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The Effect of Out-patient Dapsone in an Area of Endemic Leprosy*

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Following up the work of Charles Ross in Northern Nigeria the author has found that the prevalence of leprosy in one area in this region has fallen from a mean of 40 per 1000 of the population in 1952–5 to 1.6 per 1000 in 1967–8 after a campaign of treatment with dapsone in relatively low dosage. The limitations of the study and previously reported criticisms and drawbacks of sulphone therapy are discussed.

INTRODUCTION

Though the sulphones have been extensively used in countries where leprosy is endemic there is little information available regarding the effect of these drugs in controlling the disease. Cochrane (1964) considered there had been no decline in the world incidence of leprosy and that the widespread use of sulphone therapy for 15 years in certain areas of South India had failed to reduce the number of patients. However, no planned quantative study has yet been reported.

The work of the late Charles Ross in Nigeria is familiar to all interested in leprosy. His surveys in the early 1950's throughout the Northern Region give a good idea of the prevalence of the disease. Details of the initiation and progress of the mass treatment campaign based on the once weekly administration of dapsone have been fully described by him elsewhere (Ross, 1956, 1958, 1959, 1964). At present there are over 2000 out-patient clinics throughout the Northern Region of Nigeria where dapsone is being given.

This paper describes a study in an area of the Northern Region and attempts to assess the effect of sulphones on the prevalence of leprosy by comparing the present results with those in the pre-treatment surveys reported by Ross.

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MATERIALS AND METHODS

Area of study

Figure 1 shows the area of study and comprises the northern part of Zaria Province, including the villages of Igabi and Giwa, which Ross surveyed in 1952 before starting out-patient centres. The present study was carried out in 1967 and 1968. The results are given as prevalence rates, i.e. all the patients with leprosy at a particular time. This is in contrast to the incidence rate, which is the number of new patients over a specified interval of time. The prevalence rates have been assessed in 2 ways.

(a) *From out-patient clinics.* Twenty-nine clinics were studied in the area shown in Fig. 1. The majority of these had been visited regularly over the preceding 15 months for teaching and supervision. When it was found that patients with leprosy were much fewer than had been suspected, a decision was made to record the actual number. This was done by a single visit to each clinic at the end of 1967 and the beginning of 1968. Of these clinics 25 were visited personally and the numbers from 4 clinics were recorded by a leprosy inspector who had had 10 years experience in the diagnosis of the disease. In addition, in-patients of the Zaria Provincial Leprosy Settlement who originally came from the area under study were also included. Many people attended leprosy clinics in the hope of obtaining dapsone and, in fact,

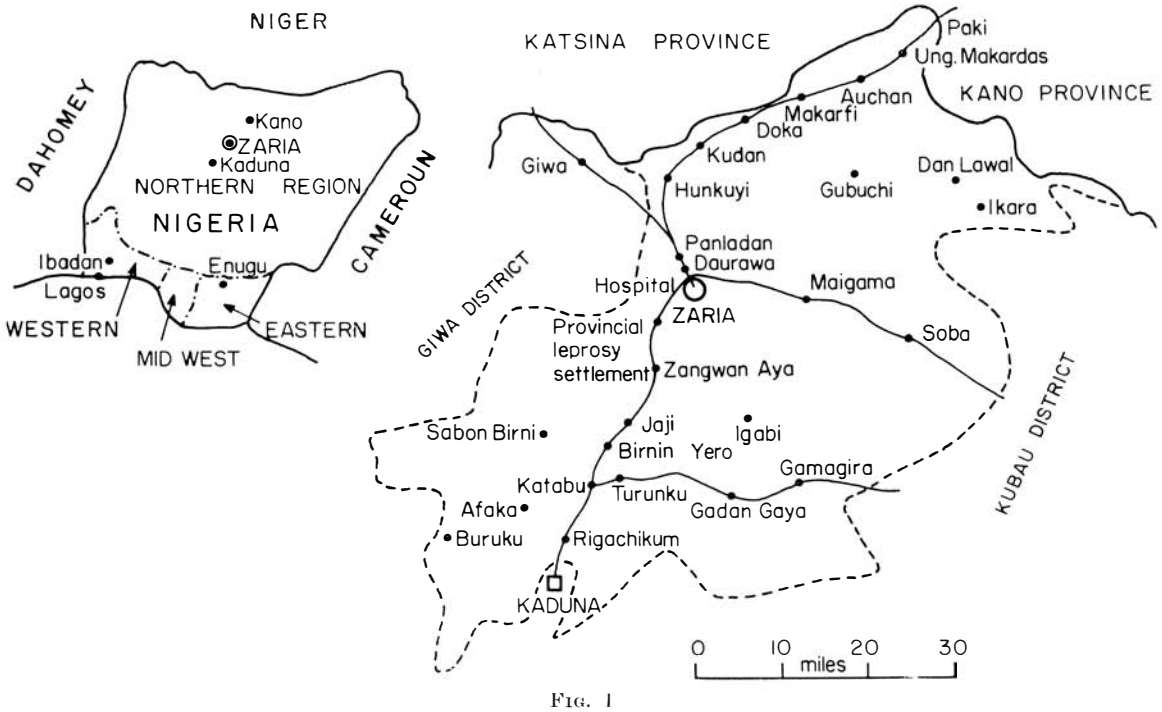

FIG. 1

Northern Zaria Province. The dotted line encloses the area from which prevalence rates have been calculated. The names indicate the position of leprosy clinics.

