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The efficacy of annual single-dose treatment with diethylcarbamazine citrate against diurnally subperiodic bancroftian filariasis in Samoa*

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Treatment of subperiodic bancroftian filariasis, which is endemic in Samoa, with diethylcarbamazine citrate (DEC-C) in single doses of 4 mg/kg, 6 mg/kg, and 8 mg/kg body weight was evaluated using the nuclepore filtration method (with 1 ml blood) and compared in terms of efficacy against the microfilariae (mf) and side-reactions produced. The 6 mg/kg single-dose treatment assessed at six months showed that the effect of DEC-C to eliminate microfilariae was closely associated with the pre-treatment microfilarial level. The treatment cured nearly 60% of the low-density carriers with ⩽20 mf/ml but only about 10% of the carriers with ⩾501 mf/ml. However, the percentage decrease in the microfilarial count, which averaged 89.3%, did not seem to differ greatly according to the level of the pre-treatment count. The age group 20–29 years showed a poorer response to the treatment compared with the other age groups. When the different dosage regimens (4 mg/kg, 6 mg/kg and 8 mg/kg) were compared at 6 and 12 months after treatment, the 6 mg/kg regimen was found to be more effective than the 4 mg/kg regimen in reducing the microfilarial count, and it produced fewer adverse reactions than the 8 mg/kg regimen. The comparison between the annual single-dose treatment at 6 mg/kg and the six-monthly two doses/year treatment at the same dosage (total 12 mg/kg/year) showed that the latter had little advantage over the former, thus indicating the effectiveness of the single-dose treatment for longer than six months.

Subperiodic bancroftian filariasis is endemic in Samoa and two nationwide mass treatment campaigns, using diethylcarbamazine citrate (DEC-C) in total dosages of 90 mg/kg and 72 mg/kg body weight were successfully carried out in 1965–66 and 1971, respectively. As a result, the microfilarial (mf) prevalence rate in blood samples from the population was reduced drastically from 21.1% in 1964 to 0.24% in 1972. A decrease in clinical cases was also apparent, but the infection still remained endemic at a low level.

Recently Kimura et al. showed that the prevalence rate of microfilaraemia in 1979 was once again up to 20% among adult males, and it became apparent that the selective treatment of known positive cases by the Samoan national team could not by itself maintain the low level of endemicity achieved by the two mass campaigns (*1*). In this situation, a new DEC-C treatment regimen, suitable for a mass campaign, was sought; the selected regimen would have to be effective, inexpensive and acceptable to the Samoan people, many of whom had lost their enthusiasm for participating in any year-long campaign.

Since Merlin et al. (*2*) had reported that in French Polynesia a spaced single-dose DEC-C treatment, given either 6 monthly or annually, had given encouraging results in reducing the mf prevalence rate and density, it was decided to try this method, which had the advantages of simplicity and low cost. The present study was designed to test several different schemes of spaced-dose treatment in the Samoan population, taking into account the side-effects produced by the different regimens.

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The object of the present study was to evaluate and compare DEC-C single dose/year regimens at 4 mg/kg, 6 mg/kg and 8 mg/kg body weight; to compare a DEC-C single dose/year regimen at 6 mg/kg with a 6-monthly two doses/year treatment at 6 mg/kg (total 12 mg/kg/year); to study the outcome of a village-level mass treatment by the single dose/year treatment in several sample villages; and to study the side-reactions caused by the single-dose DEC-C regimens.

MATERIALS AND METHODS

A total of 158 carriers of *Wuchereria bancrofti* microfilariae from 9 villages in Upolu Island, who had been identified by the nuclepore filtration method (using 1 ml blood), were treated with DEC-C in a single dose of 6 mg/kg body weight. Six months later, 112 of these treated subjects were traced and re-examined by the same method; immediately afterwards 68 of them in seven villages were given a second treatment at the same dosage, the remaining 44 persons in two other villages being left untreated for another 6 months. At the second follow-up study, one year after the first treatment, only 96 out of the 112 treated people could be traced, 41 of whom had received a single dose and 55 two doses of DEC-C.

In another group of 145 microfilaria carriers, 73 were treated with a single dose of DEC-C at 8 mg/kg body weight and 72 with one dose at 4 mg/kg. Follow-up studies were conducted after 6 months (97 subjects traced) and 12 months (96 subjects traced).

