MASS TREATMENT OF LEPROSY WITH D.A.D.P.S. (Dapsone).

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INTRODUCTION.

The following is an account of the administration of Dapsone (D.A.D.P.S.) to over 9,000 patients in 30 different treatment centres, which, starting in April 1950, now has run for 13 months.

The changeover from hydnocarpus treatment was effected mainly during the first 4 months of this period.

It is not intended that this account should demonstrate the efficiency of treatment because a longer time would be necessary for assessment of results. Other workers elsewhere, particularly Dr. J. Lowe, have shown the efficacy of both daily and twice weekly treatment on smaller series of cases under close observation. This report does, however, show that Dapsone can be administered with reasonable safety on a very wide scale with that minimum of medical supervision normally attainable in many parts of Africa.

Care has been taken to find out reasons for absence from treatment in the case of out-patients, by questioning the staff and other patients about absentees. The clinical picture of the main complications, dermatitis, lepra and nerve reactions and jaundice, are well known, so that if there are any who have had these complications without our knowledge, we believe they are very few Of course a group of 9,000 patients of all ages has had its death roll due to natural causes.

Some description of the leprosy control organisation in this area is necessary in order to appreciate the methods we have adopted. Similarly to other areas of Nigeria, a central Settlement of a little over 1,000 patients is the centre of a control scheme which covers Onitsha Province. Onitsha Province constitutes an area of about 75 miles by 75 miles, with a population of over one million people and an estimated number of leprosy patients of between 20 and 30 thousand. Roads are good in two thirds of the area; the remainder is swampy or waste land, which is largely inaccessible, though with a heavy incidence of leprosy.

Of the area accessible by road, nearly half is within 5 miles' range of out-patient treatment, and over one quarter has facilities for segregation in the form of villages in which infectious patients live separately from the rest of the community. All clinics and villages are built and maintained by the patients themselves with varying assistance from their fellow-townsmen.

The medical staff consist of two doctors (one of whom was on leave for two months of the period under review), two nursing sisters, both of whom were on leave much of the time and one newly qualified trained nurse. To assist these 1 to 3 European lay "Leprosy Control Officers" are responsible for buildings, hygiene and supervision of routine treatment and have also assisted in examination of patients and in selection of those who require to be seen by the Medical Officer.

In direct charge of each clinic, or pair of clinics there is a "Leprosy Inspector." Only one of these has had more than a primary education plus a year's training at the Central Settlement. In a few cases an intelligent patient has been trained and has been given the same responsibility. In all stages, the experience of Dr. Lowe at Uzuakoli has been taken into account and his advice followed, though much greater caution in dosage has been necessary because of the absence of close qualified supervision of patients and lack of laboratory facilities at clinics for the examination of out-patients.

2. PATIENTS TREATED.

Nearly all patients with active leprosy have been accepted for treatment provided that they live within approximately 5 miles of the clinic and are able to attend regularly twice weekly or, if infectious, are willing to segregate themselves in one of the villages or at the Settlement. Patients, from areas which are not provided with these facilities have been refused dapsone treatment and will have to wait until their towns people have procured land for the erection of a clinic and village.

Anaemic patients, first have been treated with Ferri Sulph for a period and then dapsone started with caution, when the anaemia is under control.

Under-nourished and cirrhotic patients mostly have been able to stand dapsone in small dosage but adequate to influence their disease.

3. ROUTINE TREATMENT.

At the Settlement 0.1 gm (1 tablet) was given daily for the first 6 weeks and 0.2 gm daily thereafter for 6 days a week. After 5 weeks of this regime it was found that complications were not more numerous and violent than conveniently could be controlled and a more gradual induction was started. At out-patient clinics and villages, still greater caution was used in induction as follows:—

0.1 gm twice weekly 3 weeks,
0.2 gm twice weekly 3 weeks,
0.3 gm twice weekly 3 weeks up to the maximum of 0.4 gm twice weekly for a strong adult. Children started with ½ tablet (0.05 gm).

