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Contribution of relapses to total infection sources of leprosy in Guadeloupe

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Summary In Guadeloupe between 1970 and 1984, the incidence of new cases of leprosy, analysed through the computerization of data collected by the Leprosy Control Unit on OMSLEP record cards, showed a decline from 24 per 100,000 inhabitants in 1970 to 11 per 100,000 inhabitants in 1984 ($y = -1{\cdot}44$). The decline was not significantly different in paucibacillary forms ($y = -0{\cdot}94$) and in multibacillary forms ($y = -0{\cdot}45$) but was much stronger among children below the age of 15 years ($y = -3{\cdot}22$) than among adults ($y = -0{\cdot}67$). During the same period 117 relapses were noted among the annual mean pool of 624 multibacillary patients who had been receiving lifelong treatment with dapsone alone for more than 5 years. The average number of relapses was 7·8 per year and the mean relapse rate 1·2% per year. The relapses have not in general been due to discontinuation of treatment by the patients because all cases of relapse for which a mouse inoculation has been carried out since 1980 harboured dapsone-resistant *Mycobacterium leprae*. Prevention of relapses by chemotherapy of inactive multibacillary cases still under treatment with dapsone alone appears as a priority for the control of leprosy in Guadeloupe.

Introduction

It is difficult to study the epidemiology of leprosy in any country for many reasons, more especially operational ones. Nevertheless, there are more favoured areas, especially those that are geographically small and that have good health infrastructures. Guadeloupe is one such more favoured area because it is a small island with considerable medical facilities, a specialized leprosy control unit and diagnostic-treatment facilities similar to those of metropolitan France.[1] Furthermore, in line with the recommendations of WHO,[6,7] a multidrug therapy programme has been systematically applied since 1980. All these factors, taken in conjunction with the computerization of data, led us to analyse the main epidemiological indicators of leprosy, more especially the detection rate and the relapse rate of multibacillary leprosy. The following study gives information for the period 1970–84, from which it is possible to determine present priorities for

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leprosy control in Guadeloupe. Among the annually detected sources of infection, relapses of multibacillary leprosy play an ever-increasing part, having risen from 16% in 1970 to 47% in 1984.

Material and methods

THE POPULATION AND THE LEPROSY CONTROL UNIT

Guadeloupe, which is a part of the Caribbean archipelego, consists of 2 main islands and 5 smaller islands or dependencies with a total area of 1790 km^2. According to INSEE records[4] the population of Guadeloupe remained stable at 350,000 between 1970 and 1984. Given, on the one hand, the reduction in the birth rate of more than 30% between the 1960s and the 1970s and, on the other hand, the outflow of persons between the ages of 30 and 40 towards metropolitan France, the fact that the population has remained stable has meant that it has also aged. It will be assumed for calculation purposes that the total population remained at 350,000 during the period 1970–84 and that the population below the age of 15 years remained at 100,000.

Leprosy control is provided by the departmental leprosy control unit with technical direction from the Pasteur Institute of Guadeloupe. This unit organizes active case-finding among contacts living under the same roof as known patients, persons at school and persons subjected to systematic screening for administrative reasons, and passive case-finding; it is responsible for the prescription, distribution, supervision and evaluation of leprosy chemotherapy. Lastly, it keeps the departmental leprosy records. The leprosy control unit has the full-time services of 2 doctors, 6 nurses, a medical secretary and a driver plus vehicle. The multipurpose clinics scattered over the island and its dependencies (some 30) are participating the activities of the leprosy control unit.

METHODS

The data analysed in this work come partly from the departmental records and partly from the medical files of patients registered between 1970 and 1984. Multibacillary cases remain on the departmental file throughout their lives, while paucibacillary cases remain on average for 15 years. Between 1970 and 1978 the administrative and medical facilities of the leprosy control unit were regrouped at first in part and then completely; this resulted in better standardization of detection and treatment methods and a temporary increase in the number of cases detected.

The screening of schoolchildren is so organized that 25,000 to 35,000 children are examined every year and that the whole school population below the age of 15 years is examined every 3 years. Detection among individuals living under the same roof as known patients (intra-domiciliary contacts) is organized by annual mail summons to attend the clinics.