In six villages, the nuclepore filtration method was used in blood surveys of the whole population (excluding infants under 1 year of age) both before and one year after DEC-C treatment. In three of these villages, mass single-dose treatment was given to all the inhabitants except children under 3 years of age, using a different dosage (4 mg/kg, 6 mg/kg, or 8 mg/kg) in each village. In the fourth and fifth villages, selective single-dose treatment was given to the mf-positive subjects detected at the first blood survey, using 6 mg/kg in one village and 8 mg/kg in the other. In the sixth village, initial mass treatment in a dose of 6 mg/kg was given, followed after 6 months by a second treatment of the known mf-positive subjects using the same dosage.

No assessment of signs and symptoms was made at the time of initial treatment because of the disadvantages of emphasizing this aspect of the treatment. However, between 5 and 15 days after the single-dose treatment at 4 mg/kg, 6 mg/kg or 8 mg/kg, most of the treated microfilaria carriers, and as many treated mf-negative subjects as possible were questioned about the occurrence of side-reactions that might have been produced by DEC-C. These reactions included gastrointestinal signs and symptoms (nausea, vomiting, abdominal discomfort or pain, diarrhoea, etc.), allergic reactions (fever, itching, and rash), and less-well-defined symptoms such as headache, dizziness, dullness, weakness, drowsiness, and lumbar or other joint pains.

All doses were given under direct observation. The DEC-C tablets used had been kept in sealed tins for nine years under tropical climatic conditions before being used, but a quality screening test (kindly performed by the Wellcome Foundation Research Laboratories in 1979) showed that the drug was still 100% active and contained no toxic by-products.

This study was started early in 1979 and completed in May 1981.

RESULTS

The effect of DEC-C treatment was assessed according to three indicators.

(1) The rate of successful treatment, which is the proportion of mf-positive persons treated in whom there was a reduction in the microfilarial count.

(2) The percentage cure rate, i.e., the proportion of mf-positive persons treated who became mf negative after treatment.

(3) The decrease in the microfilarial count following treatment.

Comparison of the effect of DEC-C by the pre-treatment microfilarial level, age and sex

For this study, data obtained from the 6 mg/kg treatment group at the 6-month follow-up were analysed; 112 mf-positive subjects, as determined by the nuclepore filtration method, were available.

The DEC-C effect was first analysed by the pre-treatment microfilarial level of carriers and the results are summarized in Table 1. The rate of successful treatment appeared to be higher in persons whose original microfilarial count was high, but it was not statistically significant ($P = 0.15$). The cure rate of microfilaraemia had a strong association with the pre-treatment level of the microfilarial count ($P < 0.005$). Nearly 60% of the low-density carriers, who were defined as carriers with $\leqslant 20$ mf/ml, became negative after treatment, whereas the corresponding figure in those whose original count was over 500 mf/ml was only about 10%. From our previous study (*3*), it is known that 15.4% of the low-density carriers and 2.3% of carriers with a microfilarial count in the range 21–500/ml, who had been left untreated, showed up as negative when re-examined 60–252 days later. Even if allowance is made for such spontaneous negative conversions, the difference between the

Table 1. Effect of DEC-C single-dose treatment at 6 mg/kg assessed at 6 months after treatment by the nuclepore filtration method

	Initial microfilarial level (mf/ml)					
	1–20	21–200	201–500	501–1000	⩾1001	Total
No. examined (original mf-positive)	29	29	18	17	19	112
No. successfully treated	24 (82.8)[a]	25 (86.2)	17 (94.4)	17 (100)	19 (100)	102 (91.1)
No. mf-negative after treatment (cure rate)	17 (58.6)	5 (17.2)	10 (55.6)	2 (11.8)	2 (10.5)	36 (32.1)
Decrease in mf count expressed as mean of log (mf + 1)						
Before treatment (A)	0.848	1.823	2.529	2.825	3.354	2.096
After treatment (B)	0.379	1.089	0.889	1.904	1.854	1.126
Change	0.469	0.734	1.639	0.921	1.500	0.969
% decrease[b]	66.0	81.6	97.7	88.0	96.8	89.3

[a] Figures in parentheses are percentages.
[b] Calculated as 100 x (antilog (A) – antilog (B))/antilog (A).

groups with different microfilarial levels was highly significant ($P < 0.001$).

