

made from the neurologist's standpoint; it was not our diagnosis. These cases were chosen because none of the usual causes were found in this particular group. That is, we had a large group of otalgias and mastoidalgias in which the contributory factors were easily found; but this was another group. In that respect I may say that we used every differential diagnosis measure we knew of or could learn of, and we took pains to eliminate all the usual, and some of the unusual, causes for this syndrome.

EXPERIENCE WITH CHAULMOOGRA OIL DERIVATIVES IN TREATMENT OF LEPROSY*

HOWARD MORROW, M.D.

ERNEST L. WALKER, S.D.

AND

HIRAM E. MILLER, M.D.

SAN FRANCISCO

The recent encouraging reports¹ on the treatment of leprosy with the esters of chaulmoogra acid in the Hawaiian Islands induced us to give the leper patients at the San Francisco Hospital the benefits of this remedy. The extensive chemotherapeutic studies of Walker and Sweeney² at the Hooper Foundation of the University of California furthered our interest in the subject. Only by their active cooperation has this work been made possible. There have been from twenty to twenty-five patients with leprosy at the San Francisco Hospital for many years. When we began treating these cases, we did not anticipate the publication of our findings. The results, however, have been so at variance with our expectations and the impression obtained from the literature, that we feel some record should be made of them.

EARLY USE OF CHAULMOOGRA OIL

Chaulmoogra oil has long been recognized as the best remedy in the treatment of leprosy. Old Buddhist records in India of ten or more centuries ago refer to the improvement in infected persons after eating the raw chaulmoogra seeds. In modern times, Dyer,³ Heiser,⁴ Hopkins,⁵ Connell⁶ and Hollman¹ have reported improvement and even cures due to the administration of the whole oil by mouth over a long period of time. Marked gastric disturbances, and the length of time required to obtain results, made this mode of treatment unsatisfactory.

To overcome these disadvantages, the mixture of chaulmoogra oil with other substances to make it suitable for subcutaneous or intramuscular injection was attempted. The formula proposed by Mercado and Heiser,⁷ consisting of chaulmoogra oil, 60 c.c.; camphorated oil, 60 c.c., and resorcin, 4 gm., has been used extensively. Heiser⁸ reports the cure of twenty-eight patients by the use of this formula. Hopkins,⁵

McCoy and Hollman,⁹ Armellini,¹⁰ Bercovitz,¹¹ Coghill,¹² Hall,¹³ Cadbury,¹⁴ Connell,⁶ Hollman and Dean,¹ and others report cures or improvement in cases after the use of this and other combinations.

In 1916, Sir Leonard Rogers,¹⁵ in India, reported the preparation of soluble salts of fractions of the fatty acids of chaulmoogra oil and their use intramuscularly and intravenously. He made three preparations of the chaulmoogric acids containing fractions of the lower, the medium and the higher melting points. The first preparation he called, arbitrarily, sodium gynocardate; the second, sodium hydnocarpate, as it contained a preponderance of hydnocarpic acid; and the third preparation, sodium chaulmoograte, as it contained more chaulmoogric acid than the other preparations. The latter preparation formed sodium salts too insoluble for use unless combined with other substances. After experimentation, he decided that the sodium hydnocarpate was more active than the sodium gynocardate. It was found¹⁶ that sodium hydnocarpate could be prepared more readily and in larger quantities from hydnocarpus oil than from chaulmoogra oil. Rogers,¹⁷ Cadbury,¹⁴ Carthew,¹⁸ Muir,¹⁹ Peacock,²⁰ Connell,⁶ Neve,²¹ and others report the use of sodium gynocardate subcutaneously and intravenously with very good results. Rogers²² and Muir²³ report even better results with the use of sodium hydnocarpate.

Rogers²⁴ tested the action of other oils with a large content of unsaturated fatty acids, namely, cod liver oil, linseed oil, Japanese sardine oil, and soya bean oil. He found the cod liver oil preparation, called by him sodium morrhuate, to be most effective. Advanced cases, treated with it, cleared entirely, and some patients who had ceased to improve with other preparations recovered completely when given sodium morrhuate intramuscularly or intravenously. Rogers concluded that the preparation of these different oils may be used to advantage in the treatment of leprosy. If a patient ceased to respond to one oil, the preparation of another oil should be substituted.

Harper²⁵ of India reports excellent results in the treatment of leprosy by intravenous injections of a mixture of chaulmoogra oil, sulphuric ether and iodine. Muir²⁶ also reports good results by this method of treatment; but he believes that better results are obtained by the intramuscular or intravenous administration of a formula consisting of ethyl esters of the fatty acids of hydnocarpus wightiana, 1 c.c.; pure creosote, 1 c.c.; camphor, 1 gm., and olive oil, 2.5 c.c.

At the present time, Muir²⁶ is giving small doses of the ethyl esters of chaulmoogra acids intravenously at frequent intervals, with encouraging results.

The ethyl and other esters of chaulmoogric acids were first prepared by Power and his collaborators in

* From the Department of Dermatology and the George Williams Hooper Foundation for Medical Research of the University of California Medical School.

* Read before the Section on Dermatology and Syphilology at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Hollman, H. T., and Dean, A. L.: *J. Cutan. Dis.* **37**: 367 (June) 1919. McDonald, J. T., and Dean, A. L.: *Pub. Health Rep.* **35**: 1959 (Aug. 20) 1920. McDonald, J. T., and Dean, A. L.: *The Constituents of Chaulmoogra Oil Effective in Leprosy*, *J. A. M. A.* **76**: 1470 (May 28) 1921.

