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THERAPEUTIC VALUE OF CHAULMOOGRA IN THE TREATMENT OF LEPROSY*

by

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PRELIMINARY CONSIDERATIONS

Although chaulmoogra oil is the oldest known and most widely used medication in the treatment of leprosy, no uniform criterion for evaluating its therapeutic value has yet been evolved. In all epochs and within the same epoch there have existed various schools of thought, some enthusiastic defenders of chaulmoogra, and, at the other extreme, the pessimists and disbelievers in its therapeutic value.

Henderson (1) has grouped the diverse opinions in the efficacy of chaulmoogra into four types: (a) that it is fully efficacious, (b) that it is efficacious but not infallible, (c) that it has no specific therapeutic action but acts merely as a simple co-agent in improving the general condition of the patient, (d) that it has no therapeutic value whatever in leprosy.

To what is due such diversity of opinion upon results obtained from the use of chaulmoogra? Is it attributable to the use of different derivatives of chaulmoogra; to differences in methods of application or in dosages administered, or to differences in clinical types upon which the treatment is used? We believe that the dosage factor may play a highly important role, but that it is a lack of uniformity in the selection of experimental cases for therapeutic tests with chaulmoogra which is the real cause of the diversity of results obtained, and, consequently, of the variance in opinion upon the therapeutic value of this medication. Such discrepancy is un-

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derstandable, because, there are often included within the same groups of cases, lepromatous and tuberculoid types (norms established by Rabello (2)), differing not only in clinical, bacteriological, histological, and immunological aspects, but also in behavior with respect to chaulmoogra, which acts more slowly in the first type and more rapidly and surely in the second.

Today, with our greater knowledge of matters of classification, with our more basic knowledge of the two fundamental opposing forms of leprosy, namely, the tuberculoid and the lepromatous, we are in a better position to appreciate the efficacy of chaulmoogra treatment. We should take into consideration the benefits obtained *exclusively in lepromatous cases*. In this, all leprologists should be consistent in order to judge the therapeutic value.

PURPOSE OF THE PRESENT WORK
TO EVALUATE OUR OBSERVATIONS AND EXPERIMENTS

The observation of the action of chaulmoogra upon lepromatous cases only has day by day become a more generally recognized criterion. However, there has risen a new current of pessimism among some leprologists, with the result that some use it with reluctance and others have abandoned it altogether, believing that the benign tuberculoid cases are spontaneously cured, whereas the lepromatous are not curable even with chaulmoogra. This pessimistic wave which has risen in recent years within important leprologic centers has given us serious concern and has caused us, at the end of the year 1944, to review our treated cases, and to analyze the diverse results obtained with the purpose of strengthening our position regarding this medication in the treatment of leprosy.

In 1945, at a meeting of leprologists in Cordoba, we confirmed our old position as defenders of chaulmoogra, consolidated finally through the analytical study to which I just made reference. The objective of this presentation is to bring to the heart of this Pan-American Leprosy Congress some of our optimism with regard to the efficacy of chaulmoogra, an optimism which I can assure my distinguished colleagues is not improvised nor precipitate, but which is based upon experience throughout seventeen years of contact with leprosy patients in our Leprology Service at Carrasco Hospital in Rosario. In this Service, we have 60 in-patients and an out-patient clinic where 300 are treated. Half of these are lepromatous. We also treat a like number who are registered at other centers. This number of patients is not very large, and consequently we have been able to study them periodically and with due