In order to study the decrease in the microfilarial count as a result of treatment, the mean of log (mf count + 1) at each microfilarial level was computed, before and after treatment, and then the difference was expressed as the percentage decrease. The decrease ranged from 66.0% to 97.7%, with an average of 89.3%.

Comparisons by age group and by sex are summarized in Table 2. No difference was found by age in the occurrence of successful treatment and cure rate. Also, there was no significant difference in the mean of log (mf count + 1) in each group before and after treatment. However, the change in the microfilarial count after treatment was significantly different ($P < 0.05$) between those in the 20–29-year age group, where the DEC-C had a very poor effect, and those in the other age groups.

A comparison by sex showed no significant differences in the occurrence of successful treatment, cure rate, or decrease in microfilarial counts.

Table 2. Effect of DEC-C single-dose treatment at 6 mg/kg assessed at 6 months after treatment by the nuclepore filtration method: classification by sex and age group

	Sex		Age group (years)				
	Male	Female	⩽19	20–29	30–39	⩾40	All persons
No. examined (original mf-positive)	79	33	18	18	28	48	112
No. successfully treated	71 (89.9)[a]	31 (93.9)	16 (88.9)	14 (77.8)	26 (92.9)	46 (95.8)	102 (91.1)
No. mf-negative after treatment	24 (30.4)	12 (36.4)	6 (33.3)	4 (22.2)	8 (28.6)	18 (37.5)	36 (32.1)
Decrease in mf count expressed as mean of log (mf + 1)							
Before treatment (A)	2.119	2.040	1.972	1.924	2.212	2.139	2.096
After treatment (B)	1.194	0.966	1.073	1.502	1.039	1.057	1.126
Change	0.925	1.075	0.899	0.422	1.173	1.082	0.969
% decrease[b]	88.1	91.6	87.4	62.1	93.3	91.7	89.3

[a] Figures in parentheses are percentages.
[b] Calculated as 100 x (antilog (A) – antilog (B))/antilog (A).

Comparison between a single annual dose of DEC-C and two annual doses given at 6-monthly intervals

A total of 112 mf-positive cases determined by the nuclepore filtration method were treated with a single dose of DEC-C at 6 mg/kg and their microfilarial counts were again determined at follow-up 6 months later. The changes in microfilarial counts are shown in Table 3 (see (i)). Of these 112 cases, 55 were treated at this follow-up with the same dose a second time, and 6 months later (i.e., one year after the first dose) their microfilarial counts were again determined. A third group of 41 mf-positive subjects were treated initially and their counts determined at 12 months without any intervening dosage. Conversion rates for these latter two groups are also shown in Table 3 (see (ii) and (iii)). A comparison of efficacy at 12 months was made between the single-dose treatment and the two 6-monthly treatments. By application of the conversion percentages of the two 6-month periods (Table 3, (i) and (ii)) to the pre-treatment distribution of the microfilarial counts of the 41 mf-positive subjects (Table 3, (iii)), it was possible to estimate the distribution of microfilarial counts at 12 months that would be expected if the 41 subjects had been treated 6-monthly (Table 4). Although this was a very small group, the comparison suggests that there is little advantage to be gained from a six-month dose regimen rather than a 12-month one.

Table 3. Changes in microfilarial counts following various regimens of DEC-C treatment at 6 mg/kg

		Microfilarial count						No. of persons[a]
		0	1–20	21–200	201–500	501–1000	⩾1001	
	Initial count:	*Count at 6 months:*						
(i) Conversion percentages in microfilarial counts of 112 subjects, six months after treatment with a single dose of DEC-C	⩽20	58.6	31.0	10.3				29
	21–200	17.2	44.8	31.0	6.9			29
	201–500	55.6	–	33.3	11.1			18
	501–1000	11.8	–	58.8	23.5	5.9		17
	⩾1001	10.5	26.3	21.1	15.8	10.5	15.8	19
	No. of persons[b]	36	27	32	11	3	3	112
	Count at 6 months:	*Count at 12 months:*						
(ii) Conversion percentages in microfilarial counts of 55 subjects from (i), six months after a second dose of DEC-C	0	93.7	6.3					16
	1–20	72.7	27.3					11
	21–200	14.3	28.6	52.4	4.8			21
	201–500	20.0	20.0	60.0				5
	501–1000	(11.8)[c]	(–)	(58.8)	(23.5)	(5.9)		0
	⩾1001				50.0	50.0		2
	No. of persons[b]	27	11	14	2	1	0	55
	Initial count:	*Count at 12 months:*						
(iii) Conversion percentages in microfilarial counts of 41 subjects, twelve months after treatment with a single dose of DEC-C	20	100.0						11
	21–200	50.0	21.4	21.4	7.1			14
	201–500	28.6	71.4					7
	501–1000	20.0	–	20.0	40.0	20.0		5
	⩾1001	25.0	25.0	25.0	–	–	25.0	4
	No. of persons[b]	22	9	5	3	1	1	41

[a] Pre-treatment distribution.

