS/mg creatinine.

TABLE 2

Mean D/C concentration ratios and estimates of percentage of prescribed DDS doses taken by each population: OUT-PATIENTS

Origin of samples (map ref.)	No. of subjects	Prescribed DDS dosage (mg/day)	D/C concentration ratio* Mean ± S.E.M.	Range	Estimated % of doses taken
Special skin clinic, Mandalay General Hospital (3)	22	100	26.2 ± 5.4	0 –120.0	52
Mandalay General Hospital	24	25	17.3 ± 3.5	0 – 69.0	64
Mandalay General Hospital	28	50	20.7 ± 4.0	0 – 66.7	62
Outpatient clinic Rangoon General Hospital (4)	45	50	31.6 ± 4.3	2.7–116.3	100
Htauk Kyant hospital (2)	44	50	23.1 ± 2.9	0.7– 66.9	71
(sub-total	117	50	25.8 ± 2.2		80
ALL PATIENTS	163	25–100			74

* µg DDS/mg creatinine.

TABLE 3

Mean D/C concentration ratios and estimates of percentage of prescribed DDS doses taken by each population: URBAN & RURAL CLINICS

Origin of samples (map ref.)	No. of subjects	Prescribed DDS dosage (mg/day)	D/C concentration ratio*		Estimated % of doses taken
			Mean ± S.E.M.	Range	
Htauk Kyant village (2)	33	50	14.7 ± 2.4	2.1 – 59.7	40
Madaya township, Mandalay (5)	58	50	14.7 ± 2.7	0.7 – 100.0	40
Patheingyi township, Mandalay (6)	56	50	5.2 ± 0.9	0 – 37.0	6
Amarapura township, Mandalay (7)	61	50	7.7 ± 1.1	0.4 – 44.0	15
Maymyo town, Mandalay (8)	22	50	5.8 ± 0.5	0.9 – 16.6	8
(sub-total	230	50	9.7 ± 0.3		22)
Madaya township, Mandalay (5)	38	100	6.8 ± 1.5	0.2 – 53.1	7
Taik Kyi area, Rangoon (9)	59	100	21.9 ± 3.3	0 – 120.5	42
Hlegu area, Rangoon (10)	47	100	14.7 ± 2.6	0 – 60.6	26
Hmawbi area, Rangoon (11)	48	100	13.2 ± 1.7	0 – 56.8	22
(sub-total	192	100	15.0 ± 1.3		26)
ALL PATIENTS	422	50–100	12.1 ± 0.5		24

* μg DDS/mg creatinine.

TABLE 4
Estimate of urine samples negative for DDS (urine D/C concentration ratios > 6.8)

Origin of samples (map ref.)	No. of subjects	No. negative	%
IN-PATIENTS			
Leprosy Hospital, Mandalay (1)	82	4	5
Htauk Kyant hospital (2)	56	5	9
ALL	138	9	7
OUT-PATIENTS			
Mandalay General Hospital (3)	88	25	28
Rangoon General Hospital (4)	45	8	18
Htauk Kyant (2)	44	9	20
ALL	177	42	24
URBAN AND RURAL CLINICS			
Madaya township (5)	118	62	53
Patheingyi township (6)	74	58	78
Amarapura township (7)	75	53	71
Maymyo township (8)	30	20	67
Hlegu area (10)	47	26	55
Hmawbi area (11)	48	19	40
Taik Kyi area (9)	59	22	37
Htauk Kyant village (2)	33	9	27
ALL	484	269	56

TABLE 5
Analyses of variance

Source of variation	Sum of squares	Degrees of freedom	Mean square	*F*	*P*
(a) % DOSES TAKEN					
Between regions	1162.88	1	1162.88	0.31	N.S.
Between sources within regions	7397.36	2	3698.68	61.21	< 0.001
Between dosage within sources	241.72	4	60.43	0.26	N.S.
Within dosage	1379.25	6	229.87		
TOTAL	10,181.21	13			
(b) % URINES NEGATIVES FOR DDS					
Between regions	1411.87	1	1411.87	1.19	N.S.
Between sources within regions	4759.55	4	1189.89	11.29	< 0.01
Within sources	737.50	7	105.36		
TOTAL	6908.92	12			

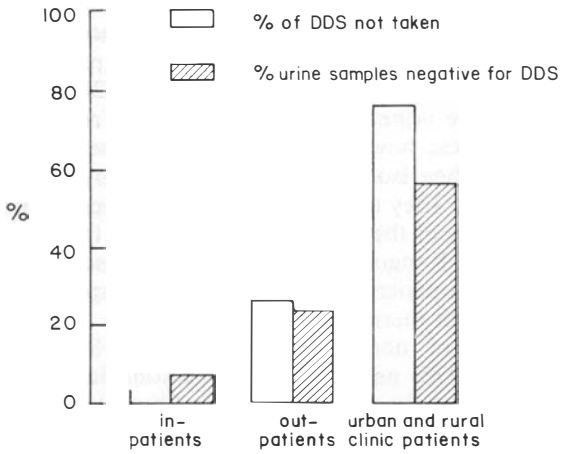

Fig. 2. Percentage estimates of non-compliance among different groups of leprosy patients.

results must, however, be interpreted with care. Leprosy patients attending out-patient departments in Mandalay and Rangoon weekly do not receive direct supervision of medication. Attendance at weekly intervals does, however, ensure continued motivation for compliance and continued supply of DDS tablets. The findings of an overall compliance rate of 74% and a totally non-compliant rate of 24% could be taken to indicate that a proportion of such patients are irregular attenders rather than poor tablet takers. This conclusion is supported by the observation that those urine samples which were positive for DDS contained on average as much drug as did the samples obtained from in-patients. By comparison, urban and rural clinic patients are not directly supervised at all. The estimates obtained in this group of 24% overall compliance and 56% total non-compliance are therefore likely to indicate more directly failure to adhere to the treatment regimen as such. In this case, for example, it is apparent that those patients who did comply took only half their tablets. In either instance, however, the findings show that there is substantial failure to take the drug in the absence of supervision. Such a conclusion warrants further discussion, as follows.

Because of the uncertainty of overlap in D/C concentration ratios between patients who are fully compliant and those not compliant with DDS therapy, no attempt was made to classify out-patients into those taking their doses regularly, irregularly or grossly irregularly (Ellard *et al.*, 1974*b*). Instead urines were classified as either positive or negative, by the use of the highest D/C concentration ratio in the blank values range. It is inevitable that some patients will be misclassified by this procedure and this is borne out by the finding that 5% of the in-patients from Mandalay and 9% of those from Rangoon had negative urines. It is, however, also possible, although unlikely, that even supervised in-patients do not absolutely reliably receive their medication, some patients consistently evading it.

The number of hospital out-patients found to have negative urines represents an unacceptable level of non-compliance. Those who attend hospital clinics are known to be well motivated to take their prescribed therapy and most are regular attenders. Even so, the finding that 24% of those attending the clinics had negative urines is of major concern. Urban and rural patients attending mobile clinics, however, present a more serious problem. These patients, by virtue of their isolation and life in a leprosy community, lack the motivation to be cured. They often fail to collect supplies of tablets, so it is not surprising to find many of them with negative urines. In the Taik Kyi, Hlegu and Hmawbi areas of Rangoon, the patients are prescribed higher doses of DDS than hospital out-patients in an attempt to compensate for the lack of motivation in taking their therapy.

The consequences of non-compliance with DDS therapy have been emphasized (Ellard, 1975) and it is clearly reasonable to conclude that the current prevalence of the disease in Burma (Tin Shwe, 1970) is at least partly a consequence of poor compliance among inadequately supervised patients. The practical solution appears to be to increase supervision with medication and our results support Ellard's suggestion that those patients who are relied upon to self-administer their DDS therapy require fully supervised intermittent therapy. This additional supervision could be given at clinic sessions with the proviso that those patients who default clinic attendances would be followed up.

This study has reinforced the idea that increased supervision with DDS therapy, both in hospital out-patients and urban and rural clinic patients in Burma, is urgently needed in order to reduce the prevalence of leprosy and the persistent emergence of new cases of this disease.

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References

Balakrishnan, S. (1977). Monitoring self-administration of dapsone by patients. *Lepr. India* **49,** 364.

Bratton, A. C. and Marshall, E. K., Jr. (1939). A new coupling component for sulfanilamide determination. *J. biol. Chem.* **128,** 537.

Ellard, G. A., Gammon, P. T., Helmy, H. S. and Rees, R. J. W. (1974*a*). Urine tests to monitor the self-administration of dapsone by leprosy patients. *Amer. J. trop. Med. Hyg.* **23,** 464.

Ellard, G. A. Gammon, P. T. and Harris, J. M. (1974*b*). The application of urine tests to monitor the regularity of dapsone self-administration. *Lepr. Rev.* **45,** 224.

Hagan, K. J. and Smith, S. E. (1979). Variability of urinary dapsone/creatinine concentration ratios in leprosy patients fully compliant with dapsone therapy. *Lepr. Rev.* **50,** 129.

Huikeshoven, H. C. J., Honhoff, C., Van Eys, G. J. J. M., Anten, J. G. F., Mayer, J. M. A. and Van Helden, H. P. T. (1976). Weekly self-medication of leprosy patients monitored by DDS/creatinine ratios in urines. *Lepr. Rev.* **47,** 201.

Kin Ma Gyi, Maung Maung Lwin, Yi Yi Myaing, Khin Maw Oo and Tin Shwe (1978). Reliability of dapsone self-administration by leprosy patients in the Rangoon area. *Lepr. Rev.* **49,** 283.

Low, S. J. M. and Pearson, J. M. H. (1974). Do leprosy patients take dapsone regularly? *Lepr. Rev.* **45,** 218.

Naik, S. S. and Ganapati, R. (1977). Regularity of dapsone intake by leprosy patients attending urban treatment centre. *Lepr. India,* **49,** 207.

Snedecor, G. W. and Cochran, W. G. (1967). *Statistical Methods,* 6th Edit., p. 285. Iowa State University Press, Ames.

Tin Shwe (1970). Leprosy in Burma. *Lepr. Rev.* **41,** 121.

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Immune Complex Glomerulonephritis in Leprosy

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Twenty patients with lepromatous or borderline leprosy selected at random were investigated for evidence of immune complex glomerulonephritis. Light, immunofluorescence and electron microscopy findings suggested that glomerulonephritis in leprosy results from the accumulation of immune complexes in glomeruli. Fluorescence and electron microscopy findings may be attributed to the fact that the deposits are less soluble immune complexes. A comparison was made between glomerulonephritis in the BSA-rabbit system and leprosy.

Introduction

Renal lesions in leprosy have been recognized by Mitsuda and Ogawa in 1937, in an autopsy analysis of 150 cases. Similar findings were also reported by Kean and Childress (1942). Impaired renal functions and abnormal urinary sediment have also been observed in patients with leprosy (Drutz and Gutman, 1973; Gokhale and Kurkure, 1958; Granells, 1968; Gutman *et al.*, 1973; Rea and Levan, 1975; Thomas *et al.*, 1970). After the introduction of percutaneous renal biopsy, the nature of renal lesions was shown by some authors (Bullock *et al.*, 1974; Date and Johny, 1975; Drutz and Gutman, 1972, 1973; Iveson *et al.*, 1975; Johny *et al.*, 1975; Mittal *et al.*, 1972; Sachdev *et al.*, 1969; Shwe, 1971). Renal amyloidosis, interstitial nephritis, pyelonephritis and proliferative glomerulonephritis were the significant lesions found in these studies. Recently, the immunological basis of the proliferative lesions was studied (Bullock *et al.*, 1974; Date and Johny, 1975; Drutz and Gutman, 1972; Iveson *et al.*, 1975; Shwe, 1971), but the number of patients was inadequate to support the idea. Therefore, we examined a large group of leprosy patients.

The purpose of the present study is to describe the changes seen by light, immunofluorescence and electron microscopy in the glomeruli of leprosy patients, and to get more information about the frequency of immune complex glomerulonephritis in leprosy as well as the dependency of the lesion on ENL reaction of the disease.

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Patients and Methods

From the patients admitted to the Bakırkoy Leprosy Sanatorium, of different clinical types with or without ENL and varying stages of therapy, 27 were selected at random. They were classified into lepromatous and borderline lepromatous groups according to the Ridley–Jopling immunological method. Twenty-four hour urine and blood samples of these patients were examined for proteinuria, urinary sediment, urea and creatinin clearance and electrolytes. ASTO levels in the sera were also determined. Percutaneous renal biopsy was performed with a Vim-Silvermann needle. The specimen was trisected for light, immunofluorescence and electron microscopy.

Paraffin sections from the specimens were stained with haematoxylin eosin, PAS, PASM, Cresyl violet, Masson's trichrome stain, and TRIFF.

Cryostat sections of the unfixed material about 5 μm in thickness were washed for 10 min in Coons' buffer (pH 7) and incubated for 30 min in a moist chamber with rabbit-anti-human gamma globulin G,M,A, and anti-complement conjugated with FITC. The preparations were examined by dark field fluorescent microscopy using a Zeiss photomicroscope equipped with an ultraviolet high pressure mercury lamp (HBO 200 W, barrier filter 244).

For electron microscopy, the tissues were fixed by immersion in 3% glutaraldehyde. They were then rinsed, postfixed in 1% osmium tetroxide in a Veronal acetate buffer, dehydrated in acetone and embedded in Vestopal-W. Sections were cut on a LKB ultratome. Survey sections were stained with Toluidine blue and examined by light microscopy. Ultrathin sections were picked up on hole grids and stained with uranyl acetate and lead citrate. They were examined in a Zeiss EM 9s-2 microscope.

Results

Table 1 shows the clinical, laboratory and light microscopy findings of the cases.

Adequate renal biopsy was obtained from 20 patients examined for this study. Sixteen of the 20 patients were males. The ages ranged from 23 to 70 years. Mean duration of disease was 18 years and ranged from 3 to 33 years. All of the patients had been on dapsone therapy. There were 18 cases of lepromatous type and 2 of borderline lepromatous type. Abnormal renal histology was seen in 12 of the 20 patients. Only 7 patients in the lepromatous group had recent history of ENL, and 4 of these patients had abnormal renal histology: 3 mesangioproliferative glomerulonephritis, 1 rapidly progressive glomerulonephritis. The kidney lesions were observed in 7 of the 13 patients without ENL reaction: 5 mesangioproliferative glomerulonephritis, 1 amyloidosis, 1 chronic pyelonephritis. One of the 2 borderline lepromatous group patients had mesangioproliferative glomerulonephritis. Acid-fast bacilli were not observed in the sections stained with TRIFF.

The main laboratory findings of the mesangioproliferative glomerulonephritis were trace proteinuria and haematuria. The patient with rapidly progressive glomerulonephritis had oedema, proteinuria, casts, leucocyturia and hypertension. A nephrotic syndrome was observed in the patient with

TABLE 1

Group	Age; sex	Type of disease	ENL	Pu	Hu	Lu
Proliferative						
Mesangioproliferative	46; M	LL	–	T	+	+
	28; M	LL	+	T	+	+
	36; M	LL	–	T	+	+
	53; M	BL	–	T	+	+
	42; F	LL	+	T	–	+
	25; F	LL	–	–	+	+
	35; F	LL	–	T	+	+
	32; M	LL	+	T	+	+
	48; M	LL	–	T	+	+
Rapidly progressive	34; M	LL	+	1*	+	+
Amyloidosis	35; M	LL	–	5*	M	–
Chronic pylonephritis	36; M	LL	–	T	+	+
Normal	31; M	LL	+	–	M	–
	57; M	LL	–	T	–	–
	23; M	LL	+	–	M	–
	46; M	LL	+	–	–	+
	37; M	BL	–	–	–	–
	42; M	LL	–	–	–	–
	46; M	LL	–	–	–	–
	70; F	LL	–	–	–	–

Pu: proteinuria; Hu: haematuria; Lu: leucocyturia; T: trace; M: micro.
*gr/lt.

amyloidosis. Pyuria, haematuria and trace proteinuria were found in the patient with chronic pyelonephritis.

(1) PROLIFERATIVE GLOMERULONEPHRITIS (10 patients)

(a) *Mesangioproliferative type*

Nine of the patients had mesangioproliferative changes. There was no suggestion of thickening of the GBM. There appeared to be a definite increase in mesangium (Fig. 1). It was not possible to view the small spike-like projections on the epithelial side of the GBM with PASM stain. Most of the glomeruli in the examined cases showed segmental and peripheral (Bowman capsule) adhesions. In two of the cases, protein substances were observed in the tubuli. Interstitium generally appeared to be normal. In the immunofluorescence study, there was a wide variation in the extent of deposition from patient to patient, which appeared to correlate with the histological findings and the clinical course of the disease. All of the accumulations were of granular pattern (Fig. 2). The mesangium appeared to be the most predilected area. In mild cases of mesangial proliferation, staining of the immune deposits was slight (Fig. 3). In more severe cases, granular deposits of IgG, IgM and C3 were seen in the mesangium. IgG, IgM and C3 were observed in all of the

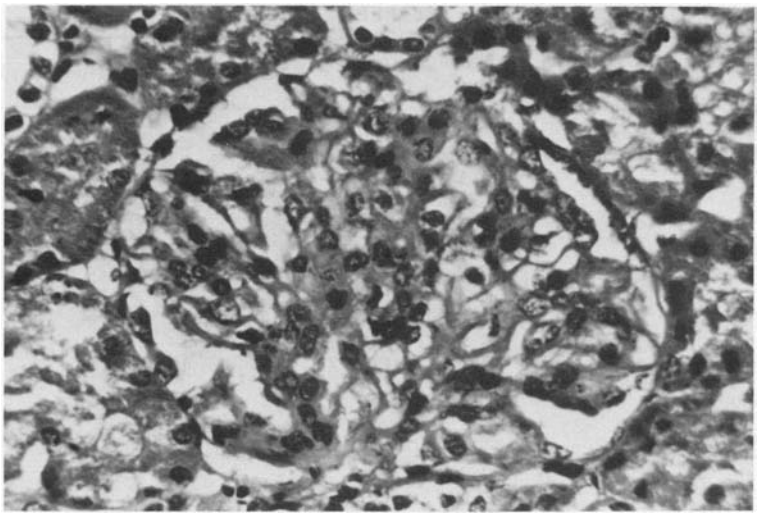

Fig. 1. Increase in matrix material in the mesangium with hypercellularity. (Case from mesangioproliferative group.) HE, × 500.

