Chemoprophylaxis of leprosy in the Southern Marquesas with a single 25 mg/kg dose of rifampicin. Results after 10 years

L. N. NGUYEN*, J. L. CARTEL** & J. H. GROSSET†
**Institut Louis Malarde, Tahiti, French Polynesia, **Institut Pasteur, Guadeloupe, France, and †Faculté de Médecine Pitié Salpêtrière, Paris, France*

Summary In 1988, a programme of leprosy chemoprophylaxis, employing a supervised, single 25 mg/kg dose of rifampicin, was implemented in the Southern Marquesas Islands. Of the 2786 inhabitants, 2751 (98·7%) were treated. In addition, 3144 South Marquesans living elsewhere in French Polynesia were administered the same chemoprophylaxis. During the following 10 years, seven leprosy patients were detected among those who had been administered chemoprophylaxis. Of these, two were very likely missed cases of leprosy, and cannot be considered a failure of chemoprophylaxis. The epidemiometric projection model, based on cases of leprosy observed in the Southern Marquesas during the 20 years preceding implementation of the programme, predicted that 17 leprosy cases could be expected in the South Marquesan population if no chemoprophylaxis were given. In fact, only five cases were detected in the treated population, a number significantly smaller than 17, suggesting that the chemoprophylaxis was 70% effective, assuming that no change of detection rate would have occurred without chemoprophylaxis. However, during the 10 years following implementation of the chemoprophylaxis programme, the detection rate in the Polynesian population that was not administered chemoprophylaxis declined by about 50%. Therefore, the effectiveness of the chemoprophylaxis was only 35–40%.

Because studies conducted in India demonstrated that chemoprophylaxis with dapsone, administered to the entire population in an endemic area, might contribute to leprosy control, and because rifampicin is much more active against *Mycobacterium leprae* than is dapsone, a programme of chemoprophylaxis for leprosy employing a supervised, single 25 mg/kg dose of rifampicin was launched in January and February 1988 in the Southern Marquesas Islands. These remote islands of French Polynesia were chosen because of the limited size of their population (slightly fewer than 3000 inhabitants), and because the detection rate of leprosy had been very high (48·9 per 100,000—six times higher than in the general population of French Polynesia) for decades. Also, the decision to conduct such a chemoprophylaxis programme was made because an epidemiometric projection, based on cases detected during the past 20 years, had shown that a significant reduction of the number of expected cases could be observed in as few as 6 years if the chemoprophylaxis were 80% effective (Table 1).

In 1987, all of the villages in all of the valleys of the three inhabited islands were visited, and the objectives of the programme were explained to the local authorities and the

Table 1. Expected numbers of cases of leprosy in the South Marquesan population without and with chemoprophylaxis of 80% effectiveness

Year	Expected population	Expected numbers of cases Without chemoprophylaxis	With chemoprophylaxis
1988	2880	1·4	0·28
1990	8901	4·34	0·86
1992	15,289	7·46	1·49
1994	22,065	10·77	2·15*
1996	29,255	14·01	2·85
1998	34,992	17·08	3·42

* Significantly different from 10·77 expected without chemoprophylaxis ($P < 0·05$).

population. All known patients had a clinical and bacteriological examination, and the household contacts of these patients were also examined. Also, the 1983 census of the population born in the Southern Marquesas and living in the Southern Marquesas or elsewhere in French Polynesia was brought up to date, and a computerized list of inhabitants was prepared by island, valley and village. Using this list, two teams, each consisting of a medical doctor, a nurse and a health worker of the leprosy control unit, supplemented by a South Marquesan primary health worker, carried out the programme between 18 January and 20 February 1988. During the post-chemoprophylaxis period, follow-up of the treated population was carried out by the staff of the leprosy control unit in Tahiti, the main island of French Polynesia, in collaboration with the personnel of the Public Health Service in the Southern Marquesas. Each treated person suspected of being a new leprosy patient was referred to the Public Health medical doctor in Southern Marquesas and, subsequently, if necessary, to the leprosy control unit in Tahiti.

Of the 2786 inhabitants, 2751 (98·7%) were given a single, supervised 25 mg/kg dose of rifampicin. An additional 3144 persons were also given chemoprophylaxis, either because they were born in the Southern Marquesas (678), or because they were members of a family from the Southern Marquesas (2466).