[b] Post-treatment distribution.

[c] As the calculation was not possible due to the zero frequency, the figures in (i) for the same microfilarial count were utilized.

Table 4. Observed and estimated distribution of microfilarial counts at 12 months if the subjects had been treated 6-monthly

	Microfilarial counts at 12 months						
	0	1–20	21–200	201–500	501–1000	⩾1001	Total
No. observed	22	9	5	3	1	1	41
No. expected	23.2	7.8	8.6	1.0	0.4	0	41

Comparison of the 4 mg, 6 mg, and 8 mg/kg dosage regimens

The successful treatment rate, the cure rate and the decrease in the microfilarial count were compared at 6 and 12 months after the single-dose treatment at the above dosages (Table 5). The results indicated that there were no differences in the occurrence of successful treatment and the cure rate between the three dosage levels, either at 6 or 12 months. However, the decrease in the microfilarial count did show a clear difference. At 6 months, a significant difference was found in the change of microfilarial count ($P < 0.05$), although the mean values of the counts before and after treatment were not different. At 12 months, there were significant differences in the post-treatment mean ($P < 0.05$) and in the change in counts ($P < 0.01$) for the three dosage levels. The 8 mg/kg treatment, which produced the greatest reduction in microfilarial count at 6 months, was not very different from the 6 mg/kg dosage level, but the 4 mg/kg dosage produced a less marked fall in counts than either the 6 mg/kg dosage ($P < 0.005$) or the 8 mg/kg dosage ($P < 0.01$).

Comparison of mass treatment and selective treatment of mf-positive subjects

About one year after the initial prevalence study and the first treatment with DEC-C which followed it, a second total blood survey was conducted in the six villages. Mass treatment was given in four of these villages; in the remaining two, only the mf-positive cases were treated. The results are summarized in Table 6.

Regardless of whether mass or selective treatment was used, the mf prevalence rate in each village did not decrease noticeably. In fact, some villages showed an even higher prevalence rate after the treatment. This is probably due to the considerable movement of the people from one village to another. At one village, for example, more than half of the mf-positive individuals detected in 1979 could not be traced one year later. In four villages, some 40% of the positives detected in 1980 were newcomers to these villages.

Side-reactions by sex, age and microfilarial count

Answers concerning side-reactions were obtained from 119 people (51 mf-positive and 68 mf-negative

Table 5. Comparison of the effects of different DEC-C dosages assessed at 6 and 12 months after treatment

	Dosages in the 6-month follow-up			Dosages in the 12-month follow-up		
	4 mg/kg	6 mg/kg	8 mg/kg	4 mg/kg	6 mg/kg	8 mg/kg
No. examined	47	112	50	51	41	45
No. successfully treated	45 (95.7)[a]	102 (91.1)	50 (100)	42 (82.4)	38 (92.7)	43 (95.6)
No. mf-negative after treatment (cure rate)	13 (27.7)	36 (32.1)	22 (44.0)	15 (29.4)	22 (53.7)	18 (40.0)
Decrease in mf count, expressed as mean of log (mf + 1)						
Before treatment (A)	2.278	2.096	2.250	2.117	2.003	2.198
After treatment (B)	1.271	1.126	0.900	1.384	0.751	1.010
Change	1.006	0.969	1.350	0.733	1.251	1.188
% decrease[b]	90.1	89.3	95.6	81.5	94.4	93.5

[a] Figures in parentheses are percentages.

[b] Calculated as 100 x (antilog (A) – antilog (B))/antilog (A).