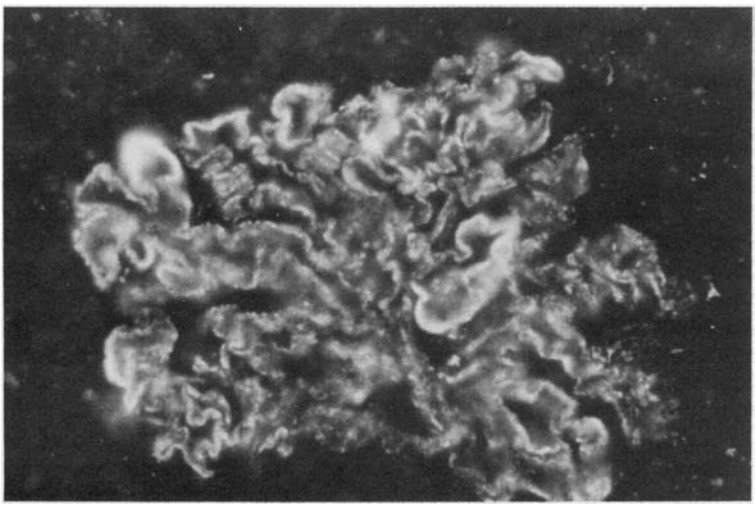

Fig. 2. Irregular deposits occupy the mesangium and occasionally the contiguous portions of the capillary walls. (Case from mesangioproliferative group.) Antibody specific for IgG, × 500.

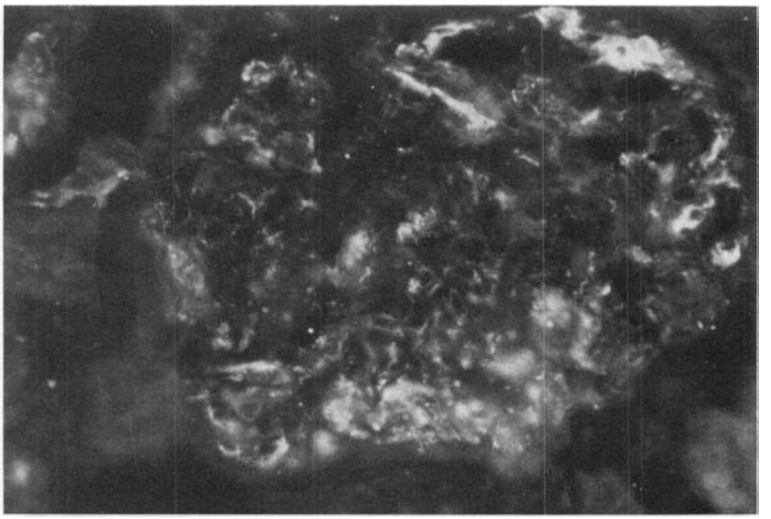

Fig. 3. Granular and patchy distribution of deposits. (Case from mesangioproliferative group.) Antibody specific for C3, × 500.

patients with mesangioproliferative changes. IgA was seen in 2 patients. In one of these cases, IgA was found in the glomeruli, and in the other one, it was observed in the epithelium of the proximal tubuli.

Electron microscopy study showed various structural abnormalities. Proliferation of mesangial cells and increase of mesangial matrix were the prominent findings. Another significant finding was that of electron-dense deposits (Figs 4 and 5). The deposits were seen within the proliferating mesangial matrix with occasional extension into the contiguous basement membrane and between the endothelium and basement membrane. Subepithelial deposits were not observed. There was focal fusion of epithelial foot processes.

(b) *Rapidly progressive glomerulonephritis*

One of the patients had severe clinical and laboratory findings. Light microscopy of specimen showed crescent formation in all of the examined glomeruli (Fig. 6). Tubuli were filled with a proteinaceous substance and there were interstitial inflammatory cells. Necrotizing arteritis was not observed. Fluorescence microscopy showed a slight granular staining of IgG and C3, in both mesangium and capillary walls. Electron microscopy failed to demonstrate the electron-dense deposits. The proliferating epithelial cells showed a great increase of cytoplasmic organelles.

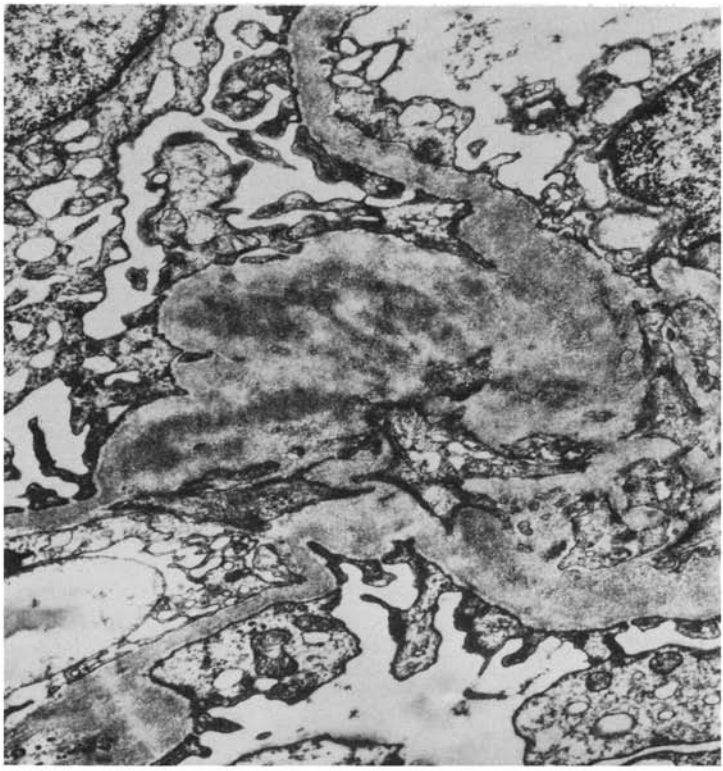

Fig. 4. Electron-dense deposits in an expanded mesangium. These extend for a short distance along the inner aspect of the glomerular loops, and are seen in subendothelial and intramembraneous position. Note the focal fusion of foot processes. (Case from mesangioproliferative group.) × 20,000.

(2) AMYLOIDOSIS (1 patient)

A pink, homogenous material was seen in the glomeruli and the walls of the arterioles. The substances showed a remarkably positive metachromasia when the section was stained with Cresyl violet. Thus, further study of this case was not commenced.

(3) CHRONIC PYELONEPHRITIS (1 patient)

Two hyalinized glomeruli surrounded with inflammatory cells were seen in the paraffin sections. Other studies were not performed.

Discussion

Kidney diseases are the most common causes of death in leprosy (Brusco and Masanti, 1963). The main problem is the relationship between disease and

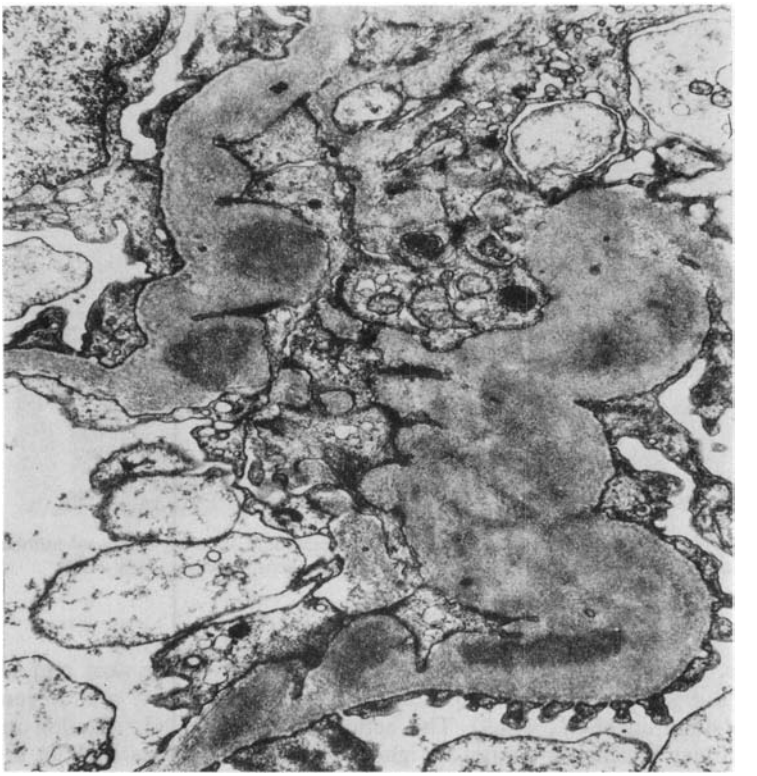

Fig. 5. Mesangial, subendothelial and intramembraneous deposits. (Case from mesangioproliferative group.) × 20,000.

the nephropathy. Much evidence speaks in favour of the existence of two different immunologic mechanisms in experimental as well as human glomerulonephritis. One involves deposition in the glomerular capillary walls and mesangium of antigen–antibody complexes formed in the circulating blood. The principal event in the other mechanism is deposition of antibody in the glomerular capillary walls due to the occurrence in the blood of an antibody which can react with the GBM. The last mechanism seems to be the least common in human glomerulonephritis.

Urine and renal abnormalities in leprosy are reported to be associated with ENL reactions (Bernard, 1971; Brusco and Masanti, 1963; Date and Johny, 1975; Drutz and Gutman, 1972; Gokhale and Kurkure, 1958; Granells, 1968; Gutman *et al.*, 1973; Johny *et al.*, 1975; McAdam *et al.*, 1975; Thomas *et al.*, 1970). Wemambu *et al.* (1969) suggested that ENL is a manifestation of the Arthus phenomenon. Waters *et al.* (1971) and Drutz *et al.* (1973) proposed that ENL is a result of the accumulation of immune complexes. During ENL

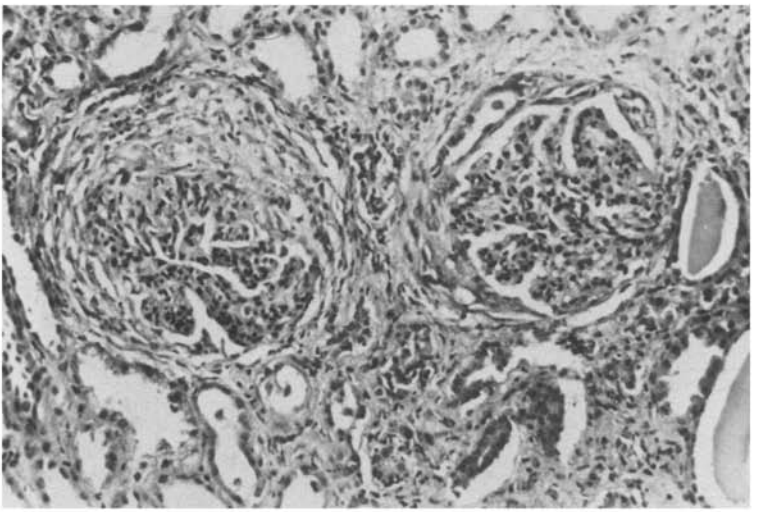

Fig. 6. Epithelial crescents surrounding two glomerular tufts showing increased numbers of mesangial cells. (Case from rapidly progressive glomerulonephritis group.) HE, × 200.

reactions, immune complex depositions were shown in the skin and blood vessels (Bullock *et al.*, 1974; Quismorio *et al.*, 1975; Turk and Bryceson, 1971; Wemambu *et al.*, 1969). The aetiologic role of ENL reaction in the nephropathies in leprosy cannot be ignored, but in 6 patients without a past history of ENL reaction, mesangioproliferative glomerulonephritis was found when our study was over. It seems quite well established that proliferative glomerulonephritis belongs to the broad class of immune complex glomerulonephritis, as seen in the present study. According to Job *et al.* (1964), ENL has 3 phases. The first is an acute phase, with subacute and chronic phases following the first phase. This description is similar to an experimental disease called the BSA-rabbit system. The results of the studies on the BSA-rabbit system indicated that immune complex size is the main determinant of the site of location of circulating complexes within the glomerulus and thus of the nature of the glomerulopathy (Germuth and Rodriguez, 1973). In the acute BSA-rabbit system a single injection of antigen is followed by an acute diffuse glomerulonephritis as a result of antigen–antibody complexes formed in the antigen excess. There are 3 different phases of disappearance of circulating immune complexes and lesions. In ENL, the acute release of mycobacterial antigens in the circulation, as a result of either normal breakdown of bacilli or drug therapy, permits the formation of circulating immune complexes formed in antigen excess. Thus, an acute diffuse glomerulonephritis may develop, as in cases reported by Drutz and Gutman (1972, 1973) and Date and Johny (1975). Haematuria and proteinuria are common findings in ENL, but do not indicate current renal disease, and the lesions may show a complete recovery within a period of several months if the

patient has a high antibody response. In the low antibody response form, it appears morphologically as a rapidly progressive glomerulonephritis, as shown in a case presented here. Clinically, there was a rapidly evolving renal failure terminating in irreversible uraemia in a few months. These kind of lesions found in patients with ENL resemble those produced in the acute BSA-rabbit system, and they are probably produced by the same mechanism.

Chronic glomerular lesions may develop when animals are exposed to prolonged antigen. In these animals, diffuse mesangioproliferative glomerulonephritis is found in a high proportion of those experiments which show a moderate antibody response, and circulating complexes are less soluble. Complexes developed in the moderate antibody response are localized primarily in the mesangium with occasional extension into the contiguous capillary walls. The mesangium responds eventually in the expansion of the mesangial cells and matrix that contain the deposited immune complexes into the capillary walls. In the present study, fluorescence and electron microscopy findings were attributed to the fact that the deposits are less soluble immune complexes and our patients with or without ENL had moderate immune response because the deposits were found primarily in the mesangium.

In the study of Johny *et al.* (1975), no definite relationship could be observed between the occurrence of glomerulonephritis and the presence of ENL. In 50% of the cases reported by Mittal *et al.* (1972), consisting of 6 lepromatous without ENL, 4 lepromatous with ENL and 5 non-lepromatous, histologic changes were seen in the kidneys. These results are very close to ours. In our cases, none of the 3 patients with ENL and 5 patients without ENL had any renal lesions, this finding may be related to the very high antibody response of these patients. The complexes formed are very large and are rapidly removed from the circulation by the RES, when there is a large amount of circulating antibody. These kinds of complexes are not responsible for glomerular lesions.

In this study, we have seen cases in which the patients with or without ENL had mesangioproliferative glomerulonephritis, which was established by three microscopical methods. According to our opinion, the incidence of renal involvement in leprosy depends mainly on the antibody response of the patients, thus the size of immune complexes. These results may be related to the selection of the patients, since the patients were selected at random and our findings are similar to the results of the studies made by Johny *et al.* (1975) and Mittal *et al.* (1972) who chose their patients at random as well.

In one biopsy specimen, granular deposits in the epithelium of proximal tubuli were observed with anti-human IgA. The pathological significance of tubular epithelium deposits is unknown, since it was not accompanied by any apparent lesion observable by light microscopy.

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References

Bernard, J. C. (1971). Estudio anatomopathologica de la distribucion de amiloidosis. *Leprologia* **16,** 15.

Brusco, C. M. and Masanti, J. G. (1963). Causes of death of leprosy patients; influence of lepra reactions and renal disease. *Int. J. Lepr.* **31,** 14.

Bullock, W. E., Callerame, M. L. and Panner, B. J. (1974). Immunohistologic alteration of skin and ultrastructural changes of glomerular basement membranes in leprosy. *Am. J. trop. Med. Hyg.* **23,** 81.

Date, A. and Johny, K. V. (1975). Glomerular subepithelial deposits in lepromatous leprosy. *Am. J. trop. Med. Hyg.* **24,** 853.

Drutz, D. J. and Gutman, R. A. (1972). The kidney in leprosy: an immunologic target organ. *Int. J. Lepr.* **40,** 217.

Drutz, D. J. and Gutman, R. A. (1973). Renal manifestations of leprosy. *Am. J. trop. Med. Hyg.* **22,** 496.

Germuth, F. G., Jr. and Rodriguez, E. (1973). *Immunopathology of the Renal Glomerulus.* Little, Brown and Company, Boston.

Gokhale, B. B. and Kurkure, N. B. (1958). Phenol red excretion test of kidney function in leprosy patients. *Ind. J. med. Sci.* **12,** 331.

Granells, M. (1968). Renal lesions in leprosy. *Int. J. Lepr.* **36,** 645.

Gutman, R. A., Lu, W.-H. and Drutz, D. J. (1973). Renal manifestations of leprosy. *Am. J. trop. Med. Hyg.* **22,** 223.

Iveson, J. M. I., McDougall, A. C., Leathem, A. J. and Harris, H. J. (1975). Lepromatous leprosy presenting with polyarthritis, myositis, and immune complex glomerulonephritis. *Br. med. J.* **3,** 619.

Job, C. K., Gude, S. and Macaden, V. P. (1964). Erythema nodosum leprosum. *Int. J. Lepr.* **32,** 177.

Johny, K. V., Karat, A. B. A., Rao, P. S. S. and Date, A. (1975). Glomerulonephritis in leprosy. A percutaneous renal biopsy study. *Lepr. Rev.* **46,** 29.

Kean, B. H. and Childress, M. E. (1942). A summary of 103 autopsies on leprosy patients on the Isthmus of Panama. *Int. J. Lepr.* **10,** 51.

McAdam, K. P. W. J., Anders, R. F., Smith, S. R., Russel, D. A. and Price, M. A. (1975). Association of amyloidosis with ENL reactions and recurrent neutrophil leucocytes in leprosy. *Lancet* **ii,** 572.

Mitsuda, K. and Ogawa, M. (1937). A study of one hundred and fifty autopsies on cases of leprosy. *Int. J. Lepr.* **5,** 53.

Mittal, M. M., Agarwal, S. C., Maheshwari, H. B. and Kumar, S. (1972). Renal lesions in leprosy. *Arch. Path.* **93,** 8.

Quismorio, F. P., Rea, T. H., Levan, N. E. and Friou, G. T. (1975). Immunoglobulin deposits in lepromatous leprosy skin. *Arch. Derm.* **111,** 331.

Rea, T. H. and Levan, N. E. (1975). Erythema nodosum leprosum in a general hospital. *Arch. Derm.* **111,** 1575.

Sachdev, J. C., Puri, D. and Bansal, S. (1969). Secondary amyloidosis in leprosy. *Lepr. India* **41,** 73.

Shwe, T. (1971). Immune complexes in glomeruli of patients with leprosy. *Lepr. Rev.* **52,** 282.

Thomas, G., Karat, A. B. A., Rao, P. S. S. and Prathapkumar, C. (1970). Changes in renal function during reactive phases of lepromatous leprosy. *Int. J. Lepr.* **38,** 170.

Turk, J. L. and Bryceson, A. D. M. (1971). Immunological phenomena in leprosy and related diseases. *Adv. Immun.* **13,** 209.

Waters, M. F. R., Turk, J. L. and Wemambu, S. N. C. (1971). Mechanism of reactions in leprosy. *Int. J. Lepr.* **39,** 417.

