BENEFICIAL EFFECTS OF CHAULMOOGRA IN LEPROUS NEURITIS

SALOMON SCHUJMAN, M.D.
Chief, Men's Section, Prof. E. P. Fidanza Leprosy Service
Carrasco Hospital, Rosario, Argentina

Among the serious complications of leprosy are the lesions caused by leprous neuritis, especially when the process involves the trunk and terminal nerves severely. In that event, in advanced stages, it causes serious disorders such as total anesthesia of extensive areas, muscular atrophies and retraction of fingers and toes, incapability of working, and, finally, deformities and mutilations which constitute for the patient a veritable martyrdom, physical and moral.

One can say without exaggeration that, from the point of view of prognosis, and from that of the patients themselves, the neural involvements and complications are more serious than the cutaneous manifestations. The latter, even if advanced, may regress without leaving sequelae of importance compared with the end results of nerve damage, for which so little can be done. Hence we should give serious thought to the nerve lesions, and treat them early and properly.

INADEQUACY OF THE SULFONES IN LEPROUS NEURITIS

With the advent of the sulfones, and considering their evident beneficial effects on skin lesions and even on the bacteriologic state, it was naturally expected that they would have similar effects on the leprous neuritic conditions, at least on lesions of moderate degree. Unfortunately, it has turned out that the sulfones have little effect on these lesions, when any at all. Not only are they incapable of making the nerve lesions regress, or even of arresting them, but they are also incapable of preventing the progression of such changes.

Many leprologists have reported on this matter. I will mention only a few. In 1948, Lauro de Souza Lima and associates (8) reported on their 4-½ years of experience with sulfones in the different clinical forms of leprosy. They pointed out the beneficial effects on the lesions of the skin and mucous membranes, but in discussing the nerve lesions they wrote, "In spite of these highly favorable results of sulfone therapy with respect to the cutaneous lesions of lepromatous leprosy, it must be stated that as regards the peripheral nervous system the results have been practically nil. We do not mean by this that we were expecting the regression of the usual sequelae of nerve involvement, but we have seen them appear during active treatment. This probably indicates a previous involvement of the nerve, and inability of the sulfone treatment to arrest or reverse the lepromatous process so located. This fact is manifest in lepromatous cases of moderate and advanced degrees."

Rotberg (3), in 1956, participating in the discussion of a paper by Mariano reporting on his 10 years of experience with sulfone therapy, pointed out the seriousness of the therapeutic problem posed by leprous neuritis, saying, "One of the problems I wish to bring to attention is that of neuritis which appears in the course of

sulfone therapy and which, according to some authors, may be precipitated by it. The situation is such that many patients, concerned about this possibility, have begun to avoid the treatment."

Nègre and Fontan (2), discussing the value of physiotherapy as an adjunct treatment of leprous neuritis, pointed out that the neural sequelae ". . . are still, in spite of the sulfones, the sad prospect of the lepers"; and that ". . . the present medical treatment of leprosy is insufficient. Even if the sulfones lead to bacteriological sterilization of the patients and their clinical stabilization, *the neurotrophic sequelae continue to progress as if the patient had not been treated*" (italics theirs).

With regard to my own experience, I refer especially to selected lepromatous patients treated with sulfones with strict regularity and adequate dosage, for a period of not less than four years, a period more than sufficient to evaluate the therapeutic effects of a medicament. In this connection I disregard cases with severe neurotrophic manifestations, since they are irreversible processes due to fibrosis and sclerosis which strangle the nerve fibers and terminals. I am concerned here only with moderately advanced cases in which the neural symptoms are predominantly subjective, and in which certain objective symptoms were only beginning to appear. It is in such cases, with moderate manifestations and sometimes even with incipient changes, I have found, in keeping with the opinion of other authors, that the sulfones cannot prevent the appearance of the neural symptomatology; also, that once such manifestations occur they not only do not regress but in many cases they progress and are accentuated (Figs. 1 and 2).

Details of the findings in 14 such cases, and the results of subsequent chaulmoogra treatment, are given in Table 1. Here I will only point out that it has been common for me to see in lepromatous cases, after one or two years of sulfone treatment, the appearance of the symptoms of leprous neuritis, both *subjective* such as numbness, cramps, pains, pruritus, loss of strength of the extremities, and *objective* such as the appearance of muscular atrophies and, less commonly, trophic blisters. These symptoms do not improve under sulfone treatment, but sometimes become increased and progressive.