at some clinics 70 to 80% of attenders had no evidence of the disease; none of these persons were included in this study unless they had the signs listed below. The prevalence rate has been calculated from the total number of patients attending the out-patient clinics and from the 1963 census, in the area shown.

(b) *Village surveys.* These were carried out in Igabi and Giwa in 1967. The village headman had previously been contacted with the request that the people stay in their huts on the day of the survey. Teams of leprosy attendants, each headed by a leprosy inspector, examined all the people, and all those with any type of skin lesion or deformity were referred for diagnosis.

Diagnosis of leprosy

This was made on the clinical features of the various types, supplemented by bacteriological examination where possible.

In the lepromatous (multi-bacillary) type the features were infiltration of the ears and skin, especially of the face. Other accompanying signs often present were loss of eyebrows and nasal depression. A few patients showed acid-fast bacilli on bacteriological examination and in some there was evidence of mutilation of the extremities and thickening of the peripheral nerves.

In those non-lepromatous (pauco-bacillary) patients with discrete lesions the characteristic features were hypopigmentation with some alteration of the texture of the skin, anaesthesia to light touch—though this was not invariable—and absence of itching. The common skin conditions to be differentiated were birthmarks, pityriasis versicolor, other superficial fungous infections, the facial hypopigmentation which is common in children in Northern Nigeria, and macular hypochromia (Browne, 1964).

The neurological signs in those without skin lesions taken to be evidence of leprosy were a mononeuritis or mononeuritis multiplex (Brand, 1964) and a polyneuritis involving superficial

sensory modalities (Monrad-Krohn, 1923; Crawford, 1968) when this was accompanied by some evidence of loss of protective sensibility such as blistering or ulceration of the skin or mutilation of digits.

Bacteriological studies

Smears were taken by the standard split-skin method from 168 lepromatous out-patients and from 15 lepromatous patients in the leprosy settlement. Of the lepromatous patients, 34 were from the adjacent districts of Giwa and Kubau (see Fig. 1), but were included because the aim of the bacteriological studies was to test the effectiveness of out-patient treatment in rendering lepromatous patients bacteriologically negative. These cases are, of course, not included in the prevalence rates. Initially, 6 skin sites were chosen, but because of the consistently negative results from the trunk and limbs the examinations were finally restricted to both ear lobes and the forehead. The smears were stained with strong carbol fuschin, decolorized in 0.5% hydrochloric acid and 70% alcohol, and counterstained with brilliant green or methylene blue. All the slides were personally examined.

RESULTS

Table 1 shows the decline in the prevalence of the disease over 12 to 15 years in the area of Zaria Province studied. Ross's figures are derived from surveys and relate to the whole of Zaria Province. The prevalence rates in the adjacent provinces of Katsina and Kano are included to show the equally high levels prevalent in 1952–5. The number of patients attending the out-patient clinics with leprosy was 838. As the population of the area was 525,068, this gives a prevalence rate of 1.6 per 1000.

TABLE 1
Decline in leprosy prevalence in an area of Zaria Province

Year	*Study*	*Province*	*Prevalence rate*
1952–5	Ross	Zaria	46/1000
1952–5	Ross	Katsina	39/1000
1952–5	Ross	Kano	35/1000
1967–8	Present	Northern Zaria	1.6/1000

TABLE 2
Decline in leprosy prevalence in the villages of Igabi and Giwa by survey

Year	*Study*	*Population examined*	*No. with leprosy*	*Prevalence rate*
		Igabi		
1952	Ross	1422	94	67/1000
1959	Ross	1052	51	50/1000
1967	Present	1904	4	2/1000
		Giwa		
1952	Ross	410	16	39/1000
1967	Present	1187	3	2.5/1000

TABLE 3
Bacteriological status of lepromatous patients

	Out-patients	*In-patients*
No. of lepromatous patients examined	168	15
No. positive for acid-fast bacilli	19	11

Table 2 shows the decline in leprosy prevalence as assessed by survey in the villages of Igabi and Giwa. None of the patients in the present surveys had lepromatous leprosy.