Wemambu, S. N. C., Turk, J. L., Waters, M. F. R. and Rees, R. J. W. (1969). Erythema nodosum leprosum. A clinical manifestation of the Arthus phenomenon. *Lancet* **ii,** 933.

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Methodology of Research into Social Aspects of Leprosy Control

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Given the goal of optimal dapsone intake, social scientific research needs to take into consideration *both* the socio-cultural and socio-medical settings in which dapsone is available.

Various techniques can help reveal what factors determine prompt self-reporting and regular clinic attendance, and what factors retard them. In our project (Western Province, Kenya and Mwanza Region, Tanzania 1974–76) we combined a factor analysis of data on patient registration cards (limited in value because of the low quality of the data) with in-depth interviewing (patients, relatives, neighbours, false-alarmists, community leaders, traditional doctors). With a set of "test" statements, we measured prevailing community attitudes towards leprosy patients and then compared the results with our observations. At the same time we interviewed health personnel intensively, and observed patient–staff interactions.

In-depth research is able to generate valuable suggestions for strengthening the leprosy services available, for training and retraining health personnel, and for educating patients and communities about leprosy control essentials.

Before selecting appropriate *research methods* for a particular investigation, the *problem* to be studied, and the *purpose* of the study must be carefully defined. If this problem is of a practical nature—-deficient case-finding and case-holding in leprosy control—and if the purpose of the enterprise is to propose possible solutions, then research must concentrate on gathering data immediately relevant to decision making. It should also produce results as quickly as possible, for those who take the decisions—doctors, in our case—will, presumably, be eager to implement the results. Costs must form another consideration in the choice of research procedures. Where a country's resources are barely sufficient to cover the basic needs of its inhabitants, it is imperative to take a hard look at the kinds of results yielded by some of the expensive research techniques developed in Western societies. To what extent are these techniques appropriate in a non-Western situation, and do the benefits justify the costs? Never, however, should restrictions in available time and money seduce us into coming up with results that are superficial, and thus misleading. To put it briefly: the research must be *relevant, reliable, quick,* and *cheap.*

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I should like to elaborate on these points by critically evaluating research we carried out between 1974 and 1976 in two leprosy control schemes in East Africa, our team consisting of five medical anthropologists and sociologists. The problem seemed clear: both in the Mwanza Regional Leprosy Control Scheme in Mwanza Region, Tanzania, and in the West Kenya Leprosy Control Project in Western Province, Kenya, case-finding and case-holding achievements were disappointing. Although between 65 and 80% of the estimated case-load in Mwanza Region and Western Province had been traced, when we began our research only about 30% of the patients registered were "under control", i.e., under regular (out-patient) treatment or officially declared cured. That potentially infectious cases appeared slightly more regular in attendance offered only minor consolation, when almost half of all the registered leprosy patients were lost sight of before being officially discharged. Could we, the doctors asked, help find out why most patients came forward for treatment in a relatively late stage of their disease? why so many "defaulted", and why others never showed up at all? Could we assist in formulating recommendations for the improvement of case-finding and case-holding activities, and could we suggest ways to implement these recommendations?

To start with, we redefined the problem. We identified case-finding and case-holding difficulties as *communication problems* involving two parties: the *medical staff,* with services to offer, and *patients and other community members,* with a need for these services. It was clear that both parties required study if we were to understand weak points in their mutual understanding. Such study takes time. Before a social scientist can make a useful contribution, he must both learn the ins and outs of the medical organization in question, and the ins and outs of the society within which the medical organization operates. Our research in leprosy control problems in Mwanza Region and Western Province occupied us, collectively, for almost two years. This first experience in East Africa, however, has enabled us to come to grips with essential issues more efficiently in places where we have worked since (e.g. Nigeria, and Botswana's National Tuberculosis Programme).

When selecting our research methods we could choose between two different approaches. One is the so-called *quantitative* or *survey approach,* developed by Western sociologists. Among a carefully selected sample of the population under study—which may include hundreds of informants—sociologists systematically gather information which they assume will give them insight into the problems they are investigating. To this end they devise strictly structured questionnaires. Answers are usually precoded to facilitate data processing by computer. The computer analyses which variables influence each other and to what degree. Thus, to illustrate from our own field of study, we can find out to what extent a favourable or unfavourable attendance of leprosy patients is related to their sex, age, type of leprosy, economic situation, or level of education. By means of a factor analysis, the computer is, moreover, able to reveal the comparative importance of the different variables related to patients' attendance. A patient's economic status, for example, may prove more decisive for compliance with treatment prescriptions than his type of leprosy or degree of deformities.

The other research approach stems from anthropology. It is sometimes labelled as the *qualitative* or *"understanding" approach.* The main research method has become known under the term "participant observation". By living among the people he is investigating, an anthropologist becomes *nolens volens* involved in the life of the community, even though his participation is as a rule largely passive. By keeping his eyes and ears wide open—and instructing his one or two well-trained research assistants to do the same—he will gather some extremely valuable information which he could never have obtained by means of questioning only. Even so, nowadays most anthropologists will, in addition, also question representative samples of informants on specific topics of interest. It would otherwise be impossible to generalize findings pertaining to the entire research population. Still, the anthropologist's technique of questioning differs significantly from the sociologist's. It is less fixed, and in leaving space for discussion with the informant, it creates opportunities for relevant information to merge spontaneously in the course of such discussions. . . the more, the better. An anthropologist, in trying to understand the problem he is investigating as thoroughly as possible, will prefer to go back to the same informant four or five times, rather than end up with a collection of superficial impressions by talking only once to five times as many informants. Consequently he will work with a limited number of informants, and usually in a restricted area. No matter how thought-provoking his conclusions may be, however, further research must demonstrate whether and to what extent they are applicable in other areas as well. The anthropologist's qualitative approach, therefore, has its limitations. But so does the survey approach. Sociologists themselves have expressed their doubts about the value of mass surveys, especially in developing countries, where several studies have clearly shown how difficult it is to obtain reliable answers by means of such data gathering (Pausewang, 1973).

Since both methods have their merits and weaknesses, a combination seems to offer better prospects for fruitful research. This is what we attempted in the Mwanza and West Kenya leprosy control schemes. In both areas we began with a quantitative analysis of patients' medical history cards and attendance records, a sample of 1760 cards in Mwanza Region, and of 1000 cards in Western Province. By feeding coded data to a computer, we expected to obtain detailed information about the composition of the patient population with regard to age, sex, type of leprosy, development of the disease, attendance history, geographical distribution, which would enable us to define a sample of patients for further in-depth interviewing. Also, we hoped to identify some variables affecting attendance behaviour. The preparations in the field for the computer analysis took five months. The analysis itself (2 months) took place in Holland. Within five months, a report with results was available. Our remaining year and a half in the field was spent interviewing and observing in two areas in Western Province inhabited by the Luhya, and in one larger area in Mwanza Region where the Sukuma live. The Sukuma like the Luhya, are a Bantu speaking tribe. We spoke with some 200 patients, with their relatives, neighbours, other members of the community (both prominent and less prominent), with traditional doctors, and with some 115 representatives of the leprosy and general health services scattered throughout Western Province and Mwanza Region.

The *quantitative analysis* which we undertook proved costly, both in terms of time and money. And, no matter how technologically advanced a computer may be, if data are incomplete and unreliable, computer calculations can be of only limited value. For our factor analysis of variables related to attendance, patient cards and attendance registers provided data which varied considerably in quality. They contained—or, were supposed to contain—a number of *medical variables*, which we assumed would influence a patient's motivation to come for treatment. Among them: activity of the disease, reactions, number and visibility of lesions, degree of deformity. Further, in providing data on the organization and quality of the services, they contained a number of *medical-sociological variables* such as: training of fieldworker, amount of supervision (the last date on which any assessment of the patient's clinical activity had been made proved an effective clue), the number of home-visits paid, home-clinic distance. These cards, however, contained hardly any *socio-cultural variables.* Only the patient's age and sex were recorded; there was nothing recorded about level of education or the patient's socio-economic status.

Not only were a number of crucial variables lacking, especially in the socio-cultural category, but also, data that should have been filled in were all too frequently missing, or unreliable. Attendance records sometimes seemed to have led a life of their own, irrespective of a fieldworker's presence or absence on clinic days.

The principal reason, however, for the limited utility of our attempts at finding out by means of a factor analysis which variables were related to patients' attendance was that there existed such fluctuations in the actual functioning of the leprosy services themselves. When services are provided irregularly, or even discontinued at certain clinics, complicated calculations in order to reveal which patients default and why, become meaningless. At least a rudimentary service must exist, continuously, throughout the entire area (tablets must always be available at the appointed time and place), before it makes sense to undertake such an analysis.

After these qualifying remarks it seems legitimate to ask: did we gain anything at all from the analysis? Fortunately, we did.

(1) We did not get a 100% accurate, but still the best possible picture of the composition of the patient population. From this we could select our sample of patients and ex-patients for in-depth interviews.

(2) Especially in Mwanza, where patient data were more complete and reliable than in Western Province, cross-tabulations between patients' attendance behaviour and available variables gave at least *some* insight into the identity of those who come regularly for treatment, and those who don't, e.g. deformed patients, who reported themselves with leprosy when middle-aged, and who live not further than five miles from their leprosy clinic, are predictably better attenders than those without deformities, who contract leprosy in their youth or old age, are found in a school or mass survey and/or are living further than five miles away from a treatment point.

(3) Cohort analysis of patients' disease- and attendance-history, per year of registration (the only way to thoroughly evaluate the progress made by a leprosy scheme and to compare the achievements of different schemes), became comparatively easy.

(4) Generalization about individual attendance patterns became feasible. We only did this in Mwanza, where attendance data were relatively complete. We found that by far most patients "default" within two years after being registered. Once a patient has established a stable pattern of visiting clinics, he appears to carry on. This finding proves how urgent it is to devote special attention to new patients, offering them relevant health-education, and visiting them after any early absence.

(5) The results of the computer analysis evoked more questions than it solved, thus providing a challenge for the next phase of in-depth interviewing. It was, for instance, clear that socio-cultural factors could not explain why in a culturally homogeneous, predominantly rural area, the percentage of regularly attending patients varied from 20 to 90% within a radius of 100 km. We would have to look as deeply into the organization of the service and the motivation of leprosy workers to do their jobs, as into the socio-cultural background of patients and their motivation to come for treatment. *Difference in quality of the service* became an important criterion for the choice of the areas in which we conducted our interviews. In Western Province we selected the Wanga locations because part of the services appeared to function very well, the Busuku locations because they functioned rather poorly. As fieldwork progressed we discovered that the Wanga's provided an even more interesting research situation than expected: its two fieldworkers differed significantly in dedication to their work. Under such circumstances it is as interesting to find out which patients disappear from treatment and why, even when the service is reasonable or good, as it is to know which patients will struggle to get treatment, even if the service functions poorly.

The question remains whether a computer analysis is the best way to obtain these positive results in countries where computers are scarce and have long waiting lists of clients. In our eyes the answer must be NO. Hertroys' (1974) analysis of every tenth patient registration card in Mwanza, and our own analysis (Varkevisser, 1977; Paape and Varkevisser, 1978) of some 2000 TB patient cards in Botswana, by hand, with the assistance of a small calculator only, produced simple but relevant information many times more cheaply, and more quickly.

Far more rewarding and revealing than our quantitative analysis of medical records—both for ourselves and, we feel, for the doctors—were our in-depth interviews. The technique we used when speaking with patients and ex-patients can be described as a *topic-wise, loosely structured interview*. Together we developed a schedule of items we wanted to cover, rather than a strict questionnaire. Generally, we would pose some leading questions: "How did your disease begin?" and "How do you feel now?" . . . then letting the patient determine the further course of topics. Within limits, of course. In the evenings we organized notes, making sure that we had obtained all the information we wanted. Wishing to understand the full process each patient had gone through, from the moment of first noticing a possible leprosy symptom down to the present, we time and again returned to the same informant, encouraging him or her to talk about their lives. In addition, we tried our best to speak with many

satellite informants: the spouses, relatives, and neighbours of a patient. This was not only to verify what we had heard from the patients themselves, but also to enrich our picture of reality. How had the patients, how had their neighbours and relatives reacted to the disease? Of particular importance to this stage of our research was an evaluation of the role of treatment, both traditional and modern, in patient–community relations.

Our team intentionally discarded the idea of working with fixed questionnaires such as used, for example, in KAP (Knowledge, Attitude, Perception) studies. One reason for this decision was that patients, when talking about their lives, are reserved. They are hesitant to reveal painful encounters with relatives or community members, reluctant to confess how long it took them to report for modern treatment. Often, it wasn't until during a later interview that we could discover how earlier on we had been deliberately deceived. Our one guiding rule was never to accept any statement at its face value. We had to develop patience, until successive interviews with patients, relatives, and fellow villagers generated a consistent picture. A fixed questionnaire would no doubt have yielded results . . . quite specific ones, quite readable and, we are convinced, quite misleading and superficial!

The stress of such probing, in-depth research on the one carrying it out is considerable. There is always that gap between what you want to know and what you get to know. It is a gap that can only be bridged slowly and gradually, if ever. Often the most valuable information, the real "eye openers" will come unexpectedly. And yet, the researcher must at all costs avoid being suggestive, especially where such relatively free interviews do entail the danger of his own personality introducing a strongly subjective element. Close cooperation with fellow researchers, however, can help correct this.

Although we judged *strictly structured questionnaires* unsuitable for teaching us much about the reality of interaction between patients, community, and health staff personnel, they did prove useful in bringing to light the generally accepted "code of behaviour" towards leprosy patients. In an attempt to specify the areas of social interaction where the stigma surrounding leprosy was relatively intense or weak, we drew up a set of statements concerning both actual and wished for behaviour on the part of leprosy patients. For example: "A leprosy patient cannot marry", and "A leprosy patient should not be allowed to marry". We then asked informants if they agreed, disagreed, or agreed in part with the statements. Then we invited the informant to comment. This aspect of our study showed us that there was a widespread discrepancy between, on the one hand, fear of "the leprosy patient" as a stereotype, with the accompanying desire to impose restrictions on his behaviour and, on the other hand, the actual tolerance we observed towards specific patients. In their dealings with a particular relative or neighbour who had leprosy, people would largely maintain ordinary forms of behaviour . . . if, that is, the patient was receiving treatment, and/or his disease "cooled down".

For interviews with health staff, we used a *combination of topic-wise, relatively free interviews,* and a number of *fixed questions, albeit open-ended.* We employed free interviews; we wanted staff's opinion on bottlenecks in the service, and on possible remedies; we were more pointed when we wished to

learn about the procedures followed in their treatment of patients, and to test their knowledge about leprosy.

Finally, *observation*, followed by discussions with research assistants about what we had seen, formed an invaluable, complementary research method. We deliberately frequented social gatherings (beer clubs, markets, celebrations), in order to observe interaction between patients and community members, and asked our research assistants to do the same, often by themselves. They, with or without us, systematically attended clinic days in our research area to observe over time the interaction between health staff and patients. This way we could evaluate the leprosy services from three angles: from what health staff had told us, from what patients had told us, and from our own observations.

By way of summary, one could say that, although the various methods we used all had drawbacks as well as merits, *in combination* they worked well. Those team members who have remained involved in this type of investigation feel, however, that research is most fruitful when it is clear from the beginning that researchers will share in the responsibility for implementing results. On this basis we are now working in Botswana, hoping to soon start in Indonesia as well. Our practical contribution principally concerns the field of health education, the training of staff, and (re)organization of treatment procedures at base level.

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Research reports are available at the Royal Tropical Institute, Mauritskade 63, Amsterdam, Holland

References

Hertroys, A. R. (1974). A study of some factors affecting attendance of patients in leprosy control scheme. *Int. J. Lepr.* **42,** 419.

Paape, M. and Varkevisser, C. M. (1978). Evaluation of attendance behaviour of TB patients who were registered at Athlone Hospital, Lobatse and at SDA Hospital, Kanye, during 1976 and 1977, and of patients' intake of medicines. Preliminary Report, Ministry of Health, Botswana, 1978.

Pausewang, S. (1973). *Methods and Concepts of Social Research in the Rural Developing Society.* Weltforum, Munchen, 1973.

Varkevisser, C. M. (1977). TB control in Botswana; problem identification. Report to the Royal Tropical Institute, Amsterdam, 1977.

Lepr. Rev. (1979) **50,** 231–237

Field Workers' Forum

If suitable manuscripts are forthcoming, we hope to revive *Field Workers' Forum* in *Leprosy Review*, and we begin by listing some of the publications which were examined in the *Workshop on Teaching Materials* at the recent *XI International Leprosy Congress in Mexico*, kindly supplied by Dr W. Felton Ross of American Leprosy Missions, Inc., 1262 Broad Street, Bloomfield, N. J. 07003, U.S.A.

[Although these are all available (somewhere) it should not be assumed that they are necessarily all still in print, or immediately available from the addresses given.]

Editor

LITERATURE ON LEPROSY

Publications in French

(1) *Acta Clinica*
Lepra. Documenta Geigy
Browne, S. G.
J. R. Geigy, Basle, Switzerland

(2) *La Lèpre*—Epidémiologie—Principes de Lutte—1976
Sansarricq, H.
WHO Leprosy Unit, 1211 Geneva 27, Switzerland

(3) *La Lèpre en Afrique*—1977
Loven
OCCGE Foundation Follereau, 33 Rue de Dantzig 75015 Paris, France

(4) *La Lutte contre la Lèpre*—1977
Languillon, J.
Institute de Léprologie Appliquée de Dakar—BP 11.23 CD Annex Dakar, Sénégal
Foundation de L'Ordre de Malte
Part 1. La Lutte—61 pages
Part 2. Physiothérapie et Education Sanitaire—44 pages (Foolscap)

(5) *Lignes Directrices de Lutte*—Contre la lèpre
Van Drogenbroeck, J.
ALERT—P.O. Box 165, Addis Ababa, Ethiopia

(6) *Lutte contre la Lèpre*
Nebout
Presse Africain

(7) *Un Manuel pour le Diagnostic et le Traitement de la Lèpre*—1978, Revis.
Look, LOC
ALM, INC, 1262 Broad St., Bloomfield, N. J. 07003
(Private circulation)
OUESSO, République Populaire du Congo—58 pages

Publications in Italian

(1) *Acta Clinica*
Documenta Geigy
Browne, S. G.
J. R. Geigy, Basle, Switzerland
(2) *Diagnosi e Terapia della Lebbra Iniziale*
Browne, S. G.
Amici Dei Leprosi
Via Borselli 4–40135—Bologna, Italy
(3) *Fondamenti de Leprologia*
Ross, W. F.
ALERT, P.O. Box 165, Addis Ababa, Ethiopia
Associazione Nazionale Amici Dei Lebbrosi, 40135 Bologna, Via Borselli 4, Italy
(4) *La Lebbra nella Bibbia*
Browne, S. G.
Amici Dei Lebbrosi, 40135 Bologna, Via Borselli 4, Italy

Publications in Spanish

(1) *Anatomia Funcional de la Mano*—1978
Exploracion Funcional de la Mano
Pathologia de la Mano en el Enforma de Lepra
Arvelo, Jose
Instituto Nacional de Dermatologia, Apartado 4043, Caracas 101, Venezuela
(2) *Donde no hay Doctor*—1975
Werner, David
Editorial Pax—Mexico
Libreria Carlo Cesarman, SA
Rep. Argentina 0, Mexico, DF
(3) *Lecciones de Leprologia*
Terencio de Las Aguas, J.
Fontilles Leprosarium, Fontilles Alicante, Spain

Publications in German

(1) *Acta Clinica*
Documenta Geigy
Browne, S. G.
J. R. Geigy, Basle, Switzerland

Publications in English

CATALOGUES

A. *Appropriate Technology Sourcebook*—A guide to practical books and plans for village and small community technology
Darrow, Ken and Pam, Rick of Volunteers in Asia
Box 4543, Stanford, California 94305, U.S.A.