The clinical examination includes examination of the skin and the large nerve trunks; any abnormality is noted in the medical record. The clinical examination is supplemented by biological tests: the lepromin intradermal reaction, the search for acid-fast bacilli in the nasal mucosa and the skin (ear lobes and skin lesions), biopsy for pathological examination (P Destombes and P Ravisse, Pasteur Institute, Paris) and, since January 1980, biopsy for mouse inoculation and drug sensitivity testing.[10] These various examinations taken together permit the diagnosis of leprosy, the classification of the form of leprosy according to Ridley & Jopling[9] and the assignment into paucibacillary or multibacillary categories.[8] A multibacillary leprosy relapse is defined by the reappearance of acid-fast bacilli with a bacteriological index ≥ 2[9] and solidly stained bacilli in one or all samples, accompanied by clinical signs in a patient treated for 5 years or longer.

Dapsone monotherapy (DDS) was the basis of the treatment prescribed until 1980 for an average of 10 years for paucibacillary patients (I, TT and BT) and lifelong for multibacillary patients (BB, BL and LL). Rifampicin (RMP) has been prescribed occasionally from 1974 onwards for 150 patients over short periods. Since January 1980 the treatment for paucibacillary patients has

been the daily administration for 6 months of 100 mg of DDS (50 mg for individuals weighing less than 50 kg) and 10 mg/kg of RMP, while for multibacillary patients it has been the daily administration for 24 months of DDS and RMP in the same doses as paucibacillary with a daily supplement during the first 12 months of 10 mg/kg of prothionamide, which was reduced to 5 mg/kg from October 1982 onwards.[2,3] All the drugs are distributed free of charge every month to the patients either in the leprosy control unit or in non-specialized clinics. Treatment is on an outpatient basis and self-administered except for patients hospitalized on account of reactions. Combinations of measures (summonses to attend, domiciliary visits, etc) are used to ensure that patients attend the dispensaries monthly, but there is no routine check on the presence of DDS in the urine.

All data in the patients' record were anonymously entered on the OMSLEP record card[8] and analysed by computer.

Results

ATTACK RATE

Between 1970 and 1984, 1058 new cases of active leprosy were detected in Guadeloupe, of which 281 were multibacillary and 777 paucibacillary (Table 1). About 80% of the cases were detected by passive case-finding and 20% by active case-finding. Among the latter, half were detected by systematic examination of children in school and half by examination of domiciliary contacts.[1] The total number of new cases detected annually fell from 85 in 1970 to 39 in 1984. Given that the population is 350,000, the incidence of all forms combined fell from 24 per 100,000 in 1970 to 11 in 1984. As is evident in Figure 1, the decline was not regular since two short-lived increases in detection are to be noted in 1971–73 and 1979–81, which correspond to the changes of organization which have already been mentioned and have no epidemiological significance. The regression curve ($y = -1{\cdot}44x + 29{\cdot}7$) plotted on the basis of the annual incidence of new cases detected between 1970

Table 1. Detection rate of leprosy in Guadeloupe from 1970 to 1984

	Newly detected new cases		Paucibacillary cases						Multibacillary cases				
							Total					Total	
Years	No.	rate†	NC*	I	T	BT	No.	rate†	BB	BL	LL	No.	rate†
1970	85	24	1	19	44	0	64	18	1	0	20	21	6
1971	119	34	2	33	51	0	86	24·5	1	0	32	33	9·5
1972	122	35	0	45	48	0	93	26·5	3	1	25	29	8·5
1973	104	29	4	28	41	0	73	21	0	1	30	31	8
1974	86	24	1	28	34	1	64	18	0	3	19	22	6
1975	67	19	4	19	27	0	50	14	0	4	13	17	5
1976	58	16	0	12	22	0	34	10	3	5	16	24	6
1977	45	12	2	15	11	3	31	7·5	1	1	12	14	4·5
1978	50	14	3	11	11	2	27	7	1	3	19	23	7
1979	64	18	5	24	17	0	46	12·5	0	1	17	18	5·5
1980	67	19	2	24	16	7	49	14	0	2	16	18	5
1981	60	17	3	28	18	3	52	14·5	0	2	6	8	2·5
1982	46	13	3	20	8	5	36	10·5	0	5	5	10	2·5
1983	46	13	3	25	8	5	41	11·5	0	3	2	5	1·5
1984	39	11	3	20	4	4	31	9	0	0	8	8	2

* Non-classified or nervous.
† Per 100,000 inhabitants.

