

Five Years' Experience With Thalidomide Treatment in Leprosy Reaction

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Five and a half years after the first trial of thalidomide treatment in the lepra reaction of lepromatous leprosy, with both male and female patients, excepting pregnant women, it can be stated that thalidomide has been effective in all lepra reactions of lepromatous leprosy. This was demonstrated in the following studies:

In a preliminary direct trial (1) of thalidomide, improvement was seen in all 13 cases treated. In a single comparison with a placebo (2) improvement was seen in all cases where thalidomide was administered, as can be seen in Table 1. Placebo was administered, with or without sulfone, in 12 lepra reactions. In none of these was there any improvement. In 22 lepra reactions where thalidomide was given either alone, with sulfone, or with sulfones and steroids, there was a quick, sometimes dramatic, regression.

Another trial consisted of a double blind study (3, 4) that lasted 129 days, the results of which can be seen in Table 2. Out of 85 reactions treated with thalidomide, improvement was seen in 91.76 per cent. No change was found in 8.24 per cent, which included patients suffering from dimorphous leprosy. In the 88 reactions treated with a placebo, the following results were obtained: 27.27 per cent showed improvement, 50 per cent had no change, and 22.73 per cent deteriorated. Statistical analysis showed that such a result can occur by chance only once in more than a million cases. Photographs from these studies are reproduced in Fig. 1, a and b.

In order to evaluate thalidomide as the sole long-term medication in lepra reaction (5) it was found that the best results were obtained when treatment was started with

thalidomide at 400 mgm. daily, and this dose continued until the lesions lost their acuteness. Then thalidomide was gradually reduced to a maintenance dose of 100 mgm. or less. Fairly good results have been obtained with a lower initial dosage, but improvement was slower to appear, and the reactional manifestations did not remit completely. In patients who had been taking steroids for long periods, the usual dose of thalidomide was given while cortico-

TABLE 1. Immediate effect of 34 therapeutic trials with placebo or thalidomide (400 mgm./day) in 22 lepra reactions.

Treatment	No. of therapeutic tests	Clinical improvement within 48 hrs.
Placebo and DDS	6	0
Placebo alone	6	0
Total placebo	<u>12</u>	<u>0</u>
Thalidomide and DDS and corticosteroids	1	1
Thalidomide and DDS	8	8
Thalidomide alone	13	13
Total thalidomide	<u>22</u>	<u>22</u>

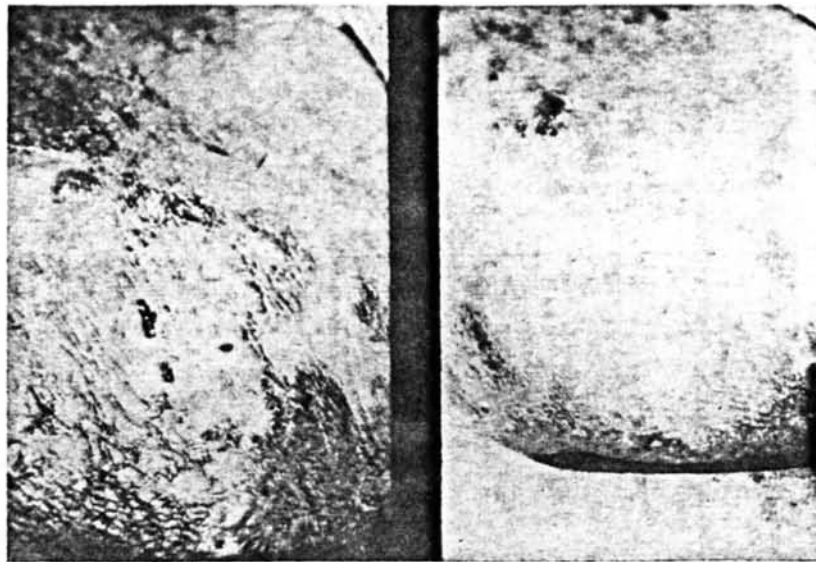
steroids were slowly and gradually reduced. The impression in this trial is that results were not as favorable as in other patients who had not taken hormones, improvement being slower.

Neural pains are among the first lepra reaction symptoms to respond to thalidomide treatment, and we have used a more objective method, which confirmed the subjective impression of improvement. It consists of measuring the motor conduction velocity before, during, and after the

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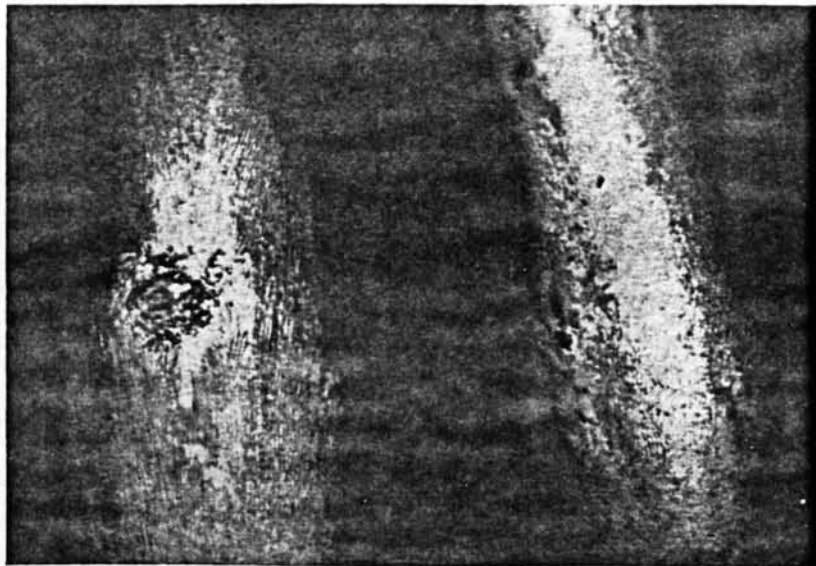
TABLE 2. Comparative results of the treatment of 173 lepra reactions with thalidomide (400 mgm./day) in a 7 day double blind study.

