Further Observations on Streptomycin Combined with Sulfones in Relapsed Lepromatous Leprosy[1]

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A previous communication ([1]) presented data on 10 patients who had each relapsed despite what was considered to be adequate and continuous sulfone therapy and who were thereupon treated with a combination of streptomycin and sulfones. At that time the patients had been observed for up to 24 months. The present paper deals with an additional 12 months' observations on this same group of patients.

MATERIALS AND METHODS

Procedures for monitoring the patients' progress remained the same as reported earlier ([1]). Each patient who remained in the study continued to receive streptomycin, 1.0 gm. intramuscularly three times weekly and sulfone in a dosage of 600-700 mgm. of DDS (dapsone) per week, or alternatively six or seven 330 mgm. tablets per week of sulfoxone (Diasone) by mouth.

Clinical examinations and skin scrapings for acid-fast bacilli continued to be performed at monthly intervals, as were skin biopsies at intervals of six months from the same site in each patient.

Random blood sulfone measurements were performed, and nursing records were reviewed to determine the actual number of streptomycin injections taken by each patient.

RESULTS

Clinical data, including duration of combined treatment, regularity of taking treatment, clinical evidence of relapse, and presence of erythema nodosum leprosum, are given in Table 1 for all the original 10 patients studied. Blood sulfones determined by the method of Simpson ([2]) were considered positive at 0.10 mgm. per cent or more and negative below 0.10 mgm. per cent.

The morphologic index (MI) ([5]) of the acid-fast bacilli from skin scrapings is given in Table 2 for the five patients with clinical evidence of relapse. For the remaining five patients in the original study the morphologic index in skin scrapings remained at 0 to 1 per cent for the time they were under treatment.

The results of skin biopsies, expressed as the biopsy index ([3]) over the morphologic index obtained on the biopsy specimen, are given in Table 3 for the five patients with evidence of relapse. No further biopsies are available on the remaining five patients except for Case No. 1. In this patient, a biopsy taken during the 24th month of treatment from the left arm (the same site as earlier biopsies) was negative for acid-fast bacilli. At the same time, however, skin scrapings for acid-fast bacilli were positive with a morphologic index of 0, some 15 cm. distant from the biopsy site. This finding still obtains.

DISCUSSION

The obvious conclusion from the present observation is that the combination of streptomycin and sulfones is of only temporary benefit in cases of lepromatous leprosy which relapsed despite apparently regular and adequate sulfone treatment. Combined therapy apparently results in no greater benefit than that which might be expected if streptomycin were given alone to such cases ([4]), or at best the time of

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TABLE 1. *Clinical data.*

Case No.	Duration of observation on sulfones and SM[a] (Mo.)	Regularity of taking treatment				Blood sulfones[b]	New lepromatous lesions clinically	ENL
		Percentage of ordered streptomycin actually taken						
		1st yr.	2nd yr.	3rd yr.	Overall			
1	34	98	81	62	80	Pos.	No.	5th.–present
2	34	97	91	72	87	Pos.	Yes, 33rd mo.	No
3	25	91	64	—	79	Neg. × 1	No	Throughout until death 2 mo. p S .I[a] stopped.
4	23	95	65	—	80	Pos.	No	15th mo. until 6 mo. p SM[a] stopped.
5	29	94	95	97	95	Pos.	Yes, 27th mo.	12th mo.–present
6	32	99	89	83	92	Pos.	Yes, 28th mo.	14th mo.–present
7	33	96	89	92	92	Pos. × 2 Neg. × 1	Yes, 31st mo.	2nd mo.–present
8	13	95	—	—	95	Pos.	No	5th mo.–present
9	34	98	92	87	91	Pos.	Yes, 31st mo.	10th mo.–present
10	25	95	97	—	97	Pos.	No	No.
Mean		95.8	84.8	82.2	88.8			

[a] SM = streptomycin.
[b] See text.

TABLE 2. *Morphologic indices of skin scrapings.*

Case number	After streptomycin				
	Months				
	9th–21st	22–24th	25–27th	28–30th	31–33rd
2	1	1–5	1–2	5	20
5	1	1	1	1	0–9[a]
6	1	1	1	1	1
7	1	1	1	1	0–20[a]
9	1	1	1	0–1[b]	0.5[a]

[a] Multiple sites scraped. Original site still 0–1%.
[b] Five sites scraped at the 28th month and all had MI of 1%.

relapse on steptomycin is merely delayed temporarily by continuing the sulfone.

Several points should perhaps be mentioned concerning the present observations.