Table 6. Results of total blood surveys performed before and 12 months after different regimens of DEC-C mass treatment in four villages and the treatment of only mf positives in two villages

		Mass treatment				Only mf-positive subjects treated	
	1979→1980[a]	4 mg/kg	6 mg/kg	6 mg/kg	8 mg/kg	6 mg/kg	8 mg/kg
Data from mf-positive subjects in 1979:	(+) → (+)[b]	18(60.0)[c]	26(48.1)	15(48.4)	16(47.1)	7(25.0)	11(42.3)
	(+) → (−)[b]	6(20.0)	17(31.5)	13(41.9)	6(17.6)	11(39.3)	1 (3.8)
	(+) → ?[d]	6(20.0)	11(20.4)	3 (9.7)	12(35.3)	10(35.7)	14(53.8)
	No. positive	30(100)	54(100)	31(100)	34(100)	28(100)	26(100)
No. examined in 1979		291	446	443	258	500	317
Data from mf-positive subjects in 1980:	(+) → (+)	18(46.2)	26(70.3)	15(50.0)	16(53.3)	7(30.4)	11(45.8)
	(−) → (+)	5(12.8)	5(13.5)	3(10.0)	4(13.3)	7(30.4)	4(16.7)
	?[d] → (+)	16(41.0)	6(16.2)	12(40.0)	10(33.3)	9(39.1)	9(37.5)
	No. positive	39(100)	37(100)	30(100)	30(100)	23(100)	24(100)
No. examined in 1980		302	402	448	201	622	264
Village prevalence rate (%)	1979	10.3	12.1	7.0	13.2	5.6	8.2
	1980	12.9	9.2	6.7	14.9	3.7	9.1

[a] As the surveys were not always conducted exactly at 12 months interval, some results were obtained early in 1981.
[b] (+) = microfilaria positive; (−) = microfilaria negative.
[c] Figures in parentheses are percentages in relation to the number positive.
[d] Not registered in 1979 or not examined in 1980, i.e., newcomers or absentees in the 1980 survey.

individuals) treated at 4 mg/kg, 230 people (142 mf-positive and 88 mf-negative) treated at 6 mg/kg, and 109 people (68 mf-positive and 41 mf-negative) treated at 8 mg/kg. No unusual reactions were recorded throughout the study.

A total of 230 people treated at 6 mg/kg were analysed; 57.0% of the mf-positive and 33.0% of the mf-negative subjects experienced side-reactions of some sort, among which the less-well-defined symptoms were the most frequent.

Table 7 (i) summarizes the reactions classified by sex and by age group among the treated mf-positive subjects. There was no difference between the sexes with regard to side-reactions of any type. A significant difference was observed in the occurrence of "any reaction" when analysed by age group ($P < 0.025$). This was due to the very high occurrence of reactions in the age group 20–29 years (86.4%). A similar tendency was observed when the combined data of 4 mg/kg and 8 mg/kg treatments were compared by age group, but the difference was not significant. There was no evidence that the 20–29 year age group had a higher mean microfilarial density than the other groups.

Table 7 (ii) shows the relation between the occurrence of side-reactions and the pre-treatment microfilarial count. Very strong associations were observed in the less-well-defined symptoms and in "any reaction". The occurrence of allergic symptoms was also associated with the microfilarial count at a significant level ($P < 0.05$). Although more gastro-intestinal symptoms were noticed at the higher microfilarial levels, this was not significant. The treated mf-negative subjects and the low-density carriers did not show any difference.

Comparison of the frequency of side-reactions in association with different dosage schemes

Before comparing the frequency of side-reactions among the populations of mf-positive people receiving treatment at three different dosage levels, it was necessary to compare first the microfilarial density (mean of log mf) and the variance among the three groups. This comparison revealed no difference in the mean ($P > 0.05$) or the variance. Another factor which may influence the result is the proportion of persons in the age group 20–29 years in each treated population. The 4 mg/kg, 6 mg/kg, and 8 mg/kg treatments included respectively 7 (13.7%), 22 (15.5%) and 8 (11.8%) mf-positive persons in this age group. The results of the comparison are shown in Table 8. There was no difference in any of the individually categorized reactions, but there was a signifi-

Table 7. Side-reactions produced by DEC-C single-dose treatment (6 mg/kg)