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One of the most serious charges which the opponents of chaulmoogra have proffered against this medication is that there are in the leprosaria many patients who are deformed and mutilated by the disease in spite of the fact that they had been treated with chaulmoogra for many years. It does not occur to these authors that many of these patients had, when admitted, already presented advanced neurotrophic lesions which were and still are irreversible with any available antileprosy drugs. Nor do they take into consideration the fact that in the presulfone era it was often the practice to use, for moderately advanced lepromatous cases, extremely low doses—sometimes even less than 300 cc. a year. Such doses I consider to be without therapeutic value, especially for leprous neuritis which re-

quires that the treatment should be the earliest and most intensive possible.

Although I adopted the new medicaments as soon as they were available (I began to use the sulfones in 1946), I have not abandoned the old chaulmoogra medication. This is because I am convinced of its activity (e.g., Figs. 3 and 4), and especially in order that I can continue to compare it with the new treatments. For more than 10 years now I have maintained, on the basis of this comparative study, that "chaulmoogra when used in sufficient doses is by no means less active than the sulfones." I have never asserted that it is superior. It is only now that for the first time I can say, on the basis of comparative therapeutic studies, that as regards leprous neuritis chaulmoogra is definitely superior to the sulfones (Figs. 5 and 6). This statement is based on the following findings:

1. In advanced lepromatous cases with manifest bacillary invasion of the nerves, treated with chaulmoogra alone in adequate doses, no serious neuritic disturbances have appeared in many years of observation. I refer to a group of such L_2 and L_3 cases with evident manifestations of leprotic involvement of the nerves—numbness, loss of strength, in some instances confirmed bacteriologically by nerve puncture—with no previous antileprosy medication of any kind, who were subjected to chaulmoogra treatment, intensive in the first year and moderate after that, which group has been followed from 8 to 10 years.

The results of this very interesting experience will be dealt with in a separate report. I wish to say here in passing that the majority of those patients who were constant in their treatment became clinically and bacteriologically negative and continued so for periods ranging from 4 to 8 years, in spite of the fact that the treatment was suspended during all of those years. With respect to the evolution of the nerve disturbances, no manifestations of peripheral neuritis have appeared so far, except in 2 cases in which, during the second and fourth years after treatment was suspended, there appeared some paresthesias with numbness and mild muscular atrophy of the hands.

2. In advanced lepromatous cases first given prolonged and adequate chaulmoogra treatment and later treated with sulfones, no serious manifestations of peripheral neuritis have appeared. Here I refer to a group of such patients who had been subjected to chaulmoogra medication in adequate dosage but who, although they had benefited from that treatment, were transferred to sulfone medication for one or another of the following reasons:

(*a*) Because the clinical and bacteriological improvement, although evident, was not fully satisfactory compared with other cases.

(*b*) Because the patient's tolerance to the medicament had decreased.

(*c*) Because the patient had moved to a distant community where it was not possible for him to continue the injections.

(*d*) Because we did not have available in our country sufficient chaulmoogra drug, and we preferred to reserve what we had for cases we thought to be of most interest.

Now, in all of these cases which initially received chaulmoogra treatment, adequate in dosage and prolonged in time (2 to 4 years), not only did there not appear serious neuritic disturbances, but they likewise did not occur during subsequent prolonged periods of sulfone treatment.

3. Lepromatous and tuberculoid cases with neuritic disturbances which did not respond to sulfone treatment were clearly benefited when they were transferred to chaulmoogra treatment. As has been said, most other authors have found, as I have, that in moderately advanced lepromatous cases, and also in some tuberculoid cases, the cutaneous lesions subside under the action of the sulfones, while the disturbances caused by the peripheral neuritis persist or increase despite active and persistent sulfone treatment.

Therefore, because of the beneficial effects of chaulmoogra observed in leprous neuritis, I decided to place under chaulmoogra medication the cases with peripheral nerve disturbances which did not respond to sulfones. For considerations of space I do not include in this report clinical histories, but instead present a consolidated table dealing with 14 illustrative cases. I will confine myself to summarizing the pertinent facts related by the patients which show that, during thorough and prolonged sulfone treatment, they had developed numbness, cramps, pains, diminution of sensation and of strength of the extremities, which symptoms had persisted and even increased despite the continuation or intensification of the sulfone treatment. Placing these patients under chaulmoogra treatment in adequate doses (20-30 cc. weekly), I observed definite improvement of these symptoms in most instances, sometimes as early as the second or third week; and that improvement increased with the progress of that treatment, and persisted for months and years after its suspension.

