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THE STATUS OF STREPTOMYCIN AND DIHYDROSTREPTOMYCIN IN THE TREATMENT OF LEPROSY

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Conflicting reports concerning the action of streptomycin in human leprosy have appeared in the medical literature. Cuttle (2), after treating one patient for fifty-five days with 185 gm. of the drug, concluded that the course of the disease in this patient had not been significantly altered. On the other hand Grillo (6), after treating one patient with lepromatous leprosy on doses varying from 2 to 4 gm. daily for a total dose of 360 gm., reported very favorable results. The report of Faget and Erickson (5) from Carville, the first to be made on the use of streptomycin in leprosy, summarizes the results obtained after the treatment of 10 patients of the lepromatous type with doses varying from 1 to 2 gm. daily for a period of seven months. Although stating that streptomycin produced encouraging results, they were of the opinion that further investigations would have to be made before any definite conclusion regarding its clinical effect could be reached. They also emphasized the need for a less toxic product than was then available, and the utilization of a lower dosage regimen than was ordinarily recommended at that time.

In advanced murine leprosy, Carpenter (1) has reported, after employing daily dosages of 25,000, 50,000 and 100,000 γ per kilogram of body weight for 5 days, streptomycin produces minimal therapeutic effects.

Cuttle did not specifically state the type of leprosy presented by his patient, but judging from the description in the case history it was undoubtedly lepromatous. He described the development by his patient of pain in the nodular lesions of the

skin and in the lobule of the right ear, where a nodule had formed on the twenty-ninth day of treatment. It appears that this occurrence would indicate the development of erythema nodosum rather than that of specific leprous nodules, which are usually anesthetic. Erythema nodosum reactions have been found to follow sulfone therapy, and have been experienced by the patients treated at Carville with streptomycin. Erythema nodosum lesions are nodular in appearance, are accompanied by pain or discomfort, and have an abrupt onset as indicated in the case history of this patient. The development of this condition can usually be considered a favorable prognostic sign, indicating a beneficial outcome of treatment. Moreover, I believe that the duration of treatment in this case was not sufficient to justify any definite conclusion as to its effects.

Grillo stated that early in the course of treatment of his patient a strong febrile reaction occurred and lasted for ten days, with deterioration of all skin lesions. Definite and progressive improvement then followed, with steady retrogression of all the lepromata. The occurrence of a febrile reaction of the type described obscures the evaluation of the results of the treatment itself. It is known that, quite often, febrile reactions in leprosy initiate in all leprous lesions spontaneous improvement which may be progressive and actually lead to an arrest of the disease.

At Carville, the experimental use of streptomycin in leprosy has been continued since the initial report was published. When reports become current that dihydrostreptomycin was less toxic than streptomycin, the former product was substituted for the latter. The present report is an evaluation of these drugs in a group of 114 patients, including the 10 original ones previously evaluated. It is believed that the findings in this larger group of patients will help to clarify some of the uncertainty that has prevailed relative to the value of these drugs in human leprosy.

METHODS AND CLINICAL MATERIAL

In the first report from Carville it was concluded that the use of streptomycin in large and continuous dosage produced toxic manifestations whose severity might preclude a successful termination of treatment. Accordingly, in pursuing the study further the dosage was reduced from 2 to 1 gm. daily, and for patients showing any toxic manifestations on the latter dose a further reduction of dosage to 0.5 gm. daily was made. With dihydrostreptomycin, used in place of streptomycin after January 1, 1949, the treatment regimen consisted of giving intramuscularly doses of 0.25 or 0.5 gm., as might be indicated, every 12 hours for 120 days for determination of the effect upon the specific lesions of leprosy. If the results

then seen warranted continuing, another trial of 120 days was made, provided toxic manifestations were minimal. After this the drugs were continued as long as they were well tolerated by the patients.

Experience gained in the treatment of the original group, which indicated that leprous lesions of the mucous membranes responded favorably and healed well after streptomycin, led to the use of this drug concomitantly with the sulfones for patients who, despite sulfone treatment, continued to have nasal obstruction, crusting and scabbing of the nasal mucosa, epistaxis, and hoarseness. The use of the streptomycin drugs was later expanded for trial in any acute or chronic complication of leprosy which seemed to persist despite sulfone therapy. These complications were leprous iridocyclitis, episcleritis, and keratitis, leprous neuritis and orchitis, and lepra reactions. Courses of treatment varying from 2 weeks to 1 month were employed for acute manifestations. Prolonged treatment was given for any chronic involvement.

