

Response to Dapsone (DDS) Monotherapy in Leprosy Patients of Gudiyatham Taluk, South India: Comparison Between the 1960s and the 1970s¹

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Dapsone (DDS) has long been the cornerstone in the treatment of leprosy. The low cost and relative rarity of toxic effects are outstanding features of DDS therapy. However, the efficacy of therapy must be the prime consideration in the choice of therapeutic agents. The recent reports of *Mycobacterium leprae* which are resistant to DDS (¹⁻⁶) suggest the need to determine whether the efficacy of DDS has changed over the years.

A direct measurement of the response to DDS in a patient can be obtained by noting the clearance of *M. leprae* from skin smears. Patients infected relatively long ago can then be compared with patients infected more recently, for response to DDS.

Gudiyatham Taluk, with a population of 425,000 (1971 census), is hyperendemic for leprosy. In 1963, the leprosy control program was launched by the Schieffelin Leprosy Research and Training Centre, Karigiri, employing DDS monotherapy given as domiciliary treatment; backed by repeated house-to-house surveys and health education, and careful maintenance of individual patient records. DDS monotherapy remained in use until 1981.

The objective of this study was to determine whether the efficacy of DDS in the treatment of leprosy showed a change with the passage of time.

PATIENTS AND METHODS

All residents of Gudiyatham Taluk registered for the treatment of leprosy in the years 1964 to 1966 or 1971 to 1973, with a clinical diagnosis of lepromatous (LL) or borderline lepromatous (BL) leprosy and acid-fast bacilli in skin smears, were included in the analysis. Data for each of these patients were obtained from the individual patient record. Skin smears had been done annually from four routine sites (ear and chin on the right, forehead and buttock/thigh on the left) as well as apparently active sites and read by trained personnel at the base hospital. Techniques and criteria for skin smears remained unchanged throughout the period under consideration. The attainment of skin smear negativity in a patient during the initial seven years of treatment was compared in two groups of patients: 1) those first registered in the years 1964 to 1966, and 2) those first registered in 1971 to 1973.

For the purpose of this study, "maximal" DDS treatment has been defined as the collection of $\geq 80\%$ of the prescribed DDS tablets, with no interruption of treatment exceeding six months.

The standard error of a proportion was determined by the formula $\sqrt{(p \times q/n)}$ where p is the number of n individuals in one category and q the number in the other.

RESULTS

A total of 391 patients registered in the years 1964 to 1966 and 148 patients registered in the years 1971 to 1973 were included in the analysis. The proportion of patients in each group who were "smear negative" after each year of treatment is shown in Table 1 and Figure 1. Among patients registered in 1964 to 1966, the proportion of patients smear negative rose from 0% at the start of treatment to 51.9% after

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TABLE 1. Attainment of smear negative status by period of treatment in two groups of patients on DDS monotherapy.

Period of treatment (yrs)	No. (% \pm standard error) of patients smear negative registered during the years	
	1964-1966 ^a	1971-1973 ^b
0	0	0
1	48 (12.3 \pm 1.66)	23 (15.5 \pm 2.97)
2	98 (25.1 \pm 2.19)	43 (29.1 \pm 3.73)
3	143 (36.6 \pm 2.46)	56 (37.8 \pm 3.99)
4	165 (42.2 \pm 2.50)	66 (44.6 \pm 4.09)
5	165 (42.2 \pm 2.50)	81 (54.7 \pm 4.09)
6	179 (45.8 \pm 2.52)	98 (66.2 \pm 3.89)
7	203 (51.9 \pm 2.53)	114 (77.0 \pm 3.46)

^a A total of 391 patients were registered in 1964 to 1966.

^b A total of 148 patients were registered in 1971 to 1973.

seven years of treatment. Among patients registered in 1971 to 1973, the corresponding figures were 0% at the start of treatment and 77.0% after seven years of treatment. After 5, 6 and 7 years of treatment, respectively, the occurrence of smear negative status was significantly more frequent among patients registered in 1971 to 1973 than among those registered in 1964 to 1966 (p in each case < 0.05).

