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AN EFFECTIVE PROGRAMME FOR THE CONTROL OF FILARIASIS IN TAHITI

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SYNOPSIS

An effective filariasis research and control programme has been recently established in Tahiti. This article describes the methods used for preliminary investigation of the clinical manifestations of the disease, the prevalence of the parasite and the role of the vector mosquitos. Control was effected by eliminating mosquito breeding-places and administering diethylcarbamazine to the population. An estimate is made of the costs and comparative value of the various procedures which were tried.

A high prevalence of filariasis, including elephantiasis, has long been noted in the Society Islands (Gros,[11] Tribondeau,[40] Villaret,[41] and Iyengar [16]). Galliard, Mille & Robinson[10] and Beye et al.[4] showed more than 30% of the population of Tahiti to harbour microfilariae; 20% or more exhibited acute filariasis or lymphangitis, and from 5% to 10% showed some degree of elephantiasis. Such findings constituted a medical, social and economic problem of significance. That the prevalence of microfilariae was higher in Tahiti than in other areas of Polynesia when this study began is apparent by comparing the findings in Tahiti with those of the Administration of Fiji during the period 1947-52 (as cited by Iyengar [16]), of McCarthy & Fitzgerald [27] in Western Samoa, and of Jachowski & Otto [20] in American Samoa, who reported prevalence rates ranging between 17% and 20.3%.

The high rate of clinical filariasis in Tahiti, together with the high microfilaraemia, warranted the organization of a filariasis control programme, the early results of which have been reported by Beye and co-workers [3-5], and Kessel and co-workers.[24, 25]

The purpose of the present report is to outline the procedures that have proved to be most successful and to summarize important results obtained.

SURVEY PROCEDURES AND PRELIMINARY RESULTS

Organization of a control programme against any arthropod-borne disease requires the possession of basic data concerning the host, the parasite and the vector. In filariasis, preliminary surveys in an area should determine:

(*a*) the prevalence of the clinical disease in man;

(*b*) the prevalence and density of the parasite in man;

(*c*) the mosquitos present and their significance as vectors, which in turn demands information on the bionomics of the vector mosquitos;

(*d*) the prevalence and density under natural conditions of *Wuchereria bancrofti* larvae in vector mosquitos.

These data should be arranged according to the sex and age groups commonly employed in health statistics, or presented in a manner which will enable them to be compared with other reports.

Clinical Surveys

Clinical filariasis has been divided by Manson-Bahr [29, 30] into *primary*, which includes acute filarial fever or lymphangitis; *secondary*, in which adenopathy occurs; and *tertiary*, which includes hydrocele and elephantiasis. In Tahiti these stages are often found to overlap with each other, and division into the two categories *acute* and *chronic* has been adequate. Usually specific clinical manifestations are indicated, as shown in Table I, which summarizes the prevalence, before the control programme was instituted, of four common clinical conditions observed by Beye et al.[4] It will be seen from the table that, on the whole, in the four categories

TABLE I. PERCENTAGES OF MALE TAHITIANS WITH CLINICAL MANIFESTATIONS OF FILARIASIS

Manifestation	Age group (years)						All ages
	0-9	10-19	20-29	30-39	40-49	50 +	
History of lymphangitis	0.0	8.2	16.3	37.6	50.0	61.2	22.7
Enlarged epitrochlear glands	6.5	32.4	37.2	56.1	84.5	67.0	40.9
Hydrocele	0.0	0.0	9.3	15.6	27.0	22.2	9.8
Elephantiasis	0.0	0.3	1.8	8.3	19.6	32.0	7.0

here listed, clinical filariasis increased with age. Elephantiasis began in the second decade and hydrocele was first observed in the third decade. Actually the youngest person to exhibit elephantiasis in Tahiti was a girl aged 14 years.

Evaluation of the final success of a filariasis control programme on a clinical basis is much more tedious than evaluation of programmes for most arthropod-borne diseases, because of the length of time required for the etiologic agent to reach maturity and of the prolonged development-period of the clinical disease. The effect of a control programme on primary filariasis may be apparent within a year or two, but a minimum period of from 5 to 10 years may be required to evaluate significant reductions in the occurrence of chronic filariasis.

Blood Surveys

Routine detection of the adult parasite in man is impractical, and the prevalence of microfilariae must therefore be determined by blood surveys before and during a control programme to ascertain the effectiveness of the procedures employed. Two methods are in practice for making blood examinations: (1) The Knott method,[26] by which 1 ml of venous blood is added to 10 ml of 2% formalin, left for sedimentation for 18 hours, and the microfilariae in the sediment counted; (2) the "thick-film" method, by which 20 mm^3 of peripheral blood, taken from the finger, is distributed in a circular film about 1.5 cm in diameter, dried, and stained with Giemsa. An exact count of the microfilariae can then be made, and the slides can be saved for future reference. Two or more 20-mm^3 films may be collected, usually on the same slide. If only one film is reported, the count indicated is for 20 mm^3 while, if microfilariae in three films are counted, 60 mm^3 is the designated unit.

Comparison of the 20-mm^3 standard with the Knott method as used in Fiji by Amos,[1, 2] and with the 60-mm^3 procedure, have shown that the Knott method and the 20-mm^3 procedure produce similar results while the 60-mm^3 procedure may yield between 3% and 5% more positives, and these are among the persons with a low microfilaraemia. This percentage may vary with the intensity of infection in different areas. Since there is so little difference in results by the three procedures, it is considered that the extra time and effort required to perform tests by the Knott and 60-mm^3 methods can be used to better advantage elsewhere in a control programme. Therefore, in this study examination of a single 20-mm^3 film has been accepted as the standard for surveys. However, in critical experimental work, for example, in evaluating a treatment experiment, 40- to 80-mm^3 counts are used.

In the data cited on page 633, the Knott method was used in Fiji; the 60-mm^3 method in American Samoa; and the 20-mm^3 method in Western

Samoa and Tahiti. Had the 60-mm^3 procedure been used in the surveys in Tahiti, the results would probably have been slightly higher.

From the blood surveys in this study it has been considered of value to determine:

(1) the frequency distribution of positives at the following microfilarial levels: 0; 1-5; 6-10; 11-30; 31-50; 51-100 and 100+;

(2) the percentage of persons positive for microfilariae; and

(3) the density of microfilariae in a given population. The density is obtained as follows:

$$\frac{\text{number of people positive}}{\text{total number of people examined}} = \text{percentage of people positive}$$

times

$$\frac{\text{total number of microfilariae}}{\text{number of people positive}} = \text{average number of microfilariae per positive person.}$$

The result is synonymous with the " average number of microfilariae per 20 mm^3 " reported in previous papers by Kessel and fellow workers.[24, 25]

Table II shows the analysis sheet of a blood survey in a typical district of Tahiti before the institution of a control programme and may be compared with the field results during the progress of the programme listed on pages 650-654. It will be noted from Table II that:

(*a*) 30.9% of the people of the district were positive for microfilariae.

(*b*) At the several microfilarial levels listed, the percentages of positives ranged from 2.2% at 31-50 to 9.1% at 100+.

(*c*) There were two microfilarial counts between 1101 and 1300. Actually the highest count observed was 1259. The highest microfilarial count per 20 mm^3 observed in Tahiti was 2302.

(*d*) The microfilarial density was 33.1.

The frequency distribution of the population at the selected microfilarial levels (1) affords the most complete picture of the occurrence of microfilariae but it is cumbersome to use in comparative tabulations. It is apparent that neither the percentages of persons positive—(2)—nor the microfilarial density—(3)—when taken alone furnish a complete picture of the occurrence of microfilariae in a given population. When taken together, however, they provide information of significance with reference to the prevalence of microfilariae in an area, and this in turn will determine the exposure rate and ultimate density of *W. bancrofti* larvae in mosquitos. In this study all three indices are considered when evaluating the results in a given area, but in summarizing tabulations it is considered adequate to cite only the percentage of persons positive and the microfilarial density.