2. Walker, E. L., and Sweeney, M. A.: *J. Infect. Dis.* **26**: 238 (March) 1920.

3. Dyer: *New York M. News* **87**: 199, 1905.

4. Heiser: *Pub. Health Rep.* **28**: 1855, 1913.

5. Hopkins, R.: *New Orleans M. & S. J.* **69**: 223 (Sept.) 1916.

6. Connell: *J. Trop. Med. & Hyg.* **22**: 37, 1919.

7. Mercado and Heiser: *Pub. Health Rep.* **28**: 1855, 1913.

8. Heiser, V. G.: *New York M. J.* **103**: 289 (Feb.) 1916.

9. McCoy and Hollman: *U. S. Pub. Health Bull.* **75**, 1916, p. 3.

10. Armellini: *Clinical Dermosifilopat d. r. University di Roma* **35**: 109, 1917.

11. Bercovitz, Nathaniel: *The Hypodermic Use of Chaulmoogra Oil in Leprosy*, *J. A. M. A.* **68**: 1960 (June 30) 1917.

12. Coghill, H. S.: *Ann. Trop. Med.* **11**: 205 (Aug.) 1917.

13. Hall: *Trop. Dis. Bull.* **13**: 13, 1919.

14. Cadbury, W. W.: *China M. J.* **32**: 226 (May) 1918.

15. Rogers, Leonard: *Lancet* **1**: 288 (Feb. 5) 1916.

16. Rogers, Leonard: *India J. M. Res.* **5**: 227, 1917.

17. Rogers, Leonard: *Brit. M. J.* **1**: 147 (Feb. 8) 1919.

18. Carthew, M.: *India M. Gaz.* **53**: 407 (Nov.) 1918.

19. Muir, E.: *India M. Gaz.* **53**: 209 (June) 1918.

20. Peacock, P. M. C.: *India M. Gaz.* **53**: 95 (March) 1918.

21. Neve: Report of a Conference on the Leper Problem in India, February, 1920, p. 41.

22. Rogers: Report of a Conference on the Leper Problem in India, p. 23.

23. Muir: Report of a Conference on the Leper Problem in India, p. 30.

24. Rogers, Leonard: *Lancet* **1**: 1178 (June 4) 1921.

25. Harper, in Muir's *Handbook of Leprosy*, Cuttack, 1921.

26. Muir: *Handbook of Leprosy*, Cuttack, 1921.

1904, during their extended investigation²⁷ of the chemistry of chaulmoogra oil at the Wellcome Chemical Research Laboratories in London from 1904 to 1907.

Notwithstanding the previous preparation of the esters by Power and the ancient use of chaulmoogra oil in leprosy, Ludwig Taub of Elberfeld, Germany, obtained patent rights in Germany in 1909 for the preparation of esters of chaulmoogra acids and their use in therapeutics. This patent right was assigned to a German chemical company, which put the ethyl esters on the market under the trade name of "antileprol." A little later, patent rights were also obtained in Great Britain and the United States. Following the war, and the confiscation of German patent rights, the alien property custodian sold the rights of this patent in the United States to the Winthrop Chemical Company of New York, which is preparing and distributing the ethyl esters of chaulmoogra acids under the trade name of "chaulmestrol."

In 1919, Hollman and Dean¹ reported the preparation and use by intramuscular injection of the ethyl esters of fractions of the fatty acids of chaulmoogra oil for the treatment of leprosy in Hawaii. These acids were separated into fractions by fractional crystallization, and these fractions converted into their ethyl esters. Four fractions in all were used. Groups of cases were treated with each fraction. It was decided that the therapeutic agent in chaulmoogra oil was distributed through all four fractions. This work was later carried on by McDonald and Dean, and is at present under the supervision of Dr. H. E. Hasseltine of the United States Public Health Service.

In 1919, Hollman and Dean¹ reported the treatment of twenty-six cases for less than two years, eight (30 per cent.) becoming bacteriologically negative in this time. In 1920, McDonald¹ reported the paroling of forty-eight cases; and in 1921,¹ ninety-four more cases were added, making a total of 150 cases.

These patients had been treated with weekly injections of the mixed ethyl esters of the acids of chaulmoogra oil, with 2 per cent. of iodine in chemical combination. This was supplemented by capsules containing the fatty acids of chaulmoogra oil with 2.5 per cent. of iodine chemically combined, given by mouth three times a day. In 1921, McDonald¹ reported series of cases treated without iodine and without chaulmoogra oil capsules. He concludes that "the oral administration is by no means necessary," and "the rôle of the iodine is at most a minor one."

This extended and varied empiric use of chaulmoogra oil and its derivatives in the therapeutics of leprosy was put on a scientific basis by the investigations of Walker and Sweeney,² at the Hooper Foundation for Medical Research of the University of California, in 1920. It was demonstrated experimentally that chaulmoogra oil contains substances having a high bactericidal activity in vitro. This bactericidal activity was found to reside in the fatty acids of the chaulmoogric series, and to be a function of the carbon ring structure which is peculiar to the chaulmoogric acids. The bactericidal action of these cyclic fatty acids was shown to be specific against the acid-fast groups of bacteria, and to be inactive toward all other bacteria. Furthermore, it was demonstrated that other unsat-

urated fatty acids, notwithstanding the therapeutic claims of Rogers and his colleagues, did not possess the specific bactericidal activity of the chaulmoogric acids. From the results of this experimental investigation, it was concluded that the empiric use of chaulmoogra oil and its derivatives in leprosy was justified, and that its therapeutic effect was due to the bactericidal action of the chaulmoogric acids on *Bacillus leprae*.

TREATMENT OF LEPERS AT THE SAN FRANCISCO HOSPITAL

In August, 1920, we began treatment of the lepers at the San Francisco Hospital, and they were under treatment up to March, 1922, when they were transferred to the national leprosarium at Carville, La.

