

# A Comparative Study of the Relative Efficacy of Ethyl Hydnocarpate and Ethyl Morrhuate in Leprosy.

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## INTRODUCTION.

**I**N the Croonian lectures on "Researches on Leprosy and their Bearing on the Treatment of Tuberculosis," delivered before the Royal College of Physicians of London, on the 26th June, 1924, Sir Leonard Rogers (1924) (1) mentioned that sodium morrhuate was found to be effective in leprosy; and the same author states elsewhere Rogers (1928) (2) that "Good results could also be obtained by injections of sodium morrhuate, etc.," and illustrates this by the results of his own observations published in his 1921 paper, quoting from which he states that out of 51 cases treated for three months and upwards, 41 per cent. were completely cured, 39 per cent. greatly improved, 18 per cent. improved, and 2 per cent. stationary. As this latter paper could not be consulted in the original, it is difficult to find out what types of cases were mainly benefited and what types did not respond to morrhuates.

Muir et al (1924) (3) as a result of their collective studies on the therapeutic value of hydnocarpus, cod liver, linseed, olive, and cocoanut, ethyl esters, concluded that "both the closed carbon ring and the amount of unsaturated fatty acids appear to be factors of value." Apart from other papers by workers in different parts of the world, dealing with attempts at evaluation of the "in vitro" bactericidal activity of the morrhuates along with other ethyl esters and sodium salts of unsaturated and saturated oils, a perusal of the available literature shows a paucity of papers dealing with comparative experimental studies carried out with a view accurately to assess the relative efficacy of the ethyl esters of cod liver *vis-a-vis* the ethyl esters of hydnocarpus wightiana.

In view of the favourable opinions expressed by Sir Leonard Rogers, and because, next to linseed oil, cod liver oil has the highest "iodine value" (which indicates the degree of unsaturation of the fatty acids); and further, no records of comparative studies from the therapeutic standpoint were available in the literature up to the end of 1931, Dr. E. Muir of the Calcutta School of Tropical Medicine suggested to the writer that he should carry out the experiment on which this article is based. Dr. Muir kindly supplied large quantities of ethyl morrhuate.

#### MATERIAL FOR STUDY.

Five C3 cases of leprosy and one N2 case with very marked symmetrical lesions (four out-patients attending the clinic and two in-patients of the Purulia Leper Colony) were chosen and examined thoroughly for the existence of other concomitant diseases that might vitiate this experiment. After dealing with the predisposing factors by appropriate treatment, they were subjected to this study. Half per cent. iodised ethyl hydnocarpate was injected intradermally into the lesions on the right side of the body, while diluted ethyl morrhuate (ethyl morrhuate one part and ethyl oleate two parts) was injected intradermally into the lesions on the left side, once a week, keeping the doses of both the preparations the same, *viz.*,  $\frac{1}{2}$  ccm. to 6 ccm. At each weekly injection, the respective doses of the preparations injected, were, as far as possible, kept the same. Pure ethyl morrhuate was found to be too irritant and therefore had to be diluted with ethyl oleate to permit of its continuous use. Even after dilution, it was found to be comparatively more irritant than the iodised ethyl hydnocarpate.

Of the six cases taken for this study, one C3 case (inmate) suddenly absconded and another C3 case (out-patient) was found to be too irregular in attendance and was therefore excluded from this experiment. The rest, three C3 cases (two out-patients and one inmate) and one N2 case, took the treatment regularly for a period of from one year and eight months to two years and four months; and the observations recorded here are based chiefly on the results of treatment in these four cases who, evidently, have had adequate and prolonged treatment. One N2 case was purposely included in this study as he had well-marked symmetrical macules (hypopigmented patches) some of them with slight anæsthesia, and it was considered desirable to study the influence of the drugs injected intradermally, on the pigment of the skin as well as on the sensory disturbances noticed.

Ser. No.	Name and Sex Inmate or out-patient	Type on admission	Dosage range in CCM.	Total No. of Injections	Total period of Treatment	Final results (Clinical)	Final Bacteriological results	Remarks
1	Shanta, F., O.P. Elderly woman nearing 40 years of age	B <sub>3</sub> (C <sub>3</sub> )	$\frac{1}{2}$ to 3	49	yrs. mts. 1 8	(N <sub>2</sub> ) much improved	RTBS <sub>2</sub> & LTBS <sub>2</sub> —neg., RHC & LHC—neg	Had to int rupt 7 mont treatment domestic reasons
2	Soi Rajwar, F., O.P. Adolescent	B <sub>3</sub> (C <sub>3</sub> )	$\frac{1}{2}$ to 3 $\frac{1}{2}$	51	1 8	(C <sub>3</sub> -N <sub>2</sub> ) im- proved	LHC.20/50, RHC- Very few coc- coids, LHE- 16/20, RHE- few small groups of coccoids, nose -M/1 ++	Had to int rupt 7 mont treatment domestic reasons
3	Moti Rajwar, M., O.P. below 16 years of age	(A <sub>1</sub> ) N <sub>2</sub>	$\frac{1}{2}$ to 2 $\frac{1}{2}$	52	1 10	(N <sub>2</sub> ) much improved	nil	ni
4	Sraban Majhi, M., House, No. 5, adult	(B <sub>3</sub> ) C <sub>3</sub> -N <sub>2</sub>	$\frac{1}{2}$ to 2 $\frac{1}{2}$	86	2 4	C <sub>3</sub> -N <sub>2</sub> improved	RHE-M/1, LHE- M/1 + RHF- 5/10, LHF-9/10, nose-M/1 +++	nil