The clinical material evaluated in this report, a total of 114 patients, can be best classified as follows:

Group I.—Eleven patients treated with streptomycin or dihydrostreptomycin alone for evaluation of the effect of these drugs, primarily, upon the specific leprous skin lesions. If complications of leprosy were present, these were also studied for evaluation of effect. All except two of these patients had had no previous antileprosy treatment except chaulmoogra oil. One patient was of the intermediate type; the rest were all of the lepromatous type.

Group II.—Fifteen patients treated with streptomycin drugs together with sulfones for evaluation of the effect of combined treatment, from the same point of view as with Group I. Three of these patients had had no previous antileprosy treatment; the others had been treated with sulfones, but the skin lesions had approached a stationary stage or one of imperceptible improvement. All patients were of the lepromatous type.

Group III.—Thirty patients treated concomitantly with sulfones for evaluation of this treatment upon lesions of the nasal or laryngeal mucous membrane which continued to give symptoms despite sulfone therapy.

Group IV.—Forty-three patients treated concomitantly with sulfones for evaluation of such treatment upon acute, acute recurrent, and chronic eye lesions which made their appearance during or persisted in spite of sulfone therapy.

Group V.—Eleven patients currently treated with sulfones and given streptomycin or dihydrostreptomycin for acute lepra reactions.

Group VI.—Four patients on sulfone therapy for leprosy treated with dihydrostreptomycin for pulmonary tuberculosis. Leprous lesions were observed for any added beneficial effect.

RESULTS

GROUP I

Definite beneficial effects upon the skin lesions were noted in all except one of the 11 patients in Group I about six weeks, on an average, after treatment was begun. Improvement consisted of a definite fading of macules and infiltrated patches and decrease in the turgescence of the infiltrations. A few weeks later this initial improvement was followed by decrease in thickness of the macules and infiltrations and in the size of the nodules. Often such promising signs of regression occurred earlier than they do under promin or diasone therapy. The improvement was progressive as long as therapy was continued. Since all patients except one were definitely of the lepromatous type and improvement was consistent in the group, spontaneous regression does not seem to be a likely explanation. Improvement in the patient with an intermediate type of the disease was similar to that in the others; two months after treatment was discontinued, however, the skin lesions became clinically worse. The patient in whom no improvement could be detected was a case of lepromatous leprosy of the diffuse form. The skin of this patient, although strongly positive for leprosy bacilli, showed only very slight thickening without much pigmentary change. Any improvement that might have occurred clinically would have been difficult to detect.

There were no changes in the concentration of leprosy bacilli in the skin lesions of any of these patients. The longest treatment period was about fifteen months, so that in this respect the effects of treatment with streptomycin are paralleled to those with the sulfone drugs. In frank lepromatous cases no change is usually noted at that period in the concentration of bacilli as such reports are made by the laboratory from skin smears.

In the first few days of treatment, usually by the end of the first week, definite beneficial effects upon lesions of the mucous membrane of the nose and throat occurred. Such improvement was much more rapid than that noted from the sulfones. There was relief of nasal obstruction through rapid healing of the ulcerations of the mucous membrane, resulting in decrease of scabbing and crusting of these lesions. Ozena, if present, was relieved, and epistaxis was reduced in frequency. One patient with extensive leprous ulceration of the soft palate improved with healing of the ulcerations after one month of treatment. Four patients in this group had acute iridocyclitis when treat-

ment began; all of them soon experienced relief of the acute symptoms, although the basic eye changes did not appear to be materially benefited.

It became necessary to discontinue streptomycin as well as dihydrostreptomycin in 9 patients because of unpleasant toxic effects. The usual cause for discontinuing the treatment was persistent vertigo, sometimes associated with tinnitus and in one patient with loss of hearing. Another patient developed severe erythema nodosum for which the drug was discontinued. The remaining patient did not experience toxic effects, but left the hospital without permission after three months of therapy. The duration of treatment and other data for each patient are summarized in Table 1.