CASES WITH MARKED IMPROVEMENT, BECOMING NEGATIVE CLINICALLY AND BACTERIOLOGICALLY

Name	Clinical forms	Length of treatment in years	Total Amount of chaulmoogra oil in c.c.	Dosage per year	Oil given intradermally	Results — Comparative study				Remarks
						Clinical		Bacteriological		
						Previous condition	Present condition	Previous	Present	
Fran, M.	L 3	6	2910	455	Yes	Abundant tubercles on the face, chest, buttocks, upper extremities and thighs. Nodules on lower extremities.	Complete disappearance of the tubercles and nodules, leaving atrophic areas and secondary atrophies.	(+++)	(-)	8 months since last treatment.
Ali, S.	L 3	6	2536	424	Yes	Tubercles and nodules on face, back, upper and lower extremities. Erosions on palate.	Absorption of all the nodules, and tubercles, leaving atrophies and secondary pigmentation.	(+++)	(-)	Intensive lepra reactions.
Fruc, A.	L 3	4	2162	540	Yes	Leonine facies — giant nodules and tubercles, lepromas on the upper extremities.	Absorption of all the lepromas and nodules, leaving pigmented patches and secondary atrophies.	(+++)	(-)	
Fran, A.	L 2	6	3912	652	Yes	Tubercles and nodules on face, neck, buttocks, upper and lower extremities. Deformity of nose.	Subsidence of all the tubercles and nodules, leaving acromic spots and secondary atrophies. Gynecomastia.	(+++)	(-)	
Juan, T.	L 2	5	2012	475	No	Tubercles on face. Coppery diffused patch on the lumbar region and buttocks, partly infiltrated.	Subsidence of all the lesions without leaving any trace. Acromic and atrophic scar on left buttock.	(++)	(-)	No previous treatment. No response to diphtheria toxoid.
Ern, N.	L 2	4	1960	490	No.	Erythematous and infiltrated lepromatous macules on arms, buttocks and lower extremities.	Disappearance of all the lesions leaving erythematous atrophic secondary lesions.	(+)	(-)	Intensive prolonged lepra reaction.
Vivi, B.	L 2	6	2618	435	Yes	Giant lepromatous infiltrations on the forearms and lower extremities. Tubercles and large nodules on face.	Complete absorption of the lesions without any traces except atrophies and pigmentations.	(+++)	(-)	
Deme, Z.	L 3	7	3730	530	Yes	Abundant tubercles and nodules on the upper and lower extremities, buttocks, and back. Coppery patches present.	Disappearance of the tubercles and nodules. Only acromic areas and secondary atrophies remain.	(+++)	(-)	
Raim, R.	L 3	6	2730	455	Yes	Face, upper and lower extremities practically completely covered with tubercles and nodules. Deformity of nose. Inguinal adenopathy.	Complete absorption of the tubercles and nodules leaving behind acromic spots and atrophies. Subsidence of the adenopathies.	(+++)	(-)	
Mig, D.	L 2	5	2148	430	Yes	Macules on face, extremities. Abundant tubercles on abdomen and buttocks.	Disappearance of all the tubercles leaving acromic areas and secondary erythematous atrophic lesions.	(+++)	(-)	No response to diphtheria toxoid.
Ram, C.	L 1	3	2020	670	No	Erythematous and coppery macules on face, thighs, and knees. On left knee is a giant macule.	Regression of all the macules leaving no trace. Residual pigmentation on left knee only.	(+++)	(-)	No previous treatment.

attention to each. Therefore, we have obtained data and made observations of real value in supporting our position.

CRITERION FOR JUDGING THE THERAPEUTIC VALUE OF CHAULMOOGRA

To formulate a clear concept of the true therapeutic value of chaulmoogra in leprosy, we have separated 50 lepromatous cases treated with its ethyl esters. Of these, 25 were not benefitted by this medication, whereas the remaining 25 manifested indisputable improvement, ranging from slight modification to extraordinary improvement in which clinical and bacteriological negativeness was attained. For these two groups, treated under the same clinical conditions and with the same medication, we have made a comparative study of the most important points and factors which we judge most responsible for such differences in results obtained. We bring these factors and observations before you today for your consideration.

OBSERVATIONS ON THE CAUSES OF SUCCESS AND FAILURE IN THE USE OF CHAULMOOGRA

From the analytical examination of our cases we have selected the most important points for comment.