	Total Cases and per cent	Improved Cases and per cent	No change Cases and per cent	Worse Cases and per cent
Thalidomide	85 100	68 91.76	7 8.24	0 0
Placebo	88 100	24 27.27	44 50.0	20 22.73



a.

b.



a.

b.

FIG. 1. Photographs of 2 patients before (a) and after (b) 2 weeks' treatment with thalidomide.

administration of thalidomide, steroids, analgesics or placebo (⁶). In reactional patients of Hansen's disease suffering from neuritic symptoms, 96 motor conduction velocity tests were performed. Results can be seen in Tables 3 and 4. After thalidomide treatment there was a marked improvement of motor conduction velocity, which started as a rule within 48 hours to one week. After steroid treatment too there was an improvement, but it was slower and less striking.

In four lepra reactions of lepromatous leprosy, in which iridocyclitis was one of the main features, the usual dose of thalidomide plus topical application of 1 per cent atropine drops suppressed the symptoms (⁷).

As regards *thalidomide in Hansen's disease without reaction*, the drug has been evaluated both as a sole treatment and in combination with DDS. A trial in which 24 patients received thalidomide alone for periods of up to 19 months confirmed that thalidomide is ineffective as a sole treatment for Hansen's disease (⁸). In another trial of 31 months in 18 patients in whom sulfones had been provoking lepra reac-

tions, combined treatment of DDS (25 to 100 mgm./day) with thalidomide (400 to 100 mgm./day) enabled them to tolerate sulfones. As for the types and forms of the disease, thalidomide was very effective in lepra reactions of lepromatous leprosy, and less effective in the few cases of dimorphous and reactional tuberculoid leprosy that we have treated (⁹).

During the five years when thalidomide was used in the therapeutic trials cited above, repeated laboratory investigations were carried out. These investigations included the following: leucocyte and erythrocyte counts, erythrocyte sedimentation rate, serum proteins and electrophoresis, liver function test, and transaminase. No deviations from the normal values that could be ascribed to the thalidomide, were found in these examinations.

Side-effects encountered were edema of the extremities, usually unilateral, drowsiness, dizziness, vesicular skin or mucous membrane lesions, dryness of oral and nasal mucosa, and constipation. Burning of the palms and soles of the feet was also observed during thalidomide therapy, but it occurred too in leprosy patients who did

TABLE 3. Motor conduction velocity time of ulnar nerves following thalidomide therapy in lepra reaction.

	Before reaction	During reaction	Thalidomide therapy (started 29 Oct. 1967)
Rt. N. ulnaris	1 Oct. 67 65 m/sec.	29 Oct. 67 30 m/sec.	31 Oct. 67 63 m/sec.
Lt. N. ulnaris	60 m/sec.	25 m/sec.	60 m/sec.

TABLE 4. Motor condition velocity time of ulnar nerves following placebo and thalidomide therapy in lepra reaction.

	Before therapy		During therapy		
	Before reaction	During reaction	Placebo therapy (17 Oct. 67)	Thalidomide therapy 400 mgm./day (22 Oct. 67)	
Rt. N. ulnaris	17 June 67 48 m/sec.	16 Oct. 67 14.5 m/sec.	18 Oct. 67 0	23 Oct. 67 43 m/sec.	30 Oct. 67 49 m/sec.
Lt. N. ulnaris	18 m/sec.	7.7 m/sec.	0	0	12 m/sec.

not receive thalidomide. None of these side-effects was ever severe enough to necessitate stopping the treatment, and most disappeared with continued therapy.

SUMMARY

After a five year trial it may be stated that thalidomide is very effective in lepra reactions of the lepromatous leprosy type, but is not effective as the sole treatment for leprosy itself. For patients who do not tolerate sulfone alone, the addition of thalidomide is recommended.

The optimal initial dose of thalidomide was found to be 400 mgm./day (6 mgm. per kgm. body weight), and the optimal maintenance dose 100 mgm./day (1.5 mgm. per kgm. of body weight). In patients who have been under long-term treatment with corticosteroids it is advisable to start with the optimal dose of thalidomide even before the gradual reduction of the steroids is completed.

Thalidomide might possibly play a role in reducing or even perhaps preventing neural, muscular and osseous changes following reactional neuritis. Side effects were mild and did not necessitate withdrawal of treatment. Repeated laboratory examinations of blood and other body fluids did not reveal any pathologic deviation from normal values.

Thalidomide should not be given to pregnant women.

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