B. *A Short List of English Titles*
Scientific Publications series, PAHO, Washington DC, U.S.A.

C. *Books for Health Workers in the English-Speaking Countries of East, Central and Southern Africa*
Commonwealth Regional Health Secretariat, African Med. and Research Foundation
Printer—AMREF, Box 30125, Nairobi, Kenya—47 pages

D. *Catalogue of Educational Materials*
VHAI, C–14 Community Centre, Safdarjung Development Area New Delhi, 110–016, India

GENERAL LITERATURE

(1) *A Book of Home Study Courses*
A Self Instructional System
U.S. Dept. of Health Education and Welfare, Public Health Service

(2) *A Laboratory Manual for Rural Tropical Hospitals*—1976
Cheesbrough, Monica (1 page on leprosy)
Churchill Livingstone, 15–17 Teviot Place, Edinburgh EH1 2XX
London/New York

(3) *A Medical Laboratory for Developing Countries*—1973
(A six page section on leprosy)
King, Maurice
Oxford University Press, Ely House, London W1, England

(4) *A Textbook for Auxiliary Nurse Midwives*
(Two pages on leprosy)
Chalkey, A. M.
Christian Literature Crusade, P.O. Box 501, Parktown, Madras 600–003, South India—491 pages

(5) *Diagnostic Pathways in Clinical Medicine*—1976
An Epidemiological Approach to Clinical Problems
Essex, B. J.
Churchill Livingstone, Edinburgh, London, and New York—1976 173 pages

(6) *Learning with Modules*—Facilitating Teaching
An Approach for Nurse Midwife Teachers
Produced by Division of Health Manpower Development
WHO 1211 Geneva 27, Switzerland

(7) *The Book of Outlines*—1977
Hasan, S.
Hind Kusht Nivaran Sangh, 1 Red Cross Rd., New Delhi, 110001, India

(8) *Teaching for Effective Learning*—A short guide for teachers of health auxiliaries
Wakeford, Richard E.
WHO—Health Manpower Division

(9) *Where There is No Doctor*—1977
(A village health care handbook)
Werner, David
The Hesperian Foundation, Palo Alto, California
T.A.L.C. London, Rural Communications, England

JOURNALS

(1) *AFYA—A Journal for Medical and Health Workers*
Editor: Dr H. de Glanville—Six issues annually
AFYA, P.O. Box 31025, Nairobi, Kenya
(2) *News Bulletin of the National Leprosy Organization*
Periodical suitable for Health Workers 2 & 2
National Leprosy Organization of India
Published by: Secretary, National Leprosy Organization, Hindinagar, Wardha, India
(3) *Partners—Magazine for Paramedical Workers in Leprosy* (also in French)
The Leprosy Mission, 50 Portland Place, London, W1N 3DG, England
(4) *International Journal of Leprosy, Leprosy Review, Leprosy in India,* and many others: these are not listed in full here; details are readily available from current issues *(Editor).*

LEPROSY LITERATURE

(1) *Additional Leprosy Notes for Senior Leprosy Assistants*—1978
Blenska, W.
St. Francis leprosarium, P.O. Box 151, Bukoba, Uganda—typed
(2) *A Footwear Manual for Leprosy Control Programs*—Parts 1 & 2—1978
Neville, P. Jane
ALERT, Box 165, Addis Ababa, Ethiopia and DAHW, Postfach 348, 8700 Würzburg 11, Germany
(3) *A Guide to Health Education in Leprosy*
Neville, P. Jane
ALERT, Box 165, Addis Ababa, Ethiopia
(4) *A Guide to Leprosy and Leprosy Control*—1975
Kapoor, P.
Poona Dist. Leprosy Committee, Red Cross Blood Bank Bldg, Rastre Post, Poona 411–011 (Dr J. M. Mehta)
(5) *A Guide to Leprosy for Field Staff*—1977
All Africa Leprosy and Rehab. Training Centre—Director and Staff (62 pages)
ALERT, Box 165, Addis Ababa, Ethiopia or African Medical Research Foundation, Nairobi, Kenya
(6) *An Introduction to the Understanding and Diagnosis of Leprosy*—1968
Wiersna—Jan. P.—AFIP
Washington, DC 20305, U.S.A.— A book and slide set

(7) *A Practical Guide in the Diagnosis and Treatment of Leprosy in the Basic Health Unit*—1978
Wheate, H. W.—Pearson, J. M. H.
ALERT, Box 165, Addis Ababa, Ethiopia—26 pages

(8) *A Window on Leprosy*—1977
Chatterjee, B. R. and others
Hind Kusht Nivaran Sangh (Indian Leprosy Assoc.), 1 Red Cross Road, New Delhi 110001—395 pages

(9) *Basic Knowledge about Leprosy*
West African leprosy Secretariat, P.O. Box 673, Freetown, Sierra Leone, West Africa
Associazione Naz. Amici Dei Lebbrosi, 40135 Bologna, Via Borselli 4, Italy

(10) *Better Care in Leprosy*—Before Treatment, After Treatment—1978
Laugesen, Murray
Voluntary Health Association of India, c14 Community Center Safdarjang Development Area, New Delhi 110 016, India—64 pages

(11) *Dermatoses in Dark-skinned people*—8 Booklets
Verhagen, A. R.
Ciba-Geigy, Medical Dept (Publications), Basle, Switzerland

(12) *Essentials of Leprosy*—1977
Pearson, J. M. H. and Wheate, H. W.
ALERT, Box 165, Addis Ababa, Ethiopia, also available from:
German Leprosy Relief Association, 87 Würzburg 1, Dominikanerplatz 4, Postfach 348, Würzburg, W. Germany

(13) *Evaluation Tests for Leprosy Assistant Students*
Blenska, W.
St. Francis Leprosarium P.O. Box 151, Bukoba, Uganda—typed

(14) *Greater Calcutta Leprosy Teaching and Health Education Notes*—1978
Chaudry, D. S.
Vol. 1 Leprosy; Vol. 2 Anatomy and Physiology; Vol. 3 Communicable Diseases; Vol. 4 First Aid.
Private Circulation—14/2A Broad St, Calcutta 70019, India

(15) *Guidelines for the Campaign Against Leprosy*—1976
Text: Medical Commission of ILEP—22 pages
Also available from DAHW (German Leprosy Relief Association), 87 Würzburg 1, Dominikanerplatz 4, Postfach 348, Würzburg, W. Germany

(16) *Handbook on Leprosy*—Second Edition—1978
Jopling, W. H.
Heinemann Medical Books Ltd, London

(17) *Health Centre Laboratory Manual*
For Tropical Countries
Cheesbrough, Monica
Rural Communications, South Petherton, Somerset U.K. TA13 5BS
Cost £1.50 + 54p postage ($4.00 U.S.)

(18) *Hints on Diagnosis and Treatment of Leprosy*—Third Edition—1975
Wardekar, R. V.
Gandhi Memorial Leprosy Foundation, Post Kindingar, Warda 442103 Maharashtra, India

(19) *Insensitive Feet*—Revised 1977
Brand, P. W.
The Leprosy Mission, 50 Portland Pl., London W1N 3DG, England—88 pages

(20) *Leprosy and Other Diseases in the Three Wangas: Community Thought Patterns About Health Care and Their Consequence for Emergent Patients*—(One of four monographs on social aspects of leprosy)
Bijleveld, Iman
Royal Tropical Institute, Dept of Social Research, Amsterdam OOST, 63 Mauritskade, Netherlands

(21) *Leprosy Diagnosis and Management*—1975
Job, C. K., Selvapandian, A. J. and Kurliar, P. V.
Hind Kusht Nivaran Sangh, New Delhi, 1 Red Cross Rd, New Delhi 11000, India—93 pages + illustrations

(22) *Leprosy for Medical Students & Practitioners*—1978
Koticha, K. K.
Acworth Leprosy Hospital, Bombay 400–031, India—32 pages

(23) *Leprosy for Paramedicals*—In Process
Ross, W. F.
American Leprosy Missions, Inc. 1262 Broad St, Bloomfield, N. J. 07003

(24) *Leprosy for Students of Medicine*—1979, Second Edition
Bryceson, A. and Pfaltzgraff, R. E.
Churchill Livingstone, 15–17 Teviot Place, EH1 2XX, Edinburgh–152 pages

(25) *Leprosy in Children*—1976
Noussitou, F. M.
WHO 1211 Geneva 27, Switzerland—28 pages

(26) *Leprosy in England, Yesterday and Today*—1977
Browne, S. G.
The Leprosy Study Centre, 57A Wimpole St, London W1M 7DF, England

(27) *Memorandum on Leprosy Control*—1971
Browne, S. G.
Issued jointly by Oxfam, Lepra and The Leprosy Mission—27 pages
TLM, 50 Portland Pl., London W1N 3DG, England

(28) *Notes on Hansen's Disease*—1973
Coffin, D.
Kumi Leprosy Centre, P.O. Box 9, Kumi, (S. Teso), Uganda—55 pages

(29) *Notes on Hansen's Disease*—1978
Blenska, W.
Kumi Leprosy Centre, Kumi, Uganda, P.O. Box 9

(30) *Physical Therapy in Leprosy for Paramedicals*—1978
Kelly, Ellen Davis
American Leprosy Missions, 1262 Broad St, Bloomfield, N. J. 07003

(31) *Questions People Ask About Leprosy*
Ross, W. F.
American Leprosy Missions, 1262 Broad St, Bloomfield, N. J. 07003

(32) *Take Care of Your Feet*
Produced by participants—Workshop on Development, Educational Manual of Leprosy
Philippine Leprosy Mission, P.O. Box 718, Manila, Philippines

(33) *Textbook of Leprosy for Students and Paramedicals*—1975
Thangaraj, R. H.
The Leprosy Mission, 50 Portland Place, London W1N 3DG, England

(34) *Teaching Material on Leprosy and Leprosy Control*
Korean Leprosy Institute, San 87, Ojeon-ri, Euwang-myun, Shihung-gun, Kyeonggi-do, Korea—66 pages

(35) *The Care and Prevention of Injuries to Insensitive Feet*
Bonnette, Allen R.
U.S. Public Health Service Hospital, Carville, 70721, Louisiana

(36 *The Diagnosis and Management of Early Leprosy*
Leprosy Today—1976—35 pages
Browne, S. G.
The Leprosy Mission, 50 Portland Place, London, W1N 3DG, England

(37) *The Memories and Reflections of Dr Gerhard Armauer Hansen*
German Leprosy Relief Association, D–8700 Würzburg 11, Postfach 348, Germany—135 pages

(38) *Watch Those Eyes*
Brand, Margaret
The Leprosy Mission, 50 Portland Place, London W1N 3DG, England

(39) *What You Should Know About Leprosy*
Koticha, K. K.
Acworth Leprosy Hospital, Bombay 400–031, India—22 pages

(40) *The Book of Outlines*—1977
Hasan, S.
Hind Kusht Nivaran Sangh, 1 Red Cross Rd, New Delhi, 110001, India

Lepr. Rev. (1979) **50,** 238–242

Leprosy and the Community

THE INTERNATIONAL YEAR OF THE CHILD AND WHO

The following summary appeared in the *WHO Chronicle* **33,** 3–6 (1979)—

1979 is the International Year of the Child (IYC), the general objectives of which are fully in line with one of the basic principles of WHO, as indicated in the preamble to the WHO Constitution, adopted in 1948. This states that "healthy development of the child is of basic importance; the ability to live harmoniously in a changing total environment is essential to such development". In addition, one of the main functions of the Organization is "the promotion of maternal and child health and welfare". The major emphasis in WHO's efforts in relation to the International Year of the Child will be to bring out the importance of investment in children and the interrelationships between child health, education and welfare, and socioeconomic development. In other words, the child is both a beneficiary of and a potential contributor to the development process.

A WHO Press Release WHO/9 of 22nd March, 1979 drew further attention to—

Focus on the Child in World Health Day Issue of *World Health*

Of the 125 million children born in 1978, twelve million—mostly in developing countries—are not likely to live to see their first birthday. Dr Halfdan Mahler, Director-General of WHO, reports this appalling figure in the February–March issue of *World Health*, which commemorates both the International Year of the Child and the World Health Day theme—"A healthy child, a sure future".

Dr Mahler states that over 80% of all children alive today live in developing countries, a majority of them in an environment characterized by malnutrition, infection, poor housing, lack of safe water and sanitation, and inadequate health care. He goes on: "Starting with such a serious disadvantage, most of these children have little chance of realizing their full economic and social potential. They will in turn give birth to another unhealthy generation, thus helping to perpetuate a vicious cycle".

Pointing out that World Health Day—8 April—this year will be an occasion to rouse the world's social conscience to the plight of millions of youngsters, Dr Mahler calls for a radical new approach, basing itself on primary health care and emphasizing the just distribution of health resources, to safeguard the health of today's children.

From the Institute of Child Health, 30 Guilford Street, London WC 1N 1EH (Adviser in Child Health; Dr David C. Morley, MD, FRCP), numerous publications have been issued on various aspects of preventive and curative health in children. The following is the full text of that dealing with—

"CHILD-to-Child in Leprosy Detection"

Reports come in from many parts of the world describing many different CHILD-to-child programmes. An unexpected, but we believe valuable, programme describing how leprosy education and leprosy detection can benefit from CHILD-to-child reached us from Pune, in the State of Maharashtra, India. Dr J. M. Mehta, Honorary Director of the Pune Urban Leprosy Investigation Centre, has set up an urban leprosy control programme, working through the schools and making use of the children as well as the teachers. Between April 1975 and June 1978 303 schools were covered and 146,618 children have been examined for early signs and symptoms of the disease. The following notes describe the programme and, in particular, the role that children can play in it.

In April 1975 an Urban Leprosy Control Programme was started in Pune, a metropolitan city in Maharashtra, India. The programme involves three activities:

(1) Survey
(2) Treatment
(3) Health education.

SURVEY

Surveys are carried out in all slum areas and all schools, primary and secondary. Between April 1975 and June 1978 a count of 173,966 children, boys and girls, was established and 303 schools were visited. A total of 146,000 children were physically examined.

SURVEY AND HEALTH EDUCATION

During surveys health education is carried out. Regular lectures are given to teachers, students, parents and other groups. These lectures are given in local language. Early signs and symptoms are explained in very simple terms and considerable use is made of audio-visual aids.

Health education also continues during physical examination. Brief mention is again made of early signs and symptoms to individual children and others present.

TREATMENT

Treatment is given in out-patient clinics. These have been established all over the city in easily accessible areas. It is important that no child has far to travel to receive treatment.

A lot of treatment is carried out through teachers. They bring their children to the treatment centres regularly. Every encouragement is given to the teachers to do this.

Separate clinics are conducted for school children. This prevents the mixing of early school cases with badly deformed and advanced adult cases.

TREATMENT AND HEALTH EDUCATION

During treatment further health education is provided. The early detection and prevention of the disease are talked about on a person-to-person basis. Pictures, flash cards and other exhibits are shown around the clinic.

The intention is to make the clinic *an interesting place.* Attendance at the clinic for treatment is also an educational visit. Every effort is made to create a relaxed atmosphere where the children feel comfortable, free to talk and ask questions. Full use should be made of children's natural curiosity.

ATTITUDE

The attitude of all concerned with the programme is very important. Leprosy is talked about like any other disease. Fear, dread or stigma are not mentioned at all. If a child or teacher appears to have any doubts or fears every effort is made to explain them away. This is done by a para-medical worker giving careful explanations. In doing so great stress is placed on scientific knowledge and understanding of the disease.

The disease is talked about openly and everyone is encouraged to ask questions and seek advice. *There is no need to be ashamed or afraid of leprosy.* Openness and a willingness to cooperate are essential in any leprosy control programme.

EFFECTS OF THE PROGRAMME

The most obvious result has been the voluntary reporting of 622 cases of leprosy, adults and children.

Of particular importance has been the attitude of teachers and children to the programme.

Teachers

Many teachers are now aware of the early signs of leprosy. As a result they have brought cases to our clinics for confirmation. A number of such cases did have leprosy.

The teachers are helpful and often accurate with their observations.

Children

The children are willing to cooperate and assist. They have shown little fear or reluctance about taking part in the programmes.

During survey many children came forward voluntarily. On seeing what the para-medical team are looking for, the children are quick to come and show hypo-pigmented lesions (paler skin patches) on their body. Some of these patches have turned out to be caused by leprosy, proving the keen and intelligent observation of the children.

At other times many children voluntarily come to show lesions on their bodies and those of friends and fellow students. They are eager to know if they have detected anaesthetic skin lesions and whether the tests they carried out for detecting and demonstrating anaesthesia were correct.

During survey and examination the children are keen to cooperate. Many assist by getting other children to form queues; by undressing them; giving their names, etc.

Attendance at the clinic for school children is good. Children are often heard persuading each other to attend regularly.

Perhaps the most vital aspect of the programme has been the development of *an open, free and cooperative attitude towards the detection and treatment of leprosy.* Without this the programme would not have succeeded to the extent it clearly has.

BOMBAY LEPROSY PROJECT

Bombay Leprosy Project (BLP) sponsored by the German Leprosy Relief Association (GLRA) started work in October 1976 with the object of establishing a model for urban leprosy control in India. Similar projects of GLRA, are in operation in two other major cities in the country namely Madras and Calcutta.

Earlier experience gained through extensive school surveys in Bombay (Ganapati, R. *et al., Lepr. Rev.* **47,** 127–131, 1976) had indicated the existence of pockets of high prevalence of leprosy in some northern suburbs of the city, presumably of the order of 10–15 per thousand especially in the slums, where more than a third of the city's population (7 millions according to mid-year estimation in 1976) reside under very poor hygienic conditions. No studies on overall prevalence rate for the city are available.