(i) By sex and age group for mf-positive persons

Reactions	Sex		Age group (years)				All persons
	Male	Female	1–19	20–29	30–39	⩾40	
Gastrointestinal	18 (17.6)[a]	8 (20.0)	5 (17.9)	6 (27.3)	8 (22.2)	7 (12.5)	26 (18.3)
Allergic	20 (19.6)	9 (22.5)	5 (17.9)	6 (27.3)	6 (16.7)	12 (21.4)	29 (20.4)
Less-well-defined	55 (53.9)	19 (47.5)	12 (42.9)	14 (63.6)	18 (50.0)	30 (53.6)	74 (52.1)
Any reaction	61 (59.8)	20 (50.0)	13 (46.4)	19 (86.4)	18 (50.0)	31 (55.4)	81 (57.0)
No. of persons	102 (100)	40 (100)	28 (100)	22 (100)	36 (100)	56 (100)	142 (100)

(ii) By pre-treatment microfilarial level (mf/ml)

Reactions	Microfilarial counts				Total
	0	1–20	21–500	⩾501	
Gastrointestinal	10 (11.4)[a]	4 (12.9)	10 (15.2)	12 (26.7)	36 (15.7)
Allergic	8 (9.1)	3 (9.7)	15 (22.7)	11 (24.4)	37 (16.1)
Less-well-defined	22 (25.0)	8 (25.8)	35 (53.0)	31 (68.9)	96 (41.7)
Any reaction	29 (33.0)	11 (35.5)	37 (56.1)	33 (73.3)	110 (47.8)
No. of persons	88 (100)	31 (100)	66 (100)	45 (100)	230 (100)

[a] Figures in parentheses are percentages in relation to the total number of persons.

Table 8. Side-reactions produced by DEC-C treatment at various dosage regimens among the treated mf-positive and mf-negative subjects

Reactions	Mf-positive subjects				Mf-negative subjects			
	4 mg/kg	6 mg/kg	8 mg/kg	Total	4 mg/kg	6 mg/kg	8 mg/kg	Total
Gastrointestinal	16 (31.4)[a]	26 (18.3)	20 (29.4)	62 (23.8)	8 (11.8)	10 (11.4)	10 (24.4)	28 (14.2)
Allergic	17 (33.3)	29 (20.4)	22 (32.4)	68 (26.1)	4 (5.9)	8 (9.1)	5 (12.2)	17 (8.6)
Less-well-defined	24 (47.1)	74 (52.1)	41 (60.3)	139 (53.3)	16 (23.5)	22 (25.0)	11 (26.8)	49 (24.9)
Any reaction	30 (58.8)	81 (57.0)	53 (77.9)	164 (62.8)	19 (27.9)	29 (33.0)	15 (36.6)	63 (32.0)
No. of persons	51 (100)	142 (100)	68 (100)	261 (100)	68 (100)	88 (100)	41 (100)	197 (100)

[a] Figures in parentheses are percentages in relation to the total number of persons.

cant difference in the occurrence of "any reaction" ($P < 0.025$). This was largely due to the very high occurrence of reactions among those treated at 8 mg/kg.

When the treated mf-negative subjects were compared, no difference was found between the various dosage regimens.

DISCUSSION

It is generally considered that mass treatment with DEC-C at a total dosage of 72 mg/kg of body weight is effective in reducing the mf prevalence rates and densities, and therefore the amount of transmission of *W. bancrofti*. However, this conventional method has several disadvantages, chief of which is that a long period (up to one year) is often required to complete the numerous doses in a course of treatment. In Samoa, where two year-long multi-dose mass treatment campaigns had been conducted in the past, it was considered that another round of such treatment would not be accepted by the people with sufficient enthusiasm to guarantee success. In addition, past experience had shown that quite large numbers of the DEC-C tablets, which were distributed to individual persons, were probably wasted during the two campaigns.

By contrast, an annual single-dose treatment with DEC-C has definite advantages in its simplicity and low operational cost. The disadvantage of this method is that it has to be repeated annually for several years in the form of mass treatment. It may be possible to facilitate the process of treatment by fixing national days for public health activities, during which the DEC-C tablets will be distributed by the villagers themselves as if it is an annual observance.

The efficacy of DEC-C single-dose treatment at 6 mg/kg was assessed at 6 months according to pre-treatment microfilarial counts, age, and sex. As found by several workers (*4–8*), the success of DEC-C in eliminating microfilariae was closely related to the pre-treatment microfilarial count. However, in our study, the average percentage decrease in microfilarial count did not seem to differ greatly according to the level of the pre-treatment count, although an exceptionally low decrease (66.0%) was observed in the low-density group. The age group 20–29 years showed a poor response to the treatment as it did to the reduction in microfilarial count, although no difference was recognized between the two sexes. It is interesting that persons in this same age group experienced more side-reactions than did those in the other age groups. The reasons are not clear.

