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Low Dose Dapsone Therapy in Lepromatous Leprosy

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Under the conditions of this study, dapsone in doses of 5 mg and 10 mg daily when administered to patients with lepromatous leprosy is an ineffective therapy in terms of killing and elimination of *Myco. leprae* from human skin and bone marrow. A real danger of facilitating the emergence of resistant bacilli exists. Therefore, until there is more evidence from long term therapeutic trials of low dose dapsone in bacillated types of leprosy, conventional dosage of dapsone is recommended.

Clinicians treating lepromatous leprosy patients before and after the introduction of sulphones as specific therapy have gained the impression that both the incidence and severity of erythema nodosum leprosum reactions in leprosy have greatly increased. There have been reports of the beneficial effects of low dose DDS in reducing the incidence of these reactions in lepromatous leprosy. The apparently effective inhibition of multiplication of *Myco. leprae* in the footpads of mice by extremely low concentrations of dapsone in the diet (of the order of 0.0001 g%) (Shepard *et al.*, 1966) had tended to breed an undue sense of optimism and confidence in the efficacy of homeopathic doses in man. This optimism was further compounded by extrapolation of reported changes in Morphological Index of *Myco. leprae* in skin smears to death of *Myco. leprae.*

A study was initiated to elucidate the precise relationship between dose of dapsone and incidence of reactions, as well as the period of viability of *Myco. leprae* in skin and bone marrow of lepromatous leprosy patients on low and high dose of dapsone.

Material and Methods

Thirty consecutive untreated lepromatous leprosy patients were randomly allocated to three therapy groups:

(1) dapsone 5 mg daily;
(2) dapsone 10 mg daily;
(3) dapsone 100 mg daily.

Skin smears were taken from 8 standard sites by slit-skin method once a month and Morphological Index (Shepard and McRae, 1965) and Bacterial Index (Ridley, 1964) were determined. Skin biopsy and bone marrow aspiration were obtained immediately prior to initiation of treatment and once in 3 months during the first year and once in 6 months for 2 subsequent years. *Myco. leprae* homogenates from these specimens were injected into hind footpads of thymectomized CBA mice which were harvested at regular intervals and harvest

counts obtained. Clinical records included specific reference to occurrence of ENL, painful neutritis, iritis or any other intercurrent complication. The reactions were treated with 4 week course of 15 to 30 mg of prednisolone.

Of the 30 patients only 15 patients—5 in each group—completed the study and the data regarding these patients is presented here.

Results

Morphological Index

In the majority of cases the MI was between 3 and 10% at initiation of treatment and came down to below 1% in 12 to 24 weeks in all the groups. There was no significant difference in rate of fall of MI between the low and the high dose group.

Bacterial Index

(a) *100 mg dapsone.* There was a fairly uniform fall in BI at the rate of 1+ per year. Three of the 5 patients were skin smear negative at the end of 3 years. However, in 4 of the 5 patients bone marrow aspirates continued to be positive for *Myco. leprae.*

(b) *10 mg dapsone.* In 1 patient the BI fell at the same rate as that seen in patients in 100 mg dapsone. In 2 patients there was no significant change in BI and in 2 patients there was a gradual rise in BI throughout the period of therapy despite the MI remaining persistently below the 0.1% in these cases.

TABLE 1

Dapsone 10 mg daily

Changes in BI over 3 years		
Steady fall	No change	Gradual rise
1	2	2

(c) *5 mg dapsone.* There was a steady fall in BI in 1 patient, no change in 1 patient and a gradual rise in 3 patients.

TABLE 2

Dapsone 5 mg daily

Changes in BI over 3 years		
Steady fall	No change	Gradual rise
1	1	3

ENL

Two patients in each of the 3 therapy groups developed ENL and there was no clinically recognizable difference between the 3 groups.

Bacilli in the bone marrow

Except for 1 patient on 100 mg dapsone whose skin smear also had become negative at 2 years, in all the other patients AFB was demonstrable in bone marrow aspirates throughout the period of study.