- (1) *Lepromatous cases not treated with chaulmoogra become unfailingly worse.*

All leprologists know of numerous persons who because of fear of submitting to examination, or through laziness and neglect, or because they live far from leprosy clinics, do not submit to chaulmoogra treatment. In these the process follows the progressive evolutionary course peculiar to lepromatous cases: spots appear which are at first erythematous and lenticular, and which become bronzed and confluent; and later tubercles, nodules, plaques, etc., appear accompanied in the more advanced cases by ulceration of the mucosa of the nose and larynx, infarcts, and ocular lesions of a serious nature, with all the alterations and deformities which leprosy is apt to cause. We shall not enter into detail upon these cases; it is enough to illustrate photographically the grave state which one of these patients has reached because of lack of treatment (Fig. 1) and the improvement following adequate chaulmoogra therapy.

- (2) *Lepromatous cases irregularly treated show an unfavorable evolution.*

This fact is frequently observed by our colleagues who treat out-patients suffering from the lepromatous type. These patients, because of economic difficulties, or for other reasons, submit only

irregularly to treatment. As a consequence, the disease follows the unfavorable course common in lepromatous cases with all the succession of signs and symptoms which we have described in the preceding case.

- (3) *Tuberculoid leprosy progresses more favorably with than without chaulmoogra.*

Patients with tuberculoid leprosy, because of their specific organic resistance to the disease, tend to improve and in some cases the lesions may even regress spontaneously. But if we make a comparative study we will find that in patients treated with chaulmoogra the lesions not only regress with greater certainty and rapidity, but that furthermore they do not have the tendency to return, particularly when adequately treated. We have a series of observations which are very convincing, one particularly so because we have been able to record photographically the changes over a period of years (Fig. 2). This is a tuberculoid case in which the only lesion, one on the face, was stationary during a period of four years. With chaulmoogra it receded in one year, but when treatment was discontinued, the lesion reappeared four years later in the same place, although smaller. We purposely withheld treatment and the lesion continued to advance slowly over a period of three years, after which the patient was again subjected to the chaulmoogra treatment in a dose of 20 c.c. per week. The lesion disappeared completely within six months (Fig. 2 f).

- (4) *Untreated lepromatous cases nearly always improve with chaulmoogra and often respond with rapidity.*

In lepromatous cases which for the first time receive treatment with chaulmoogra in sufficient amounts, encouraging results are observed not only in milder cases and in those moderately affected, but in advanced cases as well. Not only do the spots clear and disappear, the tubercles go down, and the nodules recede, but leprosy rhinitis, edema, and adenopathies disappear. It is of great importance to point out that this initial improvement requires steady and intensive maintenance of treatment to prevent recurrence. It may have been this initial improvement which caused excessive optimism among a large group of leprologists during the first years of experimentation. Many of these later became discouraged at the return of the symptoms. These relapses need not discourage us if we keep in mind the fact that such regressions may be observed under similar circumstances in other diseases characterized by a chronic evolution such as syphilis.

- (5) *In lepromatous cases in which treatment with chaulmoogra is renewed after having been abandoned, the beneficial reaction is less certain and slower.*

To support this, we have a series of observations which are interesting and convincing. Of these we will cite two examples of a mild type (L-1) with few spots of a bronze color. One of these was subjected to intensive initial treatment of 80 to 100 cc. of chaulmoogra per month by intramuscular and intradermic injections; whereas the other was given insufficient doses of 30 c.c. per month during the first two years of treatment, followed later by intensive treatment. The first case is today clinically and bacteriologically negative, whereas the second still presents active leprous manifestations.

- (6) *Non-treated lepromatous cases which do not benefit by other treatment do benefit from chaulmoogra.*

In 1933 and 1934, in collaboration with Prof. Fernandez (3), we made therapeutic tests with certain aniline dyes and we could cite a number of cases in which they failed, and in which immediate benefits were derived from chaulmoogra treatment.