Also, in some tuberculoid cases with mild but definite neuritic manifestations which did not respond to the primary sulfone medication, I have seen these disturbances decrease and even subside when they were later placed under the chaulmoogra medication (e.g., Cases 10-14).

Neural symptoms which respond best to chaulmoogra medication.— There is no need to stress the fact that the advanced neural changes in leprosy, such as extensive muscular atrophies with their attendant contractions, deformities, and distal mutilations of the extremities, are irreversible phenomena for which no medication offers benefit. These sequelae call for physiotherapy and surgical treatment.

My experience has been mostly with lepromatous cases with moderate neural disturbances in which muscular atrophy was absent or at most only incipient, and in which the principal symptoms were the subjective ones which respond to chaulmoogra treatment.

TABLE 1.—*Beneficial effects of chaulmoogra in leprous neuritis.*

Case	Form	Previous treatment	Symtoms	Chaulmoogra treatment[a]	Results
1. Acu.	L1	None	Numbness & pains, extremities; repeated trophic blisters & ulcers	20 cc. (240 cc.)	Numbness & burning gone; no more blisters, & ulcers healed
2. Bog.	L1	Sulf, 2y.	Numbness, tremor & weakness of hands, difficulty in sports	20 cc. (160 cc.)	Increased strength, hands; now plays tennis without difficulty
3. Pes.	L2	Sulf, 3y.	Numbness & weakness of hands, 1 yr. tends to drop objects	20 cc. (440 cc.)	Decreased numbness, increased strength, hands; now holds objects well
4. Gir.	L2	Sulf, 3y. TB-1, 2y.	Numbness of hands, pains in extremities; unable to shave and dress	20 cc. (70 cc.)	Less numbness; now uses hands well, shaves & dresses
5. Spe.	L2	Sulf, 4y.	Pruritus, numbness & weakness of hands	30 cc.	Frank improvement after 2 weeks treatment
6. Ban.	L2	Sulf, 1y.	After reaction, severe pains of limbs, unresponsive to treatment	20 cc.	Pains relieved after 3 weeks treatment
7. Din.	L2	Sulf, 4y.	Pains, numbess & weakness of limbs	20 cc.	Manifest improvement in 1 month
8. Cas.	L2	Sulf, 2y.	Pains, numbess & weakness of limbs	20 cc.	Diminution, numbness & pains; increased movement of hands
9. Hur.	L3	Sulf, 3y.	Pain & burning, plantar surfaces, unresponsive to treatment	30 cc.	Reported pains gone & sleeping, after second injection
10. Gen.	T	None	Numbness of limbs, atrophy lt hand & rt thenar eminence	20 cc.	Disappearance of numbness; increased strength, limbs; muscular increase, rt hand
11. Maz.	T	Sulf (?y.)	Contracture rt hand, anesthesia lt middle finger, 3m.	30 cc. (240 cc.)	Sensation lt hand recovered; rt hand unchanged
12. San.		Nerve decap. & transpos.	Weakness of hand; sl. contracture little finger; nodulation, ulnar nerve	20 cc. (160 cc.)	Increased strength of hand; ulnar nodule disappeared
13. Gay.	T	Sulf, 2y.	Numbness, 1-1/2 y.; spasm & weakness of hands	20 cc.	Diminution of numbness; increased strength hands after 1-1/2 m. treatment
14. Fre.	TR	Sulf, 2y.	Since reaction, severe pains & weakness of extremities	20 cc. (160 cc.)	Pains regressed, able to rest; increase of muscular strength

a Weekly dosage; total amount in parentheses.

Subjective symptoms: Numbness, cramps, pains, hypoesthesias, pruritus and general dulling of sensation of both the upper and lower limbs. Objective: Mild localized amyotrophies of recent appearance, blisters and trophic ulcers (Figs. 3 and 4). I wish to note here the increase and recovery of muscular strength that occurs. Some patients who, while under sulfone treatment, complained of loss of finger movement—a condition which hinders them in performing routine work such as shaving, sewing, writing, etc.—returned after a month of chaulmoogra treatment jubilant and grateful for the benefit they had experienced.

