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Preliminary Appraisal of a WHO-recommended Multiple Drug Regimen in Paucibacillary Leprosy Patients in Malawi[1]

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In 1981, a Study Group organized by the World Health Organization devised and recommended a short-course multiple-drug therapy regimen (WHO/MDT) for paucibacillary leprosy patients ([15]). This recommendation was unusual insofar as the regimen had never been subjected to a controlled trial. Nevertheless, the regimen soon became standard policy in many countries, including Malawi.

This paper reports on a study set up within the framework of the LEPRA Evaluation Project (LEP) and the LEPRA Control Project (LCP) to evaluate the WHO/MDT regimen in Malawi. The main objectives of the study were as follows: a) to study the risk of type 1 reactions during the course of treatment and during a 4-year surveillance period after completion of treatment; b) to measure the incidence rate of relapses within 4 years after completion of treatment; and c) to assess the feasibility of post-treatment active surveillance for 4 years in rural Central Africa. This paper presents data on the outcome at the end of treatment and at the end of the first 12 months of subsequent follow-up. Although this is too short a period for final conclusions concerning the relapse rate in paucibacillary leprosy patients following WHO/MDT, a preliminary report, in particular on the occurrence of type 1 reactions during and after treatment, seems appropriate.

PATIENTS AND METHODS

Patients were recruited for the study from two different areas in Malawi. Three hundred one were recruited within the context of the LEPRA Control Project (LCP) in the central and southern regions of the country, here called the "LCP area," between December 1983 and June 1985. Of these, 288 had self-reported to the LCP staff, and the remaining 13 were found during village and school surveys. An additional 202 patients were recruited from Karonga District, in the northern part of the country, between April 1983 and August 1984. Of these patients, only 40 had self-reported to LEPRA staff; the remaining 162 were found by active case detection during a total population survey carried out by the LEPRA Evaluation Project (LEP) ([13]).

Patients were examined before or on the day of recruitment by JMP in Karonga District and by GB in the LCP area. On that occasion the certainty of diagnosis ([2, 12]) and the classification were decided upon by the investigators and a 4-mm punch biopsy was taken from the most active lesion of each participant. All biopsies from Karonga District were examined by Dr. A. C. McDougall (Oxford, U.K.). The first 235 biopsies from the LCP area were examined by Dr. D. Ridley (London, U.K.) and the remaining 66 were examined by Dr. A. C. McDougall. Slit-skin smears were obtained from most patients. Patients with a history of previous treatment were not recruited into the study.

Patients with strong clinical evidence of leprosy (i.e., clinical certainty = "most likely" to "certain" [12]) were registered immediately. Such patients were not excluded from the study even if the biopsy did not show definitive evidence of leprosy. Criteria for definite histopathological evidence of leprosy were as described in reference 5 for biopsies examined by Dr. McDougall and

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as codes p4, p3 and p2 ([14]) for biopsies examined by Dr. Ridley. Suspects in whom the clinical certainty of diagnosis was considered to be low were recruited into the study only if the biopsy specimen(s) showed definite evidence of leprosy ([5, 9, 14]).

Only patients with paucibacillary leprosy according to the definition of the WHO Study Group on Chemotherapy of Leprosy for Control Programmes ([15]) were included in the study. In our context, this means patients classified as tuberculoid (TT), tuberculoid to borderline tuberculoid (TT/BT), borderline tuberculoid (BT), indeterminate, neural or borderline tuberculoid to mid-borderline (BT/BB), but with a bacterial index (BI) of less than or equal to 1 at all sites. We classified leprosy as TT if the skin lesion was well defined, had no streaming edge or satellite lesion(s), but had a healing center. We were reluctant to classify leprosy as TT if there was more than one such lesion.

The treatmeant was 100 mg of dapsone (DDS) daily self-administered (50 mg for patients under 15 years of age) plus 600 mg of rifampin (or 300 mg for patients under the age of 15), supervised, at intervals of 4 weeks or more, until six doses of rifampin had been taken. Patients received this treatment near their homes, as described in detail elsewhere ([3]). Patients who did not complete this treatment course within 9 months of recruitment were excluded from the study.