However, only 135 (34.5%) of 391 patients registered in 1964 to 1966 had received "maximal" DDS treatment; whereas 69 (46.6%) of 148 patients registered in 1971 to 1973 had done so ($p < 0.05$).

Table 2 and Figure 2 show the attainment of smear negative status among patients with "maximal" DDS treatment. Among such patients registered in 1964 to 1966, the proportion with negative smears rose from 0% at the start of treatment to 74.8% after seven years of treatment. The corresponding proportions among patients registered in 1971 to 1973 were 0% and 85.5%. The differences between the two groups do not attain statistical significance at any stage of treatment ($p > 0.05$).

The Bacterial Index (BI) (7) at the time of registration was analyzed in each group. Only 59 (15.1%) of 391 patients registered in 1964 to 1966 had a BI $\geq 3+$, as against 69 (46.9%) of 148 patients registered in 1971 to 1973 ($p < 0.002$).

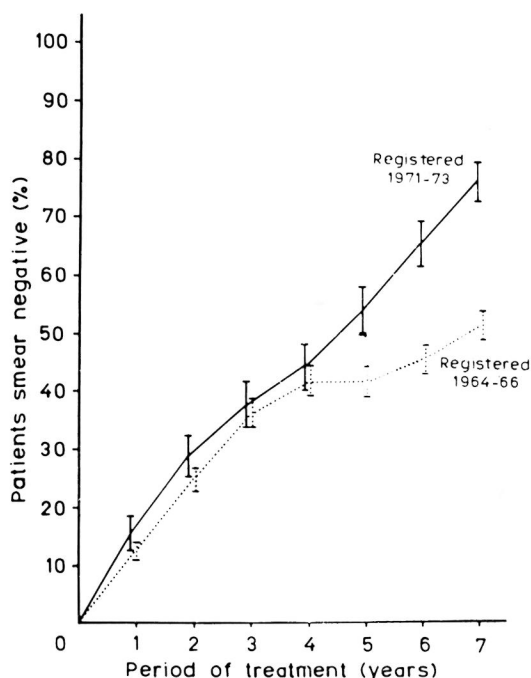


FIG. 1. Attainment of smear negative status by period of treatment in two groups of patients on DDS monotherapy. Percentages are shown \pm standard error of the percentage: $100 \times \sqrt{(p \times q/n)}$.

DISCUSSION

Patients registered in 1971 to 1973 were found to respond as well to DDS monotherapy as patients registered in 1964 to 1966, as indicated by clearance of *M. leprae* from skin smears during the initial seven years of treatment. A significantly higher proportion of patients registered in 1971 to 1973 received "maximal" DDS therapy, when compared to patients registered in 1964 to 1966. This could be explained by the steadily improving rapport between the institution and the inhabitants of Gudiyatham Taluk. This seems to explain why a larger proportion of those registered in 1971 to 1973 than those registered in 1964 to 1966 were smear negative after 5, 6 and 7 years of DDS treatment. Despite the disadvantage of including a higher proportion with an initial BI $\geq 3+$, patients registered in 1971 to 1973 did not attain smear negative status any more slowly than those registered in 1964 to 1966.

The exact date of infection in a patient is

TABLE 2. Attainment of smear negative status by period of treatment in two groups of patients on "maximal" DDS monotherapy.

Period of treatment (yrs)	No. (% \pm standard error) of patients smear negative registered during the years	
	1964-1966 ^a	1971-1973 ^b
0	0	0
1	27 (20.0 \pm 3.44)	11 (15.9 \pm 4.40)
2	44 (32.6 \pm 4.03)	21 (30.4 \pm 5.54)
3	66 (48.9 \pm 4.30)	27 (39.1 \pm 5.87)
4	79 (58.5 \pm 4.24)	32 (46.4 \pm 6.00)
5	89 (65.9 \pm 4.08)	41 (59.4 \pm 5.91)
6	95 (70.4 \pm 3.93)	51 (73.9 \pm 5.29)
7	101 (74.8 \pm 3.74)	59 (85.5 \pm 4.24)

^a A total of 135 patients registered in 1964 to 1966 received "maximal" DDS monotherapy.