TABLE II. ANALYSIS OF BLOOD SURVEY IN A TYPICAL DISTRICT BEFORE CONTROL MEASURES

Levels of microfilarial counts	Number of microfilarial counts made at each level	Persons examined		Total microfilariae per 20 mm³
		number	%	
0	—	570	69.1	0
1-5	1:14; 2:10; 3:8; 4:8; 5:7	47	5.7	125
6-10	6:4; 7:15; 8:3; 9:3; 10:4	29	3.5	220
11-30	11-20:36; 21-30:10	46	5.6	806
31-50	31-40:12; 41-50:6	18	2.2	688
51-100	51-60:12; 61-70:6; 71-80:10; 81-90:6; 91-100:6	40	4.8	2 941
100+	101-300:43; 301-500:16; 501-700:6; 701-900:7; 901-1100:1; 1101-1300:2	75	9.1	22 497
Total persons positive		255	30.9	27 277
Total persons		825	100.0	microfilarial density 33.1

Entomological Surveys

Surveys of larval and adult mosquitos have been made in Tahiti by Galliard and fellow workers,[9, 10] Edgar (Beye et al.[5]), Rosen,[33] Rosen & Rozeboom,[34] Bonnet & Chapman (unpublished data), in order to determine the species of mosquitos present and their relative abundance. At the present time (1955) 8 species of mosquitos are known to occur. In addition, a species tentatively identified as *Culex sitiens* Wiedemann was reported by Edgar in Tahiti, though not observed by Rosen. It has since been found by Bonnet on the nearby islands of Maupiti, Bora-Bora and Maiao (Tubuai Manu), but as yet has not been found again in Tahiti.

Results of experimental laboratory infections by Rosen[33] and dissections of field-caught mosquitos by Rosen[33] and Bonnet & Chapman (unpublished data), have been used to indicate the significant vector mosquitos. This information has been summarized in Table III, where it is seen from experimental data in the laboratory, natural infections in the field, and the relative abundance of adult mosquitos, that only *Aëdes polynesiensis* and *C. quinquefasciatus* need be considered as vectors of importance. They are abundant and widely distributed, bite man readily

TABLE III. MOSQUITOS OF TAHITI: THEIR ABUNDANCE, HOSTS, AND EFFICIENCY AS VECTORS OF NON-PERIODIC FILARIASIS

Species	Relative abundance of adults	Primary blood hosts	Percentage* of experimentally-infected mosquitos positive for infective-stage larvae	Percentage of wild mosquitos positive for infective-stage larvae
Aëdes aegypti	abundant in urban area, rare in rural	man	0.0	0.0
Aëdes edgari	rare; flood-water mosquito; spotty distribution	man (?)	relatively efficient	0.0
Aëdes polynesiensis	abundant in rural areas, rare in urban	man; pig; dog; birds	highly efficient; 77.0	4.0-7.8
Culex annulirostris	common	birds, dog, man	0.0	0.0
Culex atriceps	uncommon	rarely bites man	inefficient	0.0
Culex quinque-fasciatus	abundant in both rural and urban areas	man; birds	host poor; 15.0	0.38
Culex sp. (*close* to *C. atriceps*)	rare; found in leaf axils of pandanus	?	?	—
Culex sp. (close to *C. litoralis*)	common	man	inefficient	1.7

*** Or standard as vector** **Compiled from Rosen [33] and Bonnet (unpublished data)**

and regularly, and are capable of developing the larvae of *W. bancrofti* to the infective stage. *C. quinquefasciatus*, however, is considered of secondary and minor importance, inasmuch as the infections observed in this species, both in the laboratory and in the field, are of a low level compared with the infections found in *A. polynesiensis*. Rosen [33] considers *C. quinquefasciatus* to be a poor host for Tahitian strains of *W. bancrofti*. Likewise, unpublished results of recent dissections by Bonnet & Chapman of 788 *C. quinquefasciatus* captured in houses known to harbour microfilarial carriers confirm this opinion. Only 10, or 1.2%, of the mosquitos were positive for larvae in all stages of development, and of these only 3, or 0.38%, harboured third- or infective-stage larvae of *W. bancrofti*, while 25.5% of *A. polynesiensis* caught from these same houses harboured larvae of all stages, 7.6% of which were infective-stage larvae. For these reasons, *A. polynesiensis* is considered to be the vector of major importance, and studies on mosquito bionomics and control have been confined largely to this species.

Manson-Bahr was the first to mention *A. pseudoscutellaris* as an important vector of non-periodic filariasis in Fiji. Byrd, St Amant & Bromberg [7] and Jachowski & Otto [19] consider *A. polynesiensis* also to be the significant vector in American Samoa. Symes [35] in Fiji recently reported 0.34% of field-caught *C. quinquefasciatus* in that area to harbour infective-stage larvae, presumably of *W. bancrofti*. This is similar to the figure quoted above by Bonnet. However, only 0.12% of *A. pseudoscutellaris* and/or *A. polynesiensis* dissected by Symes harboured similar stages, although he reported 1.9% of *A. fijiensis* with infective-stage larvae.

Bonnet and his co-workers [6] have described elsewhere the details of the " Intensive Survey " method used to procure quantitative information on the prevalence rates of mosquitos and the occurrence in them of *W. bancrofti* infections. Mosquitos are caught on human bait for a ten-minute period within 10 m of each house in a given district. The average number of mosquitos caught per minute is the unit selected by which to record prevalence rates. Standardized proportions of each catch are dissected and the numbers of larvae for each stage of *W. bancrofti* recorded. From these records the percentage of mosquitos positive for each stage of larvae, and the larval density for each stage in the mosquito, are determined. The results have been used not only to designate the existing conditions of transmission before control procedures are begun, but also to measure the progress of the control campaign against filariasis.

A summary sheet of an Intensive Survey in an area before control measures were instituted is presented in Table IV.

Of special importance are points (6), (8), (9), (10), (11). These data, from such a standardized type of survey, provide significant information

TABLE IV. ANALYSIS OF INTENSIVE MOSQUITO SURVEY FROM A TYPICAL DISTRICT BEFORE CONTROL MEASURES SHOWING COLLECTIONS AND DISSECTIONS OF AËDES POLYNESIENSIS FOR WUCHERERIA BANCROFTI LARVAE

District: 1		
(1) Number of stations		112
(2) Number of mosquitos collected		615
(3) Number of stations with mosquitos	75 or	66.9%
(4) Number of stations with 10 or more mosquitos	20 or	17.8%
(5) Number of stations with mosquitos positive for larvae of *W. bancrofti*	29 or	25.8%
(6) Number of mosquitos caught per minute		0.54
(7) Number of mosquitos dissected		422
(8) Developmental-stage larvae present in mosquitos	56 or	13.2%
(9) Infective-stage larvae present in mosquitos	32 or	7.6%
(10) Density of developmental-stage larvae per dissected mosquito		0.74
(11) Density of infective stage larvae per dissected mosquito		0.19

concerning the prevalence of *W. bancrofti* larvae in mosquitos and from them, an impression of the amount of transmission in progress can be determined. Each of the points (8) to (11) in itself might be used as an index for comparison with other surveys. However, a single index compiled from a combination of the most pertinent points provides a standard susceptible of general comparison. Jachowsky & Otto [18] recommended a potential transmission index in Samoa, determined by multiplying the " number of mosquitos per survey " by the " percentage of mosquitos infected with developmental-stage larvae ". Kessel et al.[25] suggested that the " average number of mosquitos caught per minute " be substituted for the " number of mosquitos per survey ", but retained the second factor.

However, subsequent studies indicate that the " larval density per dissected mosquito " is a more realistic factor and this has accordingly been adopted for the work in Tahiti. It is derived as follows:

$$\frac{\text{number of mosquitos positive for all stages of larvae}}{\text{total number of mosquitos dissected}} = \text{percentage of mosquitos positive for all stages of larvae}$$

times

$$\frac{\text{total number of larvae}}{\text{number of mosquitos positive for all stages of larvae}} = \text{average number of all stages of larvae per positive mosquito.}$$

It may also be expressed as " the average number of *W. bancrofti* larvae per dissected mosquito ".

The density of larvae could be based either on developmental stages present in the mosquito, that is, beyond the microfilarial stage, or on infective-stage larvae only. In this study it has been elected to use density based on all developmental stages rather than on infective stages alone, because such a factor represents a more severe test than the infective-stage figure, in that all developmental-stage larvae actually are potential infective-stage larvae.

