CORRESPONDENCE

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THE USE OF DIAMINODIPHENYL SULFONE

To The Editor:

In a letter which appeared recently in The Journal [17 (1948) 111], Dr. George Brownlee stated that I and certain others "have turned back in their tracks to the use of the parent substance, diaminodiphenylsulphone (DDS)." I think it well to explain the genesis of this treatment, which we initiated in Madras some three years ago.

When I visited Britain in 1946 I naturally made enquiries about the possibilities of further developments of sulfone therapy, and was put into touch with the laboratories of the Imperial Chemical Industries at Wimslow, Cheshire. Dr. John Francis told me of the way in which they were using DDS in mastitis in cows, and it occurred to me that a modification of this method could be used in human beings. We, therefore, devised a collapsible tube fitted with a large-bored needle instead of the usual canula and charged with the quantity of DDS required. With the needle inserted into the subcutaneous tissue, the DDS suspension was milked out, the needle withdrawn, and the area of injection vigorously massaged. Work has still to be done on this method of treatment before we are quite certain that it is suitable for general application.

Our present opinion with regard to DDS is that the dosage which we originally used—namely, 2.5 gm. weekly—was too large, and that the total dosage should not exceed 1.5 gm. per week. Even with this dosage we have not been able to eliminate the occurrence of reactions.

We are of the opinion that, until the toxicity of DDS is adequately worked out, it is an unsafe remedy for general use despite the fact that it has an effective action on *M. leprae.* While I am willing to submit to the general statement that various sulfone derivatives are probably degraded to DDS in the body, our more recent assessments indicate that sulphetrone in relatively small doses (2.5 gm. twice a week) in oily emulsions [see,

for example, THE JOURNAL **17** (1949) 299, editorial] is as effective therapeutically as DDS and less prone to cause reactions. Further, injectable sulphetrone, particularly the emulsion, appears to be almost completely free from toxic effects. If these results are confirmed it would indicate that Brownlee's original opinion that sulphetrone acts as a whole and not after degradation to DDS may be partially correct.

At the present moment I deprecate the emphasis being placed on DDS because, while it is clinically effective, serious results may follow its use unless very great care is taken in its administration. It is to be remembered that a blood level of 1.5 mgm% may be perfectly safe, but a blood level of 2 mgm% and above may cause serious toxic effects. Therefore, until we are quite certain of the dosage which can be given without raising the blood concentration to dangerous levels, DDS should not be used in mass treatment.

Our work with injectable sulphetrone preparation indicates that, for the time being, this is the safest remedy to use.

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(*Addendum*)

[From information supplied by John Lowe (personal communication) and George Brownlee (elsewhere in this department), as well as the foregoing note, it appears that the present trials of DDS in leprosy stemmed from experiences of the Imperial Chemical Industries whereby its use became established in England in veterinary medicine [McEwin, Pizer & Patterson, *Vet. Rec.* 53 (1941) 429; Francis, *Vet. Rec.* 59 (1947) 131]. Francis became convinced that the sulfone derivatives act solely by virtue of the DDS radical released by degradation in the body. In the above note Cochrane tells how, after contact with Francis in 1946, he was led to undertake in the following year experiments with that substance by injection. He told briefly of his experiences in a paper read at the Havana congress [THE JOURNAL 16 (1948) 139], and the possible usefulness of the substance was mentioned in the report of the Therapy Committee, of which he was a member [ibid. p. 213]. Molesworth [THE JOURNAL 17 (1949) 197] got his impetus from Cochrane and used the injection method.

[It also appears that early in 1947 Francis got in touch with

the British Empire Leprosy Relief Association in London to expound his ideas, and left some of the substance with them. When Lowe joined BELRA in the latter part of 1947, Muir told him of Francis' views and suggested that he try DDS at the research unit which he and Michael Smith, the biochemist, were going to Nigeria to establish. Against all advice, Lowe says, he decided that logic, to say nothing of local conditions, indicated that the trial should be with oral administration. Muir, now at Purulia in India, has adopted that method.

[Thus there began an experience which, by all accounts, holds promise of being an important new advance in leprosy therapy. Apart from the question of whether DDS, properly administered, may or may not prove more efficacious than the derivatives now in common use, it offers a tremendous advantage in the much smaller dosage of a materially less expensive substance. Lowe [*Lancet*, in press] estimates the cost of DDS per patient per year at about 14s, against some £10-15 for sulphetrone. If it proves practicable to use that substance on a large scale without increase of expensive personnel, it will obviously follow that where only limited numbers of patients now receive the benefit of treatment with the proprietary derivatives perhaps twenty times as many can be treated with DDS under the same budget. —EDITOR.]