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Letters to the Editor

OILY INJECTIONS OF DAPSONE; AN ACCEPTABLE FORM OF TREATMENT?

Sir,

Oily injections of DDS, comprising a 25% suspension of DDS in ethylchaulmograte, were in the sixties prepared by Roussel Laboratories, Paris. Many leprosy-endemic countries still have a stock of this preparation, which was provided by UNICEF, and is therefore usually called UNICEF injections.

At the All Africa Leprosy and Rehabilitation Training Centre (ALERT) in Addis Ababa, UNICEF injections have been used from the early seventies for over a hundred patients who did not respond satisfactorily to oral DDS therapy and were therefore either not taking the prescribed therapy or harbouring DDS resistant *M. leprae*. The injections were given once weekly intramuscularly in a dosage of 1·5 ml containing 375 mg DDS. The patients attended regularly and asked for a supply of tablets in case they had to travel for longer than a week. Patients who responded to DDS injections and became clinically inactive were advised to continue tablets but, almost without exception, preferred to have the injections.

These injections thus appeared a convenient way of administering DDS supervised, without occupying hospital beds. Our only worry was whether or not the dosage given was sufficient, for in some countries 1·5 ml was administered twice weekly.

We therefore welcomed the opportunity in 1981 of a collaborative study with the Biopharmaceutical Department of the University of Amsterdam. One of the projects was a study[1] of serum levels in 20 patients on UNICEF injections. The serum level curves were found to be very regular over the week and were about equivalent to that found in patients taking 1 mg dapsone orally per kilogramme bodyweight, which is acceptable. At that time, 8 patients were also questioned about possible unwanted effects of the injections and, to our surprise, 6 patients considered them painful. Other complaints were swelling at the injection site and difficulty in walking or sleeping for some days after the injections.

This unexpected finding prompted us to plan an interview of all patients on UNICEF injections, with a view to assessing side-effects and acceptability. A nurse of Ethiopian nationality, assisting in the clinic held for assessment of suspected dapsone-resistant patients, and therefore known to the patients on DDS injections, was instructed on the general purpose of the study and on the questions to be asked. The patients were first asked whether or not they liked the injections and then whether they had complaints which they thought were related to the injections. We were also interested in the opinion of the patient on the status of his disease and his desire or willingness to discontinue the injections and to change to either DDS tablets or other antileprosy treatment.

Of the 70 patients treated with injections, 67 were interviewed, of whom 35 were male patients. All except 1 were started on injections to exclude non-compliance with the DDS tablets as the cause for their relapse or unsatisfactory clinical improvement. Most of the patients were classified lepromatous (BL or LL); 4 patients had borderline tuberculoid (BT) leprosy and 1 patient, who initially had been lepromatous, presented with a BT relapse. The mean age of the females was 34·5 years and of the males 38·6 years. The duration of DDS injections in females was found on the average to be 2 years longer; 4·6 years against 2·3 years in the men. Three women were on injections

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for more than 10 years. Ten female and 12 male patients were on injections for less than 1 year but all patients had injections for a minimum of 2 months.

Six (9%) of the 67 interviewed patients did not like the injections. Particulars of these patients are presented in Table 1.

The 5 patients who preferred to discontinue DDS injections had a good reason for it, except patient 4: they were not satisfied with the effect of the therapy or had serious complaints which they attributed to the injections.

The remaining 61 patients considered their disease to have improved, except 2: 1 patient took the injections irregularly and was clinically active and the second was a BT patient who experienced a reversal reaction. All 61 patients preferred, without exception, to continue on weekly injections. In spite of this positive attitude to injections, quite a number of these 61 patients experienced unwanted effects: 9 patients considered the injections to be painful, the pain usually lasting for some days. Four patients experienced a local swelling and 6 patients experienced both pain and swelling. One patient reported local swelling with difficulty in walking.

Of the 67 patients that were interviewed, a total of 39% had complaints and there was, in this respect, no difference between males and females. However, complaints were reported in a relatively higher proportion of the patients treated for a relatively short time: 58% and 50% in the female and male patients respectively, treated for a maximum of 1 year.

This study indicated that an alarmingly high proportion of patients treated at ALERT with weekly oily DDS injections of the above composition experienced adverse effects which they attribute to the injections. However in some cases the relation between the injection and their complaints was very doubtful, e.g. pain on the third day after the injection, a hungry feeling for 7 days. But in most cases the complaints were almost certainly caused by the injections, e.g. pain and/or swelling at the site of injection for varying periods of time but in some cases as long as 7 days.

Table 1. Particulars of patients who disliked DDS injections

	Sex	Age	Duration of injections	Complaint related to injection	Opinion on disease status	Therapy preferred
1	M	34	1 year	Pain (at injection site)	Worse, due to rheumatic pains	Other drugs
2	M	45	9 months	Hungry, dry skin and weakness for a week	No change	DDS tablets
3	F	21	1 year	Local pain and swelling for a week	No change	DDS tablets
4	F	30	6 months	Pain for a few minutes	Improved	DDS tablets
5	F	13	8 months	Local pain, shivery for a week	No change	DDS injections
6	M	60	2 years	Local pain and difficulty in walking	Numbness in limbs	DDS tablets

Gluteal abscesses were not seen in this group and over 7 years, I remember only 1 abscess due to DDS injections.

At the time of the interview, the WHO recommended form of multiple drug therapy (MDT) had already been introduced at ALERT and our patients in this study must have heard about the new leprosy therapy. Nevertheless, 93% of the group preferred to continue on DDS injections and proved to be, at a later stage, very difficult to convince of the merits of the new therapy. The alleged seriousness of the unwanted effects of the injections in about 40% of the patients, has to be balanced against the fact that over 90% of them preferred to continue injections, even when they were offered a potent alternative therapy. It should be noted that in general Ethiopians seem to be less obsessed by the supposedly beneficial effects of injectable drugs, as is the case in many African countries where any form of oral therapy is considered inferior. Of the 6 patients who expressed their dislike of the injections, 4 were possibly more dissatisfied with their clinical condition, than with the inconvenience of the injections.

Under the circumstances described for this group of patients in Addis Ababa, it seems that weekly oily DDS injections are an acceptable form of DDS therapy, especially for cases where supervised DDS therapy is indicated. Intramuscular dapsone has been used for many years in Venezuela for all lepromatous and Mitsuda-negative indeterminate cases[2] and it was used in Malaysia by the British Medical Research Council group in their early controlled clinical drug trials and studies on dapsone resistance.[3–5] It was also used quite extensively (as a 25% suspension of dapsone in chaulmoograte d'ethyle in the 1950s and 1960s in several French-speaking countries of Africa (Dr Arthur Cap, personal communication). Published reports give the impression that few problems have arisen but it would be of interest to have more specific information, particularly from those who have used such preparations extensively.

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