Such a potential transmission index for the survey summarized in Table IV (see page 639) will be derived by multiplying item (6)—0.54—by item (10)—0.74—which gives 0.4. A whole number, capable of easy comparison, is desirable for such an index. If 0.4 is multiplied by 1000 and divided by 4, the figure 100 is obtained. Such computation has been followed to advantage in Table VIII (see page 653) where the transmission indices from several surveys are compared.

CONTROL MEASURES AND RESULTS

Measures in an ideal control programme should involve the host, the parasite and the vector. These have all been included in the two-point control programme in Tahiti, which aimed at the parasite by drug administration and at the vector by mosquito control.

Host

Measures directed towards the host (man) are mainly education and supervision of the population with reference to exercising mosquito control and accepting medication.

The following instructional activities have been used to advantage:

(1) well-organized talks illustrated by posters, charts, and films;

(2) illustrated pamphlets;

(3) instruction to teachers in the schools, and inclusion of an outline on the prevention of filariasis in the regular hygiene course.

Before work is begun in a new area or district, a radio talk, including a question and answer programme, is given. In districts where radios are not common, gatherings are organized in central locations at which a film on filariasis control, prepared by the Project, is shown, and followed by a discussion with questions and answers.

Early in the programme in Tahiti it was considered advantageous to institute a system whereby an inspector was appointed to each district of the island. These young men, selected from each district, were given a course of instruction at the Institut de Recherches médicales de l'Océanie française and were placed in charge of the mapping, census-taking, mosquito control and drug administration in each area. A chief inspector was appointed who visited the districts periodically to supervise the activities; once a week he was accompanied by one of the doctors of the Institute staff. Voluntary co-operation of the people has been the primary objective, but this has been enhanced by a system of fines which may be levied by the chief of a district if an individual fails to co-operate in the mosquito control programme. By and large, excellent co-operation has been obtained because of the friendly relationship established between the staff of the Institute and the population.

Parasite

A perfect filaricide against adult *W. bancrofti* to be used in mass treatment is lacking. However, the salt of diethylcarbamazine (Hetrazan, Notezine, Banocide), Lederle, was shown by Hewitt and fellow workers [12-14] to be an effective microfilaricide. The nature of its effect on the adult worm is still uncertain, although both clinical and biopsy evidence reported in this paper indicate that a direct effect does occur.

Experimental Results

Prevention

When the work began in Tahiti, the dosage schedule recommended for diethylcarbamazine by the manufacturers was 2 mg per kg of body-weight three times a day (t.i.d.) for 7 days, and accordingly was the first schedule used. One year after the completion of this schedule, it was found that 50.6% of the treated people had returned to a positive status, 28% with counts ranging from 1-5, 8% from 11-100, and 13% with more than 100 microfilariae per 20 mm^3. When these are compared with original positive rates shown in Table II (see page 637), a marked reduction is apparent.

However, Rosen [33] had by this time been successful in infecting *A. polynesiensis* by feeding them on donors with minimal microfilarial counts, and such reductions as those recorded above were not considered adequate to warrant success if applied to a control programme. Consequently the treatment was repeated, in the hope that a second similar annual dosage would prove to be sufficient. After the second year, 23.0% were still positive, although the microfilarial density had been reduced to 1.5. 14% were positive in the 1-5 level, 2% in the 6-10 level, and 1.5% in the 11-30 level. No counts above 30 were noted.

By this time several different dosage schedules had been studied (Kessel, Thooris & Bambridge [24]) and 6 mg per kg of body-weight one day a month was selected both as the most likely dosage to produce success, and as the most suitable for administration in this programme. Table V shows the results from the earlier and later schedules as follows:

A

(1) 2 mg per kg of body-weight t.i.d. for one week, as originally recommended; follow-up one year later.

(2) 2 mg per kg of body-weight t.i.d. for one week as in A(1), plus a second similar dose at the beginning of the second year; follow-up one year after second dosage.

B

6 mg per kg of body-weight once a month for 24 months.

(1) Cessation of treatment at the end of two years.

(2) Follow-up one year after treatment was stopped.

The 6 mg per kg of body-weight dosage listed above has been administered at (*a*) 3 mg per kg of body-weight twice a day (b.i.d.), and at (*b*) 6 mg per kg of body-weight once a day.

The follow-up examinations under B(2) refer to persons treated by the (*a*) schedule. Preliminary reports on schedule (*b*) indicate satisfactory results, although the final follow-up examinations have not been completed.

It will be observed from B(1) at the end of 24 months that only one out of 54, or 1.9%, was still positive, and this positive person had a microfilarial count of 1. It was pointed out by Kessel, Thooris & Bambridge [24] that the critical test would come after a period of three years—that is, when individuals had been treated for two years and a subsequent follow-up had been made one year after the close of treatment.

TABLE V. RESULTS OF DIFFERENT EXPERIMENTAL TREATMENT SCHEDULES WITH DIETHYLCARBAMAZINE *

A	One week at first of year (originally recommended) (1)		One week at first of each year for two years (2)	
Number in series	91		100	
	percentage positive	microfilarial density	percentage positive	microfilarial density
Before treatment	100.0	90.0	100.0	79.0
At end of treatment	6.6	1.0	not determined	
One year after end of treatment	50.6	8.0	23.0	1.5

B	One day a month for 24 months			
	At end of two years (1)		One year after end of treatment (2)	
Number in series	54		40	
	percentage positive	microfilarial density	percentage positive	microfilarial density
Before treatment	100.0	61.0	100.0	76.0
At end of treatment	1.9	0.02	0.0	0.0
One year after end of treatment	See (2) for 40 of these		2.5	0.05

* Based on microfilarial counts

In B(2), 40 persons who were negative at the end of two years were followed at monthly intervals throughout one year after the termination of treatment. Only one of these returned to a positive state. His original microfilarial count had been 209, well above the average. His count two months after the end of treatment was 2, and in subsequent monthly examinations during the year it varied between 0 and 2.

In addition to these results, observations may be reported on three other schedules:

(1) A group of ten positive people was continued on the monthly treatment routine for a third year, that is, for 36 months in all. One year after the end of treatment, all were found to be negative.

(2) 16 positive people were given between 21 and 28 consecutive daily treatments of 2 mg per kg of body-weight t.i.d., and examined at three-monthly intervals for one year. Four, or 25%, were positive, with a microfilarial density of 1.1 at the end of the year. This experiment indicates that daily treatments for from three to four weeks at the beginning of a period are not as effective as the same total amount of drug administered at monthly intervals for two years.

(3) 22 positive cases were given the regular one-week schedule, plus 17 one-day-a-month treatments, which also provides a total dosage identical with B. It would appear to be as efficient as the B schedule where all were negative at the end of the 18 months. However, the follow-up examination, one year later, has not yet been completed.

One may summarize as follows from these experiments:

(1) 6 mg of diethylcaıbamazine per kg of body-weight administered one day a month for 24 months reduced 98% of positives to a negative state.

(2) Of 40 such negatives, one year after the close of treatment 39, or 97.5%, were still negative. The one recurring positive exhibited a low count of 2 microfilariae per 20 mm^3.

(3) 10 persons treated by this same dosage for a period of 36 months were negative when checked one year later.

In addition, preliminary experiments in progress, in which 3 mg per kg of body-weight were administered in a single dose, once a month, for a period ranging from 12 to 18 months, have produced results similar to the early ones recorded for the administration of 6 mg per kg of body-weight.

Since only 2.5% of the negatives treated by schedule B were lightly positive one year after the close of treatment, this dosage schedule would appear to be highly successful in reducing microfilariae to a minimum, and will probably prove effective in a mass control programme. When the larval density results (see Table VIII, page 653) arereviewed, such an opinion is confirmed.