To combat anaemia 10 gr. of Ferri Sulph per diem was given in the Settlement or 20 gr. twice weekly in the clinics. This caused some gastric-intestinal disturbance in clinics and a controlled experiment with 50 patients each on 20, 10 and 5 gr. of Ferri Sulph twice weekly indicated that 10 gr. is certainly sufficient. It is likely that Ferri Sulph can be left out except for special cases, but of this we cannot yet be certain.

4. COMPLICATIONS.

(a) *Complaint of general weekness and increased appetite.*

The great majority of the patients complained of general weakness and depression with increased desire for food during the second month of treatment. The mental and physical depression was very obvious in each community of patients during the second, but during the third month and later this gradually

changed to enthusiasm as they became " acclimatised " to dapsone therapy. After about 8 months few complain of feeling weak, and many say their limbs are not so " heavy " as they were before dapsone treatment.

(b) *Dermatitis.*

This has been the most frequent and most troublesome of the severer complications. Its incidence has varied from clinic to clinic (perhaps due to tribal differences). On the average the incidence has been about 3%.

The earliest symptoms usually have been fever and skin irritation after which a rash resembling " prickly heat " or " goose-skin " has appeared. Some degree of exfoliation and superficial sepsis has been seen in nearly all cases; in severe cases complete exfoliation has occurred and the patient has been in considerable danger.

Four deaths have occurred from dermatitis. In two cases the relatives refused to accept the Leprosy Inspector's diagnosis; they believed the patients to be suffering from measles, and took them home. One occurred in a weak old man and one in a healthy adult, who appeared to be improving, but developed hyperpyrexia.

We miscalculated our great need of anti-histamines and had difficulty in getting sufficient supplies. With greater experience of our Leprosy Inspectors and with adequate supplies of anti-histamines, we feel that deaths should not occur again from this cause. All deaths occurred in the first 2,000 patients treated.

The time of onset of dermatitis seems to have been related to the dosage employed. In the Settlement, the onset was between the 4th and 9th week, but in the clinics on more gradual induction cases continued up to the 12th week, with a few very mild cases after that; there seemed no significant difference in numbers of cases of dermatitis in the two groups, but the clinic cases, on the whole, were less severe.

Rules for dealing with dermatitis had to be simple to suit the medical knowledge of those in direct charge of clinics. They were:—

(i) To stop treatment at the first suspicion of dermatitis during the first 3 months. The patients were instructed to report skin irritation and fever. If the temperature was above 100°F during the first 3 months, treatment was to be stopped. (This was to prevent incipient dermatitis from being made worse by an extra dose of 3 or 4 tablets.)

(ii) To insist on the patient staying in the sick-bay at the

clinic until the diagnosis was confirmed or refuted.

(iii) To give anthisan (or other anti-histamine) according to set instructions.

We have been able to desensitise most patients by giving sulphetrone in a mixture, starting with 0.05 gm twice weekly. Those in which this regime fails, have been sent to the central hospital for more cautious reinduction of treatment. In no case has this method of disensitisation led to a severe recurrence of dermatitis.

(c) *Leprosy Reaction (including the eyes)*

This has been mild in cases on twice weekly treatment. In those on daily treatment very severe lepra reactions have occurred any time after the first month, but were becoming less common by the sixth month. On daily treatment the incidence has been about 5% of lepromas. On twice weekly treatment it has been less than 1%. After 12 months, few reactions needing hospital treatment are occurring.

(d) *Nerve Reaction.*

This has been almost negligible in non-lepromatous patients and has been milder and rarer in lepromas under twice weekly treatment. Under daily treatment very severe nerve reactions have occurred, with great pain and some paralysis. At operation, in the few cases in which it was deemed necessary, there was acute inflammation of perineural tissue and it was found impossible to strip the nerve sheath as could be done in reactions under hydnocarpus oil. The results of operation were not encouraging.* Under daily treatment, incidence of severe nerve reactions has been about 5% in lepromatous patients.

On twice weekly treatment there have been few severe nerve reactions. This, although not dangerous to life, has been the most distressing complication in the Settlement as it has recurred and has sometimes led to paralysis. Such cases started to occur during the second month of treatment and have continued up to the 7th when all patients were changed to twice weekly treatment, but they continue to occur and some need one or more intra-neural injections of procaine. Since that time there has been less trouble with nerve reaction. Mild nerve reactions occurred in many low-resistance tuberculoid patients, but these amounted only to temporary increase in pain. After 8 months' treatment most patients say that they have less nerve pain than they had before treatment.