Of a total of twenty-one cases, there were ten of the nodular type, six of the maculo-anesthetic type, and five of the mixed type. One had shown manifestations of the disease for two months, one for thirteen years, and the others for periods intermediate between

SUMMARY OF CASES TREATED

Case	Name	Age, Years	Type of Disease	Duration	Severity	Duration of Treatment	Average Dose, C.c.	Condition
1.	F. C.	22	Nodular	6 mo.	Moderate	3 mo.	3	Unimproved
2.	W. H.	27	Nodular	5½ yr.	Moderate	3 mo.	3	Unimproved
3.	L. C.	28	Mixed	5½ yr.	Moderate	2 mo.	3	Unimproved
4.	T.	41	Nodular	1 yr.	Advanced	10 mo.	3	Unimproved
5.	A. A.	34	Nodular	6 yr.	Moderate	3 mo.	3	Slight imp.
6.	L. Y.	27	Mac. anes.	3½ yr.	Moderate	5 mo.	3	Unimproved
7.	M.	24	Mixed	3 yr.	Moderate	8 mo.	3.5	Slight imp.
8.	G. H.	33	Nodular	3 yr.	Moderate	8 mo.	3	Unimproved
9.	D.	37	Nodular	10 yr.	Advanced	12 mo.	3	Worse
10.	S.	27	Nodular	2 yr.	Advanced	18 mo.	4	Worse
11.	W. K.	24	Mixed	5 yr.	Moderate	17 mo.	4	Much imp.
12.	Y. S.	45	Nodular	13 yr.	Advanced	9 mo.	3.5	Unimproved
13.	T. L.	36	Mixed	4½ yr.	Moderate	2½ mo.	3	Unimproved
14.	S. A.	53	Nodular	5 yr.	Advanced	13 mo.	3.5	Worse
15.	J. F.	15	Mixed	2 yr.+	Advanced	5 mo.	1	Died during treatment unimp.
16.	E. L. B.	71	Nodular	12 yr.	Moderate	11 mo.	4	Died, pneumonia unimproved
17.	F. W.	19	Mac. anes.	3 yr.	Moderate	14 mo.	3.5	Slight imp.
18.	G.	22	Mac. anes.	2 mo.	Mild	3 mo.	4	Absconded, unimp.
19.	J.	29	Mac. anes.	6 mo.	Mild	2½ mo.	3.5	Absconded, unimp.
20.	E.	47	Mac. anes.	6 mo.	Mild	8 mo.	4	Unimproved
21.	M.	45	Mac. anes.	2 yr.	Moderate	4 mo.	3.5	Much imp.

these two extremes; the average duration of the disease was four and one-half years. Most of the cases were far advanced. The average period of isolation before beginning treatment was three years.

We employed chiefly the ethyl esters of the total fatty acids of chaulmoogra oil in our treatment. The injections were made intragluteally at weekly intervals, and the dosage was varied according to the weight of the patient and the amount of local and constitutional reaction after the preceding injection. The injections were not supplemented by chaulmoogra oil orally, or by the combination of iodine with the drug.

Laboratory investigations of the chemotherapeutics of chaulmoogra oil and its derivatives, which are being conducted by one of us simultaneously with the treatment of these patients, disclosed that two other esters, the butyl and propyl esters, produced much less local reaction and pain than the ethyl esters or any of a large series of derivatives prepared and tested. Therefore, these two new esters were substituted for the ethyl ester in the later treatment of our patients, and two lepers were treated exclusively with these esters. The clinical results confirmed the relative absence of local reaction obtained in the animal tests, and the

27. Power and Gornall: J. Chem. Soc. **85**:851, 1904; Power and Lees: Ibid. **137**:349, 1905. Power and Barrowcliff: Ibid., 884. Barrowcliff and Power: Ibid. **91**:557, 1907. Power, F. B.: Am. J. Pharmacol. **87**:493, 1915.

therapeutic action appeared to be as good as that obtained with the ethyl esters.

These twenty-one patients were under treatment for a period of from three to eighteen months, with an average of eight months. Of these patients, a boy, aged 15 years, with advanced leprosy, died of the disease; one man, aged 71, died of pneumonia-leprosy

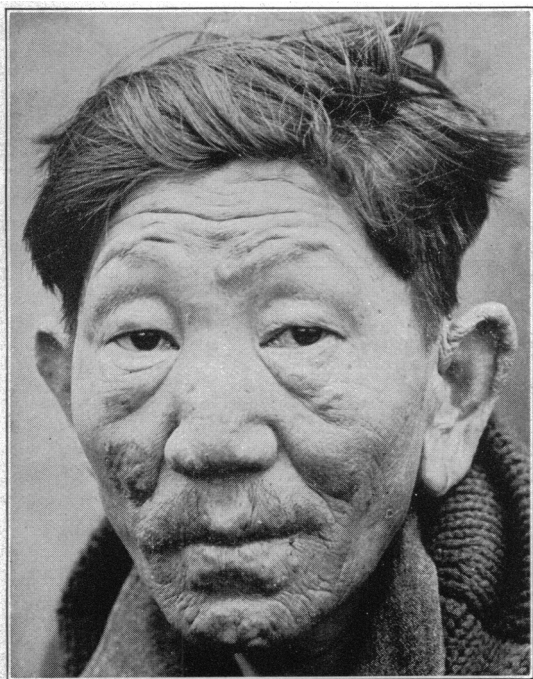


Fig. 1 (Case 8).—No improvement after eight months' treatment.

unimproved; three patients in advanced stages became definitely worse; nine showed no improvement; two patients with cases of moderate severity were markedly improved; three with cases of moderate severity were slightly improved, and two patients with the disease in an early stage absconded after three months' treatment.

None of these patients became bacteriologically negative during treatment; but the nasal discharge in one case (Case 11) became negative after more than a year of treatment. The accompanying table, case reports and reproductions of photographs illustrate the results obtained.