Clinical

Diagnosis and treatment of clinical filariasis have their place in a control programme, both because of their relation to epidemiology and of their benefit to patients, which produces a good psychological effect upon the population in gaining their co-operation for a campaign. When the programme first began in Tahiti, a central filariasis clinic was established at the Institute and smaller clinics were set up in each experimental area. These area clinics were subsequently discontinued and individuals who could not attend the central clinic were visited by the Institute staff during weekly trips around the island. Detailed reports on diagnosis, etiology, prophylaxis and therapy have been made by Thooris [36-39] and by Thooris

& Beye (unpublished data). They include the effects of diethylcarbamazine on acute and chronic filariasis, of symptomatic treatment, of the drugs suramin and sodium thiacetarsamide, of injecting sclerotic agents into hydroceles, and of bandaging elephantoid limbs.

Effect of Diethylcarbamazine on the Clinical Syndrome

Special groups of individuals, exhibiting acute or chronic filariasis, were selected during the course of the control programme, and their clinical state was observed before treatment, annually during treatment, and after treatment.

Acute filariasis or lymphangitis

In a series of 2153 persons receiving a variety of dosage schedules, under observation for four years, the average number of lymphangitis attacks per year per person was 0.82 before treatment and 0.13 during the fourth year. The reduction in acute manifestation was gradual but definite, that is, 84% during a four-year period. This gradual diminution in symptoms occurs simultaneously with the reduction in microfilaraemia and in transmission which accompanies the institution of control measures.

Chronic filariasis

The most common chronic signs are adenopathy, hydrocele, and elephantiasis, which take a long time to develop. It is difficult to judge the final effect of the control programme on chronic filariasis in the short period under consideration. However, since no new cases of elephantiasis were recorded in follow-up examinations of treated people, the method of chemotherapy here employed would appear to have an effect on chronic filariasis. Whether this is the result solely of control procedures in reducing the opportunity for reinfection, or whether the drug has a direct effect on the helminth as well, is difficult to prove.

Effect on adult Wuchereria

In order to study the possible direct effect of diethylcarbamazine on the adult worm, dissections were made on 86 biopsies of lymphatic tissues from 83 people who showed evidence of filarial involvement and who therefore might harbour adult worms.

Of 48 lymph-nodes studied before any treatment was undertaken, 14 (29%) were positive, and of 22 scrotums dissected, 4 (18%) showed the presence of adult worms. After therapy, 9 lymph-nodes and 2 scrotums failed to show the presence of helminths. Although two specimens might reasonably have been expected to be positive in such a series, such a group suggests an effect on adult worms but is too small to be statistically significant. It does, however, point the way to a procedure for clarifying the problem.

Other Therapeutic Measures

Symptomatic

Treatment of lymphangitis with penicillin and terramycin were without direct effect. Antihistamines, for example, pyribenzamine and chlorothen citrate, were used on several hundred cases in comparison with acetylsalicylic acid. All were beneficial, but the acetylsalicylic acid was the most effective in reducing pain and fever.

Because of the allergic phenomenon recognized in filariasis, and especially since sensitivity reactions to the liberation of foreign protein from destruction of microfilariae may follow administration of diethylcarbamazine, a combination of chlorothen citrate and acetylsalicylic acid was adopted as a standard treatment for acute lymphangitis and for reaction following diethylcarbamazine therapy. The reactions accompanying the seven-day schedule are discussed by Beye et al.[4] The newer dosage schedule recommended in this paper produces lighter reactions of shorter duration which may range from slight dizziness to malaise with or without headache, joint pains and fever, and may last 24 hours or longer. Urtecaria occurs in a small percentage of cases; delayed reactions consisting of bullous eruptions, and abscess formation may result. The reactions to subsequent monthly doses are decreasingly severe and are seldom observed after the third month.

Dirofilaria immitis antigen was administered to a series of 43 patients who were experiencing an average of 1.7 attacks per person per month. Attacks were reduced by 90% after five months' treatment.

Filaricides

Suramin and sodium thiacetarsamide, which have been reported to be effective against adult filaria, have each been used in an experimental series. One gramme of suramin once a week was administered intravenously for seven weeks to 20 patients with an average of 2.9 attacks of lymphangitis per person per month. At the close of treatment, the attacks were reduced to 0.37 per person per month. Sodium thiacetarsamide, administered daily in 6-ml intravenous injections for 15 days to 35 patients with an average of 0.75 attacks per person per month, reduced the attacks to 0.04.

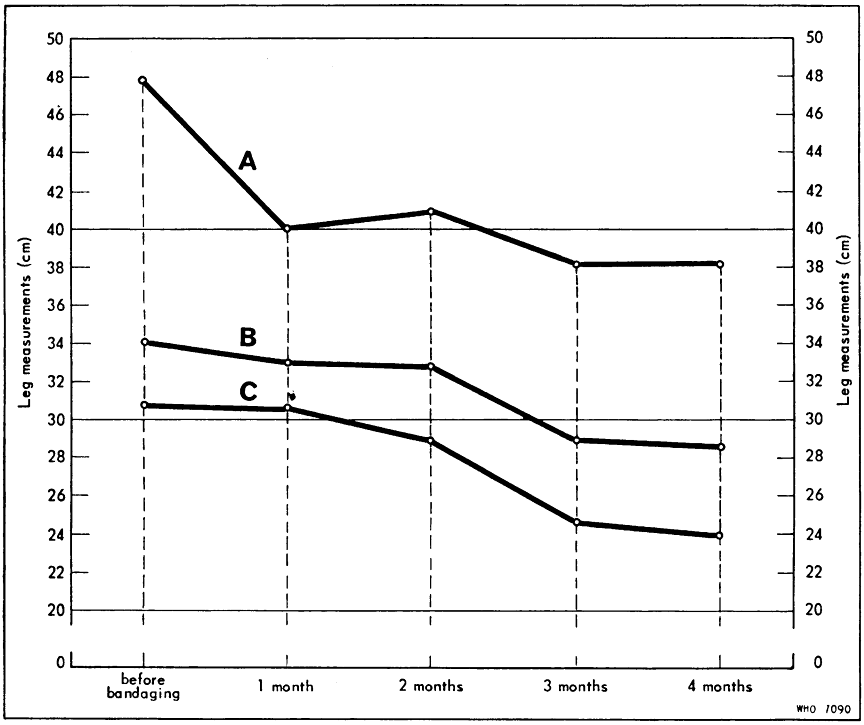
Sodium thiacetarsamide exhibited a slower but more permanent effect on microfilariae than the diethylcarbamazine when given by the dose recommended in A (1), first tried in this study (see page 642). Suramin produced an effect similar to, although less dramatic than, that of acetarsamide.

Chronic Filariasis

The two most common manifestations of chronic filariasis are hydrocele and elephantiasis. The former is satisfactorily treated by injecting sclerotic agents, such as sodium psylliate, and sodium morrhuate, with procaine into the tunica vaginalis after having aspirated the fluid.

Elephantiasis of the scrotum is best relieved by surgery. Elephantiasis of the limbs, however, presents a more serious problem since lymphatic destruction, once present, is difficult to relieve. Bandaging of the limb involved has produced the most satisfactory results. Thooris (Beye [3]) introduced the use of Unna's paste, which is applied to the skin and covered by gauze. An elastic bandage, as originally suggested by Knott (personal communication, 1948), is then applied tightly over this, and is changed once a week. The paste provides asepsis and softens the tissue, while the bandage forces the lymph to circulate through new collaterals. The treat-

FIG. 1. REDUCTIONS IN LEG MEASUREMENTS OF ELEPHANTIASIS AFTER BANDAGING



A = calf; B = instep; C = ankle

ment is applied as long as reduction of volume is apparent. The degree of improvement possible will depend on the previous amount of tissue damage and chronicity of the case. Early elephantiasis may be reduced to a normal state, while older cases will show less improvement. Fig. 1 illustrates the average reduction of the leg measurements in 200 persons who were bandaged for four months or longer. The greatest reduction noted in calf measurement of a bandaged case was from 86 cm to 43 cm, and a few individuals who had not been ambulatory for several years were sufficiently improved to be able to walk.

Recently, Markell & Kerrest [31] administered cortisone to a series of patients with elephantiasis of the limbs. They noted a marked lessening of induration in the affected members which persisted for some time after discontinuance of the drug. Further trials of maintenance dosages are in progress. At present, the greatest usefulness of cortisone seems to be in conjunction with bandaging.

