# TREATMENT OF LEPROMATOUS LEPROSY BY A COMBINATION OF DDS AND SARSAPARILLA (*SMILAX ORNATA*)

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The sometimes spectacular, but admittedly inconstant, action of decoctions of sarsaparilla on leprosy, traditionally employed by the Moroccans for its treatment, led me to investigate, beginning in 1948, the real nature of the active principles of that plant and its therapeutic possibilities.

The chemical, pharmacodynamic and phytologic studies were carried out by Paris, Vaillant and Menard ([2]), and by Cottet ([1]). The first three authors, in particular, examined the saponosides of two sarsaparillas, *Smilax ornata* and *S. japicanga,* which have been used as antileprosy medicaments. In the light of their work we have successively employed weak aqueous extracts of *S. ornata;* and then tablets containing 240 mgm. of the extract. The early results were reported by Rollier, Noury, Weissgerber and Maury ([7]) from the clinical, histologic and bacteriologic points of view. Repeatedly since then I have called attention to the antileprosy activity of red sarsaparilla, either used alone or in association with DDS ([3-6]).

## PRESENT STUDY

Here are reported observations on two groups of patients with lepromatous leprosy who were treated and examined for a period of three years, one of which (Group 1) was given an experimental combined treatment of sarsaparilla tablets and DDS, the other (Group 2) receiving DDS alone to serve as a control.

The first group comprised 111 cases—33 L1 (29%), 43 L2 (39%), 30 L3 (27%), and 5 regressive (5%). The DDS was administered in progressive doses, starting at 25 mgm. and increasing by 25 mgm. every 3 weeks, never exceeding a daily dose of 150 mgm. for adults weighing 70 kgm. The sarsaparilla dosage was increased from 4 to 10 tablets in the first week, remaining at the daily dose of 10 tablets for a minimum period of 6 months and a maximum of 1 year. Subsequently, the treatment was continued with DDS alone in the classical dose of 150 mgm. per day for adults.

The bacteriologic, clinical and biologic results, supported to some extent by pathologic findings, have been compared with those obtained with DDS alone in a comparable lot of 140 patients, distributed as follows: 42 L1 (30%), 56 L2 (40%), 38 L3 (27%), and 4 regressive (3%). The patients of this second group were given the same doses of DDS as those in the first lot. With both groups the treatment was given 6 days a week.

RESULTS

*Bacteriologic changes.*—The degrees of bacteriologic positivity in the two groups, Group 1 on the combination treatment and Group 2 on DDS alone, in the nasal mucosa and the lepromas at the beginning of the experiment are shown in Table 1. It is to be noted that all cases had positive skin lesions, but that several in each group gave negative nasal smears. It was impossible to make the groups strictly comparable, and the DDS-Smilax group had slightly the greater degrees of positivity, which makes the findings the more significant.

TABLE 1.—*Degrees of bacteriologic positivity, in percentages, before, during and after treatment of Group 1 (DDS-Smilax, 111 cases) and Group 2 (DDS control, 140 cases), in the nasal mucosa and the lepromas.*

| Period of treatment | Group 1 | | | | | Group 2 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Neg. | 1+ | 2+ | 3+ | 4+ | Neg. | 1+ | 2+ | 3+ | 4+ |
| *Nasal mucosa* | | | | | | | | | | |
| Before | 0[a] | 14 | 34 | 42 | 10 | 0[b] | 22 | 33 | 35 | 10 |
| After 6 mos. | 54 | 29 | 13 | 4 | 0 | 27 | 34 | 29 | 10 | 0 |
| After 1 yr. | 83 | 9 | 8 | 0 | 0 | 52 | 37 | 8 | 3 | 0 |
| After 1½ yrs. | 93 | 7 | 0 | 0 | 0 | 74 | 21 | 4 | 1 | 0 |
| After 2 yrs. | 100 | 0 | 0 | 0 | 0 | 86 | 12 | 2 | 0 | 0 |
| After 2½ yrs. | 100 | 0 | 0 | 0 | 0 | 98 | 2 | 0 | 0 | 0 |
| *Lepromas* | | | | | | | | | | |
| Before | 0[c] | 6 | 16 | 50 | 28 | 0[c] | 16 | 31 | 32 | 22 |
| After 6 mos. | 13 | 23 | 30 | 32 | 2 | 4 | 30 | 32 | 28 | 6 |
| After 1 yr. | 24 | 22 | 32 | 22 | 0 | 8 | 48 | 29 | 11 | 4 |
| After 1½ yrs. | 37 | 27 | 29 | 7 | 0 | 22 | 51 | 21 | 5 | 1 |
| After 2 yrs. | 51 | 41 | 10 | 0 | 0 | 41 | 42 | 13 | 4 | 0 |
| After 2½ yrs. | 57 | 32 | 11 | 0 | 0 | 57 | 31 | 11 | 1 | 0 |
| After 3 yrs. | 61 | 33 | 6 | 0 | 0 | 61 | 27 | 12 | 0 | 0 |