TREATMENT AT KALIHI AND AT MOLOKAI

In consequence of the slow progress of most of these cases after treatment for fifteen months, it was decided to check up our results by a personal study of the treatment of lepers with the ethyl esters of chaulmoogric acids in the Hawaiian Islands. During December, 1921, one of us had the opportunity to see all the patients at Kalihi Hospital, Honolulu, and practically all the patients at the Molokai Leper Settlement.

There are 176 patients with lepra at Kalihi under the supervision of Dr. H. E. Hasseltine of the United States Public Health Service. These patients present all types of leprosy, from the earliest forms of maculo-anesthetic to advanced nodular. On account of all the very early cases of lepra in the Territory of Hawaii being segregated in Kalihi, that hospital is an ideal place for experimentation with the derivatives of chaulmoogric oil.

The various preparations used in treatment are made at the University of Hawaii under the supervision of Dr. A. L. Dean. At present, both at Kalihi and at Molokai, the preparations are used without the addition of iodine. The injections are given once a week, and until recently all injections were given into the buttock. Since the early part of January, 1922, Dr. Hasseltine has been giving a few patients small doses of the ethyl esters intravenously every few days. The latter method has the advantage of being painless.

Between 1918 and July, 1921, 150 patients were paroled from Kalihi; of this number, ten at least have died; a few have gone to other parts of the islands, and twenty (8 per cent.) have returned to Kalihi for further treatment as the result of recurrence of active symptoms of leprosy. It is likely that more of the paroled patients will show activity of the disease and will need further treatment.

The present system of paroling patients and giving them weekly injections of the ethyl esters for a further period of two years is a good one. It allows the patients to work, and with the continued medication there will be fewer recurrences, and many more patients are likely to be permanently cured.

During the six months previous to January, 1922, there were but six patients paroled. This small number of paroles indicates that the present authorities are using greater caution to prevent the discharge of arrested cases which are later liable to show exacerbations of leprosy. There are many patients with an advanced stage of leprosy at Kalihi, probably fifty of whom are incurable with our present method of treatment, and many of these should be sent to Molokai.

The settlement of Molokai contains 452 patients, and during 1921 more than 300 received treatment with the ethyl esters. As no patients with leprosy have been sent to Molokai since 1919, it is quite evident that very few early cases are to be seen there, and of the 300 receiving treatment, few, if any, show indications of an early parole. Dr. William Goodhue, the physician in charge of Molokai Settlement, is conscientious in giving the injections, and hopes to see many of the milder cases cured.

From conversation with Dr. Heiser, Dr. Trotter and many others who have had extensive experience in the treatment of leprosy, it seems to be the unanimous opinion that the present treatment with the esters is by far the best of any chaulmoogric oil treatments so far advanced. From bacteriologic studies and from clinical symptoms, it seems probable that the present system of treatment will cure the early cases, especially in young subjects. The advanced cases certainly improve in time, and it is possible that many of these will be cured after years of treatment. Some of the advanced cases show little or no improvement after many months of treatment, and a very small percentage seem to do poorly under treatment.

In our cases of leprosy treated in San Francisco, the discouraging results are undoubtedly due to the age

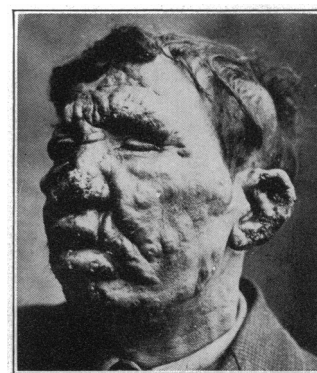


Fig. 2 (Case 9).—Lesions more extensive after twelve months' treatment.

of many of the patients and the advanced stage of leprosy in most of them. In the few early cases we have treated, we are satisfied that the present remedy is of great value, and from statistics gathered we are also of the opinion that the injections must be kept up for at least three years in the milder cases and much longer in the advanced ones.



Fig. 3 (Case 10).—Appearance of patient before treatment.

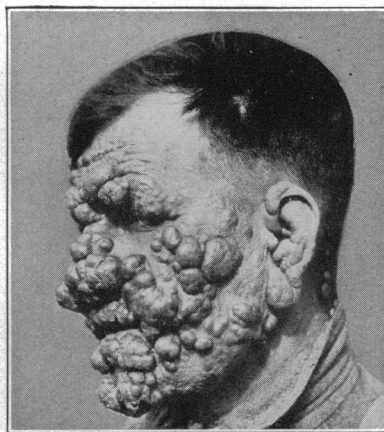


Fig. 4 (Case 10).—After eighteen months' treatment: lesions somewhat larger.

Isolation of all advanced cases of leprosy in one leprosarium in Louisiana is an excellent plan. Under government control and supervision these patients will receive much better treatment than when they were scattered in isolated county hospitals throughout the United States. We shall watch with much interest the results of treatment in this national leprosarium, and particularly the effect of further treatment in our individual cases.

REPORT OF CASES

CASE 1.—F. C., a man, aged 22, born in China, who had leprosy of the nodular type, of six months' duration, was treated three months with an average dosage of 3 c.c. There were large nodules on the brow, and many small nodules on the cheeks, neck, chin and ears. There was marked tumefaction of the lobes of the ears. The trunk was normal except for a few pigmented macular areas on the back. There were a few similar areas on the forearms and arms, and many miliary semiconfluent nodular areas around the wrists. Tumefaction and pigmentation of the hands were well marked. There was no muscle atrophy. Compulsory treatment was discontinued after three months. The leprosy was unimproved.

CASE 2.—W. H., a man, aged 27, born in Canton, China, had leprosy of the nodular type, of five and one-half years' duration. Treatment was given for three months with an average dosage of 3 c.c. There were alopecia and tumefaction of the brows; semiconfluent and confluent nodules on the nose, cheeks, chin and ears; diffuse, ill-defined, macular mottling over the shoulders, arms and forearms, and tumefaction of the backs of the hands. There was no muscle atrophy or sensory changes. Compulsory treatment was discontinued after three months. The leprosy was unimproved.