Field Results

In man

The experimental results under prevention show what could be achieved if everyone in a community accepted the prescribed diethylcarbamazine. In a mass control programme, however, irregularities in administration of the drug occur and the results procured in the field show variations corresponding to the efficiency of administration. The main problems occur with (*a*) new immigrants and visitors into a district, (*b*) a certain number of persons who object to taking medication, here designated " refusals ", and (*c*) those who are excused from treatment for medical reasons.

After evaluating the several dosage schedules discussed on pages 641-645, it was decided to establish the following routine for Notezine administration in each area or district:

(1) Perform blood survey before treatment.

(2) Administer diethylcarbamazine in the dosage schedule of 6 mg per kg of body-weight one day each month for one year to both negative and positive persons. The negatives were treated to ensure that all positive persons received the drug including (*a*) those with light infections who might have been missed by the blood survey, and (*b*) those who might have been in the incubation period at the time of the blood survey and have subsequently become positive.

(3) Repeat blood survey at end of year.

(4) Continue treatment of all current and original positives until they have been demonstrated to be negative by two annual blood surveys. After the second year few people need treatment. These are included in what may be termed the " mopping-up " part of the programme, under which (3) and (4) should be repeated annually as long as necessary.

Table VI is a census sheet compiled at the end of the third year for a district to which such treatment had been applied. As compared with Table II (see page 637), marked reductions in percentages of positives will be noted (*a*) at the microfilarial levels listed, (*b*) in the total percentage positive (3.1 %), and (*c*) in the microfilarial density (0.64). The people still positive were immigrants, persons excused treatment, or those who had received only between 1 and 5 monthly treatments; the latter are in the lowest microfilarial group of 1-5.

TABLE VI. ANALYSIS OF BLOOD SURVEY IN ONE DISTRICT IN THE THIRD YEAR AFTER INSTITUTION OF CONTROL PROGRAMME

Levels of microfilarial counts	Number of microfilarial counts made and treatment received *	Persons examined		Total microfilariae per 20 mm³
		number	%	
0	—	597	96.9	—
1-5	5 E E 4 E 5 5 3 4 I 4 5 1 1 3 3 1 1 1 4 2 1 1 5	12	1.9	24
6-10	I 6	1	0.16	6
11-30	E I I 29 11 12	3	0.46	52
31-50	I 38	1	0.16	38
51-100	—	0	0.00	0
100+	I I 117 156	2	0.3	273
Total persons positive		19	3.1	393
Total persons		616	100.00	microfilarial density 0.64
I positives		7	—	—
R positives		0	—	—
E positives		4	—	—

* The upper figures represent the number of monthly treatments administered at the time the census was taken; the lower figures represent the microfilarial count.

E = excused treatment
I = immigrants
R = refusals

Immigrants constituted the greatest problem in this particular census, and the people with the highest counts were among those who had not begun their treatment. If these untreated individuals were subtracted, it is obvious that the field results would be more in line with the experimental results recorded above. As more areas of a region come under a developing control programme there are fewer positive immigrants into a treated area, and immigrants will thus constitute a progressively minor problem.

There were no refusals in this district at the time of this census, although refusals may constitute a problem, especially in larger districts. Good personal relations between the inspector and the people of his district are paramount in securing co-operation. At times persuasion by a member of the professional staff of the Institute has proved successful when the inspector failed. The most common reasons for refusals were personal objections to taking a European drug, and fear of allergic reaction which might temporarily incapacitate the person for work. Occasional chronic objectors occurred, as are found in any public-health project in any country. These were usually among the Europeans, who insisted on their individual right to refuse.

The excused in this programme do not constitute a major problem. They usually are elderly people or others with chronic disease or an occasional pregnancy, whom it seemed undesirable to treat. A death or clinical complication, regardless of the cause, in a person previously given Notezine may at times be attributed to the drug and cause criticism by relatives or neighbours. Such complexities have been rare in the programme in Tahiti and have been more than offset by the fact that many individuals in untreated areas, upon hearing good reports of the programme, have often requested and even bought the diethylcarbamazine in advance of the start of a programme in their area. Additional data from field results are shown in Table VIII (see page 653), where it will be observed that progressive diminution both in the percentage of persons positive for microfilariae and in microfilarial density is apparent as one proceeds from the time before control to the successive years after control.

It should be emphasized that the positive people remaining in a district after 24 months of treatment, except for a very low percentage, are those who have refused treatment, have been excused, or have recently moved to the district, receiving either no treatment or an incomplete course of treatment. Continued supervision of this limited group will gradually reduce the positives to a negligible minimum where it is expected that the mosquito control measures, which are a permanent part of the sanitation programme of the island, will be sufficient to deter any future increase in transmission.

In mosquitos

Once a control programme in a district or area is well under way, marked reductions in the several items recorded by an Intensive Mosquito

Survey are apparent. This may best be observed by comparing Table VII, an analysis after control measures, with Table IV, an analysis before control measures.

TABLE VII. ANALYSIS OF INTENSIVE MOSQUITO SURVEY FROM A TYPICAL DISTRICT AFTER CONTROL MEASURES SHOWING COLLECTIONS AND DISSECTIONS OF AËDES POLYNESIENSIS FOR WUCHERERIA BANCROFTI LARVAE

District: 6

(1)	Number of stations		98
(2)	Number of mosquitos collected		107
(3)	Number of stations with mosquitos	30 or	30.6%
(4)	Number of stations with 10 or more mosquitos	2 or	2.0
(5)	Number of stations with mosquitos positive for larvae of *W. bancrofti*	1 or	1.0%
(6)	Number of mosquitos caught per minute		0.109
(7)	Number of mosquitos dissected		65
(8)	All stages of *W. bancrofti* larvae present in mosquitos	1 or	1.5
(9)	Infective stage of *W. bancrofti* larvae present in mosquitos	0 or	0.0%
(10)	Density or average number of all stages of *W. bancrofti* larvae per dissected mosquito		0.061
(11)	Density or average number of infective stages of *W. bancrofti* larvae per dissected mosquito		0.0

Actually the results in Table VII are for district 6 at the fourth annual follow-up. They were selected for this table instead of the third year follow-up results, which were negative, to illustrate that finding just one positive mosquito in a survey will alter the percentages appreciably. This mosquito contained four first-stage larvae. Since the numbers of mosquitos caught and dissected were unusually low, one positive mosquito had a marked influence on the results, being responsible for the 1.5% of mosquitos positive for developmental-stage larvae, and for the transmission index of 0.015.

Table VIII is a compilation of field results showing reductions observed both in microfilarial surveys in man and in larval surveys in mosquitos. The districts under the control programme for one, two, three, or four years may be reviewed in relation to district 1, before control measures were instituted.

This district was observed for three years as an area where no filariasis control was instituted. A blood survey was performed both at the beginning and at the end of these three years with little change being noted between the two. Intensive mosquito surveys were also performed every three months, each time with similar results. The " 0 or before " figures for district 1 in this table are those from the last of the surveys, made three months before the treatment programme was instituted. It is representative of other districts throughout the island of Tahiti (see the figures in parentheses in Table VIII, page 653, which show that the percentage of positives in each district ranged from 26.2 to 43.6, and the micıofilarial density from 17.0 to 48.1). The figures for percentages of *W. bancrofti* larvae in mosquito dissections for district 1 are likewise representative for Tahiti, as they are intermediate between the extremes of 17.8 and 10.2 for "all-stage" larvae found in other districts before the administration of diethylcarbamazine.