[a] Of the 111 cases in Group 1, only 100 were positive in the nasal mucosa before treatment, and they are taken as 100 per cent in this table.

[b] Of the 140 cases in Group 2, only 120 were positive in the nasal mucosa and are taken as 100 per cent.

[c] All cases were positive in the lepromas.

With respect to the changes under treatment, considering first the cases positive in the nose (100 of the 111 in the combined-treatment group and 120 of the 140 in the DDS control group), 54 per cent of the first group became negative within 6 months, and 83 per cent within

a year; whereas of the second group only 25 per cent had become negative after 6 months, and 52 per cent in a year. The nasal smears of all the patients in the experimental group were negative by the end of 2 years, and those of the control group in 3 years.

Turning now to the lepromas, bacteriologically positive in all cases, it is to be said that all of the patients were routinely biopsied before treatment, and simultaneously several punctures of the lepromas were made. These punctures and biopsies were, at first, repeated every month for the first 6 months, and every 6 months thereafter. The same personnel took the biopsy specimens and made the smears, and the same physician interpreted the microscopic findings, so that the coefficient of error is the same in the two groups. The percentages of changes which occurred with respect to the negativation of the leproma punctures are shown in the second section of Table 1.

It is evident that from the epidemiologic point of view there is considerable interest in the mixed treatment, for endemic areas where it is technically impossible to hospitalize systematically all open cases. The figures on negativation, of both the nasal mucosa and the lepromas, for Group 2 correspond fairly well to those observed by the majority of authors. Such was the opinion of Drs. Laviron, Lechat, Ramon Miquel and Rabello, to whom we recently had the opportunity to show our results. The notable negativizing activity of the sarsaparilla is unquestionable. Its effects persist even after cessation of its administration, since it was not until the end of the third year of treatment that the lot of patients who received DDS alone came up to the same level of negativity as those who had received the combined treatment in the first year.

*Morphology of the bacilli.*—The bacilli are greatly altered, quantitatively and qualitatively, under the combined treatment. Their numbers decrease more or less rapidly, and negativation of formerly florid lepromas has been observed in less than two months—although, unfortunately, such early negativation is rarely permanent. Morphologically, the bacilli are altered from the beginning of the second week, showing degenerative characteristics: they are shorter and granular and the globi partly lose their acid-fastness, and sometimes they show only a state of granulation.

Clinical evolution.—Here is considered only the progress in the course of the first year, since our patients were given sarsaparilla for only 6 to 12 months, after which they were maintained on DDS alone. The beneficial action of the sarsaparilla seems nevertheless to have been prolonged much beyond the time of its administration. Certain lepromatous patients have been seen who remained clinically cleared up for many months after a single 40-day course of treatment with the sarsaparilla decoction.

1. Lesions of the skin and nasal mucosa: Apart from certain exacerbations of the lepromas produced in the first months (which might go on to ulceration), as a rule the ensemble of lesions tends to subside rapidly, sometimes from the second week.

Some of the lesions of the buccal and pharyngeal mucosa healed very rapidly, in 2 to 10 weeks—two times more rapidly than with DDS alone. The more recent are the lepromatous affections of the skin, the more rapidly they subside. The more or less infiltrated erythematous patches become soft, then disappear. The papules subside, and also the nodules. The deep, infiltrated sarcoid nodules rarely persist for more than a year.

It will be seen from Table 1 that the lesions of the nasal mucosa had been cleared up after one year of treatment in 83 per cent of the cases of Group 1, against 52 per cent of those in Group 2.

In Figures 1-6 are shown clinical pictures of the faces of three cases. The second one of the first case (No. 36/56) shows the great reduction of the lesions after the full course of treatment of Group 1 described. The other cases (79/58 and 95/58), which are recent ones, illustrate the improvement that may be seen after short periods of the combined treatment.