Compliance with the treatment protocol was monitored by the examination of urine specimens collected during surprise home visits, once between registration and completion of treatment and once during the first 6 months after completion of treatment. All urine specimens were examined by the same technician (H. Tegha, in the LEP Laboratory at Chilumba) for dapsone, and for creatinine ([4]). In addition, most urine specimens (174 of 178 during treatment and 102 of 153 after treatment) collected from patients in Karonga District were also analyzed by an ELISA method in Dr. H. Huikeshoven's laboratory at the Royal Tropical Institute in Amsterdam ([6]). Negative control urine specimens were provided by the Malawian project staff with reliable histories of no dapsone intake.

Patients were examined several times during the treatment period for signs of type 1 reaction by paramedical workers trained for leprosy work (leprosy control assistants, LCAs). Patients were fully reviewed at the end of treatment and at 3, 6, and 12 months after that. Reviews at 6 months after completion of treatment were always done by medical officers (JMP or GB) who, on that occasion, usually obtained repeat biopsy specimens from a site adjacent to the scar from the first biopsy. (The histopathological findings in these repeat specimens will be reported separately.) All other reviews were done by four experienced LCAs especially allocated to this study. They recorded the presence or absence of skin lesions and the activity, if any, in such lesions. Any lesions with signs of inflammation were called "active." Any patient suspected by an LCA to have either a type 1 reaction (after completion of treatment) or a relapse was re-examined by JMP or GB.

Any tender, enlarged nerve(s) was regarded by us as evidence of type 1 reaction. However, most type 1 reactions did not show this cardinal sign and the presence or absence of type 1 reaction had to be judged from the degree of (renewed) inflammation in the skin lesion(s). If the (renewed) inflammation was judged to be considerable, a standard course of 30 mg of prednisolone (15 mg for patients under the age of 15) daily, tapered down to zero over 12 weeks, was prescribed ([3]). Even in the absence of clinically apparent type 1 reaction, such a course of steroids was given in cases of recent paresis/paralysis. The prescribed WHO/MDT was not altered during a course of prednisolone.

The appearance of a new skin lesion after completion of WHO/MDT was interpreted by us to represent a relapse, provided that there was either strong clinical or definite histopathological evidence (or both) of leprosy. A new skin lesion appearing during an episode of type 1 reaction would have posed a major difficulty of differential diagnosis, but this did not occur in this series.

RESULTS

The age and sex distribution of the patients in the two study areas are shown in Figures 1a and 1b. The excess of females is in agreement with data previously reported from Malawi ([11]). For the LCP area, the modal age was 25–29 years for males and 35–39 for females. The patients were youn-