It will be noted that, on the whole, gradual diminutions are observed in all categories as the control period is extended. These range from the 30.9% of persons positive in district 1 before treatment to the 1% positive in district 8 in the fourth annual follow-up. Corresponding reductions in these same districts were observed in microfilarial density, from 33.1 to 0.04; in percentage of mosquitos positive for developmental-stage larvae, from 13.2 to 0.0%; and in the potential transmission index, from 100 to 0.0. District 1, one year after the institution of the control programme, showed the expected reduction in microfilariae in man, and a corresponding reduction in *W. bancrofti* larvae in mosquitos. The transmission index was still quite high, however, being 25. This is explained by the fact that no mosquito control had been instituted in this district since it was the district used in the experiment (see Table IX) to determine whether the mosquito population was appreciably altered in an area under treatment with diethylcarbamazine. Once a control programme is well under way, larvae of *W. bancrofti* diminish rapidly in mosquitos caught in the field. This is especially true for infective-stage larvae; only two districts (2 and 3) showed the presence of such larvae after the institution of control measures. From this finding one may assume that infective-stage larvae are so rare by the end of the first year after institution of control measuıes that little transmission is still in progress. Clinical and epidemiological observations in this study confirm this point of view. Even so, the results from districts 2 and 3 indicate that a few infective-stage larvae were still present. As the objective of this programme has been to impose the most rigid conditions of control possible and to evaluate them by the most critical standards available, control measures are continued as long as carriers occur in a population, or until mosquitos are found to be negative for larvae of *W. bancrofti.*

The question was raised early in the work as to whether sufficient reduction in microfilarial counts in man could be realized by the use of diethylcarbamazine to produce the necessary reduction of larvae in mosquitos to constitute adequate control. The data presented in the previous tables and discussion indicate that the programme here outlined constitutes the basis for such effective control of filariasis. Likewise, the measures selected for evaluating the progress of the programme appear to be adequate.

TABLE VIII. FIELD RESULTS SHOWING REDUCTION IN MICROFILARIAE AND IN LARVAE OF WUCHERERIA BANCROFTI

District	Years of control		Persons examined	Microfilariae in man *		Mosquitos dissected	Larvae of *W. bancrofti* in mosquitos			Potential transmission index
				percentage of persons positive	microfilarial density per 20 mm³		percentage positive all stages	percentage positive infective stage	density	
1	whole district before treatment	0	825	30.9	33.1	422	13.2	7.8	0.74	100.0
1	part of district treated	1 2	289 304	7.2 4.9	1.8 0.6	270 250	4.7 2.0	0.0 0.0	0.17 0.076	25.0 4.3
1	other part not treated; resurveyed after 2 years		560	31.9	32.0	279	20.7	5.3	1.08	90.0
2		1	2248 *	(29.8) 6.3	(23.1) 1.8	279	10.0	2.5	0.51	7.6
3		2	1317	(30.3) 6.1	(35.9) 0.9	275	6.5	1.4	0.30	7.5
4		2	874	(29.1) 5.6	(17.0) 1.4	187	0.5	0.0	0.02	0.5
5		3	332	(43.6) 2.75	(48.1) 0.39	163	0.6	0.0	0.006	0.25
6		3 4	616 823	(26.2) 3.1 1.8	(25.2) 0.64 0.14	401 65	0.0 1.5	0.0 0.0	0.0 0.06	0.0 0.015
7		4	173	(27.0) 2.0	(33.0) 0.15	225	0.0	0.0	0.0	0.0
8		4	322	(35.5) 1.0	(30.0) 0.04	364	0.0	0.0	0.0	0.0

* The figures in parentheses for districts 2-8 refer to findings before treatment.

Otto, Jachowski & Wharton [32] suggested that persons with high microfilarial counts in a human population might serve as a check on the mosquito population by virtue of producing a high and fatal parasitaemia in mosquitos. They cite an example of a Samoan village where the entire population received diethylcarbamazine for a period of 14 days after which " the mosquito population apparently more than doubled within three months ".

In order to obtain additional information on this point an experiment was performed in Tahiti. Two adjacent areas of approximately equal size, and with similar human population, microfilarial counts, and mosquito population, were selected. Diethylcarbamazine was given to the whole population of one of these areas and was withheld from the other.

Table IX shows the results of Intensive Surveys which were made in both areas 2 months and 12 months later. It will be seen that in the treated area progressive reductions in larval counts of *W. bancrofti* occurred in mosquitos, while the corresponding categories of the untreated area remained unchanged. The mosquito populations in both areas remained at about the same level. These results do not indicate that the administration of diethylcarbamazine to a population which is positive for *W. bancrofti* will result in the increase of the mosquito population in that same area.

The Vector

As already indicated in this paper, *A. polynesiensis* Marks is considered to be the most important vector of filariasis in Tahiti. Consequently, mosquito control measures have been directed primarily against this species. Complete control against this mosquito, however, is difficult because of its diverse habits. It is essentially a forest-dwelling mosquito which only occasionally enters houses to bite and does not rest inside dwellings. However, in Tahiti it may be found in large numbers in the vicinity of houses which are close to bush areas. Although this mosquito regularly bites man, it may also obtain its blood meal from other animals, including the pig, dog, rat, and bird.

Larval surveys by Beye et al.,[4] Rosen,[33] and Bonnet & Chapman (unpublished data) have shown that this species is extremely adaptable in its choice of breeding-place, which includes such sites as tree-holes, rat-eaten coconuts, rock-holes, crab-holes, pirogues, metal drums, barrels, roof-gutters, bottles, tin cans, ant-cups, bamboo-stumps, fallen leaves, animal drinking-pans, automobile tyres, machinery parts and sea-shells. These sites are often small but numerous, thereby constituting important breeding-sources. The eggs show marked resistance to drying, and may remain viable in any of these containers, if dry, for long periods between rains.

Although the larvae of *A. polynesiensis* have not been found in the water which collects in the leaf axils of the pandanus (*Pandanus* sp.), banana (*Musa* sp.), taro (*Calocasia* sp.), and spider lily (*Crinum* sp.) or other

TABLE IX. EFFECT OF DIETHYLCARBAMAZINE PROGRAMME ON MOSQUITO PREVALENCE

Item	Treated area			Untreated area	
	before treatment	after treatment			
		2 months	12 months	2 months	12 months
Mosquitos per minute	0.54	0.54	0.60	0.42	0.50
Percentage of stations with mosquitos	66.9	67.4	63.5	72.5	65.0
Percentage of mosquitos positive for all stages of *W. bancrofti* larvae	13.2	5.2	4.7	11.9	12.9
Density of all stages of *W. bancrofti* larvae per dissected mosquito	0.74	0.2	0.17	0.64	0.57
Potential transmission index	100.0	26.6	25.0	67.2	71.0

similar types of plants in Tahiti, the forest areas serve as primary reservoirs for this mosquito because of the prevalence of tree-holes and rock-holes. Consequently, any attempt at complete mosquito control must include control in the uninhabited mountain-forest regions. This is only feasible in a control scheme which can operate on a budget which would provide sufficient equipment and manpower to execute control in all areas.

Fortunately, *A. polynesiensis* has a limited dispersal range, which various workers have estimated usually not to exceed 100 m (Jachowski,[17] and Bonnet & Chapman (unpublished data)). The combination of such a limited dispersal range and of breeding in small containers suggests the possibility of control through sanitation, that is, by the removal or destruction of all mosquito breeding-places in and around villages or in the vicinity of individual dwellings. This has been the method recommended in Fiji by Amos,[1, 2] in Samoa by Byrd, St Amant & Bromberg,[7] and in Rarotonga by Davis.[8]

In Tahiti, where the inhabitants do not live in well-defined villages but in houses dispersed for the most part along the coastal belt, an effort has been made to solicit the aid of the individual householder in clearing the property of breeding-places. This has been done through education of the people and organization of the system of district inspectors previously described (see page 641). At monthly intervals the chief, policeman, and council of a district visit selected houses with the inspector to determine that satisfactory compliance with instructions is being obtained. Habitual offenders are subject to fines for failure to carry out instructions. These procedures of sanitation, when adequately applied and maintained for a distance of 100 m around each dwelling, have proved satisfactory as a means of reducing mosquito numbers in Tahiti.

In certain districts, experiments have been performed with various insecticides as a supplementary aid to the method described above for control of this mosquito. The details of these trials by Bonnet & Chapman are as yet unpublished, but it can be stated in general that when these insecticides are used as exterior residual sprays their effectiveness against adults lasts for between four and six weeks. Interior spraying is ineffective against *A. polynesiensis* because this species usually does not rest in houses.