Clinical photographs taken at various stages of treatment of four of these patients are shown in Plates (1) and (2).

TABLE 1.—Clinical data and dosage regimens, Group I patients.*

Case No.	Sex	Age (years)	Race	Type of leprosy	Type of lesion	Drug given	Daily dose (gm.)	Reduced dose (gm.)	Day dosage reduced	Total do (gm.)	Days of treatment	Total period (days)	Reason for discontinuing treatment	Clinical Status			
														Before treatment		At end of treatment	
														Skin lesions	Bacilli	Skin lesions	Bacilli
1	F	49	W	L3N3	NDI, M	S	1.0	0.5	5th	79	153	155	V	P	4+	I	4+
2	F	39	W	L2N	N, DI	S	1.0	0.5	49th	80	110	110	A	P	4+	I	3+
3	M	37	W	L2N	N, DI	SD	1.0	139	139	147	V	R	4+	I	4+
4	M	64	C	L3N	N, DI	D	1.0	234	234	279	V	P	4+	I	4+
5	M	67	W	L3N	P1, DI	SD	1.0	235	235	295	V	P	4+	I	4+
6	M	W	Int	P1, DI	S	2.0	1.0-	51st	314	312	330	V	P	4+	I	3+
7	M	46	W	L2N3	N, DI	S	2.0	0.25 1.0	120th	343	223	225	VT	P	4+	I	3+
8	F	28	W	L1N	DI	S	2.0	1.0	120th	365	245	246	V	St	4+	St	3+
9	M	42	F	L2N	N, DI	D	1.0	383	383	475	VT	P	4+	I	3+
10	M	31	W	L2N	N, DI	S	2.0	1.0	120th	421	323	324	V	P	3+	I	2+
11	M	36	F	L2N	N, DI	S	2.0	1.0	120th	458	338	339	V	P	4+	I	4+

* Symbols used in table: F, female; M, male; W, white; C, colored; F, Filipino; LN, lepromatous with neural manifestations; Int, intermediate; N, nodules; DI, diffuse infiltrations; M, macules; P1, plaques; S, streptomycin; D, dihydrostreptomycin; V, vertigo; A, absconded; T, tinnitus; P, progressive; R, regressive; St, stationary; I, improved.

GROUP II

Additional evidence of a suppressive or antileprosy effect of streptomycin and dihydrostreptomycin is given by the 15

patients in Group II, under combined treatment. In many of them, improvement of the skin lesions from sulfone therapy had ceased entirely or continued to progress to an almost imperceptible degree. Some still complained of nasal difficulty despite prolonged sulfone therapy. With the addition of streptomycin or dihydrostreptomycin to the treatment regimen the nasal symptoms were rapidly relieved. After about two months of treatment renewed clearing was noted in the residual skin lesions. These beneficial effects occurred almost universally, and were progressive in character as long as the drugs were administered. Those patients, three in number, who had had no previous anti-leprosy treatment when given the combined therapy appeared to show a greater degree of clearing of the lesions in the same period of time than that observed from either drug alone.

The concentration of leprosy bacilli found in the skin smears of these patients was not materially altered. Four patients (Nos. 2, 6, 12 and 13, Table 2), having a 1+ concentration of bacilli when treatment was begun,¹ showed a greater number of negative than positive smears during the course of the treatment. One of these four (No. 13), has had 20 months of this therapy and is still being treated. It cannot be determined, however, how much of the reduction in bacilli shown in Table 2 was due to the sulfones and how much, if any, was due to the addition of the antibiotic to the treatment regimen.

As in Group I, it became necessary in most of these cases to discontinue the antibiotic because of the occurrence of continued vertigo. Since it soon became apparent that after vertigo occurred the liability of ear involvement usually increased, the drug was in most cases discontinued shortly after this condition became established. In Table 2 is shown, among other things, the period over which it was possible to continue treatment in each case.