The area chosen by the project for intensive control work is about 16 square kilometers in extent and the population at risk is approximately 325,000. The control work of three other units receiving financial aid from the GLRA and operating with uniform methodology in adjoining areas covering a total population of 1.5 million is also coordinated by the BLP so that after a few years of work, it is hoped that epidemiologically useful data on a large section of urban population would be available.

Since January, 1977, when the actual field work gained momentum, 35,089 slum dwellers (out of the enumerated population of 51,089) and 40,689 school children (out of 49,478 on roll) have been examined up to the end of July 1978. Health education has resulted in ensuring reasonably regular treatment of patients reporting voluntarily at a number of treatment centres started in the slums. So far 887 patients have been detected, out of whom 772 (10.1% lepromatous) are registered for standard treatment with DDS. Clofazimine and rifampicin are used in special situations and not as a measure to contain the infection in the community. Prednisolone and thalidomide are employed to treat reactions.

The finding of major importance so far has been the confirmation of the existence of hyperendemic slum foci. In one closely packed community of 3812 subjects, screening of 3178 members unearthed 10 proved smear-positive cases, which alone works out to a prevalence rate of 3.1 per 1000 (total prevalence rate including cases of lesser public health significance being

24.8 per 1000). It is by no means conclusive that a similar situation exists in *all* the slums. Our experience in the limited number of slums which we have surveyed so far indicates that by the standards recommended by the WHO, virtually the entire population of the project area must be regarded as exposed.

Though the prevalence of dapsone resistance has not been established by laboratory methods, the existence of persistently smear-positive patients treated irregularly earlier, and relapsing with characteristic lesions indicates this possibility, which not only enhances the risk to the exposed population but poses therapeutic problems.

Studies of population movement into and out of the area chosen for control have not been carried out and preliminary work suggests that the majority of the population in slums, especially those situated along the coastline, is quite stable.

R. GANAPATI

Lepr. Rev. (1979) **50,** 243–251

News and Notes

11TH BIENNIAL CONFERENCE OF THE INDIAN ASSOCIATION OF LEPROLOGISTS

The XI Biennial Conference of the Indian Association of Leprologists, held at Madras from 5–8 April, 1979, brought together 275 doctors, research scientists and senior leprosy workers from all over India for three days of intensive association during which 93 scientific papers were presented. Although taking place less than six months after the International Congress at Mexico City, this was no mere repetition of the scientific side of that event; indeed no visitor to this Conference can have failed to be impressed by the scale and sophistication of the research in leprosy now being undertaken in India, and the fertility of thought that lay behind many of the papers presented at this Conference. The fact that the Conference was inaugurated by His Excellency the Governor of Tamil Nadu in the presence of the Director General of Health Services is an indication of the importance now being given to leprosy in India, where the estimated prevalence of the disease now gives a total of 3.6 million people as suffering from it.

For the writer the most outstanding sessions of the Conference were those concerned with laboratory aspects and with modern trends in the treatment of leprosy. The session on treatment was concerned in the first instance with rifampicin. Following a most distinguished introduction by Professor E. J. Saerens of Geneva on the risk–benefit ratio of rifampicin in its clinical use, and experience of rifampicin in India in the treatment of tuberculosis by Professor C. V. Ramakrishnan, several papers had as their primary concern the most economical use of this drug in combined therapy in lepromatous leprosy. Among several regimens tried at the central JALMA Institute for Leprosy at Agra, B. K. Girdhar, Sreevatsa and K. V. Desikan found intermittent therapy using 900 mg rifampicin once monthly for 3 months, backed by continuous dapsone therapy the most promising. On other matters, V. G. Kothandapani, V. Ekambaran and T. D. Pandian reported 6 cases of sulphone resistance arising after only 6 years of monotherapy with dapsone.

Some very important and fascinating advances in knowledge were presented at the session on Laboratory Aspects. K. V. Desikan and Sreevasta reported on extended studies on the viability of *Mycobacterium leprae* outside the human body at different seasons of the year. They found that viability was maintained for 28 days in moist tropical conditions with a maximum humidity of 78% and a maximum temperature of 32°C, but only for 14 days during the dry season when the humidity fell to 30%. Kept at room temperature in moist pre-sterilized soil, the bacilli were found to retain viability for 46 days. It thus appears that under humid conditions *M. leprae* can remain viable outside the human body for long periods.

Equally important are the biopsy studies of the nasal mucosa reported from more than one centre. C. J. G. Chacko, M. Mohan, K. Jesudasan, C. K. Job and E. P. Fritschi found inflammation of nerves in the nasal mucosa of 35 apparently healthy contacts of lepromatous patients and also in 15 contacts of tuberculoid patients. Inflammation of smooth muscle bundles was also encountered. Acid-fast bacilli morphologically resembling *M. leprae* were found in these biopsies in 3 lepromatous contacts, and 1 tuberculoid contact who subsequently developed clinical leprosy. These findings suggest that the nasal mucosa could be a primary site of involvement in leprosy. L. Mehta, V. Kasbekar, N. H. Apte and N. H. Antia, undertaking similar studies in clinical tuberculoid leprosy, were also able histologically to diagnose leprosy as the cause of atrophic rhinitis in 8 out of 30 patients referred with that condition.

In the Clinical Session, A. Mukherjee, B. K. Girdhar and K. V. Desikan drew attention to leprous phlebitis as a clinical entity easily confused with a thickened cutaneous nerve, and a contributing element to recurrent bacillaemia. The concentration and persistence of *M. leprae* in the fingers and toes of patients with lepromatous leprosy was documented by S. Hiramalini, N. A. Joseph and C. J. G. Chacko. The Immunological Session concentrated on (a) the immunosuppressive action of dapsone in high dosage, reported by workers at the JALMA Institute; (b) the demonstration of Suppressor T cells in the peripheral blood of leprosy patients (both L and T) by Indira Nath; (c) Immuno-fluorescence studies; and (d) 9 years' experience of immunotherapy by Kunai Saha, M. M. Mittal and H. B. Maheswari.

The 20 papers in the Session on Epidemiology and Control included a report by S. K. Noordeen, P. N. Neelan and A. Munaf of a double blind trial of acedapsone, 225 mg at 10 week intervals, used for chemoprophylaxis in children over a period of 2 years. A 47% success rate was achieved, most pronounced in younger children. C. Vellut, M. F. Lechat and C. B. Mission in a major longitudinal study of non-lepromatous leprosy stressed the importance of establishing norms for maintenance chemotherapy following inactivity, and the subsequent declaration of the patient as cured. S. Balakrishnan and M. Christian, screening the self-administration of dapsone by patients attending field clinics, using DDS/creatinine ratios in urine, found in 400 samples less irregularity (15–25%) than has been reported elsewhere. C. Vellut, Leo Alex and T. Ethirajan, studying reasons for absenteeism among 1200 out-patients, found loss of wages as the main reason for non-attendance in 50%, but lack of communication regarding leprosy and the duration and dates of treatment affected 92% of patients. Here was ample evidence of the importance of health education in leprosy, a subject which received prominence in this session.

The closing session of the Conference was devoted to deformities in leprosy, and emphasized the importance and feasibility of reducing the incidence of disability. The use of nerve conduction velocities of involved peripheral nerves for diagnostic and management purposes was expounded by N. M. Prickett. A comparative study of surgical decompression by medial epicondylectomy and medical decompression by steroids in the management of ulnar neuritis and early paralysis by A. Alexander Thomas, A. J. Selvapandian, Rebecca Alexander, S. D. Joseph and P. Chellan suggested that a combination of steroid with early decompression using medical epicondylectomy will prevent

deterioration and provide maximal chances of recovery. A retrospective study over 25 years at the Sevagram Unit by M. D. Gupte, M. G. Ranade, R. Mahadevan and G. Y. Joshi revealed that both reactions and deformities were more common in patients with L and B type leprosy who were regular in treatment than they were in those who were irregular, but that patients detected at an early stage were least prone to deformity.

The writer had been invited to deliver a "Guest Lecture" at the inaugural Session of the Conference, and devoted this to a review of recent evidence regarding the transmission of *M. leprae*, and the influence of this on leprosy control procedures. It was stressed that the unique complexity of Indian village social life demanded a solution to the leprosy problem which was inspired from within India and not from sources outside the sub-continent. There already exist in India community development projects which could well hold the key to the solution of the immense problems involved, in which leprosy is integrated into general health care, not by administrative procedures imposed from above, but from below, by the will and cooperation of the people themselves. At one such project the proportion of leprosy patients on regular treatment has risen over 2 years from 50% to 90% and simultaneously other aspects of health have shown remarkable improvement.

India may have more sufferers from leprosy than any other nation, but India is fortunate to have now a rapidly growing army of sophisticated scientists and field workers devoting themselves to the fight against the disease. This Conference bore witness to this in the simple fact that sheer weight of numbers has necessitated the separation of the Indian Association of Leprologists Conference from the Indian Leprosy Workers Conference organized by the Hind Kusht Nivaran Sangh. There was much at this Conference to instruct and encourage the foreign observer. There can be no doubt that the contribution and experience of leprosy workers in India is destined, more than ever before, to affect the fight against leprosy far beyond the confines of their own great country.

T. F. DAVEY

PROFESSOR M. F. LECHAT ELECTED PRESIDENT OF THE INTERNATIONAL LEPROSY ASSOCIATION, MEXICO, NOVEMBER 1978

The Editorial Board of *Leprosy Review* wishes to record its congratulations to Professor Michel Lechat on his recent election as President of the International Leprosy Association, in succession to Dr J. Convit. Professor Lechat heads the Epidemiological Unit of the Faculty of Medicine in the Catholic University of Louvain in Belgium and is, of course, already well known for his work not only on the epidemiological aspects of leprosy but also on the methodology and economics of leprosy control. To a very wide knowledge of the subject he brings enormous energy, enthusiasm and—perhaps most important of all—great realism. We wish him every possible success as the new President of I.L.A.

THE EDITORIAL BOARD

POONA DISTRICT LEPROSY COMMITTEE
National Awards for the Most Efficient Physically Handicapped Employees, 1979; Posthumously Awarded to Mr J. G. Datar

The Honorary President of the Poona District Leprosy Committee has kindly written to us drawing attention to this award to an ex-leprosy patient:

"Mr J. G. Datar was afflicted with leprosy and though highly crippled and later blind, rehabilitated himself through sheer determination and courage, and developed a poultry farm, and a soap and disinfectant department at the Dr Bandorawalla Leprosy Hospital under the support of the Poona District Leprosy Committee. Mr Datar not only rehabilitated himself but through his efforts rehabilitated a large number of ex-leprosy patients in poultry farming and other crafts. To the best of our knowledge this is the first instance of an ex-leprosy patient being honoured in this way in our country. The honour is all the more remarkable as the Government of India went out of its way to give him a posthumous Award."

"*PARTNERS*": MAGAZINE FOR PARAMEDICAL WORKERS IN LEPROSY
To be printed also in French

The popularity and usefulness of this magazine (The Leprosy Mission, 50 Portland Place, London W 1N 3DG) has stimulated the decision to produce it in French, and the letter inviting *bona fide* leprosy workers to apply for it reads as follows—

La Mission Evangélique contre la Lèpre,
Secrétariat pour l'Europe ch. dé Rêchoz,
1027 Lonay/Suisse.
Tél. (021) 715081.

AUX MEMBRES DE L'ILEP ET AUX ORGANISATIONS ENGAGEES DANS UN TRAVAIL LEPROLOGIQUE

Chers Amis,
Comme vous le savez peut-être déjà, la Mission Evangélique contre la Lèpre produit depuis un certain temps un magazine intitulé "*PARTNERS*" en anglais, à distribuer gracieusement aux paramédicaux, aides-infirmières, etc. engagés dans un travail léprologique.

L'accueil a été encourageant et d'après les réponses reçues il semble que cette brochure réponde à un réel besoin, en informant ces groupes de travailleurs des derniers développements dans le domaine de la lèpre.

Comme nous avons reçu un certain nombre de demandes de renseignements, et pensons que ce matériel en général peut être utile en d'autres langues, nous avons décidé d'en produire une *édition française*. Elle contiendra le même matériel de base et sortira deux fois par an.

Si vous désirez recevoir des exemplaires gratuits à distribuer dans les centres

où vous êtes engagés, veuillez bien retourner le coupon ci-dessous à notre bureau à Lonay, jusqu'à *fin septembre*.

Avec nos remerciements et nos messages les meilleurs.

(SIGN.) Silvano Perotti, pasteur
et secrétaire pour l'Europe.

AHRTAG

Amongst the many agencies which may be able to contribute expertise either directly or indirectly to leprosy control, AHRTAG, based in London, is one which has so far not been adequately described in the leprosy journals, and we therefore take this opportunity to reproduce in full the following account of its aims and activities—

Appropriate Health Resources & Technologies Action Group Ltd (AHRTAG)
A WHO Collaborating Centre

85 Marylebone High Street, London W1M 3DE, U.K. Tel: 01–486 4175/6.

INTRODUCTION

The Appropriate Health Resources and Technologies Action Group (AHRTAG) is an independent, non-profit organization established in 1977 with initial financial support from WHO. It has recently been designated a WHO Collaborating Centre. Its function is to advance the concepts of appropriateness and effectiveness in health care, with particular emphasis on alternatives to high cost, high technology, hospital-based medical practice. It does this by operating an information clearing house, encouraging innovation, providing liaison and recommending technical consultants.

DOCUMENT COLLECTION AND PROJECT FILES

AHRTAG maintains a small but valuable collection of literature on primary health care and related appropriate technologies. This collection is probably unique in that it brings together many papers that are unpublished or that might otherwise remain relatively unknown and inaccessible. Many of AHRTAG's documents have been provided through a network of personal contacts throughout the world.

AHRTAG has established special technical files on important appropriate technologies for use in primary health care. Examples of current projects include: the "cold chain" for safe cold storage, transport and distribution of vaccines; oral rehydration for the treatment of acute diarrhoea; effective two-way radio communication systems for isolated communities; lightweight baby scales design for local manufacture.

TECHNICAL ENQUIRIES AND CONSULTANCIES

Some 400 technical enquiries have been received on a wide range of subjects. The number received each week is rapidly increasing, with 280 enquiries in the first 4 months of 1978 compared with 102 for the previous 6 months.

AHRTAG works closely with the WHO Expanded Programme on Immunization and has recommended consultants for the programme on the cold chain for the storage and distribution of vaccines. Educational materials and curricula for the training of technical officers who will operate the cold chain system have been developed under AHRTAG's supervision. These training materials have recently been field tested in Quito, Ecuador.

PUBLICATIONS

Dr Katherine Elliott's bibliography, *The Training of Auxiliaries in Health Care,* published by the Intermediate Technology Development Group in 1975, is currently being revised by popular demand. The new edition should be available before the end of 1978.

AHRTAG has contracted to identify and annotate 300 documents for inclusion in future volumes of the *Low Cost Rural Health Care and Health Manpower Training* series of annotated bibliographies produced by the International Development Research Centre.

Papers relevant to AHRTAG's interests have been presented at several international conferences.

Further publications are planned for the coming year.

VISITS AND CONTACTS

Between July 1977 and April 1978, 200 persons from some 30 countries visited AHRTAG. Meetings were arranged for groups of overseas postgraduate students studying for further qualifications in London.

Dr Katherine Elliott, with Mrs Arna Blum and Miss Muriel Skeet, organized the section on Health Auxiliaries at the International Hospital Federation Congress held in Tokyo during 1977. Following the Congress, visits were made to innovative health projects in Thailand and Hong Kong. Dr Elliott attended major WHO Consultations on Appropriate Technology for Health in New Delhi and Alexandria, and also visited Thailand and Iran on behalf of WHO.

AHRTAG has a list of over 4000 individuals and organizations with an active interest in health care. In addition, several thousand contacts have been obtained from the mailing lists of other organizations concerned with appropriate technology, health and development in the Third World.

LINKS WITH OTHER ORGANIZATIONS

AHRTAG developed from the Rural Health Panel of the Intermediate Technology Development Group, and enjoys close relations with the parent body. Members of AHRTAG staff continue to serve on voluntary panels of

ITDG and there is an active exchange of information between the two organizations.

The Ciba Foundation gives indirect support to AHRTAG through the continuing association of its Assistant Director as Honorary Director of the new Group.

Working closely with WHO and with the U.K. Ministry of Overseas Development, AHRTAG has identified a number of opportunities for its services. Two modest projects, funded by the U.K. Ministry of Overseas Development, are already in progress, and other proposals in collaboration with WHO and ITDG are under consideration.

A contract for the identification and annotation of documents for the International Development Research Centre, Ottawa, is nearing completion, and AHRTAG looks forward to continued association with this organization.

Council of Management: Sir Graham Bull, MD, FRCP—Chairman
Katherine Elliott, MRCS, LRCP
Dennis H. Frost, MBE
Miles C. Hardie, MA, FHA
David Morley, MD, FRCP

Staff:
Katherine Elliott, MRCS, LRCP—Honorary Director
Christopher Lomax, PhD—Administrator
Arna Blum, BSc—Information Consultant
Maureen Gadd, BA
Sunil Mehra, BA —Information Officers

AHRTAG owes its existence to the many people who have provided information, contacts, published and unpublished papers, manuals, and books on health care throughout the world. In order to provide a worthwhile service, we need a constant supply of current material. Please write to us if you have documents, data, or experience which would interest us, and which would assist us in doing our work; if you have a problem with which we might be able to help; or if you have an interest in any aspect of health care in the Third World.

Our offices are open to the public during normal office hours and we welcome visitors, but, if possible, please write or phone in advance to inform us of your intended visit.

SMALLPOX SURVEILLANCE: WHO OFFER REWARD OF US $1000 FOR DETECTION OF AN ACTIVE CASE

From time to time, in leprosy control circles, the principle of offering a financial inducement to any member of the community who reports a new case of leprosy has been discussed—and abandoned in view of the obvious possibility of doing more harm than good to doctor–patient relationships. This reward for the detection of a case of smallpox is remarkable not only because it has clearly been decided wise to adopt this principle, but also because it

marks the eradication of a potentially lethal disease, an achievement which, as little as 10 years ago, many thought unattainable.

SMALLPOX SURVEILLANCE **SURVEILLANCE DE LA VARIOLE**

REWARD US $1000 RÉCOMPENSE

A reward has been established by the Director-General of WHO for the first person who, in the period preceding final certification of global eradication, reports an active case of smallpox resulting from person-to-person transmission and confirmed by laboratory tests.[1] It is believed that such a reward will strengthen world-wide vigilance for smallpox and the continuing national surveillance in recently smallpox endemic countries.