Mosquito control as a means of control for any disease, without the eradication of the species in question, is a long-range continuing programme and as such requires long-range objectives in sanitation and health education. In the control of filariasis in Tahiti the combination of the microfilaricide, diethylcarbamazine, with mosquito control appears to be proving successful and is considered most suitable for this area. After the discontinuance of the diethylcarbamazine programme, the educational campaign for mosquito control is again especially emphasized by talks and demonstrations because at this time filariasis control becomes entirely a programme of mosquito control.

The following is a general summary of the mosquito control measures employed in the system recommended.

(1) Institute survey in area to be controlled in order to determine species of mosquito and breeding-places important to it. This may be done at the same time as a census is taken for the blood survey of the population.

(2) Perform Intensive Mosquito Survey at the same time as the blood survey is done, to determine density of mosquito population and density of larvae of *W. bancrofti* in mosquitos (see Table IV, page 639). Repeat at specified intervals.

(3) Institute mosquito control procedures by educating householders to eliminate breeding-places for a distance of 100 m around each dwelling.

(4) Emphasize continuance of mosquito programme after discontinuance of microfilaricide programme.

(5) Follow this through by repeated inspection by local district inspector and special supervisory team.

DISCUSSION

Although filariasis was the first disease known to be transmitted by an insect (Manson [28]) and although it is widespread throughout the tropics, few programmes have been instituted primarily for the control or elimination of this disease. This is surprising in view of the fact that the most common chronic stage of the disease, elephantiasis, has long been figured and discussed in medical literature as one of the most disabling and bizarre of human diseases. Probably one of the reasons for this delay is that in many parts of the world it coexists with malaria, and the acute stages of the disease, accompanied by chills, fever and malaise, have at times been confused with malaria. However, in areas in which malaria does not occur, such as Polynesia, both primary or acute filariasis and chronic filariasis are at once evident, and attention is readily drawn to their importance from a clinical and an economic point of view.

Before the introduction of diethylcarbamazine by Hewitt et al.,[12] the only means of preventing filariasis was mosquito control. In areas of the world where malaria and filariasis have a common vector, or where the vectors of both diseases display similar habits, control against filariasis has automatically occurred along with the control of malaria. The same principle would likewise apply in areas where the economic and living standards of peoples have improved to the point where programmes for destroying nuisance mosquitos have been instituted. The elimination of filariasis from Charleston, South Carolina, where a focus had been introduced during slave-trade days, is an example.[22, 23] Recent reports from Western Samoa by McCarthy & Fitzgerald [27] also illustrate this trend.

Differences in the prevalence and density of microfilariae in urban and in rural areas likewise support this tendency. Surveys in the districts of Tahiti showed that from 26% to 43% of the population were carriers, having a microfilarial density ranging between 17 and 48. In the city of Papeete, however, where a few *A. polynesiensis* occur, only 15% of the population was infected, with a microfilarial density of 14.

Jachowski, Otto & Wharton [21] reported that nurses in American Samoa who lived in the screened hospital, protected from mosquitos, for a period of five years showed lighter microfilarial rates than their relatives who had continued to live in their natural environment; Samoans who moved to Hawaii where the most common vector for non-periodic filariasis—*A. polynesiensis*—does not occur, became negative for microfilariae within a period of 10 years. It would seem possible, therefore, that as sanitation methods and dilution of microfilariae in a population are gradually extended, filariasis will automatically decrease.

The improved knowledge of mosquito control that came to light during the Second World War and the discovery of the microfilaricide, diethylcarbamazine, however, have provided new tools with which to hasten the process, and it would seem desirable to apply them to the best advantage whenever possible.

The prevalence of the clinical disease, together with the extent of microfilariaemia, will determine the importance of filariasis as a public-health and economic problem in a given region, and will therefore provide the basis for the institution of such a control programme. Each area will have to determine by the necessary blood and mosquito surveys whether a programme based on mosquito control alone, administration of diethylcarbamazine alone, or a combination of the two methods, is best for its particular needs.

Mosquito control alone

This is the method that has usually been recommended in the past for a filariasis control programme (Amos,[1, 2] Davis,[8] and Iyengar [15]). It would undoubtedly achieve satisfactory results in areas where it is possible to eradicate a vector. However, it is slow and demands that the filariae in a population, either adult or embryo, be destroyed by natural body immunity mechanisms alone. The reports of Jachowski, Otto & Wharton in areas where opportunity for reinfection was discontinued, indicate that a period of from five to ten years is required to eliminate microfilariae from the bloodstream. As long as any vector mosquitos remain in a community with a high prevalence of persons positive for microfilariae, transmission will occur. The main difficulty with this method, therefore, is to assure reduction of mosquitos to that point where transmission ceases. It has already been pointed out that where *A. polynesiensis* is the principal vector, eradication is an expensive and difficult undertaking.

Diethylcarbamazine alone

It is possible to reduce transmission to a low point by the use of diethylcarbamazine without mosquito control (see, for example, Table VIII, page 653, district 1, where the field results show a reduction in microfilarial counts from 30.9% to 7.2% after one year of recommended treatment). A corresponding reduction of microfilarial density from 33.1 to 1.8 is observed. No infective stages of *W. bancrofti* larvae were encountered after one year of treatment in mosquitos in this district, and the density of larvae of all stages was reduced to 0.17.

District 7 provides another example of such control. The area was an island with a population of nearly 200. It was not possible to appoint an inspector to this island and the resident schoolteacher and pastor were taught to administer the diethylcarbamazine. One Sunday each month was set aside as " Notezine Sunday " and the pastor administered the drug regularly to the population. In the fourth-year follow-up survey on this island, only four, or 2%, of the people were positive. Three of these were recent immigrants and one a previous refusal; they had not completed their full courses of treatment at the time the blood survey was made.

This method *alone*, therefore, may be practical to use in areas where mosquito control is difficult or impossible to institute.

Mosquito control combined with microfilaricide

The application of mosquito control together with administration of diethylcarbamazine appears to present the greatest potentialities, and is the combination that was accepted for the programme in Tahiti.

The following outline summarizes the steps and procedures that are now recommended:

(1) *By clinical survey*, determine the prevalence of acute and chronic filariasis in the population.

(2) *By blood survey*, using the 20-mm^3 thick-film method, determine the prevalence of microfilariae in the population. Evaluate these results in terms of (*a*) frequency distribution of population at the several microfilarial levels recommended in Table II; (*b*) percentage of people positive; (*c*) microfilarial density.

(3) *By mosquito survey*, determine species, important vectors and bionomic characteristics of the same, e.g., breeding-habits, feeding-habits, dispersal range, resting-habits, etc.

(4) *By Intensive Mosquito Survey* (see Table IV, page 639), collect and dissect standardized catches of important vectors—*A. polynesiensis* in Tahiti—to determine mosquito density and density of larvae of *W. bancrofti* in mosquitos. A potential transmission index may then be calculated.

(5) Institute mosquito-control procedures by eliminating breeding-places for a distance of 100 m around each dwelling.

(6) Administer diethylcarbamazine at the dosage schedule of 6 mg per kg of body-weight one day each month for one year to both positives and negatives. Negatives are discontinued at the end of one year.

(7) Repeat (1), (2) and (4) above, each year.

(8) Continue diethylcarbamazine to all original and current positives, until they have been negative by two annual follow-up examinations or until each has received a full two-year treatment.

(9) Re-emphasize importance of mosquito control programme following discontinuance of microfilaricide programme.

Table VIII (see page 653), displays representative results from six districts (2, 3, 4, 5, 6 and 8) where these combined procedures were applied. It will be observed during the second year in district 4, and in all districts thereafter, that there was a marked reduction in the figures resulting from the mosquito dissections. In fact, no infective-stage larvae were encountered after this level had been attained. When such results are compared with the parallel results of the blood surveys, it will be seen that 5.6% of the population were still positive for microfilariae in district 4, and that all districts listed later demonstrated still lower percentages. Routine surveys in other treated districts not included in this table likewise demonstrate this same break-point.

Although the objective of this programme has been to reduce microfilarial carriers to zero, this point is not always attainable. The lowest results obtained in the field in this programme were in district 8 where 1% of the population remained positive with a microfilarial density of 0.04. No larvae of *W. bancrofti* were encountered in standard dissections of mosquitos in this district.

