CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of this JOURNAL is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the JOURNAL and thus interfere with its prime purpose.

Six Cases of Dapsone-resistant Tuberculoid Leprosy

TO THE EDITOR:

Since 1979, when the Dhoolpet Leprosy Research Center was initiated, we have registered about 1000 new patients with paucibacillary (BT or TT) leprosy. Almost all have received dapsone 50–100 mg daily as monotherapy. Most of them have improved satisfactorily, but a poor clinical response in some of them led to suspicion that they were infected with dapsone-resistant *Mycobacterium leprae*. We defined a poor response as old lesions enlarging and/or new lesions appearing with a biopsy appearance of active untreated leprosy without reaction.

With only outpatient facilities available, we were not able to undertake a trial of supervised treatment in these patients; nor was it possible to use mouse foot pad tests to confirm the suspicion of dapsone-resistant leprosy. Therefore, our procedure with these patients (most of whom were anxious because they thought they were doing badly) was:

a) Education that dapsone usually worked well and encouragement to take it particularly regularly for a "trial period" and to come for checkups before they finished their supply of tablets.

b) Encouragement of outpatient visits as frequently as was reasonable for the patient, considering his work circumstances and the distance he lived from the center. Most patients were seen every 2–3 months; they were clinically assessed at each visit, including measuring the size of skin lesions.

c) The urine was tested for dapsone [dapsone/creatinine (D/C) ratio] at each clinic visit. A D/C ratio of 25 or more (μg dapsone per ml/mg creatinine per ml) was considered as positive. Patients were unaware of the purpose of the urine test.

d) Biopsy of an active skin lesion was performed every 3–6 months.

Patients whose urine tests for dapsone were consistently positive and who attended regularly for treatment during the trial period were considered to be probably reasonably compliant. Compliant patients whose lesions increased in size and/or developed new lesions or who failed to improve, and in whom serial biopsies showed active leprosy without signs of reaction, were considered to be infected with dapsone-resistant *M. leprae*.

We have identified six such patients (The Table). All were classified clinically as BT and had not received previous antileprosy treatment; skin smears were negative in five cases (not performed in case 5). All attended regularly (90–100%) during their period of initial treatment, but cases 1 and 2 deteriorated within 2–4 months, and case 3 remained clinically stationary. Cases 4–6 improved clinically for about six months and then began to deteriorate. After six months (cases 1–3) or one year (cases 4–6), it was clear to both patients and doctor that treatment was unsatisfactory. Biopsies at that time were all reported as BT active; none looked reactional.

Once their poor clinical response and active biopsy had aroused suspicion of dapsone-resistant leprosy, these patients started a period of trial treatment. All attended very regularly, and all but one of their urine tests were positive for dapsone; the average D/C

THE TABLE. *Regularity of clinic attendance, duration of treatment, proportion of positive D/C ratios, and clinical progress of six trial patients.*

Case	Initial treatment		Period of trial treatment			
	Regularity (%)	Duration (mos.)	Regularity (%)	Duration (mos.)	Positive D/C ratios	Clinical features
1	100	5	100	12	8/8	Developed slight erythema of lesions which otherwise remained stationary
2	100	7	100	7	3/3	Developed new lesions; downgraded to BL and old lesions enlarged
3	100	9	100	2	2/2	Lesions rapidly enlarged
4	100	13	100	16	5/5	Transient improvement, then lesions enlarged
5	100	15	100	3	1/2	Many new lesions rapidly developed
6	90	16	95	23	2/2	Clinically stationary

ratio of all tests was 67. (Case 6 started his trial before these tests were available to us.) Case 4 improved clinically for a month or two, then deteriorated. Cases 1 and 6 remained stationary. Cases 2, 3, and 5 rapidly deteriorated, case 2 downgrading to BL. At the end of the trial period, all but case 2 were histologically active BT; none were clinically or histologically reactional.

The duration of the trial period was two months to two years; patients with stationary lesions were observed for longer periods. When it was clear that despite regular clinic attendance and positive urine tests a patient was deteriorating or stationary with a biopsy indicating active leprosy, the period of trial treatment was terminated and the patient treated with another drug. Three of these patients have been on alternative treatment for a year or more; all have shown good clinical improvement, and in two cases repeat skin biopsy has shown definite histological regression following the change of treatment. The other three patients changed treatment less than a year ago but are improving clinically.

These patients were drawn from a population of about 1000 newly registered patients with BT or TT leprosy, suggesting that the prevalence of such cases is less than 1%. We have seen a number of other patients whom we suspect to have dapsone-resistant leprosy, but in whom the data are inadequate for final proof; but even if such cases are included, the prevalence of dapsone-resistant tuberculoid leprosy in the Hyderabad area amounts to only about 1% of newly diagnosed cases. This figure represents those patients who are infected with *M. leprae* sufficiently highly resistant to dapsone to show almost no clinical response; the proportion of patients with high-grade, dapsone-resistant lepromatous leprosy is likely to be much the same.

We consider this figure encouraging; it implies that 99% of patients will still respond (to some extent at least) to dapsone monotherapy. Therefore, in spite of the problem of primary dapsone-resistant leprosy, dapsone can still be used confidently (at least in the Hyderabad area) as an effective component of the multidrug treatment of new cases of leprosy.

—John M. H. Pearson, M.D., D.M., F.R.C.P.

Physician

—K. Uday Kiran, M.B., B.S.

Medical Officer

—John N. A. Stanley, M.B., B.S.

Research Medical Officer
Dhoolpet Leprosy Research Center
Hyderabad 500006, India