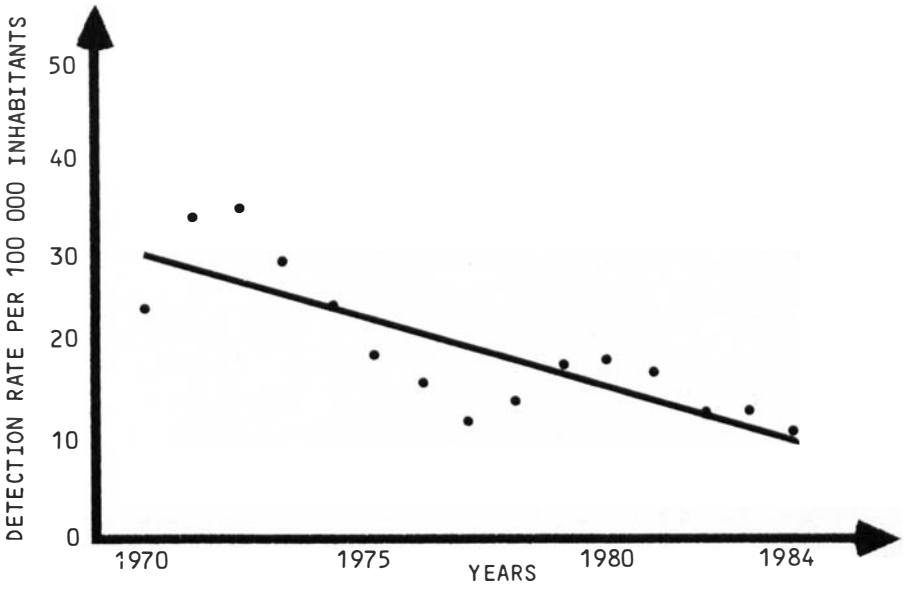

Figure 1. Evolution of the detection rate of leprosy (all cases) in Guadeloupe from 1970 to 1984. $y = -1{\cdot}44x + 29{\cdot}7$ ($r = 0{\cdot}81$).

and 1984 shows a regression of more than 60% (29 per 100,000 in 1970, 11 per 100,000 in 1984). As is shown in Figure 2, the regression of paucibacillary forms ($y = -0{\cdot}94$) is not significantly different from the regression of multibacillary forms ($y = -0{\cdot}45$). At the beginning of the 1970s the overall incidence of leprosy was two and a half times greater in children (below the age of 15) than in adults (Table 2). In 1984, conversely, the incidence in children was half that in adults. As is evident from Figure 3, the slope of the regression curve plotted from annual incidences is five times greater in children ($y = -3{\cdot}22$) than in adults ($y = -0{\cdot}67$).

RELAPSE RATE

Between 1 January 1970 and 31 December 1984, 117 relapses were noted among multibacillary patients. As is evident from Table 3, the yearly number of relapses was 7·8 on average, varying in the range, 3–14, without any marked tendency either to increase or to decrease over the years. If, as is also done in Table 3, the annual number of relapses is related to the annual total of multibacillary patients treated for more than 5 years with dapsone alone, which is on average 642, it is noted that the relapse rate is on average 1·25% per year (varying in the range 0·5–2·2%). Actually the 117 relapses correspond to 110 patients, 7 of whom had 2 successive relapses more than 5 years apart. If the relapse rate is related only to the 110 patients, the rate is 1·1% per year. The interval between the initial detection of leprosy and detection of the relapse is given in Table 4 which shows that relapses were observed as frequently after an interval of 5–9 years, 10–14 years, and so on, right up to 30 years or more and therefore seem randomly distributed. Ideally the risk of relapse should have had to be calculated by a computation of person-years exposure to risk of relapse which was not possible. However our data are consistant with the hypothesis that the risk of relapse increases with time. The average of the intervals between the initial detection of leprosy and detection of the relapse in the 110 patients is 19 years and is similar for men and women.