Viability of Myco. leprae *in skin and bone marrow while on therapy*

(a) *100 mg dapsone daily.* In all patients, *Myco. leprae* from skin biopsy homogenates were non-viable in footpads of mice between 6 and 12 months of treatment with dapsone 100 mg daily. In 2 the *Myco. leprae* from bone marrow became non-viable at 24 months, in 1 at 30 months, in 1 at 36 months; while in 1 it was viable at the end of 36 months.

TABLE 3

Viability of Myco. leprae *in skin and bone marrow of patients treated with dapsone 100 mg daily*

Time \ Site	I		II		III		IV		V	
	S	BM	S	BM	S	BM	S	BM	S	BM
0	+	+	+	+	+	+	+	+	+	+
3 months	+	+	+	+	+	+	+	+	+	+
6 months	–	+	+	+	–	+	+	+	+	+
9 months	–	+	+	+	–	+	–	+	+	+
12 months	–	+	–	+	–	+	–	+	–	+
18 months	–	+	–	+	–	+	–	+	–	+
24 months	–	–	–	+	–	–	–	+	–	+
30 months	–	–	–	+	–	–	–	–	–	+
36 months	–	–	–	–	–	–	–	–	–	+

(b) *10 mg dapsone daily.* In 1 patient the bacilli from the skin became non-viable at 18 months and in another at 36 months while in the rest of the 3 patients the bacilli were still viable at 36 months. However, in all the patients the bacilli from the bone marrow remained viable at 36 months.

TABLE 4

Viability of Myco. leprae *in skin and bone marrow of patients treated with dapsone 10 mg daily*

Time \ Site	I		II		III		IV		V	
	S	BM	S	BM	S	BM	S	BM	S	BM
0	+	+	+	+	+	+	+	+	+	+
3 months	+	+	+	+	+	+	+	+	+	+
6 months	+	+	+	+	+	+	+	+	+	+
9 months	+	+	+	+	+	+	+	+	+	+
12 months	+	+	+	+	+	+	+	+	+	+
18 months	–	+	+	+	+	+	+	+	+	+
24 months	–	+	+	+	+	+	+	+	+	+
30 months	–	+	+	+	+	+	+	+	+	+
36 months	–	+	+	+	+	+	–	+	+	+

(c) *5 mg dapsone daily.* In 1 patient the bacilli from the skin became non-viable at 18 months and in another at 36 months. In none of the patients the bacilli from the bone marrow attained non-viability at the end of 36 months (Table 5).

TABLE 5

Viability of Myco. leprae *in skin and bone marrow of patients treated with dapsone 5 mg daily*

Time \ Site	I		II		III		IV		V	
	S	BM	S	BM	S	BM	S	BM	S	BM
0	+	+	+	+	+	+	+	+	+	+
3 months	+	+	+	+	+	+	+	+	+	+
6 months	+	+	+	+	+	+	+	+	+	+
9 months	+	+	+	+	+	+	+	+	–	+
12 months	+	+	+	+	+	+	+	+	–	+
18 months	+	+	+	+	+	+	+	+	–	+
24 months	+	+	+	+	–	+	+	+	–	+
30 months	+	+	+	+	–	+	+	+	–	–
36 months	+	+	+	+	–	+	+	+	–	–

Comments

(1) There is no evidence to show that ENL reactions can be reduced by reduction of dosage of dapsone. The occurrence of reactions in lepromatous leprosy seems to follow an "all or none" law as far as dapsone is concerned.

(2) Morphological Index, under the conditions of these experiments, appears to be an unreliable measure of viability of *Myco. leprae.*

(3) Dapsone when administered orally in dosage of 100 mg daily, renders the *Myco. leprae* in human skin non-viable in 6 to 12 months. However, a significant lag period exists between killing of *Myco. leprae* in skin and in bone marrow, the latter being viable for 12 to 24 months after the bacilli in the skin are dead.

(4) Dapsone when administered in daily doses of 5 mg and 10 mg over a 3 year period is far less effective in both killing and eliminating *Myco. leprae* from skin and bone marrow.

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