With the exception of Case No. 6 in which we have, to date, been unable to demonstrate an increase in the MI, the presence of relapse has been documented in five of the original 10 patients by the appearance of new lepromatous skin lesions from which skin scrapings have revealed an increase in the morphologic index. Thus, of the six patients followed for more than 25 months, five have shown evidence of relapse, four of these unequivocally. It is of interest that in three cases (Nos. 5, 7, and 9) the original single sites from which skin scrapings were routinely taken throughout the study, continued to show a morphologic index of 0 to 1 per cent, whereas the newer lesions have an increased MI.

In the present data (Table 3) when biopsies are taken serially from the same site, the biopsy index rises prior to the appearance of an increased MI, or the appearance of new lepromatous skin lesions. This is rather difficult to explain if indeed all nonsolidly-staining *M. leprae* are nonviable in humans. Also of interest is the rather wide variation in the readings of skin biopsies taken at various sites in the same individual at the time of relapse. The first biopsy taken from Case No. 7 at the 30th month was interpreted as an old regressing lepromatous lesion. The second biopsy taken from the same patient at the same time, was 10 mm. distant from the first and from a freshly-developing leproma. It was interpreted as a progressive lepromatous lesion. The third biopsy taken from the same patient at the same time was from his left forearm, whereas the first two were from the left deltoid region. The third biopsy was interpreted as a lesion of erythema nodosum leprosum. This diagnosis corresponded with the clinical interpretation.

It is also of interest that four of the five cases with evidence of relapse had erythema nodosum leprosum (ENL) at the time relapse was noted, and the reaction has continued to date. Case No. 4 refused further streptomycin injections because of ENL, and his reaction continued until approximately six months after stopping treatment. The ENL gradually subsided, but at the present time he has progressive nodular lepromatous disease, despite therapy with 1.0 ml. of Solapsone (Sulphetrone) administered twice weekly intramuscularly for the last six months.

SUMMARY

Five of an original group of 10 patients with lepromatous leprosy who relapsed despite apparently regular and adequate treatment, and who were then treated with a combination of streptomycin and sulfones, have shown evidence of relapse once more after 23 to 31 months of treatment with both drugs. This combination appears to have very little, if any, advan-

TABLE 3. *Biopsy index/biopsy MI of serial biopsies*[a].

Case No.	Streptomycin						
		After					
	Before	6 mo.	12 mo.	18 mo.	24 mo.	30 mo.	34 mo.
2	1.24/35%	1.24/1	1.00/1.5	0.88/2	1.01/<1	1.13/<1	—
5	2.93/20%	1.51/5	0.88/1.5	0.63/<1	1.58/<1	3.50/1–5%[b]	—
6	3.38/50%	2.10/<1	1.38/<1	0.70/<1	—	1.50/0 1.80/0[b]	—
7	4.68/25%	2.44/1	1.35/<1	1.24/<1	1.75/0	1.38/0 2.13/10%[b] 3.60/0[b]	—
9	1.58/30%	0.50/<1	0.88/<1	0.45/<1	1.00/<1	2.06/0	1.38/0 1.07/3.5[b]
Mean From the same site in each patient	2.76/32%	1.56/1.7	1.10/1	0.78/1	1.07/<1	1.52/0.<1	
Change since previous biopsy, in biopsy index (per cent)		↓ 43.5%	↓ 29.5%	↓ 29.1%	↑ 37.2%	↑ 42.1%	

[a] See text.
[b] New site biopsied is not same area as serially biopsied throughout the study.

tage over streptomycin alone in the management of clinically sulfone-resistant leprosy.

RESUMEN

Cinco pacientes de un grupo de 10 con lepra lepromatosa que recayeron a pesar de tratamiento aparentemente regular y adecuado, y que fueron entonces tratados con una combinación de estreptomicina y sulfonas, han demonstrado evidencia de volver a recaer una vez mas despues de 23 a 31 meses de tratamiento con ambas drogas. Esta combinación parece tener muy poca, si realmente hay alguna, ventaja sobre la estreptomicina sola en la atención de la lepra clinicamente resistente a la sulfona.

RÉSUMÉ

On a étudié un groupe de 10 malades atteints de lèpre lépromateuse, qui avaient présenté des récidives malgré un traitement approprié et apparemment régulier, et qui avaient alors été traités par une combinaison de streptomycine et de sulfones. Cinq de ces 10 malades ont à nouveau présenté des manifestations de récidive après une période de traitement par ces deux médicaments s'étendant sur 23 à 31 mois. Cette combinaison médicamenteuse semble avoir très peu d'avantages, ou même aucun advantage sur la streptomycine seule, dans le traitement de la lèpre cliniquement résistante aux sulfones.

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