2. Neuritic disturbances: It is very difficult to arrive at an objective opinion of the action of a given therapy on trophic disorders, especially perforating ulcers. In fact, during the period of hospitalization the daily local treatment, better general hygiene, adequate diet, and rest, may suffice—apart from the effects of any general therapy—to produce spectacular improvement and even healing of the torpid ulcerations.

On the contrary, recovery of the perception of heat and pain is for the most part unrelated to the general conditions of life; it would seem to be a direct response to therapy. The majority of the patients in the two groups studied showed comparable segmental thermo-analagesias. While in Group 2, under DDS alone, it was exceptional to see noteworthy improvement before the sixth month, yet in Group 1, under the combined treatment, it was the rule to see marked improvement, often total, of the sensory changes in less than 6 months. This very special effect has been obtained with the sarsaparilla alone, not only in lepromatous cases but also in those with the tuberculoid form of the disease.

Lastly, combined treatment seems to result, quite regularly, in a certain degree of improvement, increased mobility, of contractures of the hands (*griffes*). However, knowing the unpredictable course of these manifestations, we draw no definite conclusions from these observations.

The clinical changes observed after 6 months and 1 year in the two treatment groups are summarized in Table 2.

TABLE 2.—*Clinical evolution after 6 months and 1 year of treatment, in percentages.*

| Condition | Status | Group 1 (Combined treatment) | | Group 2 (DDS control) | |
|---|---|---|---|---|---|
| | | 6 months | 1 year | 6 months | 1 year |
| Lesions of skin and nasal mucosa | Worse | 0 | 0 | 0 | 0 |
| | Unchanged | 2 | 0 | 10 | 2 |
| | Improved | 28 | 2 | 43 | 46 |
| | Much imp'd | 50 | 18 | 25 | 46 |
| | Cleared up | 20 | 80 | 2 | 13 |
| Sensory changes | Worse | 0 | 0 | 0 | 0 |
| | Unchanged | 6 | 0 | 18 | 6 |
| | Improved | 30 | 10 | 41 | 23 |
| | Much imp'd | 46 | 30 | 39 | 47 |
| | Recovered | 18 | 60 | 3 | 24 |

*Biologic evolution.*—The following routine examinations were made every six months: red-cell sedimentation rate, Vernes resorcin test, total protein determinations, albumin-globulin ratio, total cholesterol, blood urea, and the tests of Hanger and of MacLagan.

Although it is difficult to compare the results of some of these examinations (e.g., the sedimentation rate and the albumin-globulin ratio) in those patients with unstable biologic constants, yet it seems clear that the combined treatment was the more beneficial. Thus, the sedimentation rate was improved in 35-38 per cent of the cases so treated in the sixth or twelfth months, as against 25-29 per cent of the group receiving DDS alone. The albumin-globulin ratio improved after a year in 28 per