Between 1974 and 1980, 150 patients were given RMP in addition to their treatment with DDS. As regards 125 of them, RMP was prescribed for various reasons (reactions, at the patient's request,

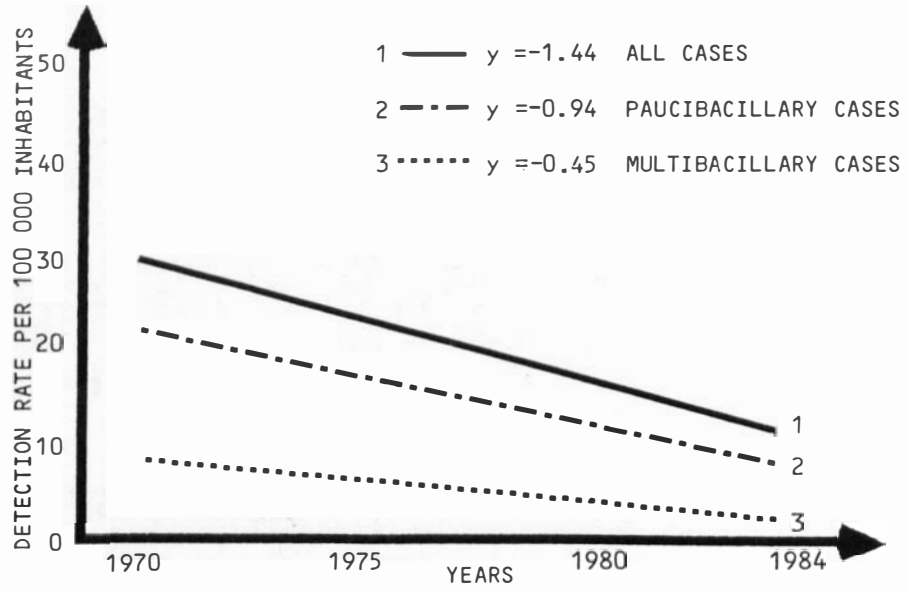

Figure 2. Evolution of the detection rate according to the type of leprosy in Guadeloupe from 1970 to 1984.

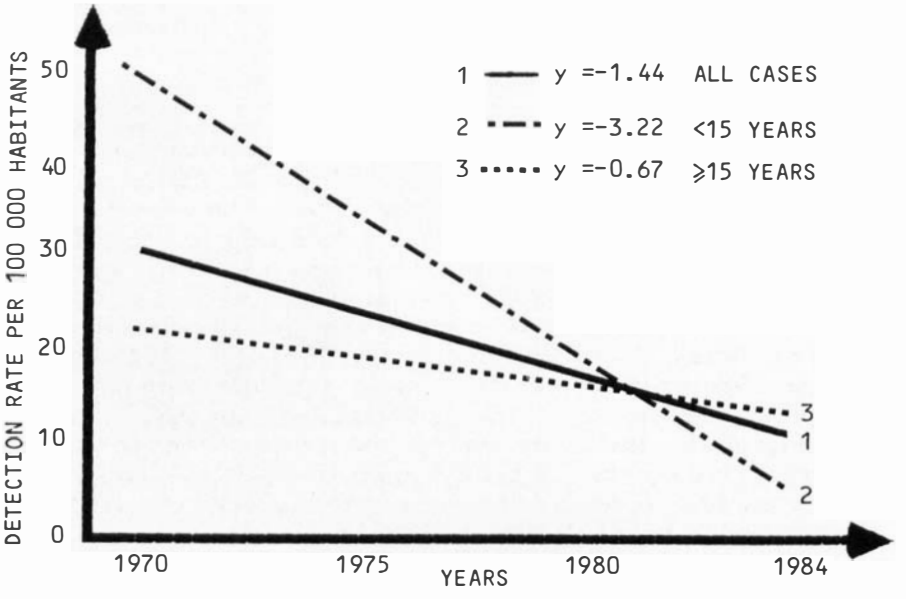

Figure 3. Evolution of the detection rate of leprosy according to the age in Guadeloupe from 1970 to 1984.