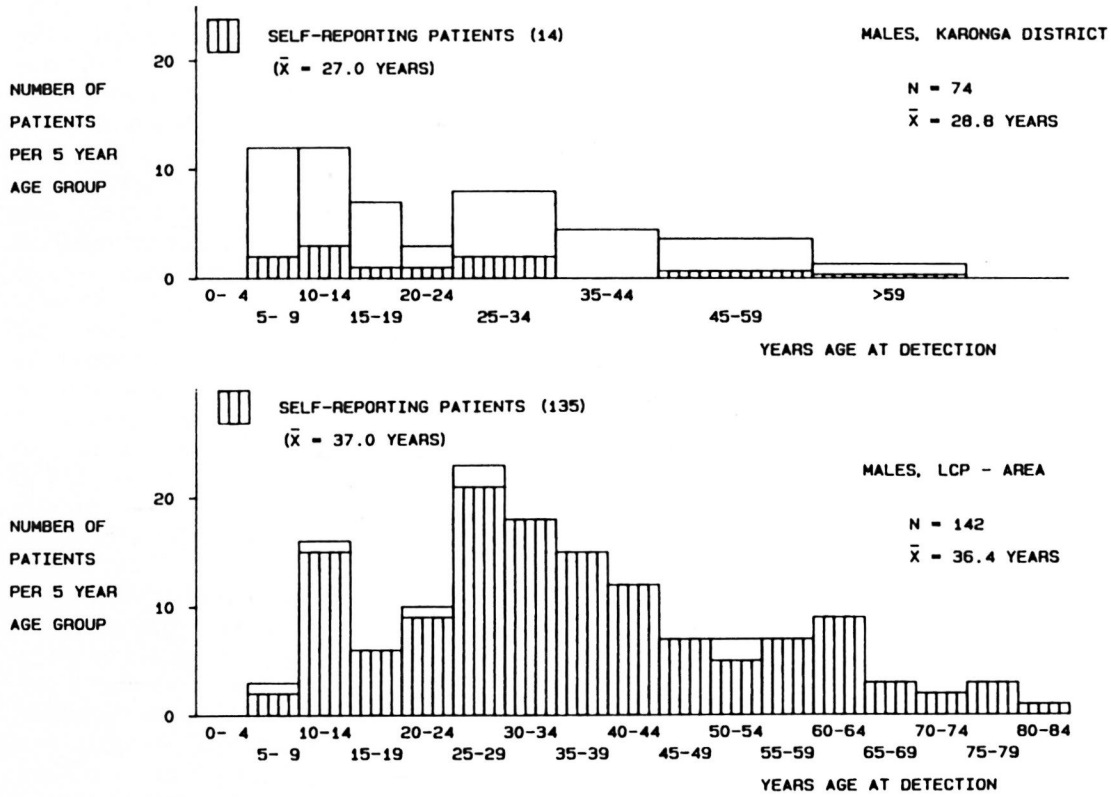

FIG. 1a. Age distribution of male patients included in the two study areas, Karonga District and LCP area.

ger in Karonga District, with modal ages of 5–14 for males and 10–14 for females. The mean age of self-reporting patients in Karonga District was slightly lower than that of patients found during the total population survey. Because of these differences, we have analyzed the results separately by type of detection and by area.

Of the patients recruited into the study, 297 of 301 (98.7%) had strong clinical evidence of leprosy in the LCP area and 170 of 202 (84.2%) in Karonga District. The histopathologists concurred by finding definite biopsy evidence of leprosy in 226 of 297 (76.1%) patients from the LCP area and in 133 of 170 (78.2%) of those from Karonga District. The remaining 36 subjects all had definite histopathological evidence of leprosy.

Table 1 shows a breakdown of patients included in the survey by area, mode of detection, classification, proportion with a single skin lesion, and proportion with palpably enlarged nerves at intake. The proportion classified as polar tuberculoid (TT) was lower in the LCP area (9.6%) than in Karonga District (15.3%), although the difference did not reach statistical significance ($\chi^2 = 3.23$, $0.05 < p < 0.1$), and lower among self-reported (5.0%) than among actively detected (17.9%) cases in Karonga District ($\chi^2 = 3.18$, $0.05 < p < 0.1$). The proportion with a single skin lesion was 79.6% among actively detected cases in Karonga District but only 32.5% among self-reporting cases in Karonga Distict and 43.2% among self-reporting cases in the LCP area. Similarly the proportion with palpably enlarged nerves at intake was much higher in the LCP area (49.5%) than in Karonga District (24.2%) ($\chi^2 = 31.2$, $p < 0.001$), and higher among self-reported (45.0%) than among actively detected (19.2%) cases in Karonga District ($\chi^2 = 10.3$, $p < 0.001$).

Dapsone/creatinine ratios and corresponding ELISA results in 25 "negative" controls are shown in Figure 2. The results suggest a lower limit of 11 μg DDS/mg creatinine and of 3.5 μg DDS/ml urine as an indication of dapsone intake. The two neg-