[1] *(Resolution WHA31.54, World Health Assembly, 1978)*

Le Directeur général de l'OMS a institué une récompense à attribuer à la première personne qui, au cours de la période précédant la certification définitive de l'éradication mondiale, signalerait un cas actif de variole résultant de la transmission d'un être humain à l'autre et confirmé par des essais de laboratoire.[1] En offrant cette récompense, on pense inciter à la vigilance dans le monde entier et contribuer à renforcer la surveillance nationale continue dans les pays où la variole était récemment encore endémique.

[1] *(Résolution WHA31.54, Assemblée mondiale de la Santé, 1978)*

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WEEKS WORLD FREE FROM ENDEMIC SMALLPOX

*The recent laboratory associated outbreak in Birmingham,[1] United Kingdom, in which two persons contracted smallpox is not considered of epidemiological significance with respect to the reckoning of the period during which the world has been free of endemic smallpox. Hence, the number of weeks is counted from the week when the last known endemic case occurred in Somalia; this patient had onset of rash on 26th October 1977.

[1] Birmingham was declared free on 16th October.

SEMAINES SANS VARIOLE ENDÉMIQUE DANS LE MONDE

*La poussée récente, associée à un laboratoire, de Birmingham[1] (Royaume-Uni) au cours de laquelle deux personnes ont contracté la variole est considérée comme sans importance épidémiologique pour l'estimation de la période depuis laquelle le monde est exempt de variole endémique. Les semaines sont donc comptées à partir de celle où s'est produit, en Somalie, le dernier cas connu de variole endémique, l'éruption étant apparue le 26th Octobre 1977.

[1] Birmingham a été déclaré indemne le 16 Octobre.

WHO Weekly Epidemiological Record No. 44, 3 November, 1978.

EXCERPTA MEDICA

(1) Leprosy and Related Subjects, Vol. 1, Issue 1, 1979

This first issue, published with the aid of the Netherlands Leprosy Relief Association, Amsterdam, Member of ILEP, has now appeared, with 26 pages of excerpts, following the usual high standard of this series. The one annual volume of 10 issues, each containing approximately 150 abstracts ". . . will provide a single convenient source of information on subjects currently scattered not only over primary journals in many different disciplines, but also in a variety of *Excerpta Medica* abstract journals. . . ." The subscription rate is Dfl. 180.00 per volume of 10 issues, including postage and handling.

(2) Selected Proceedings of the XI International leprosy Congress, Mexico City, 13–18 November 1978

Approximately 500 pages, illustrated, clothbound. Publication date: Summer 1979.

Special pre-publication price: Dfl. 150.00/US $66.75. (The list price will be Dfl. 215.00/US $95.50.)

To be published in English. Order forms to *Excerpta Medica,* PO Box 1126, 1000 BC Amsterdam, The Netherlands.

LEPRA; PRIZE ESSAY COMPETITION, 1979: "THE IMMUNO-PATHOLOGY OF NERVE DAMAGE IN LEPROSY"

Since 1972, first in Oxford, then in Birmingham and Edinburgh, the British Leprosy Relief Association (LEPRA) has annually offered prize money of £100 for essays from medical students on various aspects of the leprosy problem. In 1977 it was decided to extend the offer to all universities with a medical faculty in the United Kingdom. The response in that year, and also in 1978, was encouraging, and the competition is therefore being continued in 1979, with the above title. Posters with full details of the conditions of entry are now being printed and will shortly be issued to universities. The closing date is 31 December 1979.

EDITORIAL OFFICE CHANGE OF ADDRESS

Please note that the new address for the Editorial Office of *Leprosy Review* is *The Slade Hospital, Headington, Oxford OX3 7JH. Tel. Oxford 64841, ext. 597.*

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Letters to the Editor

Dapsone Resistance in Patients with Treated Lepromatous Leprosy

Sir,

The excellent Editorial in your June number (Vol. 49, No. 2) by Dr Rees on "Combined Therapy in Principle and Practice for the Control of Dapsone Resistance" should be widely read and widely applied.

May I make one comment? Dr Rees rightly distinguishes between the two quite different aspects of the problem:

(1) To treat established proved dapsone resistance.

(2) To prevent the emergence of dapsone resistance by combined therapy.

The latter aspect is the subject of my comment. Dr Rees says "this involves every new lepromatous patient being treated at onset with dapsone on full dosage with at least one companion drug", and certainly everyone should agree and act on this statement. In my view, however, this is not enough. There are very many lepromatous patients who have been under treatment for many years—regrettably in many cases with unsupervised, and/or inadequate dosage of dapsone—and many of these must be "incubating" dapsone resistance. It is of note, particularly in certain West African countries, that dapsone resistance was until last year considered a minor problem. Now, however, cases are being recognized and the number of such cases will inevitably increase. From the public health point of view, the *already treated* lepromatous patient presents a more immediate danger of infection, and of the spread of primary dapsone resistance than the previously untreated patient. As Dr Pearson pointed out in Mexico the situation is analogous to that of an epidemic.

We must, therefore, give combined therapy, at least for a short period, to *all* cases of lepromatous leprosy; and in the very large group of previously treated patients who are attending our clinics, one such short regimen which combines safety and cost-effectiveness would be: Rifampicin 1500 mg in a single dose, with thiosemicarbazone 150 mg daily for 6 months, combined with dapsone 100 mg daily. This may be supplemented if local conditions make it feasible by an injection of acedapsone 225 mg every 3 months.

This regimen has the advantage of allowing us the possibility of using both Rifampicin and thiosemicarbazone or one of the thionamides again in combination with clofazimine if and when proven dapsone resistance emerges; but hopefully it should at least delay this occurrence.

H. W. WHEATE

ALERT
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Reference

Pearson, J. M. H. The epidemiology and some implications of sulphone resistant leprosy. *Proceedings of the XI International Leprosy Congress.*

Reply to Dr H. W. Wheate's Letter

Sir,

While I appreciate the compliment paid by Dr Wheate on my Editorial in *Leprosy Review* (1978, **49,** 97) on "Combined Therapy in Principle and Practice for the Control of Dapsone Resistance", I fully accept his assessment that the very large pool of lepromatous leprosy throughout the world who are already on dapsone monotherapy, represent the major source from which ever increasing numbers of patients with dapsone resistance (secondary) will inevitably emerge in the next decade. Therefore, while accepting that all newly diagnosed cases of lepromatous leprosy be initiated on combined therapy to prevent them ever developing resistance to dapsone, the more immediate and greater source of dapsone-resistant lepromatous patients will evolve from the vast pool of past lepromatous patients given dapsone monotherapy.

In an attempt to halt or significantly reduce the risk of dapsone resistance emerging in these lepromatous patients Dr Wheate rightly proposes that they should all be given a short course of additional antileprosy drugs while remaining on dapsone, and continuing afterwards on dapsone monotherapy. While I fully accept the additional antileprosy drugs recommended by Dr Wheate for this short course "intervention-combined therapy" as regards their efficacy, practicability and relative low cost, I believe they need to be defined in more detail than outlined in Dr Wheate's letter. Thus, while continuing dapsone 100 mg daily the patients would receive, supervised, one dose of rifampicin 1500 mg and a 6 months course of 150 mg daily thiosemicarbazone (thiacetazone). After completion of this 6 months treatment with thiosemicarbazone (thiacetazone) the patients would continue on daily dapsone 100 mg. In addition, at the time of the beginning of the course of intervention therapy and from then onwards, Dr Wheate recommends, if locally practicable, the administration of acedapsone 225 mg by injection every 3 months. The introduction of acedapsone is to ensure that *all* patients are receiving some dapsone, whether or not they are taking unsupervised dapsone by mouth.

Finally Dr Wheate states that this intervention regimen has the advantage of allowing the use of both rifampicin and thiosemicarbazone (thiacetazone) again in combination with clofazimine in the unlikely event of the patients relapsing with dapsone resistance. Unfortunately, I think Dr Wheate is being too optimistic in assuming that such relapses could only be due to the emergence of dapsone resistance strains of *Mycobacterium leprae.* Such relapses could unfortunately be now due to the emergence of strains of *Mycobacterium leprae* resistant to rifampicin or thiosemicarbazone.

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Editorial note: in the *Journal of the Royal College of Physicians of London,* Vol. 13, No. 1, January 1979, Dr McNicol wrote on the "Treatment of Tuberculosis," referring, in his concluding paragraphs, to the attempts which are currently being made to develop a shorter course of treatment for tuberculosis, requiring fewer doses of drugs. In view of the potential importance of short course chemotherapy in leprosy and the fact that several of our drugs have come from the tuberculosis field, we invited Dr McNicol to comment further, and he has kindly replied as follows—

Short Course Chemotherapy for Tuberculosis

Sir,

The possibility of short course chemotherapy for tuberculosis is currently attracting a great deal of interest and was a topic for several sessions at the recent I.U.A.T. meeting in Brussels. The report of that Congress published by the Bulletin of the I.U.A.T. provides a useful background, particularly the papers of Fox and Grosset.

As I see it successful shorter course chemotherapy programme requires:

(1) A drug regime that is capable of being bacteriocidal and with a very high kill rate which can be given in doses pulses optimal for killing the bacterial population at some interval rather longer than one day, unless the treatment regime can be very short.

(2) As the treatment being given probably has much less safety margin than longer course chemotherapy, each dose must be supervised to ensure that the patient actually receives it. This requires:
   (a) The patient should be available to be supervised in taking the treatment.
   (b) There should be staff available to give the drugs.

Unfortunately at the moment because of drug toxicity it seems a twice weekly treatment regime based on Rifampicin and Isoniazid is the optimum. Possibly initial supplementation with the more weakly bacteriocidal drugs, Streptomycin and Pyrazinamide, may be helpful but this point is not yet clearly established. It seems now to have been demonstrated that a 6 month twice weekly supervised chemotherapy regime produces cure rates in tuberculosis comparable with that of the conventional 9 months unsupervised regime. Encouraging results have been obtained with regimes as short as 3 months in length, but the relapse rate is significantly higher than with conventional chemotherapy. This is probably not acceptable by current standards in a developed country.

My own view at the moment is that the benefit to be obtained from a reduction in the duration of treatment from 9 months to let us say 5 months, together with the need to set up the apparatus for supervision of treatment to ensure that it can be organized to deliver it at a time when the patients would be accessible does not justify the effort. I feel the present regimes which are rather longer probably carry a considerably larger safety margin and therefore are less at risk from failure of patient compliance. Given the policy of minimum clinic visits such as I outlined in the article in the *Journal of the College of Physicians* I think this probably represents less of a problem to the patient than a treatment course 2 or 3 months shorter but requiring

supervision of each dose of the drug. I have therefore not felt that the advantages offered by short course chemotherapy in our practice where we have a fairly large number of patients (about 300 a year) were such as to justify its introduction. I also see major problems in the logistics of a wider scale introduction of short course chemotherapy. With the existing drugs in the presently required dosage frequency it seems to me that if the dose interval is anything shorter than once a week, the logistics of large scale supervised chemotherapy must present formidable problems and I would not be convinced that in the third world countries where tuberculosis remains a major problem the skills that are required for this would be available.

I am sorry if my conclusion conflicts with the views of those who are enthusiastic to explore the possibilities of short course chemotherapy in leprosy. My initial reaction to the possibility of short course chemotherapy in tuberculosis was one of considerable enthusiasm, but the information presently available has, as you see, greatly tempered it.

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Technicians in Reconstructive Surgery

Sir,

This has reference to the suggestion of Dr N. H. Antia, on the floor of the XI International Leprosy Congress at Mexico City (13–18 November 1978), that "Technicians should be trained to do reconstructive surgery in leprosy because of the paucity of doctors available for this work".

It was surprising that this suggestion came from India's finest and most well-known plastic surgeon. We in leprosy seldom make attempts to analyse and evaluate the quality of our work. For a good 30 years we have tried to take several short-cuts, without stopping to think whether some of these short-cuts would contribute to the postponement of leprosy control. Dr Antia has added one more weapon to the following existing ones:

(1) Paramedical workers with an education ranging anything from IV grade to school final, being responsible for the care of the vast majority of leprosy patients. From the number of responsibilities assumed by these workers, we tend to assume and give the impression that leprosy is the most simple and uncomplicated of all diseases.
(2) We have leprosy physiotherapy technicians and leprosy shoe-workers who do not know or understand (many of them never capable of understanding) the anatomy and the complex mechanisms in the normal or leprosy hands and feet, yet they give physiotherapy in a mechanical fashion and produce shoes in a stereotype fashion.

Even the most qualified and experienced physiotherapist or shoe-maker will find his greatest challenges in leprosy but we seem to have simplified the gravity of the situation.

Of course these situations have evolved in leprosy programmes due to several constraints including financial but what is dangerous is the fact that these are accepted as "ideal" or at least "sufficient" by most leprosy workers and all government and funding agencies.

"To reach as many patients as possible and do as much as possible with as little money and personnel (as little qualified) as possible" has been our slogan but *Mycobacterium leprae* seems not to get affected by our mass-scale quantitative approach.

Perhaps a more vigorous qualitative approach is called for. It's time we did some genuine stock-taking before setting up more of our "low cost, large numbered, impressive statistics" projects. Just as we have now started to pay the price for giving dapsone the monotherapy "crown", I would hazard the guess that we shall pay the price for every one of our short-cuts including the one suggested by Dr Antia if implemented, by taking a much longer time to reach our final destination—the eradication of leprosy.

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Reply from Mr N. H. Antia, FRCS

Sir,

Thank you for referring Dr Lobo's letter to me. My comments are as follows:

I agree that under ideal conditions it would be best to have fully qualified surgeons with special training in reconstructive surgery of leprosy to undertake all leprosy surgery. Unfortunately experience tells us that this is not possible for several reasons. Some of these are as follows:

(1) Most surgeons are not interested in working in leprosy because of fear, social stigma and lack of adequate remuneration.
(2) Those who do undertake such surgery do so only for a short period at the beginning of their career when they have little alternative work and drop it when other avenues are open.
(3) Even in proper surgical departments where leprosy surgery is integrated with other forms of surgery, the constant turnover of surgical and ancillary staff does not permit development of a coordinated team. This applies to all aspects of surgery and certainly to leprosy which seldom receives high priority. The poor overall quality of results bears testimony to this.
(4) The achievements of a few centres which are run by people with dedication can hardly fulfil the vast demand for this type of surgery.
(5) The expertise of surgeons not trained in this aspect of surgery leaves much to be desired.

The large number of leprosy surgery centres that operate at an appallingly low level of efficiency should convince us that our present approach cannot deliver the goods. Fortunately the deformities of this disease are of a repetitive nature and lend themselves to correction by a few standardized surgical procedures under local or regional anaesthesia. While one does not wish to minimize the extent of knowledge and skill required for these procedures, I feel that it should not be impossible to train persons like physiotherapists working with this disease to undertake such procedures after sufficient apprenticeship. In fact, we know of many physiotherapists in this field who have a superior knowledge of the anatomy and function of the hand and foot in leprosy to many a surgical specialist. I have had personal experience of nurses and physiotherapists who make excellent assistants and who with some encouragement and training can undertake some of these standard operations quite adequately. Some of these could well have become surgeons if the opportunity had been provided to them. We have mystified medicine and feel nobody else can undertake any of our functions even though we ourselves cannot deliver the goods.

The ability of simple unqualified persons to undertake routine abdominal operations like tubectomies on a large scale, with results comparable to those of qualified surgeons, as demonstrated in Bangla Desh, should encourage us to harness the latent human talent so readily available in developing countries to solve their own problems, rather than wait for the day when sufficient numbers of well trained surgeons will be motivated to tackle the surgical problems of leprosy.

I suggest that all existing centres take a few suitable candidates, preferably leprosy physiotherapy technicians, and give them the necessary theoretical and practical surgical training. Within a few years we should have sufficient trained personnel to utilize the idle capacity of many of the existing centres for leprosy surgery and provide a much needed service to the patients. Such a person will have the additional advantage of seeing the patient from the start to the finish of his treatment, will develop intimate rapport with him and avoid all the frustrations of a "team approach". He is also likely to serve the institution for a substantial period, if not a lifetime, at a cost which the institution can afford.

Medico-legal problems are bound to be raised, but then medicine is meant more for the benefit of the patient rather than for the benefit of the doctor or the lawyer.

N. H. ANTIA

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Palatal Involvement in Lepromatous Leprosy

Sir,

I read the three articles by Dr Girdhar and his colleagues with great interest (Girdhar, B. K. and Desikan, K. V., *Lepr. Rev.* (1979) **50,** 25–35. Mukherjee, A., Girdhar, B. K. and Desikan, K. V., *ibid* (1979) **50,** 37–43. Hubscher, S., Girdhar, B. K. and Desikan, K. V., *ibid* (1979) **50,** 45–50). Their finding that *Mycobacterium leprae* is discharged from the mouth in a high proportion of

patients with lepromatous leprosy, even when no oral lesion is seen, is of particular significance.

I have discussed previously palatal involvement in lepromatous leprosy (Barton, R. P. E., *Lepr. India* (1974) **46,** 130–134) and, like Girdhar and Desikan, I have not seen perforation of the palate in over 300 patients. I would therefore suggest that such perforation be described as "rare" rather than as "quite often seen", particularly as perforation of the palate may also be caused by syphilis and tuberculosis.

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Unnecessary Laparotomy for Abdominal Pain and Fever due to Clofazimine

Sir,

A 24-year-old Indian man was admitted to hospital in October 1974 with acute lymphadenitis and severe erythema nodosum leprosum (ENL), which were his first manifestations of lepromatous leprosy. He was treated with rifampicin for 6 weeks and dapsone; prednisone was used to control the ENL which was causing extensive skin ulceration. One unusual manifestation of his reaction was the appearance of haemorrhagic blisters on, and around the margins of, his palms and soles, which rendered his skin prone to ulceration from the slightest pressure or trauma. For this reason, prolonged immunosuppression was necessary and this could not be achieved with acceptable doses of corticosteroids. On 8 November 1974 treatment was started with clofazimine in a dose of 200 mg daily, which was gradually increased, reaching 500 mg daily on 25 December 1974, as it was still not possible to withdraw steroids. At the end of January 1975 he began to experience a series of fevers which were attributed to ENL, and on 29 January 1975 he complained for the first time of sudden, severe epigastric pain. There was marked epigastric tenderness, but a gastrograffin meal failed to show an ulcer or a perforation. Two subsequent bouts of fever were not associated with other detectable evidence of reaction but extensive investigations failed to show a cause for them. The second bout from 8–15 March 1975 was accompanied by severe generalized abdominal pain and tenderness. It was though that he might have a paracolic abscess secondary to a perforated duodenal ulcer and laparotomy was performed on 16 March 1975.

Laparotomy showed the intraperitoneal fat to be stained red. The liver, stomach, duodenum, gall bladder, pancreas, spleen, kidneys and large bowel were normal and within the mesentery and about the aorta there were firm lymph nodes that were coloured black. Frozen sections showed chronic low grade inflammation with intracellular crystalline structures. Histology of the mesenteric lymph node showed non-specific inflammation with few reactive follicles but prominent sinus histiocytes. The brown pigment crystals seen in frozen sections had dissolved in processing.