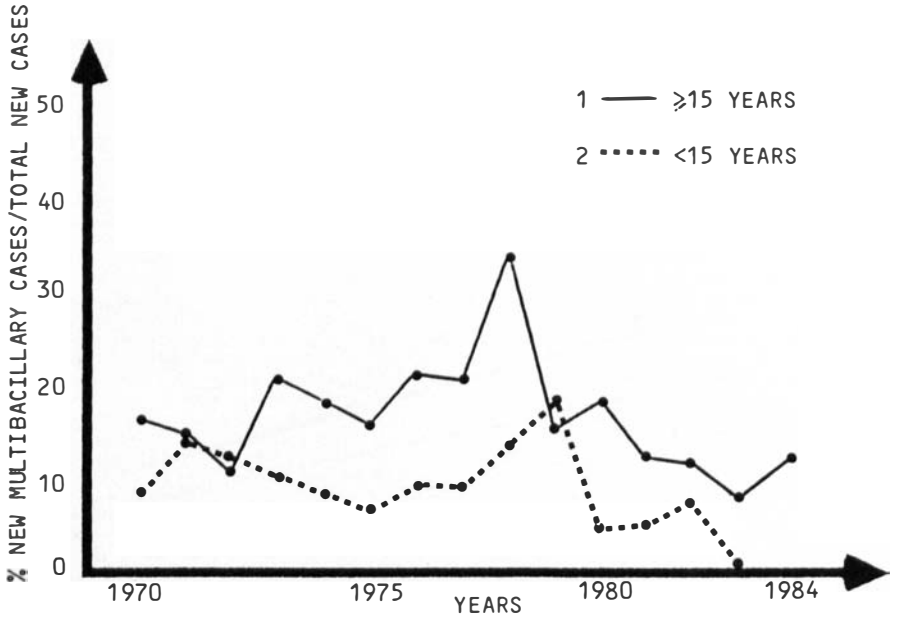

Figure 4. Evolution of the percentage of newly detected multibacillary cases/total of newly detected cases per year in Guadeloupe from 1970 to 1984.

Table 2. Detection rate of leprosy according to the age in Guadeloupe from 1970 to 1984

	< 15 YEARS*						≥ 15 YEARS					
	Total		Paucibacillary		Multibacillary		Total		Paucibacillary		Multibacillary	
Years	No.	rate†	No.	rate†	No.	rate†	No.	rate†	No.	rate†	No.	rate†
1970	42	42	35	35	7	7	43	17	29	11·5	14	5·5
1971	49	49	35	35	14	14	70	28	49	19·5	21	8·5
1972	56	56	42	42	14	14	63	25	49	19·5	14	5·5
1973	56	56	45	45	11	11	48	19	28	11	20	8
1974	42	42	35	35	7	7	44	17·5	28	11	16	6·5
1975	23	23	20	20	3	3	44	17·5	30	12	14	5·5
1976	11	11	9	9	2	2	47	19	27	11	20	8
1977	11	11	9	9	2	2	34	13·5	20	8	14	5·5
1978	19	19	14	14	5	5	31	12·5	10	4	21	8·5
1979	19	19	12	12	7	7	45	18	31	12·5	14	5·5
1980	23	23	21	21	2	2	44	17·5	28	11	16	6·5
1981	23	23	21	21	2	2	37	15	28	11	9	4
1982	7	7	6	6	1	1	39	15·5	30	12	9	3·5
1983	13	13	13	13	0	0	33	13	28	11	5	2
1984	6	6	6	6	0	0	33	13	28	11	8	3

* From 1970 to 1984 the population in Guadeloupe was 350,000 inhabitants: 100,000 in the age group 0–14 years and 250,000 in the age group 15 years or more.

† Per 100,000 inhabitants.

Table 3. Relapse rate of multibacillary cases of leprosy treated for life by DDS alone in Guadeloupe from 1970 to 1984

Years	Multibacillary patients treated for 5 years or more	Relapses	
		No.	%
1970	581	4	0·6
1971	618	6	1·0
1972	620	4	0·6
1973	628	3	0·5
1974	640	12	1·9
1975	630	5	0·8
1976	616	13	2·1
1977	630	14	2·2
1978	646	10	1·6
1979	644	7	1·1
1980	639	14	2·2
1981	643	8	1·7
1982	644	3	0·5
1983	587	7	1·2
1984	602	7	1·2
Total	9638	117	1·2
Mean	642	7·8	1·2

Table 4. Interval between the detection and the relapse in the 110 relapse cases of leprosy in Guadeloupe

No. of relapses	Interval (year)
22	5–9
17	10–14
21	15–19
16	20–24
18	25–29
16	≥30

Table 5. Dapsone sensitivity of *Mycobacterium leprae* in Guadeloupe from 1980 to 1984