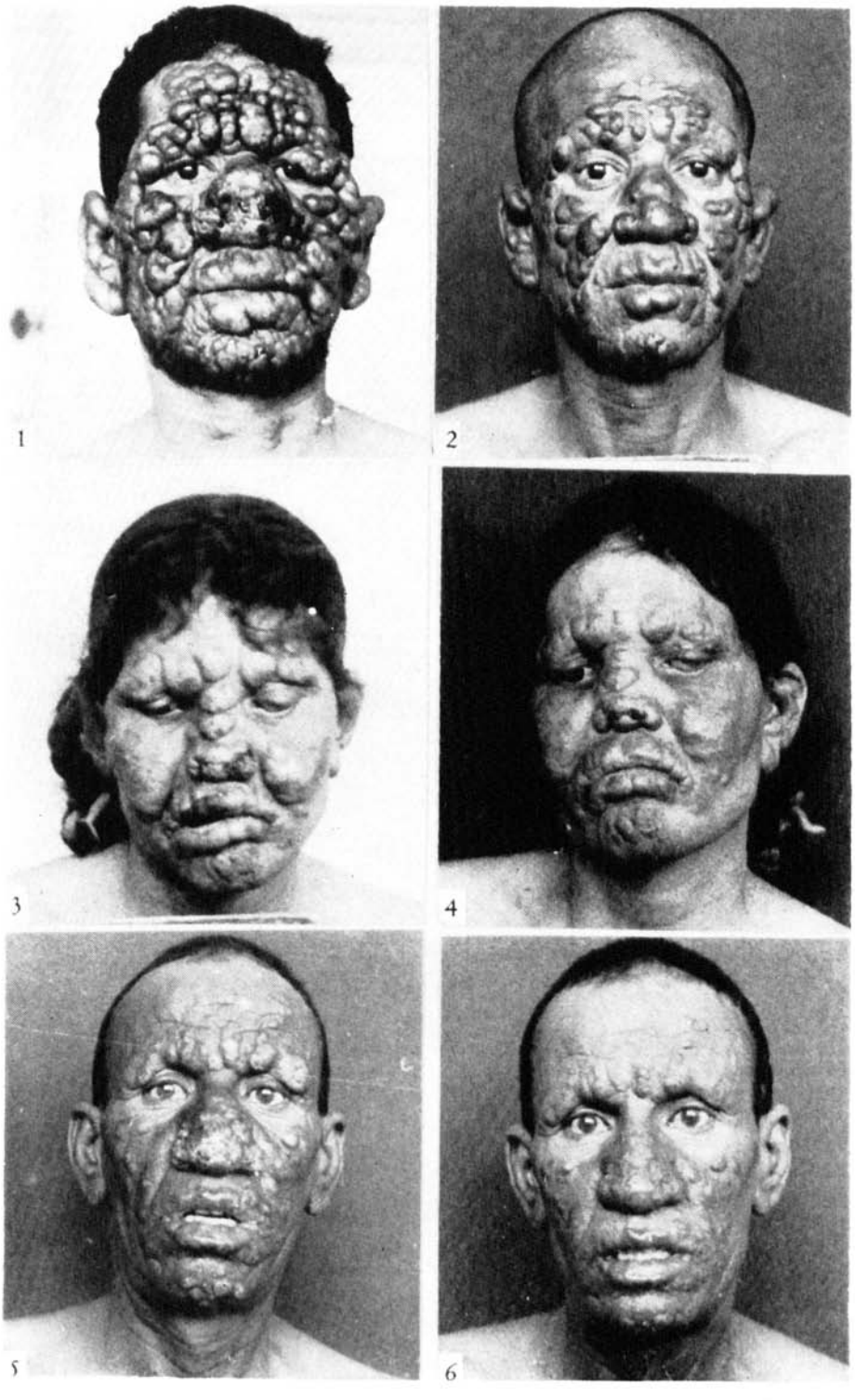
DESCRIPTION OF PLATE

The pictures of the first case in this group illustrate the degree of improvement in a very severe case of Group 1 after the entire treatment period as described. Those of the other two cases, recently put under treatment, show the notable improvement that may be seen after only a few weeks of the combined DDS-sarsaparilla therapy.

FIGS. 1 and 2. Case 36/56. On February 28, 1956, the disease in this patient was reactional and actively progressive, of $L_3$ grade (Fig. 1), the nasal mucosa and the lepromas 4+ for bacilli. (A picture taken two months later, not reproduced, shows a short-time effect comparable to those in the other two cases here shown.) After six months of treatment (on August 22) there was considerable bacteriologic improvement, especially with respect to the nasal cavity, the smear from one side being 1+ and that from the other side negative. At the time of the last examination, on August 25, 1958, there was marked improvement (Fig. 2).

FIGS. 3 and 4. Case 79/58. When this patient was put under treatment on April 2, 1958, the condition was florid, progressive, $L_3$ (Fig. 3). Within less than two months there had been definite clinical improvement (Fig. 4, May 21). When last examined, after four months of treatment, both clinical and bacteriologic improvement were notable; nasal smears, both 4+ at the start, were 1+ and negative.

FIGS. 5 and 6. Case 95/58. On May 6, 1958, the disease was florid, progressive but not reactional, $L_3$ (Fig. 5). In less than two months there was obvious clinical improvement (Fig. 6, June 26). After 2½ months—at the last examination—there was clinical improvement of a degree never observed in so short a time with any other therapy.


1
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6

cent and 18 per cent, respectively. For certain patients proteinograms were made, and the decrease of the gamma globulin and the increase of the albumin confirmed the impression of improvement in the status of the proteins.

Although the Vernes resorcin test showed changes comparable to those of the sedimentation rate, no notable change was found in the sixth and twelfth months in the flocculation of the Hanger and the MacLagan tests in either group.