Clofazimine was withdrawn and there were no further attacks of abdominal pain or of unaccountable fever. The ENL was adequately controlled with thalidomide.

It seems likely that this patient's abdominal pain was caused by lymphadenitis, produced by clofazimine in high dosage over a period of 11 weeks. His fever may have been due to clinically undetected leprosy reaction, for example in a deep lymph node, but one must also consider the possibility that it was due to clofazimine. The case emphasizes that this valuable drug should be used in high dosage for only a limited period of time, and under expert supervision, before an alternative such as thalidomide is introduced.

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Lepr. Rev. (1979) **50,** 260–263

Book Reviews

Ethiopia. A Geomedical Monograph, by K. F. Schaller and W. Kuls, 1972. Published by Springer-Verlag, Berlin, Heidelberg, and New York.

This is one volume (number 3) of a remarkable series from a world-famous publishing house, the others being *Libya* (vol. 1), *Afghanistan* (vol. 2), *Kuwait* (vol. 4) and *Kenya* (vol. 5). Volume 3 has 159 pages (this comprises a combined English-German text), and there is a superb set of maps in a pocket at the end of the book, which is hard cover. In view of the important data on dapsone resistance in Ethiopia which appear in this number of *Leprosy Review* and the numerous research links between Ethiopia and research units in Europe, we reproduce here the major part of Professor K. F. Schaller's text. Tables IX, X and XI, and Section D; "Ethiopia and its Diseases–a Geomedical View" should be consulted in the original.

3. LEPROSY

"Leprosy is one of the oldest diseases known in Africa and the Middle East. In Egypt it was a common disease long before the Exodus. Ethiopia and Egypt are neighbouring countries, that have maintained contacts since time immemorial. In the east their traffic proceeded via the Red Sea and through the Sabaean kingdom, in the west through ancient Nubia. Leprosy was spread towards the south and the west of the African continent by migrating Cushitic tribes probably after the disease had been brought to the Ethiopian highland by the pre-nilotes [335].

"Even in the oldest *folk-tales*, leprosy occupies a special position among the diseases. Nowadays, leprosy patients still revere St. Gabrechristos as their patron [338]. It is generally believed that leprosy is a God-given malady.

"According to another conception, leprosy is transmitted by *heredity*. People blame the Evil Spirit or the Evil Eye for causing leprosy. Victims of leprosy must endeavour to pacify the evil spirits by making offerings. Another superstition is that a man will develop leprosy if he has sexual intercourse with a woman in the open—a superstition encountered, by the way, in the Far East as well.

"The habits of the 'Lalibellas' appear mediaeval to us. Originally, they were patients who came from the Welo Province in pairs, and wandered about the country begging. With veiled faces they used to sing at doors of the villagers' huts before sunrise. Today's 'Lalibellas' are not sick. They suppose that the aforementioned way of life will save them from catching leprosy. Customs, traditions and philosophy show that the population of this country has been preoccupied with leprosy for a long time.

"Previous travellers' reports indicate that leprosy once prevailed in the Ethiopian Highland in particular [282]. Reports dating from Italian authors [51] are very similar. Agostini [2]; and Talotta [383] describe 559 cases of leprosy in Eritrea. Thirty years later, in 1961, Greppi [164] estimated the number of sufferers in Eritrea at 1000, half of whom had come there from other provinces. At all times, leprosy patients felt attracted by hot springs and by the warm water of the Red Sea, which they hoped would cure them. Fadda [128] reported in 1936, that Tigre, Adis Abeba, Jima and Dire Dewa has 'very' many sick. In 1938 Mariani [235] estimated the prevalence of leprosy at Adis Abeba at somewhat less than 0.5%.

"By *mass* surveys of school-children, the author tried to get an idea of the extent to which the population is infected with leprosy. Table IX shows the results obtained at 30 places during the period 1957 to 1959. These results are not conclusive as to the *prevalence* among the whole population, and any conclusions must be made with reservations since children attending school in Ethiopia themselves represent a minority. Around 1960 only 5% of the children of school-age went to school.

"The percentage of leprous Ethiopian children who *heal spontaneously* is not known. The investigations confirmed, however, that the prevalence of leprosy is particularly high in the

provinces of Gojam and Shewa. The *leprosy-index* for all age-groups in the Gojam Province was 49 in 1000, and an almost equally high index, i.e. 42 in 1000, was found in the western part of Gurageland near Welkite. The index of 25 in 1000, found among the school-children of Fiche, Salale, in the Shewa Province, suggests that the endemic occurrence of leprosy in this area is very high.

"The *prevalence* of leprosy in the individual provinces has been estimated on the basis of the statistics kept by the leprosy control service, which have existed since 1954, and on the basis of data collected at numerous places.

"Table X also provides information on the 'open' cases registered in 1961.

"The fact that leprosy is irregularly *distributed* even in countries like Ethiopia, where the disease is highly endemic, renders any estimates as to its total prevalence very problematic.

"If the prevalence is determined only on the basis of one investigation, repeated studies are absolutely necessary to substantiate the results. Even 'official' estimates must be taken with reservation, as will be shown in the instance of Ethiopia. Prior to 1950, the number of leprous patients was estimated at 9000, in the following years at 15,000, and in 1954, eventually, the estimate amounted to 36,000 cases. The fact, that ten years later 80,000 persons were registered, proves that all these estimates were incorrect. Besides, less than half of the vast country is medically cared for by the health services provided. The leprosy rate can be estimated at 10 to 12 per 1000 people, Thus, the number of leprosy patients in Ethiopia may well exceed 200,000.

"The estimated *indices* for the individual provinces vary from 1 to 25 (Fig. 27, back of Map 6). The Gojam Province shows the highest prevalence, i.e. 25 per 1000. The neighbouring Welo Province, Begemdir Province and Shewa Province, situated on the central high plateau of the country, together with the Arusi Province in the lake district, have also very high endemic rates of 10 or more per 1000.

"The examples of the Gojam Province (Fig. 28) demonstrate that leprosy is not evenly *distributed* over a given province. On the basis of data collected Jungk [203], in 1969, takes the prevalence for the Harer Province to be 8 to 13 per 1000 instead of 4 in 1000 as previously estimated.

"Price [312] considers in 1969 that a genetic susceptibility of the Amharas to leprosy cannot be ruled out. The inhabitants of the Arusi Province belong to the Galla-tribes. According to Jungk [203], the Amharas and Gallas living in the Harer Province are affected equally. The Gurage and the Kambata in the Shewa Province as well as the Agaus in the Gojam Province are also very susceptible to leprosy, as shown by the indices determined. Thus it is difficult to distinguish plainly any of the many Ethiopian tribes as being especially susceptible. In a country like Ethiopia with a prevalence of 5 and more per 1000 for most of this province's exposure to leprosy, or rather to *Mycobacterium lepra*, is unavoidable. The percentage of '*open*' cases of leprosy living in isolation is negligible, since the majority of patients share the life of the community without restriction. Owing to the fact that in Ethiopia people are exposed to leprosy to a great degree, a maximum of morbidity is to be expected. The results obtained by the examinations of school-children in the Gojam Province sufficiently confirm this hypothesis. It may be assumed that up to 10% and more of the population are susceptible to leprosy and contract the disease at some period of their lives.

"Seventy-one of every 100 patients are males. In children up to the age of 12, the sex-ratio of boys to girls is 60:40. Approximately one-fifth of the patients are children up to the age of 15. An analysis of 4000 cases of leprosy seen at the Princess Zenebe Work Hospital in Adis Abeba provides information as to the *age* of the patients when leprosy became manifest in them (Table XI). Twenty per cent of the patients had contracted leprosy by the age of 15. More than 90% of all cases had become leprous before they reached the age of 40. Two cases of leprosy occurred in children during their first year of life. During puberty, the curve of morbidity rises steeply. More than 9% of the patients contracted leprosy after the age of 40 (Table XI).

"A *breakdown* of 26,195 cases, registered in 1963, into the various types and groups of leprosy shows an increase in tuberculoid leprosy at the expense of indeterminate leprosy, while lepromatous leprosy together with the 'Borderline'-group, i.e. the interpolar forms, continuously averages nearly one quarter of all cases in the country. The occurrence in the various provinces differs considerably, ranging from nearly 11% in the Tigre Province to more than 56% in the Kefa Province. Rates above average of 'open' cases are also encountered in the provinces of Harer, Welo, Sidamo and Eritrea. These data will have to be confirmed by further investigations and must be considered as preliminary results. However, comparison of results has become

difficult, as the extended conception of intrapolar leprosy is now generally applied. Leprosy is subdivided into three groups according to the place the respective type holds within the immunity spectrum, so that it is practically impossible to render the previous results accordant with the statistics of the present time. However, for epidemiological purposes it is sufficient to determine the respective proportion of '*open*' cases of leprosy. They are those forms that discharge *mycobacteria* in larger quantities (Photo 59).

"Among others, Bucco [48], in 1946, studied the problem of the *primary lesion* of leprosy in Ethiopia. In adults, the initial lesion consisted of a solitary macular focus accompanied by sensitivity disorders, with no evidence of free mycobacteria. The author [338] studied the localization of primary lesions and compared his findings with those of Chaussinand in Vietnam (Table XII). The characteristics, which in part deviate highly, may be explained by the different life styles of the two groups compared.

"*Deformities* due to leprosy are seen in about one-fifth of the cases. According to Price [312], paralysis of the hands, feet and eyes was found in a proportion of 5:2:1. Three per cent of the patients were completely, and 6% were partially disabled by leprosy. The high proportion of deformities may be explained, not least, by the belated treatment of the infected persons. Only a very low percentage of patients came under treatment during the first year of their illness, as shown by the records of the Princess Zenebe Work Hospital on 2091 patients. In fact only 15% of the sick came under treatment during the first year of illness. Half of all patients were treated only after they had been suffering from leprosy for more than three years. A change for the better has nevertheless occurred following the institution of the Leprosy Control Service and the rural health services. However, the objective of tracing patients for treatment during the early stages of the disease has not nearly been accomplished.

"The Leprosy Control Service, under the direction of the Ministry of Health, was instituted in 1954 in order to *control leprosy systematically*. Its headquarters is the Princess Zenebe Work Hospital in Akaki, a suburb of Adis Abeba. Approximately 40 leprosy-stations, distributed throughout the country, and staffed with one dresser and providing out-patient treatment, were integrated into the public health service, the health-centres and health stations in 1962. In 1964, this process was prematurely discontinued owing to problems which, at the beginning, did not appear to be insoluble. A factor contributing to this development was the foundation of the supra-national All Africa Leprosy and Rehabilitation Training Centre (ALERT), with headquarters at the former leprosarium of the Princess Zenebe Work Hospital. ALERT is supported by a number of leprosy relief organizations of various countries and is still in the process of organization. The services of the institution include treatment and rehabilitation of sick at a hospital, urban and rural leprosy control, as well as the administration of rehabilitation and reintegration programme. Since 1970 the Armauer Hansen Institute (ARHI) for research on leprosy and its causative organism—an institution supported by the Norwegian and Swedish relief organizations—has been affiliated to ALERT. The Princess Zenebe Work Hospital with its capacity of 250 beds is the main teaching institution of ALERT.

"Most of the other institutions for in-patient treatment of leprosy are supported by European and American relief organizations. One of the most important institutions is the leprosarium of the Deutsches Aussätzigen Hilfswerk (DAHW) (German Leprosy Relief Organization) at Bisidimo in the Harer Province with 120 hospital beds, which is treating 500 in-patients and about 5000 cases as out-patients. Attached to the leprosarium is an outpatient department for the medical care of non leprous patients from the near and farther vicinity. Bisidimo is the centre of the leprosy control activities for the Harer Province [203], where the number of cases is estimated at more than 20,000. At the beginning of 1970, the institution at Bisidimo provided medical care for more than 3000 patients by operating a regular mobile service along the surfaced roads.

"Other leprosaria and segregation villages are found at Boru Meda near Dese in the Welo Province, at Shashemene, Hosaina and Gindeberet in the Shewa Province, at Tibela in the Arusi Province, at Finote Selam in the Gojam Province and at Asmera in Eritrea, where a ward of 30 beds for leprosy is attached to the general hospital. It was also planned to set up a leprosy-centre at the former Maltese-Leprosarium at Selekleka in the Tigre Province. The leprosarium and the segregation village at Harer are being shut down, and their functions have been taken over by the facilities at Bisidimo. The leprosarium at Finote Selam, developed with Swedish funds, has not started work yet. The total capacity of the facilities for in-patient care is approximately 3000 cases. This meets the requirements, as in Ethiopia as well as elsewhere the centre of leprosy

control is the *out-patient* treatment. In the long run it will be mandatory to *integrate* leprosy control into the general rural health services.

"In vast areas of Ethiopia leprosy represents a major problem for the public health service, with which the country will be confronted for many years to come. According to experience the disease will be eradicated only when the basic conditions have been established, which will increase the living standard for the whole population."

A Practical Guide to the Diagnosis and Treatment of Leprosy in the Basic Health Unit, by H. W. Wheate and J. M. H. Pearson, 1978. Published by All Africa Leprosy and Rehabilitation Centre, Addis Ababa, Ethiopia.

In preparing this booklet of 26 pages the authors have drawn on their long experience of teaching medical auxiliaries how to diagnose and treat leprosy. They describe, in these pages, the main symptoms and signs of early leprosy, the way to test for sensory loss and enlarged nerve trunks, the technique of taking skin smears, routine treatment with dapsone, and simple exercises which the patient can be encouraged to do for fingers which are weakened or deformed. The risks associated with loss of sensation in hands and/or feet are outlined, followed by the basic treatment of dry skin, plantar ulcer, and weakness of eyelids due to facial nerve damage. The clearly and concisely written text is illustrated by four black-and-white photographs, four drawings, and one "flow chart".

The reviewer would like to offer some constructive criticism: (1) The importance of asking the patient about nasal symptoms has not been mentioned; only those who *ask* patients about nasal symptoms will discover how commonly they occur and how helpful they can be in diagnosing early lepromatous leprosy, for frequently they make their appearance before any skin lesions are noticed. (2) Testing for touch sensation by means of a wisp of cotton wool is the only method of sensory testing described. It would have been better to advise the medical auxiliary that, having found absent touch sensation, he should then proceed to establish impaired pain sensation by means of pinprick, for a number of skin diseases with thickened epidermis are likely to be anaesthetic to cotton wool but, unlike lesions of tuberculoid and borderline leprosy, will be fully sensitive to pinprick. This is particularly important as the booklet tells the medical auxiliary that he can diagnose a leprosy lesion if touch sensation is absent (facial skin excepted) and can, on the strength of this single finding, initiate treatment. (3) In describing the nerve trunks which should be systematically palpated for thickening, two important nerves have been omitted, namely, the superficial peroneal nerve and the sural nerve. (4) Why allow the patient to keep his underpants on when being examined, when it is stressed that the examination should be in private? The authors can be excused for being bashful on the subject of underpants, but they cannot be excused for not insisting that they must be pulled down so that the buttocks can be seen—a very important site for early leprosy lesions. (5) When advising sites for skin smears, no mention is made of smears from fingers. Since the original publication from the Hospital for Tropical Diseases, London, in 1976, studies in India have confirmed that fingers are the most informative sites. (6) Every medical auxiliary treating leprosy should be warned that patients are adept at defaulting on treatment or on clinic attendances, yet in the chapter on routine dapsone therapy this vital and all-too-common problem is not mentioned. Furthermore, a warning on the subject of dapsone resistance would not have been out of place.

This booklet is a brave attempt to meet its stated objective, namely, to enable any member of a medical team to diagnose leprosy in its early stages and to initiate treatment with confidence, using the booklet in association with clinical demonstrations of the methods it describes.

W. H. JOPLING

Lepr. Rev. (1979) **50,** 264–270

Abstracts

80. CHANG, W. P. **Ethiopian experience in health manpower training.** *Trop. Geogr. Med.*, v. 30, 147.

However great the benefits of modern medicine might be, these are of little use to "the man in the street" when they are not available to him at the moment of need. The problem of availability of such care is universal, even in the highest developed countries but it is—obviously—greatest in the underprivileged countries of the world. Modern medical care is a demanding mistress. Only when material resources are plentiful, a solid infrastructure is available, communications (roads, public and private transportation, telecommunication) are optimal and health manpower is present in adequate numbers of properly trained personnel, can its blessings be reaped.

A tendency towards "maximalization" has until recently been a guiding principle in the affluent parts of the world: an almost malignant proliferation (to speak in Ivan Illitch's terminology) of hospitals and medical institutions, sophisticated diagnostic facilities, huge increases in medical manpower, all needing longer and more expensive training periods before being allowed to become productive, because "health is priceless" and "for health care only the best is good enough, regardless of costs".

The infection with the "maximalization-trend" can be ruinous to the health-care services of underprivileged countries because it creates super-services for the privileged few and leaves the rest out in the cold, as can be illustrated by far too many unhappy examples.

The principle of "minimalization" in which the number of hospital beds, diagnostic facilities, medical workers etc. is just enough to provide proper care within the limits of the national budget is a sounder one, certainly for developing countries.

In the field of health manpower training, the Ethiopian experience as described by Chang is a valuable one that deserves careful consideration by all involved with the training of such manpower for underprivileged countries.

The experience started in 1954 with the establishment of the "Public Health College" in Gondar, a small rural town in the North of Ethiopia, far away from the capital with its university, big hospitals etc. At that time, Ethiopia had no indigenous doctors available and almost no "para-medical" personnel. After extensive surveys, studies and discussions by UNRRA, WHO, and US TCA groups it was decided to train three types of health workers: *Health officers,* receiving 4 years of medical training after 12 years of general education, *community nurses* receiving 3 years of medical training after 10 years of general education and *sanitarians* also receiving 3 years of training after 10 years of general education. Much of the training took place in the rural setting of Gondar and surrounding area, which is very similar to the Ethiopian rural areas in general, the future working area of these health workers. Preventive medicine was emphasized throughout the courses and teams consisting of a health officer, a community nurse and a sanitarian were formed during the training with the intention of staying together to work in the "Health Centres" of which 94 were created between 1954 and 1974. The curriculum was constantly evaluated and has been modified several times during the 20 years of experience described. The "Health teams" trained in Gondar have generally functioned very well and it was clear that the Gondar Health College had managed to maintain a high standard without losing contact with the rural way of life of the Ethiopians. The health teams possessed the rare combination of qualities of being capable health workers and still feeling at home in a rural setting. The main problems came from the Ethiopian ministry of public health of the period, which often broke up efficient teams by transferring one or more of its members, which often could not provide the essential drugs, equipment, means of transportation etc., and which was sometimes in arrears for several months in paying the salaries. A major blow to the "Gondar concept" also was the affiliation of the college to the Haile Selassie I university in 1962, when the health officer's curriculum was modified to meet a science degree of the university and became

"too academic and less service-oriented". Capable health officers got the opportunity to be "upgraded" to fully qualified doctors which resulted in the breaking-up of a number of health teams and a regression of the rural health services, to the benefit of the urban ones.