CASE 3.—L. C., a man, aged 28, born in China, had leprosy of the mixed type of five and one-half years' duration. The symptoms began six months before entrance. The patient was under treatment for a period of two months, with an average dosage of 3 c.c. There was diffuse but not marked thickening of the forehead, brows, nose and cheeks. The ears were enlarged, especially in the lobes. There was a geographic macular eruption on the neck; a coin-sized, well defined macular eruption on the trunk, anterior and posterior; diffuse macular areas on the arms and forearms; multiple, miliary nodules on the wrists, and tumefaction of the hands; a diffuse, leprosy thickening of the right palm. The ulnar nerves were moderately enlarged; there was thenar and hypothenar

atrophy, especially of the right hand. There were confluent nodules over the right elbow tip simulating xanthoma. There were geographic areas on each thigh, and nodules on the right buttocks. The patient took treatment under compulsion, and discontinued it after two months. No improvement was noted.

CASE 4.—T., a man, aged 41, born in Greece, had leprosy of the nodular type, of five years' duration. The patient was under treatment for a period of ten months. The average dosage was 3 c.c. each week. There was worm eaten alopecia of the scalp of six years' duration, simulating syphilis. The eyes were normal; the trunk, thighs and arms clear; the cheeks shiny and red, with many telangiectases and comedones. Small nodules and stains were scattered over the face. The brows and lashes were gone. The ears were enlarged and wrinkled. The hands and forearms were nodular. There was passive congestion in the hands; the normal lines of the palms were accentuated. On the legs, around the knees, were deep, dark scars. There were ulcers on each calf. There were nodules and hyperkeratosis of the soles. The condition in March, 1922, was more advanced.

CASE 5.—A. A., a man, aged 34, born in India, had leprosy of the nodular type, of one year's duration. Treatment was given for three months. The average dosage was 3 c.c. There was alopecia of the brows. There was thickening with scattered small nodules over the face, cheeks and chin. The nose was broadened and flattened. The trunk was practically clear. There was marked tumefaction of the



Fig. 5 (Case 10).—Back of patient before treatment.

hands and feet, and considerable ulceration and secondary infection on the feet. In March, 1922, all the areas were slightly improved. The patient's general health was improved.

CASE 6.—L. Y., a man, aged 27, a Chinese, had leprosy of the maculo-anesthetic type, of three and one-half years' duration

The patient was under treatment for a period of five months. The average dosage was 3 c.c. The brows, nose and ears were normal. There were confluent and diffuse macules on the face and neck. A few chicken-egg sized anesthetic rings were noted on the chest. The hands were distinctly claw-shaped, and all the muscles were atrophied. The arms and thighs were covered with diffuse, anesthetic, geographic areas. Compulsory treatment was discontinued after five months, with the leprosy unimproved.

CASE 7.—M., a man, aged 24, born in Hawaii, with leprosy of the mixed type, of three years' duration, was given treatment eight months. The average dosage was 3.5 c.c. There were about a dozen discrete and comparatively flat nodules on the forehead, cheeks and chin, confluent on the right cheek. There was faint tumefaction of the ears. There was a diffuse, confluent and semiconfluent macular eruption on the trunk and thighs. Tumefaction was noted on the backs of both hands. A few small nodules were located on the wrists and forearms. There was no disturbed sensation or muscular atrophy. Compulsory treatment was discontinued after eight months. The nodules on the face were smaller. The macular areas on the body were less distinct.

CASE 8.—G. H., a man, aged 33, a Japanese, with leprosy of the nodular type, of three years' duration, received treatment for eight months. The average dosage was 3 c.c. There were about two dozen small, flat nodules on the cheeks, lips and chin. The ears were large, nodular and pendulous. There was a faint, miliary, papular rash over the trunk and thighs. There was tumefaction over the back of the hands. The palms were dry, the normal lines increased. After eight months' treatment, the patient complained of general malaise and severe pains all over the body a few hours after each injection. The injections were discontinued. The leprosy was unimproved.

CASE 9.—D., a man, aged 37, an American, with leprosy of the nodular type, of ten years' duration, was given treatment for twelve months. The average dosage was 3 c.c. There

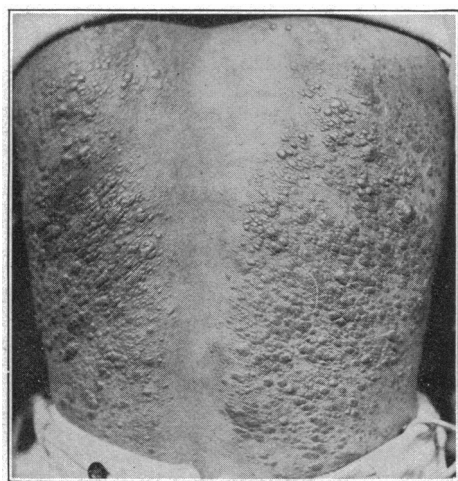


Fig. 6 (Case 10).—After eighteen months' treatment: individual lesions smaller, but much more numerous.

were discrete and confluent nodules over the entire face. The nose and ears were ulcerated. There was total alopecia of the brows. The patient was blind in both eyes. There was a diffuse, lichenoid, leprosy dermatitis from the scapulae to the buttocks. A similar condition existed on the buttocks, with scattered nodules throughout. There were crenated skin and lichenoid dermatitis on the thighs. A diffuse and marked tumefaction was present on the backs of the hands and fingers. In March, 1922, the condition of the lesions was more advanced.