In 1941, in collaboration with Dr. Mercou, we subjected 11 patients to treatment with diphtheria toxoid. Among these were some who had not had treatment of any kind whatsoever. The results, published by us in the JOURNAL (4) were all unfavorable, some of the patients remaining in the same condition, others becoming worse. When those who had had no treatment of any kind prior to this test were submitted to chaulmoogra treatment, a rapid improvement took place, and these today are clinically and bacteriologically negative in the periodic examinations. Highly illustrative is the photographic documentation which is attached hereto (Figs. 3 and 4).

- (7) *Lepromatous patients which are not benefitted by small and medium doses of chaulmoogra, are benefitted by large doses.*

Many of you doubtless remember (before 1930) the time when almost homeopathic doses of chaulmoogra were employed (4 to 6 c.c. weekly), doses which, after the Cairo Conference, were raised to 10 c.c. With these minute doses mentioned and even with those of 10 c.c. weekly, we have not obtained satisfactory results in many lepromatous cases. In 1938, inspired by the work of Moura Costa (5), we selected, in collaboration with Dr. Vaccaro, a group of 12 lepromatous patients who did not respond to small and medium doses, and subjected them to intensive treatment with doses of 25

to 30 c.c. weekly. The results were presented at the VIth National Congress of Medicine in Cordoba, and were later published (6). In eight months of this intensive treatment noticeable improvement occurred, manifested clinically by diminution and disappearance of a good part of the tubercles. The cases did not become completely negative bacteriologically, but granulation of bacilli was observed, a probable indication of bacterial destruction. Now it may be added that many of these cases intensively treated have become clinically and bacteriologically clear (Figs. 5 and 6).

- (8) *Method of using chaulmoogra: within tolerance, inject the maximum quantity in the minimum time.*

Convinced that with high dosages benefits in lepromatous cases are obtained which are not obtainable with small and medium doses, we have been able to demonstrate that among in-patients all who became clinically and bacteriologically negative had received a total dosage greater than 1500 c.c., whereas of those demonstrating only a slight improvement, only 27 per cent attained this total dosage.

- (9) *Derivatives of chaulmoogra used—manner of administration—importance of intradermal injections.*

We prefer the ethyl-ester creosates (4 per cent), and in second place the iodates (0.5 per cent) for muscle injection, and assign special importance to the intradermal injection described by Lara (7). We now believe that it does not merely produce a local esthetic effect but that such intradermal injections also act at a distance, and that the local inflammatory process resulting from the infiltration which is often accompanied by a general reaction (increase in sedimentation rate, hyperthermia, etc.) stimulates the organic defenses of the patient; and that the bacillary destruction which is manifested by granulation may perhaps contribute to slow immunization.

- (10) *Bacteriologically strongly positive cases rendered clinically and bacteriologically negative.*

With the intensive treatment which is now systematically employed in hospitalized cases and even in out-patients (aiming to reach 30 c.c. weekly including 10 c.c. by intradermal injection) we have rendered clinically and bacteriologically negative 40 per cent of our cases who were only slightly improved previously, and another 40 per cent have become *definitely* (instead of being only slightly) improved. In 1945 our bacteriologically negative cases from previous heavily bacilliferous cases were only 6 but are now double this number.

Of the cases that were *definitely improved*, 33 per cent have become clinically and bacteriologically negative and the others we confidently believe will become *markedly improved*.

The following comparative table showing the important modifications, both clinical and bacteriological, as well as the photographs shown, illustrate the above mentioned results.

(11) *Action of chaulmoogra on leprous adenopathies, on lesions of nasal and laryngeal mucosa, etc.*

In those cases evidencing improvement and especially in those demonstrating extraordinary improvement, we have accomplished, with our chaulmoogra treatments, along with the regression of cutaneous manifestations, first the diminution, and later the regression of hypertrophied leprous ganglia, and this has been accompanied by bacteriological regression (Fig. 6).