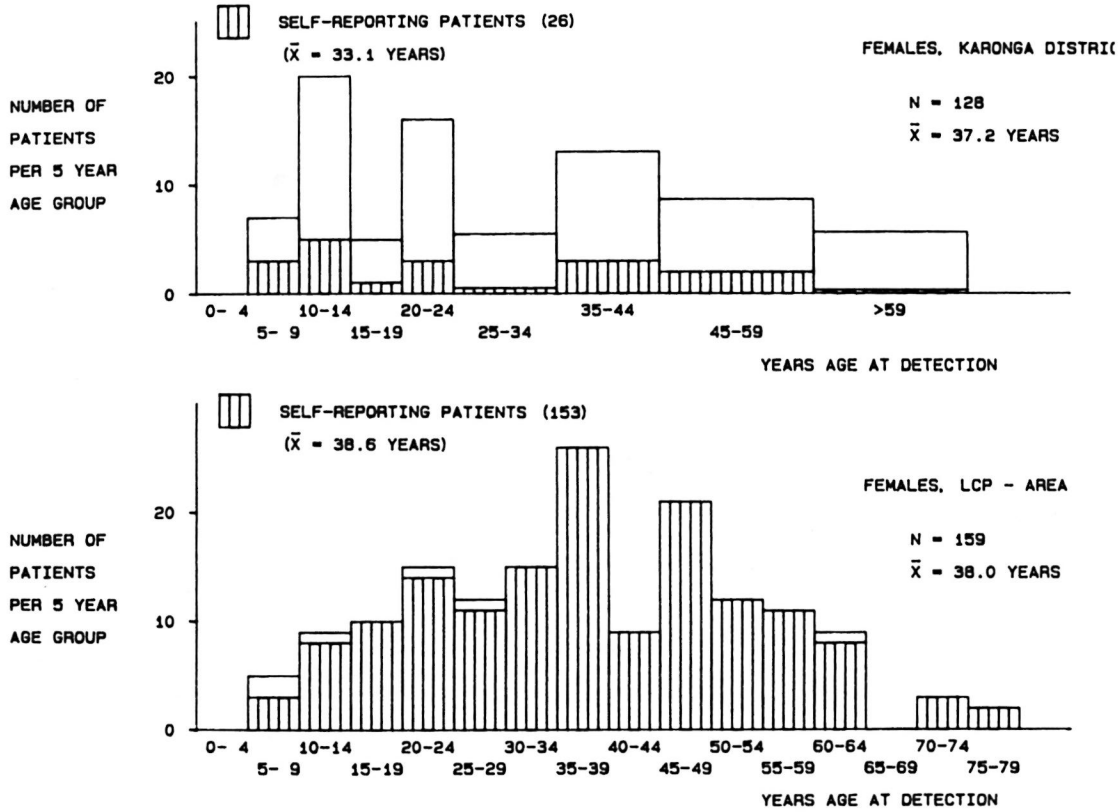

FIG. 1b. Age distribution of female patients included in the two study areas, Karonga District and the LCP area.

ative control individuals with dapsone/creatinine (D/C) ratios of 36.1 and 39.8 admitted to taking sulfonamides for enteritis at the time of urine collection.

The results of compliance studies are presented in Table 2. Dapsone/creatinine ratios are broken down into three categories, D/C ratios (in μg dapsone per mg creatinine) of <11, 11 to 30, and >30. They are usually interpreted as indicating "no intake," "irregular intake" and "regular intake," respectively. Compliance during the treat-

TABLE 1. *Distribution of patients included in the study by area, mode of detection, classification, proportion with a single skin lesion, and presence or absence of palpably enlarged nerves at intake.*

	Patients										
	Total no.	Indeterminate leprosy		TT leprosy		TT/BT – BT/BB leprosy		With single skin lesion at intake		With enlarged nerves at intake	
		No.	%	No.	%	No.	%	No.	%	No.	%
LCP area	301	0		29	9.6	272	90.3	130	43.2	149	49.5
Karonga District											
Self-reported	40	1	2.5	2	5.0	37	92.5	13	32.5	18	45.0
Actively detected	162	0		29	17.9	133	82.1	129	79.6	31	19.2
District total	202	1	0.5	31	15.3	170	84.2	142	70.3	49	24.2
Totals	503	1	0.2	60	11.9	442	87.9	272	54.1	297	59.0