GROUP III

The group of 30 patients who continued to complain of nasal obstruction and hoarseness despite prolonged treatment with sulfones responded unusually well to this antibiotic treatment. (4) Objectively, these patients showed limited ulceration of the mucous membrane of the septum associated with crusting and

¹ The concentration of bacilli found in the skin and nasal smears is graded according to numbers, as follows: 1+ or rare, less than 1 bacillus per field; 2+ or few, 1 to 10 bacilli per field; 3+ or moderate, 10 to 50 bacilli per field; 4+ or numerous, more than 50 bacilli per field.

TABLE 2.—Clinical data and dosage regimen, Group II patients.

Case No.	Sex	Age (years)	Race	Type of leprosy	Type of lesion	Drug given	Daily dose (gm.)		Day dosage reduced	Total dose (gpn.)	Days of treatment	Total period (days)	Reason for discontinuing treatment	Clinical		Status	
														Before treatment	At end of treatment		
														Skin lesions	Bacilli	Skin lesions	Bacilli
1	M	64	W	L3N3	R	D	1.0	0.5-0.25	28th	41	56	56	St	1+	Irc	1+
2	M	38	W	L3N2	R	D	1.0	99	99	101	V	St	1+	Irc	0
3	F	30	W	L3N	Pl	S	2.0	0.5	28th	116	141	155	VH	St	4+	I	1+
4	F	48	W	L2N3	N, DI	S	1.0	0.5	43rd	102	160	160	V	P	4+	I	3+
5	M	59	W	L3N3	R	SD	0.5	131	262	262	V	St	1+	Irc	1+
6	M	42	W	L2N	R	D	1.0	0.5	102nd	159	216	295	V	St	1+	Irc	1+
7	M	44	W	L1N	M, DI	D	0.5	198	395	425	St	2+	I	1+
8	M	59	W	L2N	Pl, M	D	1.0	220	220	236	V	P	4+	I	4+
9	M	C	L3N	N, DI	S	2.0	1.0	120th	318	263	263	V	St	4+	I	4+
10	M	29	C	L2N	N, DI	D	1.0	323	323	365	P	4+	I	2+
11	F	W	L2N	N, DI	S	2.0	1.0	120th	353	228	229	V	P	3+	I	2+
12	M	41	F	L2N	R	D	1.0	355	355	425	St	1+	Irc	0
13	M	63	W	L3N	R	SD	1.0	0.5	215th	372	544	611	St	1+	Irc	0
14	M	40	W	L3N	N, DI	S	2.0	1.0	120th	379	347	350	V	St	4+	Irc	3+
15	M	28	W	L2N	DI	S	2.0	0.5	176th	452	342	360	V	St	4+	Irc	3+

Symbols used in table: M, male; F, female; W, white; C, colored; F, Filipino; LN, lepromatous with neural manifestations; R, residual following sulfone therapy; Pl, plaques; N, nodules; DI, diffuse infiltrations; M, macules; D, dihydrostreptomycin; S, streptomycin; V, vertigo, H, loss of hearing; St, stationary; I, improved; Irc, improved with renewed clearing.

scabbing. Those complaining of hoarseness continued to have limited residual infiltration of the pharyngeal mucous membrane.

Symptomatic improvement was first noted by these patients after five to seven days of treatment. Objective improvement consisted of healing of the ulcerations with discontinuation of crusting and scabbing. It was usual for recurrences to appear if the antibiotic treatment was of short duration (two weeks to one month), whereas resumption of the treatment resulted in renewed improvement. Patients who were continued on the drug for periods of from three to six months usually had no further trouble, and those who had had chronic ozena from mucous membrane involvement were exceedingly grateful; this symptom

improved remarkably with the disappearance of the underlying cause.

The dosages given these patients were as follows: 7 to 30 gm., 11 cases; 31 to 60 gm., 9 cases; 61 to 120 gm., 5 cases; and 121 to 192 gm., 5 cases.

GROUP IV

The group of 43 patients who developed acute eye complaints while on sulfone therapy have been divided into subgroups depending upon the severity of the basic pathologic changes in the eyes. Those who developed acute iridocyclitis with minimal corneal infiltration, nodular iritis, and circumcorneal nerve beading have been designated as subgroup A, while those with advanced keratitis, nodular iritis, and nerve beading have been designated subgroup B. One patient whose eye changes were unusual, consisting of nodules of the fundus, has been placed in a separate subgroup, C.