The lepromatous patients in Table 3 have been divided into 2 groups, as the aim has been to show the effect of out-patient treatment on the bacillary state. Of the 11 positive in-patients, 6 had episodes of erythema nodosum leprosum (ENL) and 3 of these had in addition recurrent bouts of pain and tenderness in the ulnar nerve at the elbow.

DISCUSSION

The results show the marked decline in the prevalence of the disease. There seems little doubt that this is due to out-patient dapsone therapy, as, apart from the establishment of a segregation village at Giwa, no other means of control have been employed.

There are obviously several limitations to a study such as this. For example, not enough information was available to trace individual patients included in Ross's surveys; also the out-patient figures are recorded from a single attendance and census records are liable to be

inaccurate. However, the prevalence rates agree closely with the more accurate results from surveys. Despite these limitations, all the results point to a decline in the disease and are interesting if only to emphasize the need for planned studies on the subject. There is a danger that a potent method of eradicating leprosy may be needlessly abandoned, as the discussion of control methods has now shifted almost exclusively to the use of BCG vaccination and the administration of prophylactic sulphones to contacts (*Lancet*, 1966, 1968; *British Medical Journal*, 1966, 1968). The conflicting results to date of BCG vaccination will inevitably mean further delay before its efficacy can be decided. The results of giving sulphones prophylactically have been more encouraging, but even if both these methods are found in trials to be ultimately effective, there is still a practical point to be considered. In countries which have not conducted mass-treatment campaigns against leprosy, some way will obviously have to be devised to find the patients before their contacts can be treated.

Sulphone therapy has been criticized from a number of points of view. One of the main criticisms is the long time they take to render the patient bacteriologically negative. Thus Lechat (1961) found that, on average, it took 8 years to clear 50% of lepromatous patients of bacilli. However, Shepard *et al.* (1968) have recently demonstrated the decreased infectiousness for mice of bacilli from lepromatous patients beginning treatment with dapsone, and have emphasized how greatly reduced the chances are of these patients infecting others even after a few months of therapy. Further, the present study does show that lepromatous patients will attend regularly enough to become bacteriologically negative, even though this may take more than 10 years.

The lower dosage of dapsone now employed has led to a diminution of toxic effects, and in this study only one patient was observed with a mild dermatitis, although admittedly observation was limited. Heinz-body anaemia could not be excluded in the present study, but Smith and Alexander (1959) found that in patients taking dapsone in dosages comparable to those in leprosy there was no fall in the haemoglobin level. Erythema nodosum and pain, with swelling in the peripheral nerves occurred, as stated, in 6 of the in-patients, but was not seen in out-patients and thus were complications in only a small percentage of the total number of lepromatous patients. The sulphones have also been implicated in precipitating the onset, and producing exacerbations, of nerve damage in leprosy, but no definite conclusions can be drawn, as the natural history of nerve damage has never been studied. The most common and severe form of nerve damage encountered in Northern Nigeria is the acute onset of sensory loss associated with oedema of the hands and feet (Crawford, 1968). A similar process, also with oedema and nerve damage in the extremities, has now been reproduced experimentally (Rees and Weddell, 1968) without ingestion of sulphones, so that the syndrome in the leprosy patient is likely to be part of the natural history of the disease.

The reports of bacterial resistance to sulphones have led to justified concern. Pettit and Rees (1964) have, however, estimated the frequency to be of the order of only 3 per 1000 lepromatous patients and hence as a factor in mass treatment campaigns it is of little significance and nothing like the similar problem posed in the control of tuberculosis. The other virtues of dapsone, such as low cost and ease of administration, need no emphasizing here.

Any discussion about leprosy must take account of the social attitudes towards the disease. Ross (1964) from his experience in pre-treatment surveys made the following comments: "Survey has revealed that there is a degree of shame attached to infection by the disease; nevertheless, leprosy is tolerated in village and social life and any fear of detection has been associated with the dread of being segregated, which means divorce and separation from one's family". He also found that there was a good response to out-patient treatment facilities. In the present study there were few

patients who did not seek treatment where clinics were available. Leprosy is thus not a hidden disease, at least in this area.

The findings in this study and Ross's practical method of approach are relevant to the leprosy problem in the world as a whole. The latest estimate by the World Health Organization of the number of leprosy patients is 10.8 million, of whom only about 18% are receiving any form of therapy (Bechelli and Dominguez, 1966). Most of the remainder live in the rural communities of developing countries, and it is in these areas that a mass treatment campaign with dapsone should be seriously considered as a priority.

SUMMARY

A study in an area of the Northern Region of Nigeria has shown a marked decline in the prevalence of leprosy after a mass treatment campaign based on the out-patient administration of dapsone. The lack of information regarding the effect of sulphones in controlling the disease is emphasized. The properties of dapsone under conditions where leprosy is endemic are discussed.

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