(* This operation should only be attempted in the oedematous stage, when marked relief may be seen.—Ed.)

(e) *Jaundice.*

It is not certain that this has been a complication of dapsone therapy. A few cases have occurred, two of them following dermatitis. One patient died. Acute hepatitis is not uncommon in non-lepromatous patients, but occurrence of two cases following dermatitis is suggestive.

(f) *New Macules.*

Some patients (perhaps 5%) who formerly had all macules obscured under hydnocarpus oil and were approaching discharge, developed new macules. This percentage is less than would have been expected, had they continued on hydnocarpus oil therapy.

(g) *Complications in breast-fed infants.*

Five infants at the Settlement and over 100 at the clinics have been breast fed by mothers taking dapsone. Ferri Sulph has been given to these infants as a precaution. One infant has had mild dermatitis. Otherwise no complications have been seen or reported.

(h) *Psychosis.*

Twenty-four cases of psychosis have so far been observed. All of them have occurred in those who started on daily treatment except for two clinic staff who probably had access to daily treatment, though against instructions.

One committed suicide. Two were violent.

One was observed in the pre-psychotic stage when he complained of being unable to remain in company without wishing to scream. His treatment was stopped and in 3 weeks he was able to restart treatment without further trouble.

All have recovered within 8 weeks of being stopped treatment and have needed varying amounts of sedative.

Though it is too early to say, it seems that the wave of psychosis is dying down, the highest incidence being about the 9th month.

5. RAPIDITY OF TREATMENT.

Those patients (particularly tuberculoid cases) with most signs have had their clinical condition completely changed in 6 weeks (a total of 18 tablets). On the other hand those previously treated with hydnocarpus oil have shown slower improvement. have often had amazingly rapid subsidence of lesions.* A few Lepromas have shown a rapid clinical improvement. Bacteriological assessment has not yet been made on any considerable number. About 20% of tuberculoid cases continue to show definite

(* the more acute and marked the signs, frequently the more rapid subsidence of the lesions—Ed.)

clinical signs of activity after 10 or more months of treatment; others still show hypopigmented areas which look inactive, but whose significance must be judged after more experience. Nearly half of these appear completely inactive.

6. COMPARISON OF TWICE WEEKLY WITH DAILY TREATMENT.

Treatment with dapsone at clinics has been twice weekly, with not more than 0.8 gm. per week. At the settlement 0.2 gm. has been given for 6 days a week, a total of 1.2 gm. per week.

(a) *Rapidity.* Comparable tuberculoid and lepromatous cases who have never had hydnocarpus oil have been studied, and no significant difference has been seen between daily and twice weekly treatment.

(b) *Complications.* Anaemia seems much less common under twice weekly treatment. Dermatitis is no less common, but is usually less severe. Leproma, eye and nerve reactions are less common and severe under twice weekly than daily treatment.

7. SUMMARY AND CONCLUSIONS.

(a) D.A.D.P.S. has been administered to over 9,000 patients with scanty medical supervision.

(b) The results have proved the practicability of the project, and staff and patients are well satisfied with the results to date.

(c) On twice-weekly treatment most of the dangers have been less than was feared, but an earlier recognition of dermatitis, and better supplies of antihistamines would probably have saved the 4 deaths which have occurred from dermatitis.

(d) It appears safe to give dapsone to nursing mothers.

(e) Twice-weekly treatment is shown to be safer and probably as good as daily treatment, but no suggestion is made at this stage that this should be the routine in a settlement with adequate qualified staff.

(f) There may be many criticisms as the method described is obviously not the ideal method of treating leprosy. But the circumstances are briefly:— Great shortage of qualified medical staff: on the whole a backward people with few educated ones to help: very large numbers with leprosy: a flourishing black market which may lead to drug-resistant strains within a few years (Dapsone is being sold, coming from different sources under different names). There are, taken all round, as great dangers with much less success from using hydnocarpus oil, the only practical alternative.

I am indebted to the Honourable, The Director of Medical Services, for permission to publish this article