

OBSERVATIONS BEARING ON THE QUESTION OF
WHETHER THE "CHAULMOOGRA" GROUP DRUGS
HAVE ANY SPECIAL ACTION IN LEPROSY

I—CHANGES IN LEPROTIC SKIN LESIONS FOLLOWING INTRADERMAL
INJECTIONS OF VARIOUS OILY PREPARATIONS *

BY C. D. LARA, M.D., AND M. LAGROSA, M.D.

From the Culion Leper Colony, Philippine Health Service

Many if not most clinical workers consider that the "chaulmoogra" group derivatives have a definite place in the treatment of leprosy, whether the beneficial effect is due to a special, bactericidal action of the drugs (1), or to a nonspecific action through their content of unsaturated fatty acids (2), or to their influence on metabolism (3), or to the local and general reactions induced by their injection into the tissues (4,5). In our experience the chaulmoogra derivatives are the most widely applicable and have given consistently the best results of all the drugs tried in Culion. Because of this experience, and of a recent statement (5) which might be construed to mean that the chaulmoogra treatment of leprosy is practically of no special value, and which may influence less experienced workers, it was deemed desirable to make further comparative experimental observations.

Recession or disappearance of the cutaneous lesions is probably the most obvious change indicating clinical improvement. Improvement of anesthesia, perspiration, muscular power, color, nutrition and general appearance of the skin are not so easily evaluated. Changes in the number and character of the bacilli and the histology of the lesions may also be demonstrated. It is, however, usually difficult to demonstrate definite changes in the very chronic neural cases.

It has been shown (6,7) that injection of chaulmoogra derivatives into leprosy lesions causes more rapid resolution than treatment by intramuscular injections. Both types of injection produce some local irritation, but their scope of action is not the same. Because of its

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largely local effect and fairly rapid action, the intradermal method was thought to provide a ready means of showing the effect of injecting oily preparations that cause different degrees of irritation. The changes in the gross appearance of the cutaneous lesions, and in their bacterial content, after treatment with certain oily preparations are reported.

MATERIAL AND METHOD

Fourteen new patients with apparently active, bacteriologically positive, and more or less symmetrical macules or infiltrations were selected and treated for ten months. The drugs used were ethyl stearate, ethyl oleate, and olive oil ethyl esters; these were compared with the *Hydnocarpus wightiana* ethyl esters with 0.5 per cent iodine, the standard antileprotic drug in the Philippines. All patients also received intramuscular and intradermal injections of the *hydnocarpus* esters, at a distance from the test lesions. The uniodized, distilled *hydnocarpus* ethyl esters were not employed because of their highly irritant properties; they are about as efficacious as the iodized preparation.

Lesions on the left side were injected with the test drugs, corresponding lesions on the right with *wightiana* esters. Four patients received ethyl stearate, five ethyl oleate, and five olive esters. Similar lesions not too near the treated ones were selected as controls and were not injected. Injections were given every week unless contraindicated. Clinical and bacteriological examinations were made at intervals. One olive esters patient died of beriberi and two had to be dropped because of lepra reaction, so after ten months there remained four patients under ethyl stearate, four under ethyl oleate, and three under the olive esters.

IRRITANT PROPERTIES

The irritation decreased in the following order: ethyl stearate, ethyl oleate, olive esters, and the *wightiana* esters. The stearate invariably caused painful indurations, the pain usually lasted about a week, the induration longer, up to a month. The least irritating, the iodized *wightiana* esters, usually produced only slight inflammation which disappeared in one to a few days.

CLINICAL AND BACTERIOLOGICAL CHANGES

Observations were made periodically, with the precaution of first allowing the inflammatory reaction to subside. Improvement in the macules was indicated by diminished thickness, softening, wrinkling,

and loss of pinkish color, the outlines as a rule becoming indistinct. The infiltrations also showed thinning, wrinkling, and general shrinkage. The microscopic criteria of improvement were granulation and diminution in numbers of the bacilli.

The macules improved clinically in all cases, including the untreated control. All injected with the wightiana esters became negative bacteriologically, while those injected with the more-irritating esters were only improved, as were the control lesions. The infiltrations showed no improvement under the stearate and oleate; two of three olive esters cases showed some improvement; all under the wightiana esters improved. One of the control, untreated infiltrations showed a slight, and another a moderate, degree of clinical improvement. Bacteriologically, the infiltrations treated with the wightiana esters all improved slightly to markedly; those treated with the stearate and oleate were unchanged; and two of the three cases treated with olive esters showed slight and moderate improvement. All but one of the eight control infiltrations remained stationary; one showed slight bacteriological improvement.

COMMENT

All the areas injected with iodized wightiana ethyl esters showed improvement clinically and bacteriologically, 41.7 per cent of them having become bacteriologically negative after 10 months' treatment. On the other hand, not a single one of those injected with the irritant drugs, nor of the controls, became negative, although some showed both clinical and bacteriological improvement. These results suggest that irritation is not a necessary, nor even an important, factor in the disappearance of *Myco. leprae*. While the olive oil ethyl esters, which was less irritating than either the ethyl oleate or ethyl stearate, showed somewhat better results than the latter, these two irritating preparations showed practically no more improvement than was seen in the untreated control lesions.

Since all the patients continued receiving routine antileprotic treatment (the iodized wightiana esters intramuscularly and intradermally) in addition to the experimental treatment, the improvement noted in the stearate, oleate, and control areas may be attributed partly to the general beneficial effect of the routine treatment, and to the absorbed wightiana esters injected into the neighboring lesions under observation.

Incidentally, it may be pointed out that ethyl stearate is a derivative of a completely saturated fatty acid, while ethyl oleate is

derived from a moderately unsaturated acid. Olive esters and hydrocarpus esters with 0.5 per cent iodine are also moderately unsaturated.

SUMMARY

1. The rôle of local tissue irritation in the improvement following injections of oily antileprotic drugs was studied. Patients with symmetrical lesions were divided into three groups. Selected lesions on one side were given intradermal injections of ethyl stearate, ethyl oleate, or olive ethyl esters. Corresponding lesions in all cases were similarly injected with iodized wightiana ethyl esters, and similar lesions were left untreated to serve as controls. All the patients also received routine treatment with the iodized wightiana ethyl esters. The injections were given weekly when possible, and clinical and microscopic observations were made at intervals during and at the end of 10 months' treatment.

2. These drugs produced local inflammation in the following order: ethyl stearate (most irritating), ethyl oleate, olive oil ethyl esters, and wightiana esters (least irritating).

3. All lesions treated with the wightiana esters showed slight to marked improvement, clinically and bacteriologically. Most of those treated with olive esters showed some, though less marked improvement. Those treated with the stearate and oleate showed the least improvement, practically equalling that observed in the control, untreated lesions.

4. These observations indicate that local inflammatory processes produced by injections of the chaulmoogra preparations are not a necessary or even an important factor in the improvement observed with the use of those drugs.

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