Lesions of the mucosa (nasal-pharyngeal-laryngeal) react less readily to chaulmoogra treatment. We should, however, mention a lepromatous case having a tendency to nasal deformity in which, after intensive chaulmoogra treatment, the deformity was checked and the nose began to resume its normal shape. But, as a rule, mucous lesions, particularly of the pharynx and larynx, require the sulfone derivatives.

(12) *More than 80 per cent of failures of chaulmoogra in lepromatous cases are due to deficient and irregular treatment.*

A minute study of 25 lepromatous patients who became worse despite chaulmoogra treatment reveals that their treatment was irregular and deficient; 60 per cent of these patients had not attained a dosage of 300 c.c. of chaulmoogra annually. It is of no use to speak of the failure of chaulmoogra unless an average annual dose of 400 or 500 c.c. of chaulmoogra has been administered.

(13) *Lepromatous cases resistant to chaulmoogra treatment.*

We have observed a small group of lepromatous patients who, although subjected over a period of several years to treatment with an average of 400 to 500 c.c. of chaulmoogra annually, have not demonstrated any improvement. Some of the patients have even shown an unfavorable evolution. Fortunately, these constitute the exception. They are far advanced cases, occurring in persons having no organic resistance to the disease. We would like to see on the one hand how these would react to intensive chaulmoogra treatment with average annual doses of 800 to 1000 c.c., emphasizing particularly intradermal injections, and, on the other hand, how they

might respond to new medications now in vogue. We are working on these problems at the present time.

- (14) *Ninety per cent of our lepromatous cases becoming clinically and bacteriologically negative are in hospitalized patients.*

It has been observed that in-patients are in better condition to receive high dosages of chaulmoogra and to withstand more readily any discomforts and general reactions resulting from the treatment, reactions which, as we have already pointed out, we consider beneficial to the patient.

SUMMARY AND CONCLUSION

The author presents in this paper the most interesting facts he has observed during seventeen years of experience in using chaulmoogra oil in the treatment of leprosy, reaching the following conclusions:

(1) The disagreement of many authors regarding the therapeutic value of chaulmoogra oil is due essentially to the lack of uniformity in the selection of the cases to be treated. The therapeutic value of chaulmoogra should be appraised only by the results obtained in lepromatous cases.

(2) With the derivatives of chaulmoogra it is possible to achieve persistent clinical and bacteriological negativation of lepromatous cases; the treatment, however, must be administered early; it must be sufficient, and must be continued after the negative result has been achieved.

(3) In more than 80 per cent of cases the failures of chaulmoogra are due to irregular and insufficient treatment. Notwithstanding, there is a small percentage of patients which do not react favorably to customary doses of chaulmoogra oil.

(4) In obtaining favorable results in lepromatous cases, the author attributes great importance to the intradermic administration of chaulmoogra oil.

(5) New drugs should be experimented with, but we must not think of abandoning chaulmoogra oil. The scope of chaulmoogra in the treatment of leprosy will indeed be widened as less irritating derivatives are developed, thus making its benefits available to those patients who cannot tolerate full dosage of the present preparations.

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PLATE I

Figure 1. Evolution of a lepromatous case without and with chaulmoogra treatment.

- (a) Patient in 1938 without chaulmoogra therapy.
- (b) Patient in 1941 still without chaulmoogra therapy.
- (c) Patient in 1943 after 2 years of adequate chaulmoogra therapy.
- (d) Patient in 1945 after 4 years of adequate chaulmoogra therapy.

Figure 2. Evolution of tuberculoid case without and with chaulmoogra therapy.

- (a) Tuberculoid lesion on face persisting for four years without chaulmoogra therapy (1935).
- (b) Regression of lesion after one and one half years of chaulmoogra therapy (1936).
- (c) Relapse of lesion four years later after premature abandonment of treatment (1940).
- (d and e) Progress of lesion without treatment (1943).
- (f) Total regression of lesion after six months intensive chaulmoogra therapy.