Importance of adequate dosage of chaulmoogra.—Stress is to be laid on the importance, with respect to leprous neuritis, of adequate dosage in the initial chaulmoogra period. In many lepromatous cases which received prolonged but inadequate chaulmoogra treatment (irregular, and in low dosage), the lesions of the skin and mucous membranes continued to increase. Under more intensive treatment the process was arrested and the lesions improved, many of these cases becoming clinically and bacteriologically negative. On the other hand the advanced peripheral nerve disturbances were not improved. I believe that if these cases had been placed under adequate chaulmoogra treatment from the beginning, those irreversible sequelae would have been prevented.

DISCUSSION

For more than ten years I have maintained in various reports (e.g., 4-7), on the basis of comparative therapeutic studies, that chaulmoogra used in sufficient dosage (20-30 cc. weekly) is as active as sulfone medication, because with the former I have been able to obtain the regression and disappearance of all the clinical and bacteriological symptoms in a period of time not greater than is required with the sulfones. Never have I claimed that it is superior. Now, however, I say for the first time that in leprous neuritis, of mild or moderate degree, the therapeutic action of chaulmoogra—in sufficient dosage—is superior to that of the sulfones.

Such moderate nerve disturbances, expressed in the subjective and objective symptoms that have been enumerated, which symptoms have not responded to the sulfones, I have seen to regress in the great majority of cases that have been put on chaulmoogra medication in adequate dosage.

In none of my previous articles on therapy have I attempted to explain the mechanism of action of chaulmoogra, because I have not seen an explanation that satisfied me. Of the numerous hypotheses offered by different authors the most recent is that of Kátó and Gözsy (1), who hold that chaulmoogra acts by stimulating the reticuloendothelial system. Nor do I claim now to explain the mechanism of action of chaulmoogra in leprous neuritis, but I have no doubt of its beneficial effect. To make that fact known is the purpose of this article.

Considering the seriousness of these neurotrophic disturbances when

left alone, and the limited influence of sulfones on them, I would suggest that chaulmoogra be employed in these cases of moderate neuritis with the subjective and objective symptomatology described.

SUMMARY AND CONCLUSIONS

1. Attention should be given to the neural disturbances of leprosy, and they should be treated early because the grave sequelae in advanced cases cannot respond to any antileprosy medication we have at present.

2. The lesions of moderate neuritis in lepromatous cases generally respond very poorly to sulfone medication, according to the experience of many leprologists, including myself.

3. This type of neuritis, according to my experience, can be arrested and made to regress in a high percentage of cases, even those which have not responded to prolonged sulfone medication, when given chaulmoogra in sufficient dosage (20-30 cc. weekly).

4. The symptoms which are most benefited are, among the subjective ones: numbness, cramps, pains, pruritus, hot sensation, and diminution of strength of the limbs, and among the objective ones: bullae, trophic ulcers, and in some cases mild and recent muscular atrophy.

5. It is suggested that, in similar moderate cases which do not respond to modern leprosy medication, a trial of the old chaulmoogra treatment be made, employing sufficient dosage.

RESUMEN Y CONCLUSIONES

1. Debemos prestar atención a los trastornos nerviosos de la lepra y tratarlos precozmente, ya que las secuelas graves que dejan los casos avanzados (amiotrofias, retracciones y mutilaciones) no obedecen a ninguna de las medicaciones antileprosas que hoy poseemos.

2. Las lesiones por neuritis moderadas en los casos lepromatosos obedecen generalmente poco, según la experiencia de muchos leprólogos y también la nuestra, a la medicación sulfónica.

3. Ese mismo tipo de neuritis, según nuestra experiencia, se detiene y regresa en el mayor porcentaje de los enfermos, aún en los casos que no obedecieron a la medicación sulfónica prolongadas, cuando se les administra chalmougra en dosis suficientes (20 a 30 c.c. semanales).

4. Los síntomas más beneficiados son: entre los subjetivos: adormecimientos, calambres, dolores, pruritos, ardores y disminución de las fuerzas (impotencia muscular) en los miembros, y entre los objetivos: ampollas úlceras tróficas y en algunos casos, discretas y recientes atrofias musculares.

5. Sugerimos a los colegas que en casos semejantes (siempre en las lesiones neuríticas moderadas y nunca en las secuelas) que no obedezcan a los modernos medicamentos antileprosos, recurrir a la vieja medicación chalmoúgrica y administrarla en dosis suficientes.

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Description of Plate

Plate 26

Fig. 1. Condition of a patient before treatment. Note the lepromatous lesions of the face, and the distinct atrophy of interosseous muscles.