The comparison between annual single-dose and the 6-monthly (two doses/year) treatment regimens indicated that the latter had little advantage over the former. There was a slightly greater reduction in microfilariae but in view of the enormous practical difficulties in carrying out any nationwide treatment scheme, the advantage to be gained from having to do this once yearly rather than every 6 months must far outweigh any marginal loss in efficacy. However, this conclusion must raise a query about the repeated annual treatments because it may be that the effect of treatment persists beyond 12 months just as it appears to persist beyond 6 months. In the present study, no experiment could be set up to test this possibility, and another study will be needed to clarify for how long a single-dose treatment can be effective beyond 12 months.

The 4 mg/kg, 6 mg/kg, and 8 mg/kg dosages were assessed at 6 and 12 months. The 6-month assessment was largely suggestive of a dose-dependent effectiveness of DEC-C in terms of cure rate and decrease in microfilarial count. The 8 mg/kg treatment maintained the same results at 12 months as were seen at 6 months, while in the 4 mg/kg treatment, the microfilarial counts, which had been suppressed at 6 months, resurged slightly at 12 months. The 6 mg/kg treatment seemed to have given better results at 12 months than at 6 months. Taking account of the side-reactions, which were experienced more often with the 8 mg/kg treatment, the 6 mg/kg regimen was considered the best of the three dosage levels, giving a cure rate of 53.7% and a reduction in the microfilarial count of 94.4% one year after the treatment.

There are several reports on the efficacy of the DEC single-dose treatment at 6 mg/kg. Rachou & Scaff (*9*) in Brazil showed that this regimen reduced the mf prevalence rate from 100% to 62% and diminished the total microfilarial count by 91.4% when evaluated at 12 months. In French Polynesia, Merlin et al. (*2*) reported a 60% cure rate and 71% reduction in the total number of microfilariae. Laigret et al. (*10*, *11*) further confirmed the effectiveness of this regimen using 120 mf-positive subjects. They reported that three annual treatments reduced their mf-positive rate successively from 100% to 50%, 25%, and 12%. This annual single-dose treatment was applied to a Polynesian population of 50 000 persons for four years and, despite the fact that an average of only 2.76 doses/person were actually consumed in those four years, it resulted in a reduction of prevalence from 4.4% to 1.9% and a reduction in the average microfilarial count among carriers from 21.2 to 11.7 per 20 mm^3.

The effect of mass treatment in a small number of villages was somewhat disappointing in Samoa, probably because of the influx of new mf-positive cases from untreated neighbouring villages. The movement of people, especially adult males, is one of the main factors acting against good coverage in DEC-C distri-

bution programmes. In other words, the highest prevalence of filariasis would be expected among those who often migrate from place to place. The effects of an influx of untreated carriers were discussed by Burnett & Mataika (*6*) in Fiji, and their data on population movements should serve as a warning that small, piecemeal campaigns are liable to run into difficulties. These findings indicate the necessity for undertaking a nationwide mass-treatment campaign on an annual single-dose regimen, which would be quite realistic in a small island country like Samoa, provided that the whole population can be covered in a relatively short period of some 2–6 months.

The results of our study on side-reactions to DEC-C treatment were almost identical with those of some previous reports (*7*, *12*, *13*) in that the reactions were closely associated with the pre-treatment microfilarial level but not with the subject's sex. As mentioned previously, mf-positive persons in the age group 20–29 years experienced definitely more side-reactions than did those in the other age groups, but the reason for this is unknown. Another finding difficult to explain was that the 4 mg/kg treatment produced more gastrointestinal and allergic reactions among the treated mf-positive persons (at a nearly significant level) than did the 6 mg/kg treatment, whereas the occurrence of reactions seemed to be dose-dependent (not significant) among the treated mf-negatives. Sasa et al. (*12*) have likewise reported that a 2 mg/kg treatment caused more fever reactions than a 8 mg/kg treatment.