The saponifying action of the sarsaparilla should normally have produced variations in the cholesterol content, but that has not been observed. Likewise, a hemolytic action might have been evidenced by slight hemoglobinuria, which was systematically tested for from the beginning of the experiment, but no evidence of that disturbance was

TABLE 3.—*Biologic evolution, with respect to the average red-cell sedimentation rates and the albumin-globulin ratio, after 6 months and 1 year of treatment; in percentages.*

| Condition | Status | Group 1 (Combined treatment) | | Group 2 (DDS control) | |
|---|---|---|---|---|---|
| | | 6 months | 1 year | 6 months | 1 year |
| Red-cell sedimentation | Worse | 23 | 13 | 23 | 21 |
| | Unchanged | 42 | 49 | 53 | 50 |
| | Improved | 35 | 39 | 25 | 29 |
| Albumin-globulin ratio | Worse | 15 | 24 | 20 | 22 |
| | Unchanged | 51 | 49 | 41 | 60 |
| | Improved | 34 | 28 | 39 | 18 |

seen. Lastly, the urea levels remained constantly low in both of the groups studied.

The changes in the average sedimentation rates and the albumin-globulin ratios after 6 months and 1 year are shown in Table 3.

Hematologic evolution.—It was technically impossible to follow systematically the changes in the blood-cell formula in all of the patients. Many of them, however, showed improvement in repeated blood counts.

It was observed that, except in reactional conditions, the leucocyte counts were more regularly normal in the patients taking the sarsaparilla than in the others. The erythrocyte counts were similar in the two groups.

Apart from intercurrent affections and prolonged reactional conditions, anemia below 3,200,000 was not seen. (The normal red-cell count in Morocco is 4,000,000). Agranulocytosis has never been seen, but on the other hand a certain number of patients have shown hyper-

leucocytosis of 20,000 to 35,000 due to neutrophile polynucleosis; but this is not related to therapy, because similar leucocytosis has been observed before treatment, during reactional conditions.

*Histologic study.*—The activity of an antileprosy drug can be judged histologically, on the one hand, by the accelerated "aging" of the Virchow cells, and, on the other hand, by the general modifications of the infiltrate. The DDS-Smilax synergy is characterized, in the most favorable cases, by a veritable lysis of the lepromatous infiltrate and a significant fibrocytoid reaction.

1. Lysis of the young lepra cells can be recognized especially by the loss of their foamy character, which sometimes gives them a pseudo-epithelioid aspect.

2. The old foamy lepra cells lose their vacuoles, and by cytoplasmic changes they assume the foreign-body giant cell type (pseudo-Langhans cells).

These cytoplasmic changes are early, occurring in the first month. The other alterations correspond to a normal but accelerated aging of the lepra cells, namely, progressive vacuolization, alteration or disintegration of the nuclei, and disappearance of the cells due to sclerous stricture.

The fibroblastic reaction enters into the normal healing process of the leproma through marked formation of new collagen, the source of the future sclerosis. With the combination treatment employed this new collagenosis may become marked during the first few weeks, forming a veritable network which isolates the previously contiguous lepra cells. This fact explains the rapidity of the sclerosis, which may occur in a few months. No other therapy, outside of Cycloserine, has been seen to induce so spectacular a histologic effect.

To illustrate the effects of sarsaparilla alone, several particularly significant photomicrographs are shown in Figs. 7-12. Figs 7 and 8 are of biopsy specimens taken from the same lesion before sarsaparilla treatment and after 8 months treatment. The extreme regression shown is exceptional. Regression is variable with the individual; in some cases there are significant changes in 2 months, whereas sometimes it takes 2 years for the same degree of effect. Figs. 9-12 illustrate the course of the cytologic changes following the sarsaparilla treatment—changes which may occur extremely rapidly, in 2 or 3 months, although usually they are seen after 6 to 8 months.

*"Reactions" during therapy.*—To simplify the matter, it may be taken that there are only two types of reactional conditions in lepromatous leprosy, pure leprotic reactions and the hyperergic reactions commonly called erythema nodosum leprosum.

1. Pure leprotic reactions: These reactions consist of a congestive flaring up of the lepromas under the effects of treatment. This occurs

as a veritable Herxheimer reaction. The lepromas are copper-red, swollen, and warm to the touch. The congestion of the rhinopharyngeal mucosa increases and may lead to aggravation of ulcerations, especially of the soft palate. This disturbance is accompanied by fever of 38°-38.5°C.

Bearing in mind the fact that the patients placed under treatment were in the full evolutive period of the disease, in the course of which it is sometimes difficult to distinguish incidents due to the treatment, it is to be said that there were 15 per cent of manifest lepra reactions in the combined-treatment group as against 5 per cent in the DDS-control group.