O.P.—Out-Patient. M—Male. F—Female.  
Mts.—Months. The numerator indicates the  
number of bacilli found, and the denominator  
the number of fields examined. M/1—Many  
bacilli per field, the plus indicates more.

R.T.B.S.—Right lateral half of the back  
trunk, second region from above; similarly  
refers to the left. R and LHC—Right and l  
cheek. R and LHE—Right and left ears. R  
LHF—Right and left halves of the forehead.

## RESULTS.

In judging the results of a comparative study of this nature, one has carefully to bear in mind the probable systemic effects exercised by prolonged treatment with a tonic preparation like the morrhuate. Making due allowance for this factor, the influence of morrhuate *vis-a-vis* that of the hydnocarpate on (i) the various clinical signs of the disease ; (ii) the causative organisms, *viz.*, *M. leprae* ; and (iii) the total results obtained from this experimental treatment have been assessed as follows :—

(a) *On hypopigmented areas*: Undoubtedly, ethyl hydnocarpate had a much better effect on the pigment of the skin than ethyl morrhuate (in spite of the latter being more irritant) even after leaving a broad margin for the temporary but marked cosmetic effect exercised on such lesions by the iodine contained in the iodised ethyl hydnocarpate. (b) *On anaesthetic areas*: While the improvement in anaesthesia on the side treated with hydnocarpus esters was lasting, that on the other side treated with cod liver esters was transient ; and in some cases no effect on anaesthesia was noticed. (c) *On leprotic infiltrated patches and nodules*: On these also, the effect of hydnocarpus esters was more noteworthy than that of the cod liver esters, resolution being more rapid on the right side than on the left. (d) *Effect on M. leprae*: There is an appreciable difference in the bacterial contents of the lesions on both sides, as will be evident from a glance through column No. 8 in the table appended at the end of this paper. Right side lesions show comparatively fewer bacilli, the technique of taking clips, and staining the smears being the same, and the method of counting the bacilli also being the same, all done by the same observer. (e) *Total results obtained*: Of the four cases, two are considered to have “much improved,” one C3 case, Shanta (*vide* photos) becoming N2, and the other N2 case, Moti Rajwar, becoming N1 with marked clinical improvement in his lesions, the improvement being more marked on the right than the left side. Two other cases, Soi Rajwar (C3) and Sraban Majhi (C3-N1) are considered to have only “improved,” both of them becoming C2-N2 cases. The slowness of improvement shown by the former may be explained on the ground of her age, *viz.*, adolescence, which makes an increased demand on the human economy ; and in the latter case, the presence of extensive and severe seborrhoeic dermatitis on the face and to a lesser extent all over the trunk, interfering with the intradermal method of treatment and also with the absorp-

tion of the injected drug, may have minimised the benefits of treatment.

To illustrate the marked difference in the appearance of the lesions treated by the two different esters, two photos of Shanta, one taken in January, 1932, just before commencing the experimental treatment, and the other, taken in January, 1935 (*i.e.*, three years after the experiment was started, or in other words, at the close of the experiment) are included in this paper. In the interests of space, the photos of other cases are not given. From these two photos it can be seen that the left side lesions are still clearly visible in their entire outline, whereas the right side lesions have almost completely resolved. Keloids produced by irritation due to intradermal injections, are more extensive on the left side than on the right. This shows that cod liver esters are more irritating than hydnocarpus esters. While the lesions on both sides have become bacteriologically negative, the left side lesions have not completely resolved and are still visible clearly.