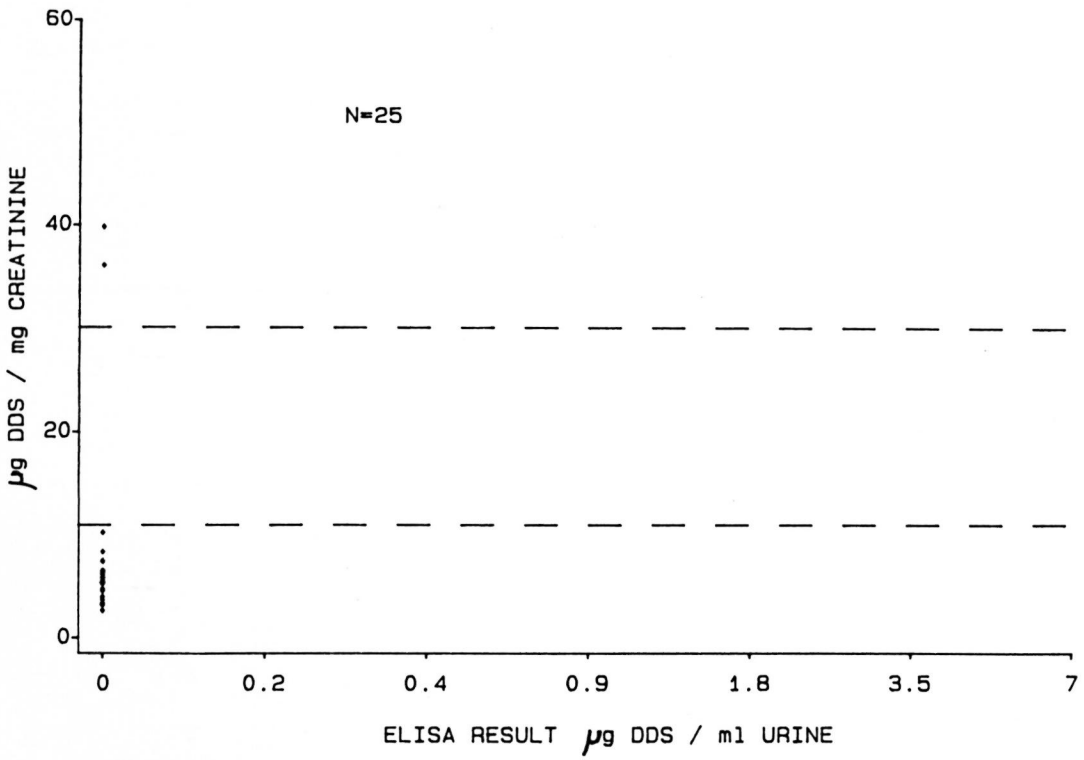

FIG. 2. Scatter diagram of dapsone/creatinine ratios versus ELISA values for 25 urine specimens collected from "negative" controls.

ment period was significantly higher in the LCP area than in Karonga District (e.g., 87.1% vs 55.1% classified as "regular," $\chi^2 = 58.9$, $p < 0.0001$). Within Karonga District, compliance was better among self-reporting than among actively detected patients (e.g., 71.1% vs 50.7%, $\chi^2 = 4.2$, $p < 0.05$). D/C ratios on urine specimens collected after treatment were similar in the two areas, with approximately 7% showing ratios >30.

WHO/MDT was evaluated in terms of a) outcome at the end of treatment and b) outcome at the end of 12 months' follow-up after treatment.

In one patient WHO/MDT had to be discontinued because of apparent allergy to both rifampin and dapsone during the third month of treatment. Four deaths occurred among the patients during the treatment period and two during the 12 months of follow-up. Three of the four deaths during treatment appear to be unrelated to the antileprosy treatment: one male (born 1928) died in congestive heart failure; one female (born 1940) died during an extended visit to a neighboring country; one male (born 1920) seems to have died from septicemia in connection with a jaw infection. However, one male (born 1956) had an episode of hematemesis and dysentery starting the day after the third dose of rifampin (600 mg), and he was admitted for this condition to the district hospital. Twelve days after his fifth dose of rifampin, he was admitted to a health center again with hematemesis, and he expired within 3 hours of admission. No further information is available.

Table 3 shows that 195 of 202 (96.5%) and 293 of 301 (97.3%) patients completed the prescribed treatment within the required first 9 months, and were reviewed at the end of treatment in Karonga District and the LCP area, respectively. The skin lesions were no longer evident at that time in 70 of 154 (45.5%) patients found by active case detection and in 10 of 39 (25.6%) self-reporting patients in Karonga District. This difference is statistically significant ($\chi^2 = 4.2$, $p < 0.05$). In the LCP area, skin

TABLE 2. *Number and percentages of urine specimens taken during treatment and during first 6 months after completion of WHO/MDT which were found with dapsone/creatinine ratios (μg dapsone/mg creatinine).*

D/C ratio	During treatment period								During first 6 months after completion of treatment			
	LCP area		Karonga District						LCP area		Karonga District	
			Actively detected		Self-reported		Total					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<11	8	2.72	29	20.7	6	15.8	35	19.7	174	60.4	90	58.8
11 to 30	30	10.2	40	28.6	5	13.2	45	25.3	96	33.4	52	34
>30	256	87.1	71	50.7	27	71.1	98	55.1	17	5.9	11	7.2
Total	294		140		38		178		287		153	

lesions were no longer evident at the end of treatment in 53 of 293 (18.1%) patients. In only 8 of 193 (4.1%) patients in Karonga District and 13 of 293 (4.4%) patients in the LCP area were the skin lesions still judged to be active at the end of treatment. Two patients with neural leprosy in Karonga District are excluded from this tabulation. Table 3 also shows the evolution of the same skin lesions that had occurred by the end of a 1-year follow-up after completion of WHO/MDT. The percentage of patients in whom skin lesions were no longer evident increased for all groups.

