made to determine sulfone resistance, but were they in fact taking their prescribed dapsone regularly? In his article "Drug resistance of Mycobacterium leprae, particularly to DDS" (Internat. J. Leprosy 35 (1967) 625-630, Part 2) R. J. W. Bees states, ". . . at least half our specially selected relapsed patients were infected with DDS-sensitive strains of M. leprae, and these same patients responded satisfactorily to a supervised course of DDS on injection. It is of course possible that a proportion of these particular patients, who, at the time of relapse, were taking DDS by mouth, may have been suffering from a malabsorption syndrome, resulting in inadequate tissue concentrations of DDS."

I realize that conditions in Malaysia or Zambia are very different from those in Carville, but it seems to me curious that malabsorption was not investigated, that the patients were not tried on injection DDS at the outset, and that prior to the trial blood-sulfone determinations were apparently not done.

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13 June 1968

To THE EDITOR:

The point raised by Dr. McDougall is entirely valid. The question of previous sulfone therapy being adequate was decided, regrettably, on the basis of prescribed oral dosage and an overall estimate of patient reliability. This is, of course, unreliable and it is entirely possible that these patients were not regularly taking their sulfones before the period of study. We remained undecided for some time, in fact, as to whether the article should be published, because of this point. Eventually it was decided to submit the observations for publication in the hope that they might prove useful in a field setting for physicians faced with similar cases. It may well be that this decision was an error of commission compounded the errors of omission so well pointed out by Dr. McDougall.

It should perhaps be mentioned at this time that a number of cases reported in the article in question have relapsed once more in recent months despite documented taking of their sulfone combined with streptomycin. We hope to communicate these additional observations and thereby amend the above article, as soon as possible.

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17 July 1968

[This paper was the subject of some similar correspondence by the Editor with Dr. Hastings and members of the IJL Editorial Board. Decision in favor of publication was made because of the importance of the question of combination therapy. Further correspondence relative to questions by the Editor and an Associate Editor was anticipated and has in fact developed.—Editor]

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 polynuereits appears even in the standard medical textbooks (4). In an extensive chapter on the neuropathies by Simpson in Modern Trends in Neurology (4), thalidomide is listed under the toxic neuropathies. Fullerton and Kremer (5) 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 (6) 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 polynuereits. 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 paralyses. 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 Opreomilla et al. (7) and Cazort and Song (8), 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 immuno suppressive 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 amonodials or antimalarias first and to restore to corticosteroids when routine treatment has failed. (8, 9).

—J. S. Berkeley

The Leprosy Mission
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17 June 1968

REFERENCES


[Editor's Notes: See also Notes and Comments. British Med. J. 2 (1968) 42.]
Correspondence

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 febrile 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.

-JACINTO CONVIT

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16 July 1968

Change in Health Departmental Designation in Brazil

To THE EDITOR:

I am pleased to inform you that a law signed on 23 July 1968, by the Governor of the State of Sao Paulo, Brazil, Dr. Roberto Costa de Abreu Sodre, changed the name of the "Departamento de Profilaxia da Lepra" of the Secretary of Health to "Departamento de Dermatologia Sanitaria."

I am sure that, just like the official substitution of "hanseniasis" for "leprosy," thereby facilitating the attendance of patients and contacts, the integration with other public health services and the activities of our health educators and social workers.

-ARALDO HORTHEN M.D.
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Departamento de Dermatologia Sanitaria
Gabinete do Diretor
Assistencia Social
Sao Paulo, Brazil
13 August 1968