The acute iridocyclitis developed by patients whose basic eye changes were minimal responded well, symptomatically and objectively, to streptomycin. The usual course of treatment consisted of a daily dose of streptomycin of 1 gm. for a period of two weeks. Symptomatic relief from pain and photophobia usually occurred after three to five days of treatment. Quite often the treatment was continued for an additional two weeks up to one month. Recurrence of the iridocyclitis occurred in 6 of the 22 patients in this subgroup. These patients were again treated, and each time they responded well. The basic eye changes, however, were not materially altered.

The symptomatic response to treatment in subgroup B was also good. The objective response was not as good as for the patients with minimal basic changes. Recurrence occurred among 10 of the 20 patients of this subgroup, and the basic eye changes either remained unaltered or continued to progress unfavorably.

Eye lesions of advanced standing offer much resistance to sulfone therapy and generally progress despite intensive treatment. It appears that this is also true of streptomycin therapy.

One patient recently reported (3) as having nodular leprosy lesions of the fundus developed while taking diasone was treated with streptomycin because his vision failed to improve after a change to promin, given in a daily dose of 5 gm. intravenously for seventeen months. No improvement occurred in the visual acuity of the left eye, which only had a blurred conception of the

20/100 characters of the trial chart. After six weeks treatment with dihydrostreptomycin visual acuity returned to 20/30, which was the reading prior to his sudden loss of critical vision when the lesions developed. Objective improvement in the lesions of the retina were noted by ophthalmoscopic examination. Although the nodular lesions of the retina in leprosy have been described as of a transient character, the rapid improvement after streptomycin therapy following failure of improvement on prolonged promin therapy would suggest that the credit for improvement in this patient's vision should be given to streptomycin.

The data on the treatment given these patients and the results with respect to the eye lesions are given in Table 3.

TABLE 3.—Clinical data and total dosage given Group IV patients.

Condition treated ^a	Total dose (gm.)	No. of patients	Clinical status after treatment					Recurrence
			Iridocyclitis		Basic eye lesions			
			SI	OI	I	U	W	
A	4-30	14	14	14	-----	14		2
	30-60	3	3	3	-----	3		2
	60-120	5	5	5	-----	5		2
B	10-30	7	6	5	-----	6	1	1
	30-60	1	1	1	-----	1		1
	60-120	4	4	0	-----	2	2	3
	120-240	4	4	4	-----	3	1	2
	240-360	4	4	1	-----	4		3
C	113	1	-----	-----	1	-----		

^a A, acute iridocyclitis associated with minimal basic eye lesions—keratitis, nodular iritis and circumcorneal beading. B, acute iridocyclitis associated with advanced basic eye lesions of the same nature. C, leprosy lesions of the fundus.

SI, symptomatic improvement; OI, objective improvement; I, improved; U, unchanged; W, worse.

GROUP V

Leprosy reactions, varying from simple erythema nodosum to the more generalized type in which there is an exacerbation of all leprosy lesions, were treated in 11 patients. It did not appear that any particular beneficial effect was secured. The febrile

phase of two of these patients improved rather abruptly after streptomycin treatment was begun, but it was impossible to correlate cause and effect. Neuritis, orchitis, lymphadenitis, edema of the mucous membrane and skin as well as iridocyclitis associated with severe lepra reactions failed to respond.

GROUP VI

Three of the four patients having pulmonary tuberculosis associated with leprosy were given a total of 90 gm. of dihydrostreptomycin over a period of ninety days. The fourth patient was unable to tolerate the drug for more than one week. Those patients who received extended therapy showed renewed clearing of their residual skin lesions.

SUMMARY AND COMMENT

Evidence is given by this study that, in dosage as low as 0.5 gm. daily, streptomycin and dihydrostreptomycin produce beneficial effects upon the specific cutaneous and mucous membrane lesions of leprosy. These beneficial effects may appear earlier in treatment than similar improvement obtained by the use of promin and diasone, and they are sustained as long as the drugs are administered. Advanced eye involvement is resistant to streptomycin treatment, as it is to the sulfones, but the symptoms associated with acute or acute recurrent iridocyclitis can often be absorbed with these antibiotics. Iridocyclitis appearing during sulfone therapy also often responds to this treatment. Little, if any, beneficial effect is exerted on acute lepra reactions, or on such complications as acute lymphadenitis, orchitis, neuritis, edema of the mucous membranes or skin associated with such reactions.