There were 11 patients with marked type 1 reaction at the beginning of treatment, 3 in Karonga District and 8 in the LCP area. One of these, in Karonga District, died in

TABLE 3. *Outcome after WHO/MDT in 503 paucibacillary leprosy patients in Malawi.*

	Karonga District		LCP area
	A[a]	S[b]	
No. patients in study	162	40	301
No. patients who died before completion of treatment	2	1	1
No. patients who did not complete prescribed treatment within 9 months	4	—	7[c]
Status and nos. of patients at end of treatment			
Lesions no longer evident	70/154[d] (45.5%)	10/39 (25.6%)	53/293 (18.1%)
Lesions visible but not active	79/154[d] (51.3%)	26/39 (66.7%)	227/293 (77.5%)
Lesions visible and active	5/154[d] (3.2%)	3/39 (7.7%)	13/293 (4.4%)
Status and nos. of patients 1 year after treatment			
Lesions no longer evident	89/150[e] (59.3%)	16/38[e] (42.1%)	75/285[e] (26.3%)
Lesions visible but not active	59/150[e] (39.3%)	21/38[e] (55.3%)	202/285[e] (70.9%)
Lesions visible and active	2/150[e] (1.3%)	1/38[e] (2.6%)	8/285[e] (2.8%)

[a] A = patients actively detected during the LEP survey.
[b] S = patients self-reporting to LEPRA staff.
[c] One allergic to rifampin and dapsone.
[d] Excluding the two patients with neural leprosy.
[e] Excluding patients with neural leprosy, refusals, and patients in whom antileprosy treatment had been re-initiated.

TABLE 4. *Outcome at the end of 1-year follow-up after completion of WHO/MDT in 480 paucibacillary leprosy patients in Malawi.*

	Karonga District		LCP area
	A[a]	S[b]	
No. patients reviewed regularly for at least 12 months after completion of treatment	153 (3/156 refused exam)	39	288 (3/293 left area; 2/293 died)
No. patients found with new additional lesion(s) during the first 12 months after treatment ("relapse")	0	0	2
No. patients found with renewed inflammation in previously inactive lesions			
Leading to steroid treatment ("marked type 1 reaction")	0	3 (3/3 histopath. confirmed)	12[c] (2/9 histopath. confirmed)
Not leading to steroid treatment ("mild type 1 reaction")	1 (0/1 histopath. confirmed)	1	7[c] (1/5 histopath. confirmed)

[a] A = patients actively detected during the LEP survey.
[b] S = patients self-reporting to LEPRA staff.
[c] All reactions occurred among the 275 of 288 self-reporting patients.

congestive heart failure. In addition, one in Karonga District and one in the LCP area developed disabilities during the course of WHO/MDT. Two of the 195 patients who completed the prescribed treatment in Karonga District and 5 of the 293 patients in the LCP area developed a marked type 1 reaction during treatment. Given that the treatment lasted 6–9 months per patient, the overall incidence rate of marked (early) type 1 reaction was 28 per 1000 person years during WHO/MDT. In none of these seven patients did the type 1 reaction lead to a disability.

Results during the 12 months following completion of treatment are shown in Table 4. New skin lesions were found during this period in two patients; both had originally self-reported in the LCP area. There were no signs of type 1 reaction clinically in the new lesions, and the biopsy specimens from the new lesions showed definite evidence of paucibacillary leprosy. We, therefore, consider these to be genuine relapses, giving a relapse rate of 2/480, or 4.17 per thousand person years (95% confidence interval 1.14 to 15.06 per 1000) during the first year after completion of WHO/MDT in paucibacillary leprosy patients.

Renewed inflammation in previously inactive skin lesions was observed in five patients in Karonga District and in 19 patients in the LCP area. In 3 of the 5 and 12 of the 19 patients, respectively, the inflammation was considered by the investigators to be serious enough to initiate treatment for type 1 reaction. Biopsies were taken from 17 of the 24 patients and the diagnosis of type 1 reaction was confirmed histopathologically in 6 of these. In the other 11 patients, the histopathologist found active leprosy but no conclusive signs of type 1 reaction. Two of the 15 patients who were put on steroid treatment (both in the LCP area) developed disabilities. Two other patients in whom steroid treatment was initiated (one in each area) were restarted on antileprosy treatment by the investigators 6 months after completion of the first WHO/MDT course because of continued type 1 reactions requiring repeated courses of steroids. In addition, 1 of the 11 patients in whom the histopathologist found active leprosy was restarted on antileprosy treatment (in Karonga District).

No patient who was clinically classified as TT or whose skin lesion(s) was no longer evident at the end of treatment developed a type 1 reaction during the first year after completion of WHO/MDT.