Patients	Tests performed	Dapsone sensitive	Dapsone resistant		
			0·0001%*	0·001%*	0·01%*
New cases	27	13	12	2	0
Relapses	18	0	1	6	11

* Drug concentration in the mouse diet.

etc). These 125 patients were excluded from the study population of the 624 multibacillary patients treated for 5 years or longer with dapsone alone. None of them had relapsed by 1984. As regards the other 25 patients, RMP was prescribed on the occasion of a first relapse: 2 of these 25 patients suffered a second relapse, 6 years after the commencement of treatment in one case, 8 years after in the other. In both cases, the secondary relapse was confirmed by clinical and pathological examination and by microscopy, but the inoculation of mice with the biopsy material was negative despite a high bacteriological and morphological index. Both patients were treated daily with 10 mg/kg of rifampicin, 5 mg/kg of prothionamide and 100 mg/clofazimine. Both were uncompliant and were finally lost from the study.

Since 1980, biopsy has been a routine practice in patients suffering a relapse of multibacillary leprosy; the biopsy material is taken to inoculate mice and to study the sensitivity of *M. leprae* to RMP and to DDS.[10] The results of the sensitivity tests currently available are set out in Table 5 in parallel with the results of 27 new multibacillary cases detected since 1980. These results demonstrate that the *M. leprae* strains isolated from relapse cases were 100% resistant to DDS and of high degree in 61 %. By contrast, the *M. leprae* strains isolated from new multibacillary cases were 48% sensitive to DDS, 44% of low degree of resistance to DDS and 8% of intermediate degree of resistance.

COMPARISON BETWEEN DETECTION RATE AND RELAPSE RATE OF MULTIBACILLARY LEPROSY

The two sources of *M. leprae* infection in the population are new cases and relapses of multibacillary leprosy, which are the two active forms of the condition. Table 6, which summarizes the annual number of new cases and relapses between 1970 and 1984, shows that relapses constituted 17·5% of the sources of infection between 1970 and 1974, 33·7% between 1975 and 1979 and 44·3% between 1980 and 1984. Multibacillary relapses now constitute practically half the sources of infection in Guadeloupe; this is of major importance for leprosy control.

Discussion

The first point to emerge from the above data is the significant reduction of the leprosy detection rate in Guadeloupe between 1970 and 1984. For it to be considered that the reduction reflects an improvement in the epidemiological situation it is necessary to ensure that the available means of diagnosis and the access of patients to the health service have not become less. There have been two changes in the organization of leprosy control in Guadeloupe, one in 1971, the other in 1978. The object and the effect of these changes were to standardize and strengthen the activities of the leprosy control unit in particular case-finding and treatment. The significant reduction in detection rate observed between 1970 and 1984 is therefore more likely to reflect an improvement in the epidemiological situation, rather than a worsening of the means of detection. It may also be verified that the detection of new cases of leprosy has not been falsified by methodological devices; this may be done by selecting from among the methods recommended for the validation of detection rates[5] the method of studying the proportion of new multibacillary cases detected to the total number of new cases detected. During the 15 years covered by the study this proportion remained relatively stable between 1970 and 1977, but rose sharply during the years 1978 and 1979 owing to the unification and strengthening of the leprosy control unit, to which reference has also already been made, after which it fell slowly for adults and more rapidly for children. Given that the decline in multibacillary leprosy in children has not been offset by a symmetrical increase of multibacillary leprosy in adults, it may be considered that there has, in fact, been a decline of leprosy in Guadeloupe and that the detection rate reflects the incidence.

The second important point to be noted arising from the analysis of the epidemiological data

Table 6. Proportion of new cases and relapses among the active multibacillary cases of leprosy in Guadeloupe from 1970 to 1984