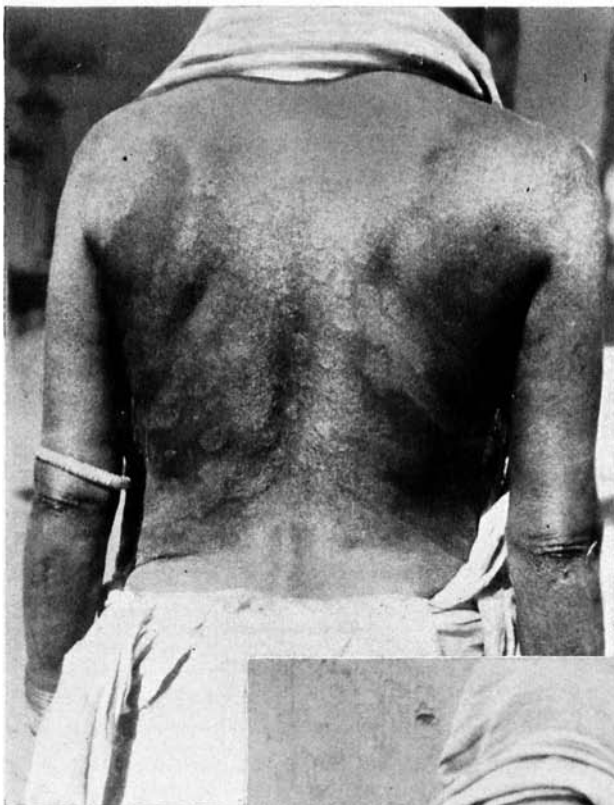
#### SUMMARY AND CONCLUSIONS.

(1) The relative efficacy of  $\frac{1}{2}$  % iodised pure hydnocarpus wightiana (ethyl esters) and cod liver (ethyl esters) diluted to one in three with olive (ethyl) esters, was studied in four cases of leprosy (three C3 cases and one N2 case) with well marked symmetrical lesions, injecting the ethyl hydnocarpate intradermally into the right side lesions and the ethyl morrhuate similarly into the left side lesions, once a week, for a period of from 1 year and 8 months, to 2 years and 4 months.

(2) On the hypopigmented, anæsthetic and leprotic infiltrated areas as well as nodules, the clinical effect was much more marked on the side treated with the hydnocarpus (ethyl) esters, than on the other side treated with ethyl esters of cod liver, even after making due allowance for the temporary cosmetic effects exercised by the iodine contained in the iodised ethyl hydnocarpate, on the hypopigmented and/or erythematous lesions.

(3) While some diminution of the number of bacilli in the treated lesions as compared with the bacterial content of the untreated lesions, as for example, the nose, was obtained with the ethyl morrhuate, the effect was distinctly more pronounced in the lesions treated with ethyl hydnocarpate. And this improvement in the bacterial content of the lesions does not appear to have been in any way influenced by the irritating quality of the drug injected.

(4) In spite of its more marked irritating effect on the

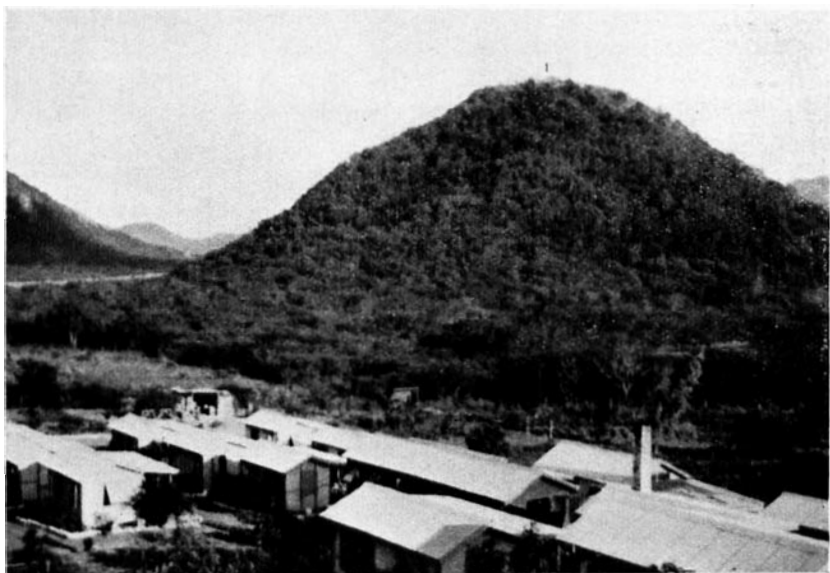


Case showing lesions on both sides of body before commencing treatment.

After 3 years' treatment. Note disappearance of lesions on right side, while those on left side are clearly visible in their entire outline. Keloids produced by irritation are more extensive on left side than on right.



(Photos by Mr. A. Donald Miller)



GENERAL VIEW OF LEPROSY SETTLEMENT, ANTIGUA.



FAMILY INFECTED WITH LEPROSY.  
NOTE SEVERITY OF INFECTION IN CHILD.

skin, ethyl morrhuate seems to be comparatively less efficacious than ethyl hydnocarpate, in leprosy. The latter seems to have some special effect on the active leprosy lesions whether of the neural type or of the cutaneous type. This special effect does not appear to be caused by the irritation produced by injecting the drug intradermally, as the more irritating ethyl morrhuate has produced a lesser degree of clinical improvement in the lesions treated with it.

#### ACKNOWLEDGMENTS.

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#### REFERENCES.

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