There was some evidence of an association between the presence of nerve enlargement at detection and the risk of developing type 1 reaction (after completion of treat-

ment). However, this association failed to achieve significance at the 5% level (χ^2 = 3.77).

DISCUSSION

We feel confident that virtually all patients included in this study had "true" paucibacillary leprosy, insofar as only those suspects with convincing clinical findings or with definite histopathological evidence of paucibacillary leprosy (or both) were included. Some of the differences found between patients in the LCP area and those in Karonga District, for example, the percentage with TT leprosy or with enlarged nerves, and even the later incidence rate of type 1 reaction, might be attributable in part to inter-observer variation between GB and JMP. However, we believe this is unlikely since the two investigators had worked together for several years. It seems more reasonable to attribute these differences to more intensive and thus earlier case detection in Karonga District. As far as relapses are concerned, it should be mentioned that one of the two relapses was examined by both investigators.

All rifampin was taken by the patients under strict supervision by the LEPRA field staff. The urine analysis results suggest that regular compliance with the prescribed dapsone component was between 51% and 87%. The lowest compliance appeared to be in actively detected patients in Karonga District. However, false-positives can arise due to certain sulfa drugs. Thus, the exact proportion of patients taking dapsone is not really known. One may suspect on the basis of Figure 2 that only those patients whose urines were strongly positive with both methods were actually taking dapsone.

Our data suggest that active surveillance of paucibacillary leprosy patients for 1 year after completion of WHO/MDT is feasible under these conditions since only 6 out of 486 patients either refused further participation or left for an unknown destination. Despite the fact that people in this population frequently change residence, it was usually possible to obtain enough information to find the patient who had moved. However, it should be empahsized that this surveillance required considerable logistic effort, in particular regular maintenance of motorcycles, spare parts and spare back-up motorcycles to keep the LCAs mobile at all times.

In view of the fact that other investigators have reported as many as 29.6% ([8]) and 50% ([1]) of paucibacillary leprosy patients still active at the end of WHO/MDT, our finding that only 4.3% of the patients were still active at that point in time seems surprisingly low. We do not know the reason for this dramatic difference. One could speculate that our patients started treatment, even in the LCP area, at an earlier stage of the disease process or that criteria for clinical activity were different compared with those reported by other investigators.

The observed relapse rate of 4.17 per 1000 person years compares favorably with the relapse rate of 12.9 per 1000 person years observed by Jesudasan, *et al.* in Gudiyatham Taluk, India, during the first year after completion of treatment with dapsone monotherapy ([7]). However, our relapse rate of 4.17 might be an underestimate insofar as we applied very stringent criteria for diagnosing relapses, and these criteria might differ from those applied in other studies. In particular, some of the lesions with renewed activity, which we judged to be type 1 reactions, might have been relapses. In this context it is worth noting that the histopathologist found only evidence of active paucibacillary leprosy, but no indication of reaction, in most (11 of 17) of these lesions. In addition, some patients seem to have continued to take unprescribed dapsone after completion of the treatment, and this might have lowered the relapse rate.

The incidence rate of marked type 1 reaction (leading to steroid treatment) after completion of WHO/MDT ranged from 43.6 (12 of 275) to 76.9 (3 of 39) per 1000 person years for self-reporting patients in the LCP area and Karonga District, respectively. We are not aware of any comparable rates in the literature. The rate may be a slight overestimate because, as discussed above, some of these lesions with renewed activity may have been relapses rather than late type 1 reactions. Of the 15 patients considered to have marked type 1 reaction, 13 were treated with prednisolone only and were not given any further antileprosy treatment. The lesions became inactive in all 13

of these patients, suggesting that they were indeed late type 1 reactions. The observed incidence rates indicate the need for active surveillance of patients for at least 1 year after completion of WHO/MDT, with the possible exception of TT leprosy patients and patients in whom all lesions have disappeared at the end of treatment.

The data presented in Table 4 indicate that the risk of late type 1 reaction was much higher among self-reporting patients than among those found by active case finding. Given that self-reporting patients generally have more advanced disease than do those ascertained by active case detection (Table 1), our findings suggest that the risk of developing late type 1 reaction is closely related to the stage of disease at detection.

We have attempted to apply strict criteria to our diagnoses of relapse and type 1 reaction. It has become increasingly clear, however, that the distinction between them is sometimes difficult and thus, to a certain extent, arbitrary. This problem has been noted by Pattyn in his discussion of incubation periods of relapses ([10]). However, it is important to note that a change in criteria would merely lower one rate at the expense of increasing the other. Both diagnoses are equally worrying to patients, the staff, and the public.