		Multibacillary active cases		
Years	Total	New cases: No.	Relapses: No.	
1970	25	21	4	
1971	39	33	6	
1972	33	29	4	17·5%
1973	34	31	3	
1974	34	22	12	
1975	22	17	5	
1976	37	24	13	
1977	28	14	14	33·7%
1978	33	23	10	
1979	25	18	7	
1980	32	18	14	
1981	16	8	8	
1982	13	10	3	44·3%
1983	12	5	7	
1984	15	8	7	
Total	398 (100%)	281 (71%)	117	29%

concerning leprosy in Guadeloupe between 1970 and 1984 is the annual rate of relapses of 1·2% among multibacillary patients detected more than 5 years previously. This 1·2% incidence is very similar to that reported in a study carried out in a leprosarium in Malaysia, although the latter study was concerned with relapses among multibacillary leprosy patients whose dapsone treatment had been discontinued.[6] Although considerable variations may be noted from year to year, the relapse rate is quite constant throughout the 15-year observation period. It could be considered that the relapses are due to discontinuation of treatment, mainly treatment with DDS alone, by patients despite the continuous urgings of the staff of the leprosy treatment unit to ensure regularity in following the course of treatment. Moreover, complete abandonment of treatment could be a possible explanation of the relapse. However, were the abandonment of treatment to be the cause of relapse, bacilli isolated from relapsing patients should be sensitive to DDS, but the opposite is noted when biopsies taken from the patients who relapse were systematically inoculated to the footpad of mice for drug sensitivity testing. Since biopsy material has only been systematically used for the inoculation of mice since 1980 it cannot be proved that the same applied between 1970 and 1980. Nevertheless it is likely that the intermediate to high degree of DDS resistance noted continuously since 1980 among patients who relapse was present in a considerable proportion of the patients who relapsed between 1970 and 1980. Should that be so, a high proportion of the relapses noted between 1970 and 1984 would be due to the acquisition of resistance to DDS in the course of treatment, possibly promoted by the irregular taking of DDS by the patients and not merely by the abandonment of treatment.

The incidence of relapses, 1·2% per year, among multibacillary patients treated for more than 5 years with DDS alone and the almost constant DDS resistance of *M. leprae* strains isolated from these patients are of great importance for leprosy control in Guadelope. Multibacillary patients who relapse are in fact sources of infection, as are new multibacillary cases. Between 1970 and 1974 relapses were only a modest proportion (17·5%) of the sources of infection whereas between 1980

and 1984 they were practically a half (44·3%). Should the present trend continue, with new cases continuing to decline at the same rate, the main source of contamination, and possibly the only source is likely to be multibacillary patients who relapse with DDS-resistant *M. leprae*. As relapses occur at a rate of 1·2% a year from the reservoir of multibacillary patients treated with DDS alone for more than 5 years, which is some 600 patients, the prevention of relapses among this reservoir is a priority for leprosy control in Guadeloupe. The difficulty is to ensure that these patients, the majority of whom are feeling in good health, accept additional treatment when they do not always understand why.

Acknowledgments

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References

[1] Cartel JL, Naudillon Y, Artus JC, Grosset JH. Epidemiologia de la lepra en Guadalupe de 1970 à 1983. *Boletin de la Oficina Sanitaria Panamericana*, 1985; **98:** 535–47.

[2] Cartel JL, Millan J, Guelpa-Lauras CC, Grosset JH. Hepatitis in leprosy patients treated by a daily combination of dapsone, rifampin and a thioamide. *Int J Lepr*, 1983; **51:** 461–5.

[3] Cartel JL, Naudillon Y, Artus JC, Grosset JH. Hepatotoxicity of the daily combination 5 mg/kg protionamide plus 5 mg/Kg rifampicin. *IntJ Lepr*, 1985; **53:** 15–18.

[4] INSEE. Recensement de la population en Guadeloupe en 1974 et 1982.

[5] Lechat MF, Vanderveken M. *Basic epidemiological indicators of monitoring leprosy control.* Sasakawa Memorial Health Foundation, Tokyo, 1983.

[6] Waters MFR et al. The rate of relapse in lepromatous leprosy following completion of twenty years of supervised sulphone therapy. *Lepr Rev*, 1986; **57:** 101–9.

[7] Organisation Mondiale de la Santé. *Guide pour la lutte anti-lépreuse.* Genève, 1980.

[8] OMSLEP, système d'enregistrement et de notification des malades de la lèpre. Unité d'Epidémiologie. Université Catholique de Louvain. Publié en collaboration avec l'O.M.S. Genève, 1981.

[9] Ridley DS, Jopling WH. Classification of leprosy according to immunity: a five group system. *Int J Lepr*, 1966; **34:** 255–73.

[10] Shepard CC. The experimental diseases that follow the injection of human leprosy bacilli into footpads of mice. *J exp Med*, 1960; **112:** 445–54.