Fig. 2. The same patient as in Fig. 1, after six years of sulfone treatment, taken regularly and in adequate dosage. Note that while the cutaneous lesions have regressed and disappeared, the neural lesions have greatly increased, with retraction and multilation.

Fig. 3. Trophic ulcers in a lepromatous case.

Fig. 4. The same case as in Fig. 3, after one year of treatment with chaulmoogra, only.

Fig. 5. Atrophy of the interosseous muscles and retraction of the little finger in a tuberculoid case, without previous treatment.

Fig. 6. The same case as in Fig. 5, after four months of chaulmoogra treatment. Observe the notable improvement achieved.

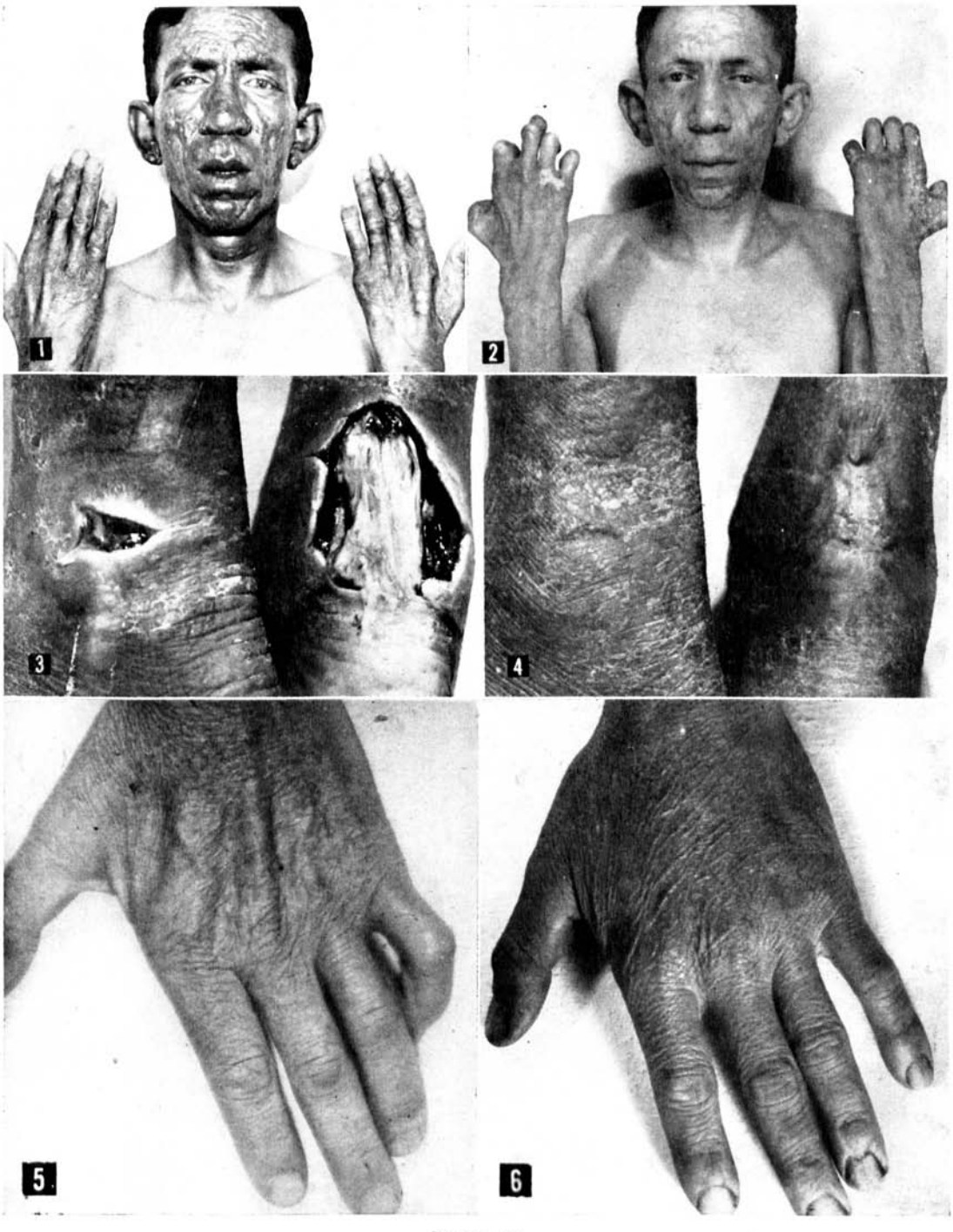

PLATE 26