The appearance of toxic manifestations, vertigo, tinnitus, and loss of hearing usually precludes the continuous administration of these drugs beyond a period of six months, and rarely will a patient tolerate them for more than one year. Although clinical improvement at the end of such periods of treatment is marked, the concentration of bacilli in the remaining skin lesions, as reported by the laboratory, remain unaltered. Since a material portion of the volume of a leproma is composed of bacilli, however, reduction in size of lepromata secured from treatment must represent a reduction in the absolute number of bacilli in the tissue. If that were not so the numbers of bacilli in the smears would increase correspondingly with decrease of the tissue elements in the lesions. In these two respects treat-

ment with these antibiotics parallel those obtained with the sulfones. The sulfones, however, can be administered indefinitely and usually a definite reduction of bacilli in nodular lepromatous lesions as reported by the laboratory, can be demonstrated after an average of two or three years of treatment. When, if ever, such a reduction can be effected by streptomycin therapy alone cannot be determined unless a much less toxic product can be created or the dose and frequency of injections can be further reduced to a nontoxic level without a loss of therapeutic activity.

The early response of mucous membrane lesions to these antibiotics, with relief from annoying symptoms, is undoubtedly due to the elimination of secondary invaders, including saprophytic organisms growing in and upon leprous lesions of the nasal, pharyngeal, and laryngeal mucous membranes. Healing of leprous ulcerations of these structures indicates that the drugs also have an effect upon these lesions themselves. This should not be surprising in view of the effect that the drugs apparently show upon the leprous skin lesions, which can hardly be ascribed to control of secondary invaders. The rapid response to these antibiotics on the part of sulfone-resistant lesions of the mucous membranes indicates that they exert a greater activity than the sulfone against secondary infection and, perhaps, the leprous lesion itself.

CONCLUSIONS

Streptomycin and dihydrostreptomycin appear to have a suppressive effect upon specific leprous lesions. Clinical improvement has been almost universal and sustained.

In view of their toxicity, precluding continuous administration in the average case beyond a maximal period of 6 to 9 months, it has not been possible to determine whether or not the drugs are capable of producing a significant reduction of lepra bacilli in the specific lesions beyond that time, as it has been possible with the sulfones which can be administered indefinitely.

Unless a less toxic product is found, or unless the dosage can be further reduced without impairing therapeutic activity, so that extended treatment can be undertaken, the value of streptomycin and dihydrostreptomycin must of necessity be limited to that of an adjuvant to sulfone therapy. For this purpose its effective utilization can be recommended as follows:

1. For hastening the resolution of specific leprous skin and

mucous membrane lesions by combining it with the sulfones at the beginning of treatment.

2. For effecting further clearing of residual leprous skin lesions which have reached a stationary stage or one of imperceptible improvement under sulfone treatment.

3. For the relief of annoying symptoms of sulfone-resistant mucous membrane lesions, and for the healing of such lesions.

4. For aborting attacks of acute leprous iridocyclitis and relieving the intense discomfort associated with this condition.

5. For treatment of patients who have an idiosyncrasy to the sulfones.

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CONCLUSIONES

Estreptomycin y dehidroestreptomycin parecen tener efecto supresivo en las lesiones específicas de la lepra. Mejoría clínica ha sido casi universal y sostenida.

En vista de su toxicidad, que precluye administración continua en el caso promedio por un período sobre 6 a 9 meses, no ha sido posible determinar si las drogas son o no capaces de producir una reducción significativa en el número de bacilos de lepra en las lesiones, como ha sido posible demostrar con drogas sulfonas las cuales pueden administrarse por tiempo indefinido.

A menos que se descubra un producto menos tóxico, o a menos que la dosis pueda ser reducida aun mas sin interferir con la actividad terapéutica, de manera que tratamiento de larga duración pueda ser administrado, el valor de la estreptomycin y la dehidroestreptomycin necesariamente se limitará a auxiliar la terapia con las sulfonas. Con éste propósito, para su uso efectivo, se recomienda lo siguiente.

