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Dapsone-resistant leprosy in Burundi

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Summary Between 1978 and 1981 a dapsone-resistance survey was performed in 4 out of 5 regions of Burundi. Among 1791 leprosy patients, 925 were multibacillary (51%) and prevalence of dapsone resistance is 3·7%, with variations in regions between 1·2 and 6·1%. Since the selection of patients was on a clinical rather than a bacteriologic basis, this should be a minimum figure. Incubation time of dapsone resistance was from 8 to more than 20 years of monotherapy. Two cases of primary dapsone resistance were also diagnosed.

Introduction

Burundi is situated in Africa between 2°45 and 4°28 S, at an altitude varying between 775 m and 2670 m above sea level. It is 28,000 km^2 with a population of $4{\cdot}10^6$ living in families dispersed in the hills, except for some commercial or administrative centres that originated during this century.

Leprosy Control Service was initiated after the Second World War, when dapsone monotherapy was introduced. This service covered the entire country from 1976 onwards. Dapsone, thiambutosine and long-acting sulphonamides were used. There was a leprosarium from 1950 to 1972 which admitted some 2000 patients.

Between 1978 and 1981 we performed a dapsone-resistance survey in Burundi.

Materials and methods

For practical reasons the survey was done in 4 (Kiremba, Rwisabu, Bururi and Kinyinya) of the 5 regions existing. Based on the latest census (1979) these regions have a population of 3,144,340 out of a total of 4,021,910, and thus comprise 78% of the population. Prevalence of leprosy in Burundi is 0·6% but in Bururi and

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Kinyinya it is 1·3–1·5%. Two hundred new cases are detected each year, 30% being multibacillary.

In the 4 regions surveyed there were 2473 patients under treatment of whom 1243 (50%) were multibacillary. Criteria for biopsy were: (a) patients with an original diagnosis of lepromatous leprosy, (b) patients treated with dapsone for at least 5 years, and (c) patients who had clinically active lesions, as judged by one of the authors (JB).

Biopsies were transported in thermosflasks on wet ice to Bujumbura and from there by air to Antwerp. Three biopsies were inoculated in 1978, 4 in 1979, the remaining 46 between January 1980 and June 1981. For each biopsy 34 mice were inoculated in both hind foot-pads with $5 \cdot 10^3$ acid-fast bacilli, 10 controls received normal food and 3 groups of 8 mice each received food containing 10^{-2}, 10^{-3} and 10^{-4} g% dapsone.

A control mouse was examined after 6 months. If the bacterial count did not reach 10^4, another control animal was examined after 8 and 10 months and 3 animals after 12 months; if it was between 10^4 and 10^5, further controls were examined at 3-week intervals. When the bacillary population reached $5 \cdot 10^5$, 3 control animals and 5 of each treated group were examined. If there was lack of time to examine the animals immediately, they were stored at $-20°C$.

Results and discussion

All biopsies except 15 were inoculated into mice within 7 days. Of those inoculated later than 7 days after having been taken, 8 were inoculated after 8, one after 9, 3 after 10, 1 after 12 and 2 after 15 days, of these 7, 1, 2, 1 and 1 respectively, multiplied in control mice. Thus the number of strains lost as a result of delay in transportation must have been minimal.

Table 1 shows the overall results. Fifty-one per cent of the patients under treatment had a multibacillary form of the disease. Of these, 53 had been treated for more than 5 years and were diagnosed as having clinically active disease. In 5 cases the biopsy did contain insufficient bacilli for mouse foot-pad inoculation. Nine strains did not multiply in mice, 4 were fully sensitive to dapsone, and 35 were resistant. The overall prevalence of proven dapsone resistance is 3·7% but varies considerably in the different regions: from 1·2% in Rwisabi to 6·1% in Kinyinya. The reasons for this variation remain unknown, but it is highest in the two regions where the disease is more prevalent. In contrast with the THELEP criteria[1] for dapsone resistance surveys, where all previously multibacillary leprosy patients treated for a minimum of 5 years are examined bacteriologically and biopsied if a skin lesion shows a bacterial index of 3 or more, in the present study, owing to lack of manpower, patient selection for mouse foot-pad testing was based on clinical impression. Therefore, patients who were incubating dapsone resistance and had not yet developed manifest signs of relapse were

Table 1. Dapsone resistance among leprosy patients in 4 regions of Burundi

Region	Population	Patients treated	Multibacillary	Suspected of dapsone resistance	Not inoculated	Results of MFI*		
						neg	S	R
Kiremba	1,274,140	291	160	5 (3·1)†	1	—	—	4 (2·5)
Rwisabi	1,020,690	281	156	6 (3·8)	1	3	—	2 (1·2)
Burundi	487,200	653	284	17 (5·9)	1	3	4	9 (3·1)
Kinyinya	362,310	566	325	25 (7·6)	2	3	—	20 (6·1)
		1791	925	53 (5·7)	5	9	4	35 (3·7)

* MFI (mouse foot-pad inoculation).

† Percentage.

S = sensitive to 10^{-4} g% dapsone in the diet; R = resistant to at least 10^{-4} g% dapsone in the diet.

probably overlooked. The real prevalence of dapsone resistance, therefore, might be higher and the figures arrived at are to be considered minimal.

The degree of dapsone resistance is shown in Table 2. Twenty-eight strains were fully dapsone resistant, e.g. they multiply in mice fed 10^{-2}% dapsone in the diet, 4 strains were median resistant, and 3 low grade resistant. In 4 cases bacillary multiplication had occurred in part of the mice receiving dapsone in the food, while multiplication had occurred in all of the control mice. This cannot be the result of inocula containing small proportions of viable bacilli and might be the result of the presence of mixed populations of dapsone sensitive and resistat organisms.

The duration of treatment when dapsone resistance was proven by mouse foot-pad inoculation varies between 8 and more than 30 years and shows a bimodal distribution, with peaks at 8–10 years and 20 years (Table 3).

However, these are most probably unreliable figures due to the patients whose files had disappeared and recall having been treated 'before independence' (1961) or not; for the latter group clinical files exist since the last 10 years (Table 3).

Finally 3 cases of suspected primary dapsone resistance were also inoculated. Two showed dapsone resistance: the results of the mouse foot-pad inoculations

Table 2. Degree of dapsone resistance

Concentration of dapsone in food:	10^{-2} g%	10^{-3} g%	10^{-4} g%
Number of strains:	28	4	3

Table 3. Number of years elapsed since start of treatment

	5	8	10	12	15	18	20	25	30	?
Number of dapsone-resistant cases		4	3	1	3	5	10	5	2	2
Number of dapsone-sensitive cases	1	1	1	1						

are presented in Table 4, one of the strains is definitely median dapsone resistant, the second has a lowered sensitivity, although it would be inhibited in man by full dosage 100 mg daily dapsone. These patients had been treated for 6–8 months.

The prevalence of dapsone resistance in Burundi (3·7%) is thus of the same magnitude as in other populations studied: 5·1% in Jiangsu Province, China, 5·0%[2] in Bamako, Mali,[3] keeping in mind that 3·7% is probably lower than reality, since patients were selected on clinical grounds.

Table 4. Results of MFI of 2 cases of suspected primary resistance

Patient No.	Dapsone concentration in mouse food		
	10^{-2} g%	10^{-3} g%	10^{-4} g%
1	1/5*	4/5	5/5
2	0/5	0/5	1/5

* Number of mice showing multiplication in the foot-pad/number of mice examined.

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