This reaction usually occurs during the first two weeks of treatment. The temperature as a rule drops in 8 to 10 days, and the congestive condition of the lepromas subsides in 3 to 4 weeks. It seems to be most severe in the more florid cases. Excluded from this group are any hyperergic reactions which have been associated with this type of condition.

2. The hyperergic reaction (erythema nodosum leprosum): The cutaneous manifestations of this kind of reaction are usually located outside of the lepromas. They occur predominantly on the extremities, but they may also involve the upper limbs, the face and even the body. The general symptoms are elevation of temperature, arthralgias and edemas. These may be absent or, on the contrary, dramatic.

The cutaneous lesions parallel the general symptoms and are a manifestation of the same hyperergic process. They present the ap-

DESCRIPTION OF PLATE

FIGS. 7 and 8. These low-power photomicrographs (60x before one-third reduction) are of biopsy specimens taken from the same lepromatous patch before treatment and after 8 months of treatment with sarsaparilla alone. The patient had advanced lepromatous leprosy, with positive nasal smears and beginning polyneuritic involvement.

In FIG. 7 is seen the general aspect of the relatively dense lepromatous infiltrate, which was 4+ before treatment but became negative after 2 months treatment, as did the nasal smears.

In FIG. 8 is seen the same lesion reduced to a vestigial state after 8 months treatment. (Fig. 12 shows a small residual focus in the same area.) The patient refused all treatment after the 8th month, but bacteriological negativity persisted for another 3 months.

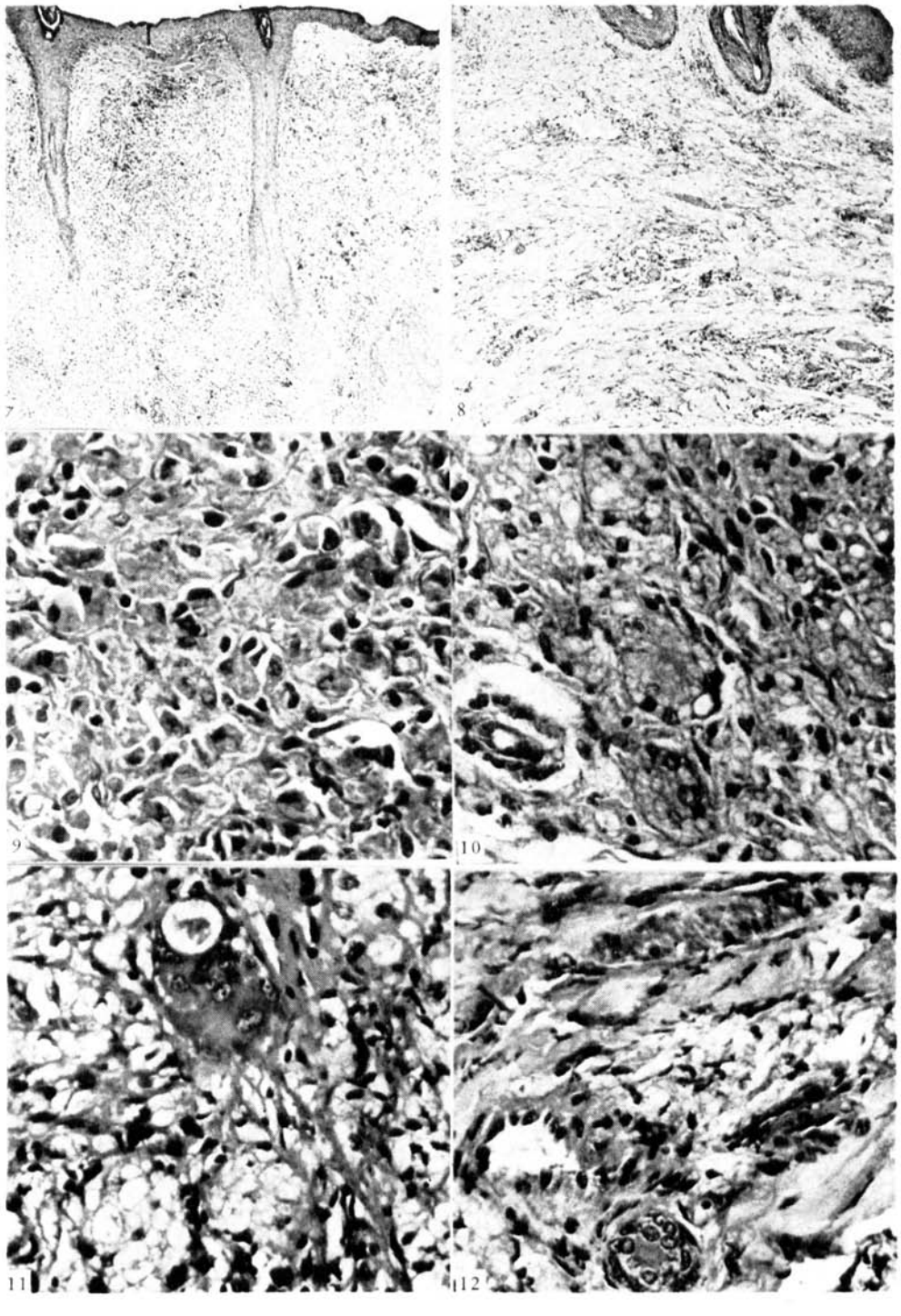
FIGS. 9-12. This series of photomicrographs, taken at higher magnification (550x before reduction) is shown to illustrate the regressive cytologic evolution of the leproma under sarsaparilla treatment. Such changes may occur very rapidly, in 2 or 3 months, although usually they take 6 to 8 months.