Judging from the data cited for districts 4 to 8, it may not be necessary to attain this low point in order to interrupt transmission sufficiently to produce the desired reduction in clinical filariasis. While in the control programme in Tahiti it is still planned to achieve as low a percentage of positives as possible with a corresponding low mosquito density, it is proposed for a mass treatment campaign that reduction of persons positive for microfilariae to a maximum of 5% with a corresponding maximal microfilarial density of 1 should be sufficient to reduce transmission to a negligible minimum. It will be necessary to continue to collect clinical data over a period of years to confirm this opinion, but the clinical observations already made in the current study definitely support such a supposition.

Unit costs

In order to give some idea of the cost of the programme here reviewed, determinations have been made per person on a number of the more significant items discussed. These are based on the actual costs of materials used, time of inspectors involved, and transportation costs of the procedures mentioned. They do not, of course, include original cost or upkeep of the Institute, cost of Institute equipment, or salaries of professional staff.

	Pacific francs	*US $*
Blood survey per person	12.2	0.19
Cost of Notezine per one 200 mg tablet	1.77	0.028
At the dosage schedule of 6 mg per kg of body-weight per month, counting both adults and children, the average used per month per person is two 200 mg tablets	3.54	0.056
Cost of administration per dose per person (this involves actual swallowing of the tablets by the recipient in the presence of inspectors)	4.08	0.065
Total cost per dose per person	7.62	0.111
Average cost per person for 12 months	91.4	1.46
Sanitation supervision by inspector per year, per person	95.0	1.52
Mosquito collections per Intensive Survey, per person	2.5	0.04
Mosquito dissections per Intensive Survey, per person	3.8	0.06
Total mosquito collection and dissection per Intensive Survey, per person	6.3	0.10

In planning a programme it will be necessary to calculate the approximate costs on the basis of the procedures it is intended to use, for example, in one group of islands where a preliminary survey was made some time ago, it was found that filariasis occurs in about the same magnitude as in Tahiti in 1949. The islands are difficult of access and it would be tedious and expensive to organize a full programme there similar to that in Tahiti. However, dispensaries with requisite numbers of nurses for medical work are already present. Without performing new blood and mosquito surveys, and without new personnel, it is a simple matter to administer diethylcarbamazine to the whole population, both negatives and positives. The only additional cost of such a mass treatment programme is that of the diethylcarbamazine, which in this instance will have to be given to the whole population for two years since a blood survey to differentiate positives and negatives was not made at the beginning of the treatment programme. Thus, treatment to negatives could not be discontinued in the second year. A follow-up blood survey and an Intensive Mosquito Survey will be performed at the close of the treatment programme for comparison with the previous survey.

The cost of such a mass programme, that is, treating the whole population, in comparison with performing a blood survey first and treating the negatives and positives for one year and the positives only for the second year, can easily be determined from the schedule of unit costs. For a population of 1000, they would be as follows:

	Pacific francs	*US $*
Treatment of all for 2 years		
Notezine: 91.4 francs × 2 × 1000	182 800	2 920.00
One blood survey at end	12 000	190.00
Total	194 800	3 110.00
Treatment of negatives for 1 year and positives for 2 years		
Notezine: 1st year—91.4 francs × 1000	91 400	1 460.00
Notezine: 2nd year—one third of 1st year	30 467	486.67
Two blood surveys, one at beginning and one at end	24 000	380.00
Total	145 867	2 326.67
Difference	48 933	783.33

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RÉSUMÉ

La filariose représente depuis longtemps un problème médical, social et économique dans l'archipel de la Société. A Tahiti, 30% de la population héberge des filaires, 20% présente de la filariose aiguë ou de la lymphangite et 5-10% de l'éléphantiasis. Les taux élevés de filariose clinique et de microfilarémie justifiaient l'organisation d'un programme de lutte. Diverses méthodes qui avaient pour objet la destruction du vecteur, et la chimiothérapie, ont été mises à l'étude.

Il est difficile de lutter contre la filariose par la destruction du vecteur seulement, dans des régions où la population est fortement infectée. La transmission se poursuit tant qu'il reste des vecteurs, ne fût-ce qu'en petit nombre. *Aëdes polynesiensis*, le principal vecteur, vit dans la brousse et ne pénètre que peu dans les habitations. Ses gîtes sont des plus variés — valves de coquilles, coques de noix de coco, pneus d'automobile, pirogues ou gouttières, etc. — et de ce fait extrêmement nombreux. Leur suppression ne peut être escomptée, car elle impliquerait l'extension de la lutte aux régions forestières inhabitées.

En revanche, il est possible d'abaisser notablement la transmission par la seule chimiothérapie. On a vu le taux d'infestation passer de 30,9% à 7,2% après une année de traitement et la densité microfilarienne s'abaisser, en conséquence, de 33,1 à 1,8, sans aucune mesure antilarvaire. La chimiothérapie peut donc être envisagée comme unique mesure de lutte, dans les régions où la destruction des gîtes est impraticable.

C'est en combinant les deux méthodes de lutte que l'on obtient les résultats les meilleurs, et le programme de Tahiti a été établi selon ces directives. La lutte proprement dite a été précédée d'enquêtes, afin de déterminer la gravité et l'étendue de l'infestation dans les zones à traiter, selon le schéma suivant:

1. Enquête clinique: prévalence de la filariose aiguë et chronique parmi la population. 2. Enquête hématologique: prévalence des microfilaires. 3. Enquête entomologique: détermination de l'espèce de moustique vecteur et étude de sa biologie. 4. Enquête entomologique intensive: dissection de *A. polynesiensis* et estimation de son infestation par les larves de *Wuchereria bancrofti.*

Les mesures 1, 2 et 4 sont répétées chaque année.

A la suite de ces enquêtes préalables, on a procédé, à Tahiti, à la lutte antilarvaire, en supprimant les gîtes de moustiques dans un rayon de 100 m autour de chaque maison. Concurremment, on a administré de la diéthylcarbamazine (Hetrazan, Notezine, Banocide) à tous les habitants, qu'ils aient été négatifs ou positifs à l'examen clinique ou hématologique. Au début de la campagne, la dose de médicament recommandée était de 2 mg de diéthylcarbamazine par kg de poids corporel, trois fois par jour pendant 7 jours. Après une année d'application de ce traitement, 50,6% des sujets étaient à nouveau positifs — 13% avec un degré d'infestation correspondant à 100 microfilaires par 20 mm^3 de sang. Malgré la réduction sensible par rapport au taux initial, la diminution était trop faible pour assurer le succès d'une campagne de masse. Une autre posologie fut alors adoptée. Elle comportait la prise d'une dose de 6 mg par kg de poids corporel, une fois par mois, pendant 24 mois pour les sujets positifs au premier examen, et pendant 12 mois pour les sujets négatifs, avec examen des sujets traités un an au moins après la fin du traitement.

Les résultats de six districts dans lesquels les deux méthodes de lutte ont été combinées sont indiqués en détail dans cette étude. Dans l'un d'entre eux déjà dès la seconde année et dans les autres ensuite, l'infestation des moustiques par les filaires avait considérablement diminué. Quant à la proportion de sujets porteurs de microfilaires, elle s'était abaissée à 5,6% au bout de deux ans déjà dans un district et, au cours des années suivantes, avait atteint dans les autres districts le niveau très bas de 2 ou de 1, auquel elle se maintenait au cours de la quatrième année après la fin du traitement. Il n'est pas facile d'atteindre le but fixé par le programme, qui est de réduire à zéro le nombre des porteurs de micro-

filaires. Il ne semble du reste pas qu'il soit nécessaire d'y parvenir pour contrôler la filariose clinique. En effet, les expériences faites au cours de la campagne de Tahiti paraissent indiquer que la réduction à 5% du nombre des personnes positives, avec une densité filarienne maximum de 1, correspond à une fréquence négligeable de la maladie. Ce point demande cependant à être vérifié par des examens portant sur plusieurs années.

L'auteur indique le coût de la campagne et suggère d'ajuster les programmes aux conditions rencontrées dans les diverses îles, certaines d'accès difficile, afin de simplifier les campagnes et d'en limiter le coût.

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