Unfortunately, the Gondar training programme has been interrupted since 1974, when the new Ethiopian government called all students and teachers from higher educational institution to participate in the "development through cooperation" campaign, which, as far as I know, is still going on. In due time, the Gondar college will probably resume its activities with some modifications and re-adjustments, but with the same basic and—to my mind—sound philosophy.

The problem of treatment and prevention of leprosy in the rural areas of Ethiopia by these health teams is not discussed in Chang's paper. As far as I know, this disease did not receive special emphasis in the curriculum. The health teams certainly had the know-how—though often not the means—to deal with the medical, preventive and sanitarian aspects of this disease but did not reach the stage of case-finding, search for defaulters etc. In some Ethiopian areas another type of health workers existed, the so called "leprosy dressers" who received some months of specialized training in leprosy, were afterwards based in a health centre or clinic and mainly travelled from market to market to meet their "clients" there and make them swallow "the tablets". At present ALERT (the All Africa Leprosy and Rehabilitation Training Centre) at Addis Ababa has a leprosy control section covering the whole of Shoa province, 15,913 patients being treated in 199 treatment centres, of which 111 are general hospitals, health centres or c inics and 88 leprosy treatment centres only. As far as can be made up from the annual report (977). ALERT is run as a separate service with little integration with the general health services f the country.

A. P. Oomen

81. HARBOE, M., CLOSS, O., REES, R. J. W. & WALSH, G. P. **Formation of antibody against *Mycobacterium leprae* antigen 7 in armadillos.** *J. Med. Microbiol.*, v. 11, 525–535.

The armadillo is already a valuable source of large numbers of *M. leprae*, but it could be exploited more efficiently if it were possible to screen newly caught animals for mycobacterial infections picked up in the wild, and also to screen animals infected in the laboratory for the development of progressive disseminated disease. If this could be recognized at an early stage, only these potentially valuable animals would need to be maintained. Professor Harboe and his colleagues have explored the possibility that antibody measurement could solve both of these problems. The authors also point out that a study of the immunology of the infections in armadillos may lead to ways of recognizing the optimum time for harvest, giving the most satisfactory balance between viability and numbers of organisms. No data are presented on this aspect.

They have employed a radioimmunoassay. Leprosy antigen labelled with ^{125}I is incubated with a suitable dilution of the serum to be tested. Then protein-A containing staphylococci are added. The protein-A strongly binds IgG. Thus the IgG in the serum sample binds to the staphylococci, which can be separated from the incubation mixture by centrifugation. If any of the IgG present was specific for the ^{125}I-labelled leprosy antigen, some of the ^{125}I is bound to the staphylococci, and this binding can be assessed in a gamma counter.

The antigen used in this study (leprosy antigen 7) is not specific to *M. leprae,* but is shared by most, perhaps all mycobacteria, and is therefore suitable for screening animals for mycobacterial infection. Most normal armadillos had lower antibody levels than a panel of Norwegian medical students. Two out of 21 animals had higher values, but there was no histological evidence of mycobacterial infection. Seven animals with mycobacterial infections at the time of capture all showed high values. The only exceptions were two animals with *M. ulcerans* infection, in which antibody was very low, but this is a known peculiarity of *M. ulcerans* infection. Several workers have failed to find antibody in mice infected with this organism. Therefore the technique appears reliable for screening newly caught animals.

The test was then applied to sera from armadillos infected 8–12 months earlier with *M. leprae.* There was significant antibody in 14 of the 17 animals with established infection, but there was no correlation with the extent of infection. Two of the three negative animals were amongst the

most heavily infected. However, the correlation was better in a small group of animals tested 2 years after infection with 10^8 *M. leprae* from a single batch of bacilli.

It is clear that detailed screening, before infection, of animals destined to be donors of *M. leprae* for experimental purposes, is essential, and the use of this technique in addition to the established procedures should be encouraged. However, it is difficult to believe that anybody will yet be prepared to discard an *M. leprae*-infected armadillo at an early stage because the antibody level has failed to rise. Such an act of faith may require support from data on armadillo sera.

G. A. W. Rook

In view of the fact that this number of Leprosy Review *carries four separate items on leprosy in Ethiopia, we take the opportunity to reproduce here a review of an important article on leprosy control in Ethiopia, originally published in 1976—*

82. CAP, J. A. & MULATU, B. **La lèpre en Éthiopie: situation actuelle. [Leprosy in Ethiopia.]** *Med. Trop.* v. 36 (1976) 11–15. (In French)

"The estimated number of leprosy sufferers in Ethiopia is between 128,000 and 135,000, of whom about 59,000 are registered. In a population of 24 million, the prevalence rate varies from 0.1 to 7.0 per thousand, or an overall rate of 2.5 per thousand. Most of the registered patients live in the central, hilly areas, but the higher prevalence rate in these districts may be a reflection of such factors as population density, activity of case-finding teams and the provision of more adequate facilities for treatment. Where prevalence is low, treatment is given at general dispensaries (1 for 28,000 persons in some areas; 1 for 220,000 persons in others); a special leprosy service is organized in areas where the prevalence is high, each trained medical auxiliary being responsible for the treatment of leprosy patients from three to five centers."
(*From* Trop. Dis. Bull.)

S. G. Browne

The abstracts which follow are reprinted from the Tropical Diseases Bulletin, *through the courtesy of the Director, Bureau of Tropical Diseases. They are classified according to subject.*

1. MICROBIOLOGY

83. HARADA, K. & KASAI, T. **Two methods of demonstrating leprosy bacilli in smears.** *Int. J. Lepr.,* 1978, v. 46, No. 2, 167–171.

84. KATO, L. **Cholesterol, a factor which is required for growth of mycobacteria from leprous tissues.** *Int. J. Lepr.,* 1978, v. 46, No. 2, 133–143.

2. IMMUNOLOGY, PATHOLOGY

85. RIDLEY, M. J., RIDLEY, D. S. & TURK, J. L. **Surface markers on lymphocytes and cells of the mononuclear phagocyte series in skin sections in leprosy.** *J. Path.,* 1978, v. 125, No. 2, 91–98.

"E, EA and EAC rosetting techniques and Ig fluorescence were used in a study of receptor sites in cryostat sections of lesions through the spectrum of leprosy, and for comparison in some other mycobacterial and granulomatous lesions. Anti-C_3, and trypsin were used as blocking agents.

"Lymphocytes in borderline lepromatous leprosy produced EA adherence and IgG fluorescence indicating B type cells. Lymphocytes in tuberculoid leprosy produced neither E or EA adherence and no fluorescence; these cells were presumed to be T cells.

"EAC and EA adherence was more marked in areas of macrophage infiltration, where there were few lymphocytes, than over the lymphocytes themselves. Two distinct patterns emerged: (i) EA binding together with IgG fluorescence was seen in active lepromatous leprosy and could be localized to the surface of individual macrophages, and (ii) EAC binding together with IgM fluorescence was seen in the granuloma of tuberculoid leprosy and sarcoidosis, but could not be definitely related to cell surface; rather it was diffusely spread over the whole granuloma; EAC adherence was diminished by anti-C_3 serum. Trypsin removed EA binding completely, but only diminished EAC adherence. It is suggested that the EA pattern indicates immunoglobulin receptors on macrophage and lymphocyte surfaces: and that the EAC binding (which is stronger than EA) involves C_3 and IgM receptors at extracellular sites as well as C_3 receptor sites on epithelioid cell surfaces.

"EA and EAC binding were enhanced in borderline tuberculoid leprosy in reaction and erythema nodosum leprosum, suggesting that immunoglobulin and complement receptor sites increase in number with enhanced hypersensitivity."

This is an important paper and merits being read in full.

M. F. R. Waters

86. VENKATESAN, K. & BHARADWAJ, V. P. **Sequential biochemical investigations in lepromatous leprosy.** *Lepr. India,* 1978, v. 50, No. 2, 166–172.

"Sequential biochemical investigations were conducted in cases of lepromatous leprosy in the reactive as well as subsided phases. Low levels of blood sugar and serum cholesterol were indicated in the reactive phase of lepromatous leprosy. Significant increase in thymol turbidity and decrease in A/G ratio were noted in most of the cases of lepromatous leprosy. Enhancement of serum levels of transaminases was observed in the reactive phase of lepromatous leprosy. Serum protein electrophoresis indicated increases in α_2-globulin and r-globulin and decrease in albumin in the reactive as well as subsided phases. The results are discussed in this paper."

87. SAOJI, A., MENE, A. & SHARMA, K. D. **Electrophoresis and immuno-electrophoresis in leprosy.** *Lepr. India,* 1978, v. 50, No. 2, 161–165.

88. CHANDI, S. M. & JOB, C. K. **The early cellular response to *M. leprae:* an ultrastructural study.** *Lepr. India*, 1978, v. 50, No. 3, 345–351.

"The ultrastructural changes that develop in mouse peritoneal macrophages from 10 min up to 14 weeks after exposure to *Mycobacterium leprae* are presented. Phagocytosis occurred by a process of engulfment by cytoplasmic processes and incorporation into a phagosome, into which lysosomal enzymes were subsequently introduced. Electron transparent zones (E.T.Z.) were not observed around phagocytosed bacilli in this study, however discrete droplets of lipid-like material appeared in the cytoplasm of macrophages, between 2 and 4 weeks after ingestion of the micro-organisms. Phagosomes with double limiting membranes were observed in macrophages harvested as early as 40 minutes after exposure to *M. leprae,* contrary to the observations of Evans and Levy (1972)."

[See *Trop. Dis. Bull.,* 1972, v. 69, abstr. 1410.]

89. SHER, R., ANDERSON, R., GLOVER, A. & WADEE, A. A. **Polymorphonuclear cell function in the various polar types of leprosy and erythema nodosum leprosum.** *Infection & Immunity,* 1978, v. 21, No. 3, 959–965.

"Polymorphonuclear leukocyte motility, both *in vivo* and *in vitro*, and reduction of Nitro Blue Tetrazolium was studied in tuberculoid and lepromatous leprosy patients and a group of lepromatous patients with erythema nodosum leprosum (ENL). A profound defect in random migration, chemotaxis, and chemokinesis was found in lepromatous patients with and without complicating ENL, and marked depletion of skin window migration confirmed these *in vitro*

findings. Tuberculoid patients exhibited a mild defect in polymorphonuclear leukocyte motility. Serum inhibitors of normal polymorphonuclear leukocyte chemotaxis were found in all types of leprosy, but sera from lepromatous and ENL patients were most inhibitory. Resting levels of Nitro Blue Tetrazolium reduction were normal in all three groups. Reconstitution of polymorphonuclear leukocyte cells from normal and ENL patients with ENL serum, however, showed increased Nitro Blue Tetrazolium reduction well above the normal range, whereas reconstitution with normal, lepromatous, and tuberculoid sera failed to increase Nitro Blue Tetrazolium reduction above the normal values."

90. STONER, G. L., TOUW, J., BELEHU, A. & NAAFS, B. ***In-vitro* lymphoproliferative response to *Mycobacterium leprae* of HLA-D-identical siblings of lepromatous leprosy patients.** *Lancet,* 1978, Sept. 9, 543–547.

"Lymphoproliferative responses to *Mycobacterium leprae* and P.P.D. were measured in 23 lepromatous and borderline lepromatous leprosy patients and in 27 of their normal siblings. At the same time siblings HLA-D-identical with the patients were identified by the absence of a mixed-lymphocyte reaction. The 7 siblings who were HLA-identical to lepromatous patients responded as well to *M. leprae* as did the 20 HLA-non-identical normal siblings. In contrast, 22 of the 23 lepromatous patients failed to respond to *M. leprae* but responded normally to P.P.D. The specific unresponsiveness of lepromatous patients thus does not result from an HLA-linked genetic defect and the defective cell-mediated immune response to *M. leprae* seems to be acquired, not inherited. Lepromatous patients may be high responders to antigens shared by *M. leprae* and other microorganisms in whom a strong antibody response has blocked the induction of an *M. leprae*-specific cell-mediated immune response."

91. REA, T. H. & TAYLOR, C. R. **Serum and tissue lysozyme in leprosy.** *Infection & Immunity,* 1977, v. 18, No. 3, 847–856.

"Mean serum lysozyme values were found to be elevated in untreated leprosy patients. Statistically significant elevations were present in each of the three major categories of leprosy, tuberculoid, borderline, and lepromatous. Values were particularly high in patients with severe reversal reactions or Lucio's phenomenon. Prolonged sulfone therapy was associated with a fall in serum lysozyme values. With an immunoperoxidase method to localize lysozyme in leprous tissues, two distinct staining patterns were found, granular and saccular. The granular pattern of lysozymal staining was found in epithelioid cells and in giant cells, and the intensity of staining showed a positive correlation with serum lysozyme levels. Conversely, a saccular pattern of lysozymal staining was found in lepromatous histiocytes, but the intensity of staining was unrelated to serum lysozyme levels; the saccular structures contained dense aggregates of *Mycobacterium leprae.* These two patterns of staining probably represent different functional responses of monocyte-derived granuloma cells, whereas the serum levels reflect, to a varying degree, both the absolute number of such cells and the rate of secretory activity of this cell population as a whole."

92. RIDLEY, D. S. **The pathology of leprosy.** *S. E. Asian J. Trop. Med. Publ. Hlth,* 1978, v. 9, No. 2, 205–208.

93. HIRSCHBERG, H. **The role of macrophages in the lymphoproliferative response to *Mycobacterium leprae in vitro*.** *Clin. Exp. Immunol.,* 1978, v. 34, No. 1, 46–51.

"Peripheral blood lymphocytes from patients suffering from lepromatous leprosy do not normally react *in vitro* to stimulation by *Mycobacterium leprae* antigens. In contrast, we found that T cells from non-responding patients in combination with macrophages from responding patients or healthy contacts did respond well to *M. leprae.* Conversely, T cells from responding patients or healthy contacts in combination with macrophages from non-responding patients

failed to respond. It seems, therefore, that the lack of response normally observed in *in vitro* tests using cells from lepromatous leprosy patients is due to a failure of their macrophages to present *M. leprae* antigens in an immunogenic form."

3. CLINICAL

94. NIGAM, P., GOYAL, B. M., MISHRA, D. N. & SAMUEL, K. C. **Reaction in leprosy complicated by filariasis.** *Lepr. India,* 1977, v. 49, No. 3, 344–348

95. FURUTA, M. *et al.* **Frequency of cerebrovascular lesions in leprosaria.** *Jap. J. Lepr.,* 1978, v. 47, No. 2, 61–65.

"Cerebrovascular diseases, especially cerebral haemorrhage, have been thought the most frequent cause of death in Japan. The Ministry of Health and Welfare has reported that cerebrovascular diseases have been the top cause of death in Japan since 1951. Pathologists, however, have not experienced so many autopsy cases who died of cerebrovascular diseases. Then, we investigated the cause of death in two leprosaria and compared it with information from the Ministry of Health and Welfare.

"One hundred and twenty-seven patients died in Komyo-en Leprosarium between 1962, January, and 1971, June. Autopsy was done on 110 cases. The average age was 62.5 years old. Malignant neoplasms (33 cases) were more frequent than cerebrovascular diseases (haemorrhage: 9 cases, softening: 3, microscopic haemorrhage: 11). The major direct cause of death was bronchopneumonia. Investigation of the death certificates in Seisho-en Leprosarium for the years 1967–1976 also revealed that cerebrovascular diseases were not the major cause of death. These results are different from information of the cause of death in Japan published by the Ministry of Health and Welfare. This discrepancy probably comes from inaccurate description of the death certificates and low autopsy rate in this country."

4. THERAPY

96. NOORDEEN, S. K. & NEELAN, P. N. **Extended studies on chemoprophylaxis against leprosy.** *Indian J. Med. Res.,* 1978, v. 67, Apr., 515–527.

"The role of dapsone as a chemoprophylactic was studied among (*a*) 955 household contacts of lepromatous leprosy when the drug was administered once a week in a dose schedule equal to about 1 to 2 mg per kg body weight per week, and (*b*) 2000 household contacts of non-lepromatous leprosy when the drug was administered twice a week in a dose schedule equal to about 4 mg per kg body weight per week. The study was double blind with comparable controls. The contacts received about 90% of the expected treatment. The results showed that chemoprophylaxis with dapsone was effective, the protection received by the contacts of lepromatous cases varying between 37 and 40%, and the protection received by the contacts of non-lepromatous cases being about 35%. The protective value of chemoprophylaxis in preventing occurrence of lepromatous cases could not be studied as no new lepromatous case occurred even in the control group. Although the protection from chemoprophylaxis was moderate, certain subgroups were found to be associated with higher protection. These subgroups, in general, had a higher risk of getting leprosy as observed from the occurrence of disease in the relevant control groups."

6. MISCELLANEOUS

97. BRAND, P. **Insensitive feet. A practical handbook on foot problems in leprosy.** 88 pp. Revised 1977. The Leprosy Mission, 50 Portland Place, London, W1N 3DG. [Free]

After describing the structure of the foot and the protective role of normal sensation, the author

discusses, in turn, paralysis of nerve supply, plantar ulceration, and damage to bones—with special emphasis to tarsal bones. On each of these subjects prevention and treatment are fully covered. The final chapter is devoted to the subject of footwear for insensitive feet.

[The management of insensitive feet is of such importance that all those engaged in treating leprosy should study this clearly written and well illustrated booklet.]

W. H. Jopling

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References:
1. Browne, S.G., Int. J. Leprosy *34,* 289 (1966)
2. Waters, M.F.R., Leprosy Review *40,* 21 (1969)
3. Hastings et al., Leprosy Review *39,* 3 (1968)
4. Warren, H.A., Leprosy Review *39,* 61 (1968)

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Tables should be typed on separate sheets and numbered in sequence, in arabic numerals; captions should be typed in double spacing.

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Photographs. A reasonable number of black and white plates will be reproduced. Glossy original photographs (positive prints) should be supplied, and clear indications (number, caption, top side) should be given. Any writing on the back of the photograph should be lightly done in pencil.

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Contractions. All weights, measures, temperatures, etc., should be given in metric units, suitably contracted. Authors may refer to "Symbols, Signs and Abbreviations Recommended for British Scientific Publications", published By The Royal Society. British (Imperial) equivalents may be added within parentheses. In the case of (body) temperatures, the Fahrenheit equivalents of Celsius (Centigrade) figures should be given within parentheses.

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