In FIG. 9 is the cytologic aspect of a lesion before treatment, showing a dense infiltrate of young Virchow cells in which smears show the bacilli to be abundant.

In FIG. 10, of a lesion biopsied after 1 month of sarsaparilla treatment. There is vacuolization of the cells, and a tendency of some of the foamy cells to assume the aspect of macrophage giant cells. The bacilli are still abundant, but for the most part granular.

In FIG. 11, after 3 months treatment, the vacuolization of the aging Virchow cells is accentuated, and there is a foreign-body-type giant cell whose cytoplasm is not foamy. Bacilli are reduced in numbers and granular, and for the most part isolated.

In FIG. 12 (showing an area in Fig. 8), the vacuolization and degeneration of the cells of this residual focus are advanced and it is difficult to identify its nature. Only a few bacilli are present, granular or in a state of fragmentation.



pearance of ordinary erythema multiform of the lesser degrees, but may eventually lead to pseudoerysipelatous and edematous sarcoid patches, showing in its course showing all phases of the nodular hypodermatitis.

Of the 11 patients on the combination treatment 34, or 31 per cent, had hyperergic reactions. Of the 34 reactions, 7 occurred in the 33 L1 cases, 13 in the 43 L2 cases, and 14 in the 30 L3 cases; there was none in the 5 regressive cases. As is logical, the more advanced the leprosy the more frequent the reactions. These reaction cases are grouped in four categories:

(*a*) In 3 cases, erythema multiforme which subsided spontaneously in the course of the first 3 months.

(*b*) In 16 cases, reactions of the nodular hypodermatitis type, with onset occurring during the first month. This condition is of variable duration and severity (there was necrosis of the lesions in 2 instances), evolving in 2 weeks to 2 months. There was relapse of the reactions in 8 cases, but each time with decreased severity. In several cases to clear up the reactions, it was necessary to administer delta-dehydrocortisone, in doses decreasing from 60 mgm. to 10 mgm., for 5 to 10 days. It was not necessary to interrupt the antileprosy medication, although in 3 cases the dosage of DDS was temporarily reduced. This type of reaction did not occur after the sixth month, or if it did it was of very mild degree.

(*c*) In 13 cases the reactions were pseudoerysipelatous, the patients arthralgic and severely febrile, with more or less severe edema of the extremities and the face. In 5 of these very marked reactions (1 in Group 1 and 4 in Group 2) it was necessary to suspend treatment during the first 4 months. All presented successive reactions of lesser and lesser severity and of shorter duration in each relapse (several weeks in Group 1 and 4 to 5 months in Group 2). Their treatment required prolonged administration of delta-dehydrocortisone in 6 cases, and plasma perfusions in 2 of them. It is to be said that the severity of the reactions was in direct relation with the degree of albumin-globulin disequilibrium, with an increase of the para-gamma globulins (Kunkel-zinc).

(*d*) Lastly, there were 2 cases with relapsing reactional conditions, highly febrile, on their arrival in the service. There were arthralgia with marked hydrarthrosis, and severe edema of the face and extremities, accompanied by erysipelatous, bullous and necrotic plaques. These cases required almost continuous administration of delta-dehydrocortisone, with alternated association of testosterone propionate, ACTH and plasma. The DDS had to be interrupted repeatedly, or reduced to 75 or 100 mgm. per day. The sarsaparilla, however, was always maintained in the regular dosage.