The present study has confirmed the usefulness of the DEC-C single-dose treatment in controlling subperiodic bancroftian filariasis. However, it must be emphasized that the use of this method does not aim to eradicate filariasis in a short period, but rather to keep clinical filariasis down to a level at which it is no longer an important public health problem in the community (*14*, *15*). We have reported elsewhere (*3*) that low-density carriers cannot be considered as an important source of infection as a whole, since the proportion of mosquito infectivity produced by them was only 2.2% of the total mosquito infectivity produced by carriers of microfilaria with all levels of counts. Thus, the approximately 90% decrease in microfilarial count to be expected following the first 6 mg/kg annual treatment is likely to bring about a substantial reduction in the transmission potential.

This method of annual single-dose treatment could probably be best applied in areas where the mf prevalence rate has been reduced to a hypoendemic level by the conventional 72 mg/kg treatment, and where the population is of reasonable size and the inhabitants cooperative.

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RÉSUMÉ

EFFICACITÉ D'UNE DOSE UNIQUE ANNUELLE DE CITRATE DE DIÉTHYLCARBAMAZINE POUR LE TRAITEMENT DE LA FILARIOSE SUBPÉRIODIQUE DIURNE DUE À *W. BANCROFTI* AU SAMOA

Au Samoa, où la filariose subpériodique à *W. bancrofti* est endémique, des études ont été effectuées du début de 1979 à mai 1981 pour évaluer et comparer des posologies différentes de citrate de diéthylcarbamazine (DEC-C) administré en une seule dose par an (4 mg/kg, 6 mg/kg, et 8 mg/kg), pour comparer un traitement par une dose unique annuelle de DEC-C de 6 mg/kg avec un traitement par la même dose administrée tous les six mois (deux doses par an, total 12 mg/kg par an), pour étudier le résultat du traitement de masse d'un village par une dose unique annuelle, et pour étudier les effets secondaires dus aux différentes posologies.

Les résultats ont été examinés 6 et 12 mois après le traitement en utilisant la méthode de filtration sur Nuclepore, et les effets secondaires ont été étudiés entre cinq et quinze jours après le traitement initial par une dose unique.

L'effet du DEC-C sur la disparition des microfilaires dépendait des numérations de microfilaires avant traitement. Le traitement par une dose unique de 6 mg/kg a guéri près de 60% des porteurs de faibles densités de microfilaires ($\leqslant$20 mf/ml), ceci d'après l'évaluation faite à six mois, alors que seulement 10% des porteurs étaient guéris par ce traitement quand le nombre de microfilaires avant traitement dépassait 500 par ml.

Cependant, la diminution en pourcentage du nombre de microfilaires, qui était de 89,3% en moyenne, n'a pas paru varier beaucoup quelle que soit la numération avant traitement. La réponse au traitement était nettement plus faible dans le groupe d'âge 20–29 ans que dans les autres groupes d'âge, ceci restant inexpliqué.

La comparaison entre le traitement par une dose unique annuelle de 6 mg/kg et par deux doses par an, faite douze mois après le premier traitement, n'a pas montré de différence très nette, ce qui indiquerait que la dose unique a un effet qui persiste au-delà de six mois.

La comparaison, en termes d'efficacité et de fréquence des effets secondaires, des différentes doses (4 mg/kg, 6 mg/kg et 8 mg/kg) a montré qu'une dose annuelle de 6 mg/kg était plus efficace que la dose de 4 mg/kg pour réduire la densité de microfilaires. Les effets secondaires étaient moins fréquents qu'avec la dose de 8 mg/kg chez les sujets positifs (porteurs de microfilaires) traités. Ces résultats montrent que la dose unique annuelle de 6 mg/kg est à la fois la plus efficace et la mieux tolérée.

Le traitement par une dose unique de 6 mg/kg a provoqué des effets secondaires (gastro-intestinaux, allergiques et avec des signes et symptômes moins bien définis) chez 57% des sujets positifs et 33% des sujets négatifs traités. En général, la fréquence des réactions était en relation étroite avec le taux microfilarien pré-thérapeutique, mais pas avec le sexe des sujets. Les personnes du groupe d'âge 20–29 ans ont présenté davantage d'effets secondaires que celles des autres groupes d'âge, pour une raison encore inconnue.

De larges mouvements de population provoquant des sorties et des entrées de cas positifs ont été observés au Samoa; il faut en conclure qu'un programme de lutte à grande échelle devra pour être efficace être exécuté sur une période de temps relativement courte.

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