1.—Para acelerar la resolución de lesiones leprosas cutáneas y mucosas, tratamiento combinado con sulfonas desde el principio.

2.—Para ayudar a resolver lesiones residuas cutáneas, las cuales hayan llegado al estado estacionario o que demuestren una evolución favorable muy lenta bajo tratamiento con sulfonas solamente.

3.—Para aliviar síntomas molestos de lesiones mucosas resistentes a las sulfonas, y para la curación de dichas lesiones.

4.—Para abortar ataques de iridociclitis leprosa aguda y aliviar las molestias asociadas a éstas lesiones.

5.—Para tratar pacientes alérgicos a las sulfonas.

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DESCRIPTION OF PLATES

PLATE 1.

FIG. 1. Case 1 of Group I, before treatment.

FIG. 2. Objective improvement shown by this patient after five months of treatment with streptomycin, 0.5 gm. daily.

FIG. 3. Case 4 of Group I, before treatment.

FIG. 4. Objective improvement shown by this patient after eight months of treatment with dihydrostreptomycin, 1 gm. daily.



PLATE 1.

PLATE 2.

FIG. 5. Case 11 of Group I, before treatment.

FIG. 6. Objective improvement shown by this patient after three months of treatment with streptomycin, 2 gm. daily to this time.

FIG. 7. The same patient after six months of treatment, the dose reduced to 1 gm. daily after 120 days.

FIG. 8. Close-up photograph of a nodule (indicated by an arrow) and infiltration of skin in Case 5 of Group I, before treatment. The areas indicated by numerals are nonleproous (fibromata).

FIG. 9. The same lesion after 1 month of treatment with streptomycin, 1 gm. daily, showing flattening and decrease of infiltration.

FIG. 10. The same lesion after five months of treatment.

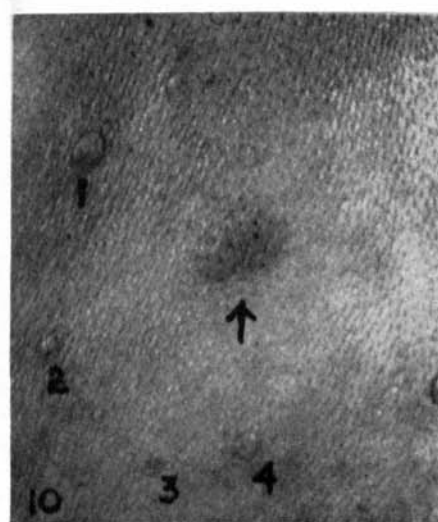
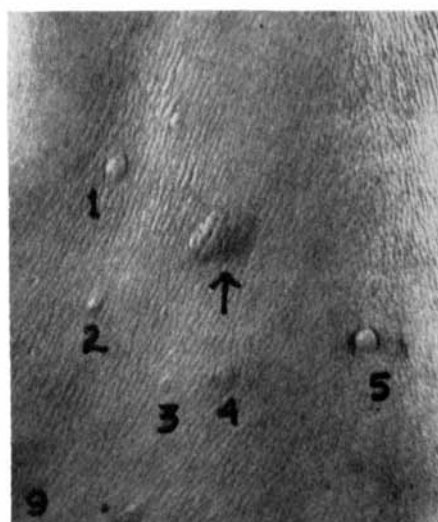
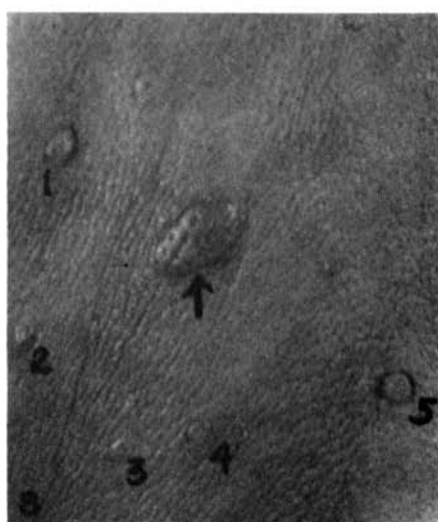


PLATE 2.