Figure 3. Evolution of patient given diphtheria toxoid and chaulmoogra therapy.

- (a) Patient before toxoid therapy.
- (b) Patient after four months of toxoid therapy.
- (c) Total regression of lesions after three and one-half years of chaulmoogra therapy.



PLATE I

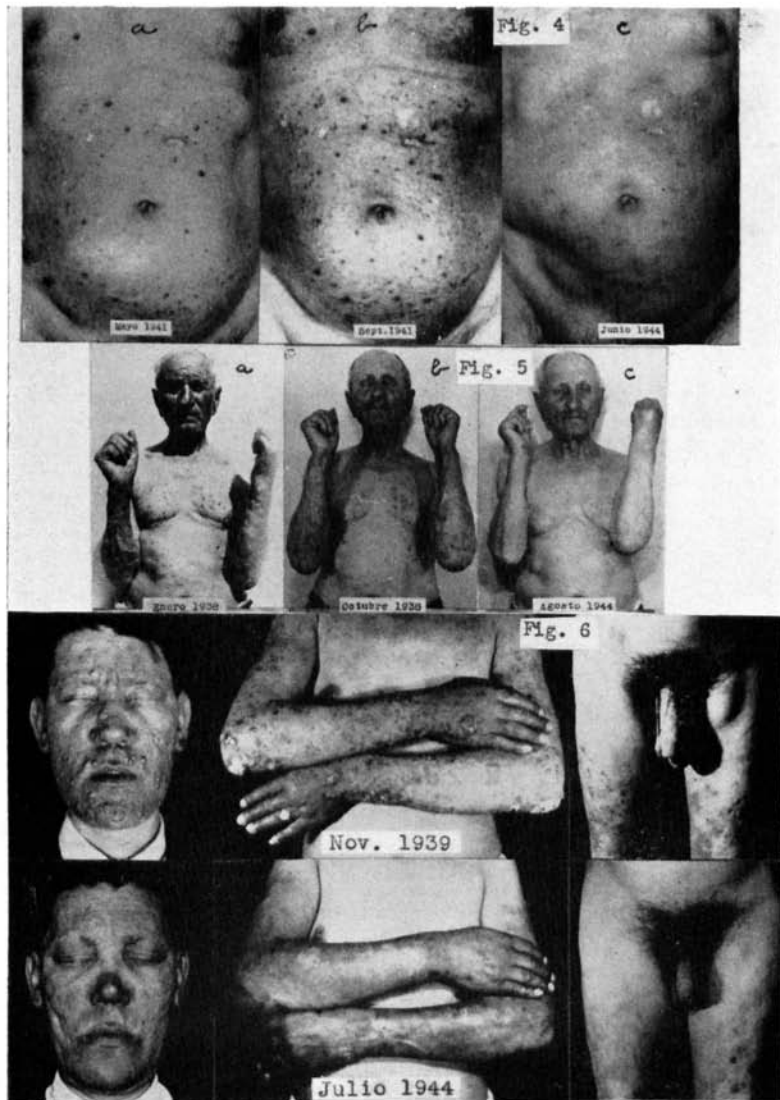


PLATE II

PLATE II

Figure 4. Evolution of patient given diphtheria toxoid and chaulmoogra therapy.

- (a) Patient before toxoid therapy.
- (b) Patient after four months of toxoid therapy.
- (c) Total regression of lesions after three and one-half years of chaulmoogra therapy.

Figure 5. No benefit from small doses of chaulmoogra, but benefit following larger doses.

- (a and b) No progression with small doses.
- (c) After intensive therapy with chaulmoogra.

Figure 6. No improvement with small doses, benefit with larger doses of chaulmoogra.

- (a) No progression with small doses of chaulmoogra.
- (b) Total regression of lesions and nodes after five years with intensive chaulmoogra therapy.