Question of Toxicity of Thalidomide in the Treatment of Leprosy Reaction

To the Editor:

I was very interested to read the article by Convit *et al.* on "Thalidomide therapy in the lepra reaction," which appeared in the October-December number of The Journal (35 (1967) 446-451). Arising out of this there are two points that I would like to raise.

The authors have strongly, and rightly, emphasized the teratogenic effects of thalidomide and the rigid precautions to be taken in administering this drug. However,

there is no mention of the neurotoxic effects. I would have thought that in the treatment of a condition such as lepra reaction, with its known tendency to produce neuritis and possible paralysis, this effect of thalidomide would have received consideration.

The fact that thalidomide is one of the known ingested causes of acute and subacute polyneuritis appears even in the standard medical textbooks ([5]). In an extensive chapter on the neuropathies by Simpson in *Modern Trends in Neurology* ([8]), thalidomide is listed under the toxic neuropathies. Fullerton and Kremer ([2]) reported 13 cases of peripheral neuritis attributed to the toxic effects of thalidomide in an average dosage of 100 mgm. (range 50-400) taken for 2-18 months. Of these cases seven showed some weakness and in two there was marked weakness—the severity apparently increasing with the duration of treatment.

In the earlier reports by Sheskin ([7]) there is no mention of this factor being taken into consideration and in the present article mention is made only of the relief of pain in the two cases of polyneuritis. I would be interested to know if the "clinical observation of vital signs," which was made twice a day, included detailed muscle assessment to detect any paresis. I am aware that this study included only 24 patients and that more extensive investigations will be required to assess the full effects, but I feel that caution should be exercised before enthusiastically employing a drug with known neurotoxic properties in the treatment of a disease with known predilection for the peripheral nervous system.

The second point that I would like to raise is in connection with the long term treatment of lepra reaction with thalidomide. The authors report that some patients suffered a relapse when treatment was discontinued. This has also been reported by Opromolla *et al.* ([4]) and Cazort and Song ([1]), and in both reports all the patients relapsed on the cessation of treatment. Three of the patients in the latter series suffered acute exacerbations of the lepra reaction. If the beneficial effect of thalidomide is due to its possible immunosuppressive activity, then any proposed treatment of lepra reaction will have to continue for a very long period.

Finally, it would be interesting to know what previous treatment these patients had received for their lepra reaction. Mention is made only of corticosteroids, whereas the generally accepted line of treatment is to administer antimonials or antimalarials first and to restore to corticosteroids when routine treatment has failed. ([3, 6]).

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REFERENCES

1. Cazort, R. J. and Song, Ye Kun. A trial of thalidomide in progressive lepra reactions. Current Therap. Res. **8** (1966) 299-311. (*Abstract in* Internat. J. Leprosy **35** (1967) 225-226.)
2. Fullerton, P. M. and Kremer, M. Neuropathy after intake of thalidomide (Distaval). Brit. Med. J. **2** (1961) 855-858.
3. Jopling, W. H. Treatment of acute phases (reactional states) in lepromatous leprosy. Erythema nodosum leprosum. *In* Leprosy in Theory and Practice. R. G. Cochrane and T. F. Davey, Eds. Bristol, John Wright & Sons, Ltd.; Baltimore, Williams and Wilkins Co., 2nd ed., 1964, pp. 418-422.
4. Opromolla, D. V. A., Souza Lima, L. and Marques, M. B. A talidomida nos surtos agudos da lepra. Eritema nodoso ou polimorfo. Hospital (Rio de Janeiro) **69** (1966) 827-844. (*Abstract in* Internat. J. Leprosy **35** (1967) 226.)
5. Price, F. W. (Ed.) A textbook of the Practice of Medicine. Oxford University Press, 1966, p. 1137.
6. Ramu, G. Treatment of lepra reaction. Leprosy in India **39** (1967) 2-5.
7. Sheskin, J. Further observations with thalidomide in lepra reaction. Leprosy Rev. **36** (1965) 183-185.
8. Simpson, J. A. The neuropathies. *In* Modern Trends in Neurology. 1962.

[Editor's Note: *See also* Notes and Comments. British Med. J. **3** (1968) 42.]

TO THE EDITOR:

I have read with great interest Dr. Berkeley's letter referring to our article on "Thalidomide therapy in the lepra reaction," published in THE JOURNAL (**35** (1967) 446-451). In relation with his comments, I have the pleasure of informing you of the following.

We have around 100 lepromatous leprosy patients who have been suffering from reactional states of long duration. These patients have been under treatment with thalidomide for periods varying between four months and one year, with a maintenance dose of 50 mgm. per day. This dose has kept their lepra reactions completely under control for as long as they continue taking the drug; because of this, they have been able to continue their sulfone treatment with the standard dose we use here in Venezuela, 100 mgm. per day orally, or 1,000-1,250 mgm. in a monthly injection.

In this group, not only have we not seen any toxic polyneuritic manifestations due to the drug, but, quite to the contrary, patients who were suffering from a severe physical deterioration due to their feverish episodes, impossible to control with the usual medications, and also from acute leprous polyneuritic phenomena, felt a general well being, which allowed them to continue treatment and return to their daily work.

In relation to the generally accepted treatments with antimalarials first, and with corticosteroids when those fail, I want to insist on the fact that we used thalidomide for treatment of lepra reaction only in cases of long duration, where the usual medications had failed and where a long term administration of corticosteroids at an adequate dose would have given rise to the secondary effects provoked by that drug.

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