Nine Cases of Rifampin-resistant Leprosy

TO THE EDITOR:

Since the first publications by Jacobson and Hastings ([3]) and Hastings and Jacobson ([2]) of two cases of leprosy with rifampin-resistant strains, much effort has been devoted to the prevention of resistance to rifampin and to the survey of *Mycobacterium leprae* rifampin sensitivity. To prevent the development of resistance to rifampin, multidrug regimens are now strongly recommended for control programs of leprosy ([1]). However, between 1970–1980, rifampin had been used in almost every country, either alone or in combination with drug(s) that have been already prescribed for long periods of time. Such was the case in metropolitan France, in Martinique and Guadeloupe, and in New Caledonia, where rifampin was used free of charge for the chemotherapy of tuberculosis as well as leprosy for as long as ten years.

Since the beginning of 1980, biopsies of new and relapsed cases of leprosy from Martinique, Guadeloupe, New Caledonia, and Paris hospitals have been inoculated into mouse foot pads ([5]) to study *M. leprae* drug sensitivity. Direct sensitivity tests were performed using 0.0001%, 0.001%, and 0.01% dapsone in the diet ([6]) and 10 mg/kg rifampin given by gavage once a week ([4]). With a standard inoculum of 5×10^3 acid-fast bacilli (AFB) per foot pad, growth was considered to have occurred when the total count per foot pad was greater than or equal to 4×10^4 AFB. Harvests of drug-treated animals were performed at the ninth and twelfth month, according to the occurrence of growth in control mice.

So far, the results of 68 sensitivity tests are available; 23 from newly diagnosed patients and 45 from relapse cases. Among the former, no rifampin-resistant strains were detected. Among the latter, 36 had rifampin-sensitive strains and nine showed rifampin resistance. The aim of this letter is to give the main characteristics of the nine patients and of the strains' drug sensitivities.

Table 1 summarizes the nine case histories. At the start of rifampin therapy all patients except one (Patient No. 3) already had a long history of leprosy treated with dapsone and/or sulfonamides. Biopsies that yielded rifampin-resistant *M. leprae* were performed for all patients except one (Patient No. 1) at least six years after the apparent start of rifampin therapy. Although it is certain that patients did not receive continuous rifampin therapy, the total duration of rifampin therapy, calculated from the patients' records, is extremely doubtful except for Patients Nos. 2, 3, and 5. For Patient No. 2 at least three courses of rifampin therapy were identified: 36 months in 1970–1972, no rifampin at all between 1973 and 1979, then two short courses of six and five months' duration in 1979 and 1980, respectively, because of clinical deterioration. Patient No. 3 received rifampin alone as soon as the diagnosis of leprosy was made.

TABLE 1. *Main characteristics of nine rifampin-resistant cases of leprosy.*

Patient no.	Date of biopsy	Age	Sex	Place of treatment	First diagnosis of leprosy	Rifampin therapy[a]		
						Start	Dose (mg)	Total duration (mo.)
1	July 1980	51	M	Martinique	1947	July 1979	600 daily	12
2	Oct. 1980	50	M	Martinique	1953	1970	600 daily	47
3	Nov. 1981	28	M	Paris	1975	1975	600 (3/7)	72
4	Jan. 1982	71	M	Martinique	1936	Mar. 1974	600 daily	10
5	Jan. 1982	50	M	Martinique	1945	Feb. 1974	600 daily	40
6	Jan. 1982	37	M	Martinique	1958	1974	Unknown	5
7	Mar. 1982	45	F	Martinique	1950	Dec. 1976	600 daily	13
8	Apr. 1982	49	M	Martinique	1946	July 1975	600 daily	19
9	Sept. 1982	56	F	New Caledonia	1942	Mar. 1975	600 daily	9

[a] Estimate.

TABLE 2. *Sensitivity tests of nine rifampin-resistant leprosy cases.*

Patient strain no.	Controls	No. positive foot pads/ No. foot pads examined			
		% Dapsone in diet			Rifampin *per os*
		0.0001	0.001	0.01	10 mg/kg
1	3/3	3/3	5/5	5/5	7/7
2	2/2	1/3	1/5	ND[a]	4/5
3	5/5	0/5	0/5	0/5	7/8
4	2/3	3/3	5/5	3/4	4/5
5	3/3	2/3	3/5	0/5	4/5
6	3/3	1/5	0/5	0/5	5/5
7	3/3	3/3	3/3	2/5	5/5
8	2/6	1/3	2/5	1/5	5/5
9	2/3	3/3	4/5	0/5	5/5

[a] Not done (mice died).

Rifampin was given mainly three times a week from 1975 until 1981, when new lesions occurred and were biopsied for mouse foot pad inoculation. For Patient No. 5, two courses of rifampin therapy were recorded: 11 months in 1974 and 29 months from 1979 on. For this patient, a biopsy taken in July 1980 had a Morphological Index (MI) of less than 0.01 and did not give growth in the mouse.

Table 2 gives the results of dapsone and rifampin sensitivity tests. It shows that only one strain was fully sensitive to dapsone—the strain isolated from Patient No. 3 who received rifampin only. Strains from Patients Nos. 2 and 6 had a partial, low-degree resistance to dapsone. Resistance to rifampin appears complete or almost complete in all nine strains. Further studies to determine the minimum effective doses of rifampin are now in progress with the last six strains.

We fully realize that precise information on the duration of rifampin therapy is lacking for the majority of our patients. However when the length of rifampin therapy is less imprecise, it approaches the 43 and 45 months observed by Hastings and Jacobson ([2]). Finally, our data emphasize the need for strictly combined chemotherapy as underlined by WHO ([1]).

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