^b A total of 69 patients registered in 1971 to 1973 received "maximal" DDS monotherapy.

difficult to pinpoint. It appears reasonable, however, to assume that patients registered in 1971 to 1973 were infected more recently than those registered in 1964 to 1966. In the interval of time between the two groups, the responsiveness of *M. leprae* to DDS appears to have shown no marked change. Although negative findings cannot be used to disprove hypotheses, these data do not support the claim that DDS-resistant infections have been increasing in frequency since the introduction of DDS monotherapy.

SUMMARY

At the Schieffelin Leprosy Research and Training Centre, Karagiri, India, 148 lepromatous (LL) and borderline lepromatous (BL) leprosy patients registered for treatment in the years 1971 to 1973 were found to respond as well to dapsone (DDS) monotherapy as 391 LL and BL patients registered in 1964 to 1966, as indicated by clearance of *Mycobacterium leprae* from skin smears during the initial seven years of therapy in each patient. Apparently, the efficacy of DDS monotherapy has not been progressively diminishing since the introduction of DDS monotherapy into the area.

RESUMEN

En un estudio realizado en el Centro Schieffelin de Investigación y Adiestramiento de la lepra, Karigiri, India, se encontró que 148 pacientes lepromatosos (LL) e intermedios (BL) registrados para tratamiento en los

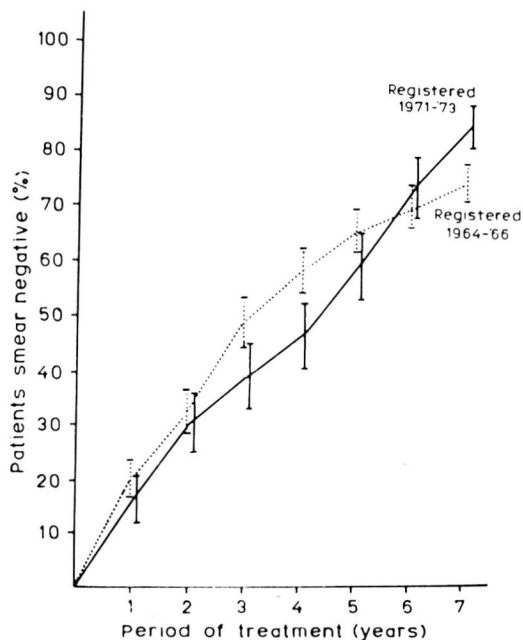


FIG. 2. Attainment of smear negative status by period of treatment in two groups of patients on "maximal" DDS monotherapy. Percentages are shown \pm standard error of the percentage: $100 \times \sqrt{(p \times q/n)}$.

años de 1971 a 1973 respondieron a la monoterapia con dapsona (DDS) tan bien como 391 pacientes LL y BL registrados de 1964 a 1966. Esto se concluyó en base a la eliminación de *M. leprae* observada en las preparaciones de piel de cada paciente durante los 7 años iniciales de terapia. Aparentemente, la eficacia de la monoterapia con DDS desde su introducción, no ha disminuido con el tiempo en el área estudiada.

RÉSUMÉ

Au Schieffelin Leprosy Research and Training Centre, à Karigiri, en Inde méridionale, on a observé que 148 malades atteints de lèpre lépromateuse (LL) ou dimorphe (BL) enregistrés au traitement au cours des années 1971 à 1973, répondaient aussi bien à la monothérapie par la dapsona (DDS), que 391 patients LL et BL enregistrés entre 1964 et 1966. Cette observation a été basée sur des études de l'immunisation de *Mycobacterium leprae* dans des frottis cutanés au cours des sept premières années du traitement chez chaque malade. Il apparaît dès lors que l'efficacité de la monothérapie par la dapsona n'a pas diminué progressivement dans cette région, depuis l'introduction de la monothérapie par la DDS.

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