In the *control group* of patients on DDS, the reactional conditions were comparable but of slightly longer duration, for each reaction considered separately, and they still occurred with severity after the twelfth month. The frequency of the ENL reactions correspond to the frequencies reported by other leprologists at the recent congress in Tokyo. In particular, Hemerijckx said that in 15,000 cases 30 per cent of the reactions were due to sulfones, and that 6 per cent were relapsing cases.

## CONCLUSIONS

In this report an attempt is made to compare, as objectively as possible, the results of treatment of two practically comparable groups of lepromatous patients, the numbers sufficiently large to make the results statistically valid, one group treated with a combination of *Smilax ornata* (sarsaparilla) extract and DDS, and the other with DDS alone as a control. The differences of the percentages of bacteriological negativation in the two groups after 12 months, 32 for the nasal smears and 16 for the lepromas in favor of the group given the combined treatment, unquestionably indicates activity on the part of the sarsaparilla. From the clinical point of view this activity, although more subjective in interpretation, is not less spectacular for those who are accustomed to observe the course of leprosy. Lastly, the severity of certain leprotic exacerbations at the beginning of the treatment gives further confirmation.

We have not had experience with certain drugs recently introduced in leprology. From reports read at the recent congress in Tokyo, none of the new medicaments seem likely to take the place of the sulfones. It was reported (Davey) that 4-butoxy-4-dimethylaminodiphenyl thiourea (Ciba 1906) is practically nontoxic and gives results comparable to the parent sulfone, and that an ethyl mercaptan derivative (Etip) has evident antileprosy activity. Certain reports, including one by me, dealt with the action of Cycloserine. From these reports it emerged that the results obtained are usually the same as, or at most very slightly better than, those obtained with DDS. If Etip shows spectacular activity at first, it is only temporary. Thus, after the VII International Congress of Leprology, I believe that treatment of leprosy by a combination of red sarsaparilla and the parent sulfone represents at the present time the best therapy, and that it meets one of the imperatives indicated by various authors, namely, a therapeutic association of different chemical medicaments to avoid drug resistance.

## CONCLUSIONES

En esta comunicación, trátase de comparar, lo más objetivamente posible, los resultados del tratamiento de dos grupos de enfermos lepromatosos, de tamaño suficiente para dotar a los resultados de validez

estadística, tratado uno con una combinación de extracto de *Smilax ornata* (zarzaparrilla) y DDS y el otro solamente con DDT como testigo. Las diferencias en los porcentajes de negativación bacteriológica en los dos grupos al cabo de 12 meses, 32 para los frotes nasales y 16 para los lepromas en favor del grupo que recibió el tratamiento combinado, indican indiscutiblemente actividad de parte de la zarzaparrilla. Desde el punto de vista clínico, aunque más subjetiva en su interpretación, esta actividad no es menos espectacular para los acostumbrados a observar la evolución de la lepra. Por fin, la gravedad de ciertas exacerbaciones lepróticas en los comienzos del tratamiento necesita nueva confirmación.

El A. no ha tenido experiencia con ciertas drogas recién introducidas en la leprología. A juzgar por las comunicaciones leídas en el reciente Congreso en Tokío, no parece probable que ninguno de los nuevos medicamentos suplante a las sulfonas. Se declaró allí (Davey) que la tiourea 4-butoxi-4-dimetilaminodifenílica (Ciba 1906) es prácticamente atóxica y da resultados comparables a los de la sulfona paternal, y que un derivado del marcaptán etílico (ETIP) posee evidente actividad antileprosa. Ciertas comunicaciones, incluso una por el A., discutieron la acción de la Cicloserina. Por estas comunicaciones se colige que los resultados obtenidos suelen ser idénticos, o a lo más, muy poco mejores, que los obtenidos con DDS. Si ETIP muestra actividad teatral al principio, esto es puramente temporal. Por esto, después del VII Congreso Internacional de Leprología, le parece al A. que el trataminento de la lepra con una combinación de zarzaparrilla roja y la sulfona paternal representa en la actualidad la mejor terapéutica, y que cumple uno de los imperativos indicados por varios autores, a saber, una asociación terapéutica de varios medicamentos químicos para evitar la fármaco-resistencia.

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