SUMMARY

A study was undertaken within the framework of the LEPRA Evaluation Project and the LEPRA Control Project in Malawi (Central Africa) to study the incidence rates of type 1 reactions and of relapses in paucibacillary leprosy patients treated with the current World Health Organization-recommended multiple drug regimen (WHO/MDT). Of 503 patients recruited into the study, 488 were reviewed at the end of treatment and 480 have now been followed for 1 year after completion of treatment. At the end of treatment the skin lesions had completely disappeared in 27.4%, but were judged to be still active in 4.3%. During the follow-up period two patients were found with new active skin lesions, giving a relapse rate of 4.17 (2 of 480) per 1000 person years during the first year after completion of WHO/MDT (95% confidence interval 1.14 to 15.06 per 1000 person years). The incidence rate of marked type 1 reaction (renewed inflammation in previously inactive lesions) during the first year after completion of WHO/MDT was 47.8 per 1000 person years in self-reporting patients but zero in patients identified by active case finding. Data are presented which suggest that the incidence rate of late type 1 reactions is closely related to the classification and stage of the disease at detection.

RESUMEN

Se hizo un estudio dentro de los proyectos de evaluación y de control (LEPRA) en Malawi, Africa Central, para estudiar los índices de incidencia de las reacciones tipo 1 y de las recaídas en los pacientes con lepra paucibacilar sometidos al esquema actual de tratamiento recomendado por la Organización Mundial de la Salud a base de drogas múltiples (WHO/MDT). De los 503 pacientes reclutados en el estudio, 488 fueron revisados al final del tratamiento y 480 se han seguido por un año después de completarlo. Al final del tratamiento, las lesiones dérmicas habían desaparecido completamente en el 27.4% de los casos pero fueron aún activas en el 4.3% de los mismos. Durante el periodo de seguimiento se encontraron dos pacientes con nuevas lesiones activas en la piel, dando un grado de recaída de 4.17 (2/480) por 1000 persona/año durante el primer año después de completar el tratamiento (intervalo de confianza—95%, 1.14 a 15.06 por 1000 persona/año). La incidencia de reacción marcada de tipo 1 (nueva inflamación en lesiones previamente inactivas) durante el primer año después de completar el tratamiento fue de 47.8 por 1000 persona/año en pacientes que se autoreportaron, y de cero en pacientes identificados durante la búsqueda de casos. Los datos presentados sugieren que la tasa de incidencia de las reacciones del tipo l tardías, está íntimamente relacioda con la clasificación y el estado de la enfermedad en el momento de su detección.

RÉSUMÉ

Dans le cadre du LEPRA Evaluation Project, et du LEPRA Control Project au Malawi, en Afrique Centrale, on a entrepris une étude en vue de mesurer les taux d'incidence des réactions de type 1 et de récidives chez les malades atteints de lèpre paucibacillaire traités par les posologies chimiothérapeutiques actuellement recommandées par l'Organisation Mondiale de la Santé. Parmi 503 malades repris dans cette étude, 488 ont été revus à la fin du traitement, et 480 ont maintenant été suivis pendant plus d'une année après la fin du traitement. Au moment où le traitement a été terminé, les lésions cutanées avaient complètement disparu chez 27,4% d'entre eux, mais chez 4,3%, elles étaient cependant considérées comme encore actives. Au cours

de la période de suivi, deux malades ont présenté de nouvelles lésions actives de la peau, ce qui donne un taux de récidive de 4,17 (2/480) pour 1000 personnes-années au cours de la première année après la fin du traitement recommandé par l'O.M.S. (OMS/PCT), ce qui correspond à un intervalle de confiance à 95% de 1,14 à 15,06 par 1000 personnes-années. Le taux d'incidence des réactions caractéristiques de type 1, soit une inflammation nouvelle survenant au niveau de lésions auparavant inactives, a été de 47,8 pour 1000 personnes-années après la fin du traitement tel qu'il est recommandé par l'OMS/PCT, chez les malades qui venaient consulter spontanément, mais il n'y a eu aucune récidive chez les malades repérés à la suite d'une détection active. Les données qui sontici présentées suggèrent que le taux d'incidence de la réaction tardive de type 1 est étroitement associé à la classification et au stade de la maladie au moment de la détection.

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