CASE 10.—S., a man, aged 27, a Portuguese, with leprosy of the nodular type, of five years' duration, was treated eighteen months. The average dosage was 4 c.c. Nodules from the size of a pea to that of a pigeon's egg covered the face. Some lesions were almost pendulous. A few ill-defined nodules were on the tongue and hard palate. There were semipendulous and semiconfluent nodules over the hands and forearms, small nodules over the palms, and scattered pea

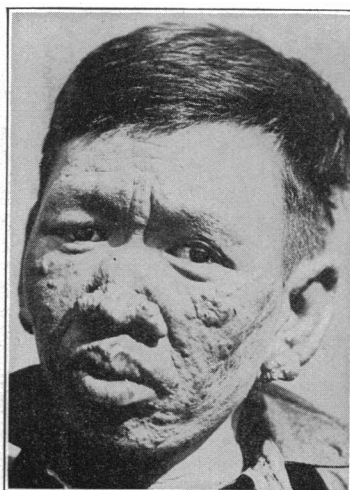


Fig. 7 (Case 11).—Before treatment.

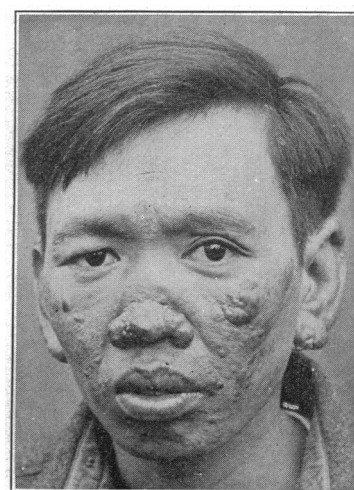


Fig. 8 (Case 11).—After seventeen months' treatment: most of nodules remaining are fibrous.

to lima bean sized semipendulous nodules over the trunk. There was no muscle atrophy. In March, 1922, the lesions were somewhat larger and more extensive.

CASE 11.—W. K., a man, aged 24, with leprosy of the mixed type, of two years' duration, was treated seventeen months. The average dosage was 4 c.c. Pea-sized nodules were scattered over the forehead, cheeks, nose and ears. Some areas were soft, and some fibrous. A few small nodules were scattered on the forearms. There were geographic, cyanotic macules on the trunk, a chronic lichenoid leprid of the thighs, and solid edema of the backs of the hands. The ulnar nerves were enlarged. There was contracture of the little and ring fingers. The nasal secretions contained many lepra bacilli. These disappeared after one year's treatment. In March, 1922, many nodules had disappeared, leaving pigmentation. The remaining nodules were fibrous and apparently inactive.

CASE 12.—Y. S., a man, aged 45 years, a Chinese, with leprosy of the nodular type, of thirteen years' duration, was treated nine months. The average dosage was 3.5 c.c. There were confluent, pea-sized, subcutaneous nodules over the entire face. The nose was flattened and partially destroyed. There were ulcerations on the nose, lips and cheeks. There was almost complete alopecia of the brows. The skin of the trunk was dry and scaly, with hyperpigmentation over the lower back. There was edema of the backs of the hands and the feet. Compulsory treatment was discontinued after nine months. The leprosy was unimproved.

CASE 13.—T. L., a man, aged 36, a Chinese, with leprosy of the mixed type, of four and one-half years' duration, was treated two and one-half months. The average dosage was 3 c.c. A few faint, indistinct nodules were seen on the upper lids. There was considerable atrophy of the skin of the face, apparently the result of the absorption of leprosy lesions. Small cutaneous and subcutaneous nodules were grouped on both forearms. There were pigmentation and crenated skin on the backs of the hands, and contracture and atrophy of all the fingers on the right hand, associated with marked anesthesia. There was very little contracture or atrophy of the left hand. The condition, after two and one-half months of compulsory treatment, was unimproved.

CASE 14.—S. A., a man, aged 53, an American, who had contracted the nodular type of the disease in the Philippines, five years before, was given treatment thirteen months. The

average dosage was 3.5 c.c. The forehead was wrinkled and hypertrophied. There were about two dozen small nodules on the cheeks, chin and lips. The left eye had been removed two and one-half years before because of corneal involvement. The entire right eye was blurred; the pupil was irregular from synechiae. The entire body had a faint, wrinkled, pigmented, scaly appearance. The condition of the hands was similar, but more advanced. Very little, if any, atrophy was present. In March, 1922, the patient was totally blind. The nodules on the face were larger. The general health of the patient was very poor.

CASE 15.—J. F., a boy, aged 15 years, a German, born in Honolulu, with leprosy of the mixed type, of probably two years' duration, was treated five months. The average dosage was 1 c.c. The patient weighed 50 pounds (22.7 kg.). There was total alopecia of the brows. The nose, ears, lips, cheeks and chin had been partially destroyed by ulcerating nodules. There were dry, faint, mottled and macular areas over the trunk and the extremities. There were tumefaction of the backs of the hands and contracture of the little fingers on both hands. The patient's general condition was much improved after two months' treatment; it became gradually worse, however, and he died of the disease after five months' treatment.

CASE 16.—E. L. B., a man, aged 71 years, an American with leprosy of the nodular type, of twelve years' duration, was treated eleven months. The average dosage was 4 c.c. The patient was blind in both eyes. The skin on the face was atrophic from absorption of nodules. There was a diffuse, leprosy, lichenoid dermatitis over the back, abdomen and the sides of the body; a faint, diffuse, gyrate mottling over the chest and the thighs and crenated skin on the forearms. The backs of the hands were dry, wrinkled, crenated and bluish. There was no muscle atrophy. The patient died of pneumonia after eleven months of treatment, with the leprosy unimproved.

CASE 17.—F. W., a man, aged 19, a Chinese, with leprosy of the maculo-anesthetic type, of three years' duration, was treated fourteen months. The average dosage was 3.5 c.c.