During the following 10 years (1988–1998), seven leprosy cases were discovered among the population given chemoprophylaxis, of whom two were not considered direct failures of chemoprophylaxis, but rather missed cases of leprosy, because they had been known before implementation of the programme. The first case was that of an 11-year-old boy found in June 1988 to have a borderline leprosy lesion located at the same site as an earlier discoloured patch, which appeared 9 months and disappeared 6 months before administration of chemoprophylaxis. The second case was that of a 28-year-old man who was found to have lepromatous leprosy in 1991; he had been examined as a household contact in 1986 and found to have an indeterminate leprosy lesion, but disappeared and was not administered multidrug therapy. The remaining five cases were discovered between 1989 and 1995; the period of time elapsed between intake of chemoprophylaxis and discovery of the disease ranged from 1 year and 8 months to 7 years (Table 2).

As shown in Table 1, the total number of expected cases of leprosy in the South Marquesan population by 1998 is 17 if chemoprophylaxis were not given, and 3·4 if the given chemoprophylaxis were 80% effective. As reported previously, five new leprosy patients

Table 2. New leprosy patients in the population administered chemoprophylaxis

Year of detection	Period of time* (years)	Sex	Age (years)	Type of leprosy
1989	1·7	F	7	I
1993	5	M	25	BL
1993	5	F	47	TT
1994	6	F	11	I
1995	7	F	8	BL

* Between intake of chemoprophylaxis and discovery of the disease.

were detected in the treated population between 1988 and 1998, suggesting that the effectiveness of the chemoprophylaxis was about 70%, assuming that no change of detection rate of leprosy would occur without chemoprophylaxis. However, this was not the case; a decrease of about 50% of the detection rate was noted between 1988 and 1998 in the population not administered chemoprophylaxis. Therefore, one may infer that approximately half of the decrease observed in the South Marquesan population was not the result of the chemoprophylaxis programme. Hence, the efficacy of the programme could at best be 35–40%.

Considering the financial (more than US $50,000) and logistic costs of such a programme, 35–40% effectiveness cannot be considered satisfactory. The fact that two persons were administered chemoprophylaxis although they had previously been examined by health workers and strongly suspected of having the disease before implementation of the programme illustrates the difficulties encountered in organizing community treatments. In addition, three South Marquesans who were not known to the team in charge of the programme and thus were not administered chemoprophylaxis developed leprosy lesions (one case of BT leprosy discovered before the end of 1988, and two cases of BL leprosy discovered in 1990 and 1995, respectively). This demonstrates clearly that, even when a carefully designed and prepared programme of chemoprophylaxis is applied, treatment of the entire eligible population cannot be guaranteed.

These findings show that a chemoprophylaxis programme never provides entirely satisfactory results and that, even with a single dose of rifampicin, chemoprophylaxis cannot be considered an effective tool for leprosy control programmes, particularly if all of the known leprosy patients are not receiving the most effective treatment.

DISCUSSION

Dr Sow: Is single-dose prophylaxis scientifically justified?

Dr Cartel: Single-dose prophylaxis was the only prophylaxis that could have been employed at that time.

Dr Sengupta: Regardless of what fraction of the bacterial population is killed by the single dose, the individual could be reinfected the day after the dose, or the day after that.

Professor Grosset: I believe you didn't fully understand the situation in the Southern Marquesas. These are small islands, with a total of approximately 3000 inhabitants. The entire population was screened and administered chemoprophylaxis. The few patients were

administered MDT; in theory, there would not have been any risk of reinfection among those who had been administered chemoprophylaxis.

Dr Klatser: Were the new cases found in the course of a population survey?

Dr Cartel: No. No active survey was carried out. On the other hand, the entire population of French Polynesia, 200,000, has been computerized, and, every year, the computer record for each new patient was checked, to learn if the patient had been administered chemoprophylaxis.

Dr Klatser: But you don't know the patients who were not diagnosed.

Dr Cartel: No, we don't.

Dr Noordeen: Particularly in single-lesion leprosy, the number of new cases detected depends upon the frequency of examination. The less frequent the examination, the greater the proportion of cases that self-heal, and the larger the number not diagnosed. Therefore, it can be very difficult to compare the results of programmes carried out by different methods.