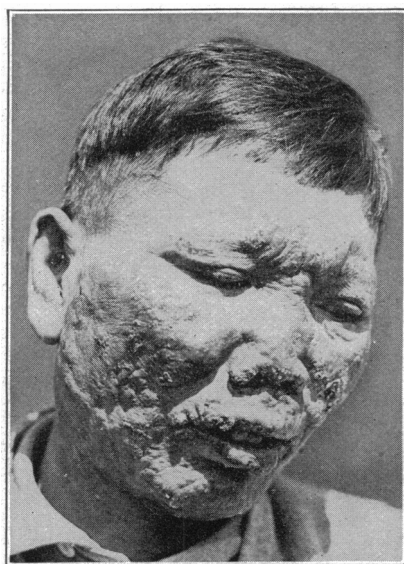


Fig. 9 (Case 12).—No improvement after nine months' treatment.

There was elephantiasis of the upper and the lower lip. On the face, neck and upper part of the back there were faint, ill-defined, macular areas. The toes and fingers were markedly contracted with considerable atrophy. Both ulnar nerves were definitely enlarged and nodular. The hands and areas on the forearms were anesthetic. In March, 1922, the macular areas were disappearing; otherwise the condition was unchanged.

CASE 18.—G., a man, aged 22, born in the Philippines, with leprosy of the nerve type, of two months' duration, was treated for three months. The average dosage was 4 c.c. each week. The right ulnar nerve was about the size of a little finger. The right little finger was contracted. The side of the wrist and palm innervated by the ulnar nerve showed a brownish pigmentation with accentuation of the normal lines. This entire area was anesthetic. The patient absconded after three months' treatment with the leprosy unimproved.

CASE 19.—J., a man, aged 29, born in the Philippines, with leprosy of the nerve type, of six months' duration, was

treated two and one-half months. The average dosage was 3.5 c.c. each week. Hyperpigmented and depigmented areas were scattered over the body. Half a dozen dollar sized rings were scattered over the buttocks and the back. There was slight tumefaction of the backs of the hands, with an accentuation of the normal markings on the palms. A similar

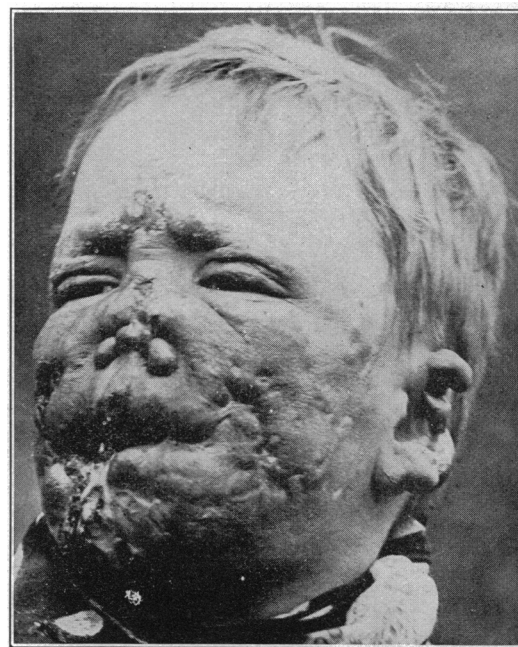


Fig. 10 (Case 15).—Boy, aged 15, died of disease after five months' treatment.

condition prevailed on the soles. There were small ulcers on the great toes. The patient absconded after three and one-half months' treatment, with the leprosy unimproved.

CASE 20.—E., a man, aged 47, an American, with leprosy of the maculo-anesthetic type, had spent some time in Brazil sixteen years before. The duration of the symptoms was six months; the duration of treatment, eight months. The average dosage was 4 c.c. A palm-sized fawn-colored, anesthetic macular area was situated just above the left internal malleolus. After seven months' treatment, erythematous macular anesthetic areas appeared on the upper lip and the right cheek. A few months after beginning treatment, the area on the leg was barely visible; at present, however, it is about the same as at the time when the patient was first seen. After eight months of treatment, he complained of general malaise with pains in the muscles and joints that were so severe that they prevented him from working. Treatment was discontinued for two months.

CASE 21.—M., a man, aged 45, an Englishman, probably contracted the disease in South Africa. The duration of symptoms was two years. The disease was of the maculo-anesthetic type. He was under treatment for a period of four months. The average dosage was 3.5 c.c. Erythematous, macular areas were situated on the left chin, left temple and left ear. The left posterior lumbar region was covered with an extensive, erythematous, macular eruption. There was a small macular area on the right anterior wrist. The macular areas were all anesthetic to pin pricks, heat and cold. After one month's treatment, the areas on the back and wrist became pigmented, and sensation began to return. At present, after four months' treatment, the pigmented areas are fading, and the skin is returning to its normal state. The areas on the face are involuting more slowly. There is general malaise, with pains in the joints and muscles of such severity that the patient is confined to bed for three or four days after each injection. Treatments were discontinued for three or four weeks. The patient was given sodium cacodylate injections during this rest period.

135 Stockton Street.

ABSTRACT OF DISCUSSION

DR. WILLIAM T. CORLETT, Cleveland: The paper is fair and comprehensive. Its conclusions, however, may be a little too optimistic; but optimism, next to the actual curative agent, is the stimulus that the leper needs. Since the parole system was adopted in the Hawaiian Islands in 1918 or 1919, the leper himself has received a new lease of life. That the community is more endangered is another question. He has felt that it is possible for him to become rid of the malady, which is a valuable curative asset in any disease. As to the treatment of leprosy with the ethyl esters: So far as I can ascertain, they bring out no beneficial properties not possessed by the old chaulmoogra oil itself—when the patient can take chaulmoogra oil. But the crude oil is often irritating to the stomach, and many patients cannot take it. In such instances the intramuscular, or better, the intravenous, administration of the ethyl esters is a decided advantage. The separation of the ethyl esters made available in 1904, or soon after, must be, therefore, considered a step in advance. A few weeks ago when I left Honolulu, Dr. Hasseltine, the marine and public health officer, was giving, when possible, the ethyl esters intravenously, and this to my mind will prove to be the future treatment for leprosy. The use of the ethyl esters intramuscularly, into the buttocks, is painful, much more so than the same method of giving mercury. Even when patients are willing to submit to it, there are disadvantages. I recall two cases in which extensive abscesses followed this procedure, while the introduction into the veins is painless. If the ethyl esters can be rendered sufficiently innocuous to be introduced safely into the veins, it would be the best treatment of leprosy so far as relates to the ethyl esters or the newer derivatives of chaulmoogra oil.

DR. R. M. WILSON, Korea: I have 800 patients with leprosy under my care. I have trained our lepers to do their medical work and use the microscope, as well as other laboratory work, and I am enthusiastic about chaulmoogra oil. I believe that chaulmoogra oil is as good as the ethyl esters because it contains many things the ethyl esters do not. We have been using chaulmoogra oil, 1 per cent., and for six months we have been using the ethyl esters, but the ethyl esters have not affected the old cases treated by chaulmoogra oil. Either the ethyl esters or chaulmoogra oil in a new case will show quite marked results in six months' time. I think that in the cases shown this morning we could hardly hope to see much improvement, because the cases are so advanced. The great hope is in the younger cases, particularly the children, who respond more readily. We find in some cases that improvement takes place under hypodermic injections before the internal treatment is effective. In our institution we have the industrial work pretty well established; these patients do brick and tile work, and they prefer to take the capsules internally and that seems to hold them in check. Many cases are not entirely healed, but they are held in check. I have 300 patients on the ethyl esters in Peking and 200 on chaulmoogra oil, and hope to report in a year's time which gives the best results. These lepers come in literally crawling in the dust, feeling that they are dead dogs, and then when they come to realize that we can do something for them they are the happiest group you can find. I am very enthusiastic about the ethyl esters, and believe there is no doubt that we can get splendid results in the early cases.

DR. I. L. MCGLOSSON, San Antonio, Texas: In San Antonio we have about thirty cases of leprosy, not that number under treatment, but that is about the number we have proved. This paper is a wonderful article on the class they have attempted to treat, but I believe that the problem in leprosy is the same as in tuberculosis and cancer—there are cases we cannot touch. I think that it is unfair to draw conclusions from the old and hopeless cases. It is the early case in which we can do the most good. I am going to advance another opinion, and that is that many cases are not recognized. They occur not in the poorer class but in the better classes, and yet they are lepers. The class in which we get the best results, in my experience, consists of early cases,

when the patients are in fine shape physically and mentally. I think the point is well taken by Dr. Corlett as to the time when they will return. A certain percentage will recur, which indicates that we have stopped treatment early. We have no means of knowing when they can be discharged as cured and when they can stop treatment. Whether this is the best treatment or not, we are on the right track to get a treatment which can offer something if we get the cases in time. My experience is that in the + and ++ Wassermann reactions that cannot be substantiated clinically, if one will investigate the nose and the skin, one will probably find some evidence of leprosy. Let us keep an open mind on this. The cases in California were far advanced, and it would take a long time before they could be influenced by the ethyl esters or chaulmoogra oil; but in the early cases I am sure that a great deal can be accomplished, and many patients cured.

DR. ERNEST D. CHIPMAN, San Francisco: The cases reported were old, but I know from personal conversation with Dr. Morrow that they have taken the cases as they found them, and that they thoroughly believe in the efficacy of the treatment in early cases. Dr. Corlett, and I think Dr. Wilson also, expressed the view that a very important feature in leprosy is the moral effect produced by the introduction of a treatment that gives the patients some hope. I have had an opportunity of visiting the hospitals in Honolulu twice during the last few years, and have been much impressed with the apparent happiness with which patients faced their hospitalization. Whereas in former times they made every effort to conceal the disease, they now come voluntarily for treatment.

DR. FLOYD STEWART, St. Louis: I had the pleasure of treating many of these patients with Dr. Isadore Dyer of New Orleans. Dr. Dyer first began using potassium chlorate, sodium salicylate and strychnin. He reported a case as a probable cure because all the lesions cleared up. The patient was dismissed from the Charity Hospital outpatient clinic, and was not taken to the leper colony. At that time it was purely voluntary; there were no laws to transport these people, and this patient, a negro, returned to work; but in about eighteen months he came back for further treatment. At that time Dr. Dyer took up another treatment, called the "antivenin" treatment. He purchased this serum from the Calmette Laboratory at Lille, France, and it gave remarkably good results at first. Following this case we had several that showed improvement for a certain length of time, and then retrogressed. Dr. Dyer discussed the use of the antivenin serum, not on account of the cost, which he had defrayed himself, but because of the poor final results. Then he took up this new treatment with chaulmoogra oil. He was rather enthusiastic about the results he was obtaining. I hope that Dr. Morrow's results are encouraging enough for him to persist in treating these cases, and that he will succeed in curing the mild cases at least, for it is quite evident that when physicians and patients are enthusiastic about a remedy, better results will be obtained.

DR. EDWARD A. OLIVER, Chicago: We have had about seven of these cases under treatment in the Cook County Hospital and have been very enthusiastic about the ethyl esters. Six were of the nodular type and one of the maculo-anesthetic type. We first started on chaulmoogra oil, and then when we received the ethyl esters we used them. There was no patient who did not improve, but they were only moderately advanced cases. One patient was a Serbian, and he improved very rapidly, all of the lesions disappearing. One man we have paroled now. Every one of these patients improved mentally, physically and in every other way under the ethyl ester treatment.

DR. HIRAM E. MILLER, San Francisco: In presenting this paper we had only hoped to moderate the impression that advanced cases of leprosy were being readily cured by the injection of ethyl esters over a comparatively short length of time. However, I would like to emphasize the fact that we feel that early cases in young persons may be cured with the present methods of treatment.