FILARIASIS AS A WORLD PROBLEM

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HISTORICAL. Filariasis is an important disabling disease, caused by a threadlike nematode. Two species are common in man, *Wuchereria bancrofti* (Cobbald 1877), Seurat, 1921, and *Brugia malayi* (Brug, 1927), Buckley, 1958. The microfilariae of *W. bancrofti* were first seen by Demarquay in 1863, more than 100 years ago, in hydrocele fluid from a patient in Cuba. They were found by Wucherer, in Brazil, three years later in chylous urine, and by Lewis in 1872 in blood from a patient in India. Bancroft recovered the first adult filaria in 1876, in Brisbane, Australia.

Sir Patrick Manson, 1878–79, working in Amoy, first described nocturnal periodicity of microfilariae and pointed out that larval stages developed in the common night-biting mosquito of the area.

Elephantiasis in Polynesia was first accurately described by Wilson (1799) in Tahiti, and the first microfilariae from Polynesia were collected by Davis in Samoa in 1884, but only reported by Manson in 1896. Earlier in the same year, Thorpe, in Tonga, was the first to report the presence of microfilariae in the peripheral blood of man during daytime in Polynesia. Bahr (1912) in an extended study in Fiji, added much to the knowledge of subperiodic filariasis in the Pacific. The line of geographic demarcation in the Western Pacific between nocturnal periodic filariasis and the subperiodic type was well defined by Buxton in 1928.

Slowness in developing control programs for filariasis was caused by difficulties in devising suitable methods for mosquito control and in discovering satisfactory filariacides. The unexpected occurrence of filariasis cases among troops in the Pacific theatre during the Second World War stimulated renewed interest in research, a most important outgrowth of which was the discovery of diethylcarbamazine, by Hewitt *et al.* (1947), a filariacide harmless to man, which held promise for use in the control of filariasis.

THE FILARIOIDEA. The main epidemiologic, clinical and morphologic characteristics of the etiologic agents of the Filarioidea are displayed in Charts 1 and 2. Filariasis, as indicated above, is caused by one of two genera belonging to this superfamily. They may cause either acute filariasis, e.g., lymphangitis with filarial fever or several types of chronic filariasis, such as elephantiasis, of arms, legs, breasts or genitalia; chyluria or hydrocele.

The photograph in Figure 1, taken in 1950 before control was begun, showing advanced elephantiasis in a man from

FIG. 1.—Advanced elephantiasis in man from Society Islands.

Society Islands, illustrates a type of Bancroftian filariasis that is disappearing through the application of control measures. Figure 2 shows a Malayan with normal legs, and another with elephantiasis of the legs. Usually elephantiasis associated with Malayan filariasis is less

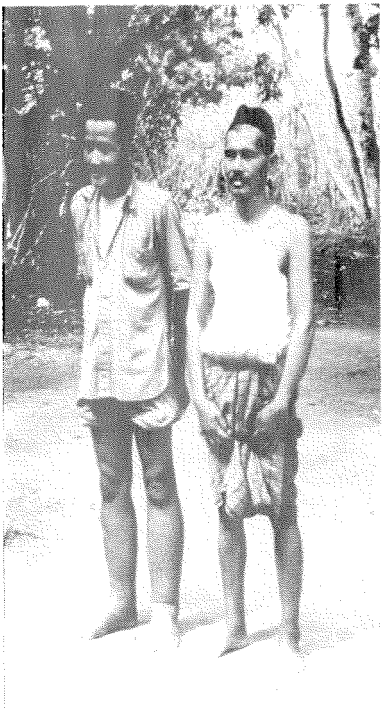

FIG. 2.—Malayan men, one with normal legs, the other with elephantiasis of the legs.

severe than that caused by Bancroftian filariasis.

DISTRIBUTION. The world distribution of the two principal types of filarioideal diseases, i.e., filariasis and onchocerciasis, is seen in Figure 3. Surveys throughout the world show some filariasis areas of low endemicity, i.e., with microfilaria rates from 1 percent to 8 percent, some areas of high endemicity, with microfilaria rates of 25 percent or more, and others with intermediate rates.

The use of diethylcarbamazine and of DDT or other new insecticides developed during and soon after World War II, led to field investigations in many parts of the world to evaluate methods for their use in filariasis control programs.

INTERNATIONAL MEETINGS. The first international meeting was sponsored by the South Pacific Commission at the Institute of Medical Research, in Tahiti, where in 1951 some 30 workers met for a two weeks' conference. Soon after this, in 1955, the World Health Organization called the first Study Group on Filariasis to meet in Kuala Lumpur, Malaya, to observe the epoch-making discoveries that were taking place with reference to Malayan filariasis in Pahang. The WHO Secretariat called a Scientific Committee in 1959, and an Expert Committee in 1961, both of which met at WHO Headquarters in Geneva. This last committee summarized most of the available literature, in the form of guides rather than rules, which was published in 1962, (WHO Tech. Report Series No. 233).

In November, 1965, the first Inter-Regional Seminar on Filariasis was held in Manila under the auspices of the WHO. Twenty-five countries where filariasis occurs accepted invitations to attend, as follows:

African Region:	1. Madagascar
	2. Mauritius
Eastern Mediterranean Region:	3. Sudan
	4. United Arab Republic
Southeast Asia Region:	5. Ceylon
	6. India
	7. Thailand
Western Pacific Area:	8. American Samoa
	9. Australia
	10. British Solomon Islands
	11. China (Taiwan)
	12. Fiji
	13. French Polynesia
	14. Gilbert and Ellice Islands
	15. Japan
	16. Korea
	17. Malaysia
	18. Philippines
	19. Ryukyu Islands

Parasite	Periodicity	Vectors	Reservoirs	Clinical Type
Wuchereria bancrofti	Nocturnal	Culex Anopheles	Man	Acute Lymphangitis, filarial fever
	Diurnal in Polynesia	Aedes		Chronic Lymphadentis, Hydrocele Elephantiasis
Brugia malayi	Nocturnal	Mansonia Anopheles	Cats, dogs, Macaca, Slow loris	Same, but elephantiasis less severe
Loa loa	Diurnal	Chrysops	Probably monkeys	Migratory. Calabar swellings
Acanthocheilonema perstans	Modified Nocturnal	Culicoides	Monkeys	Pathogenicity ? allergic dermatitis
A. streptocerca	None, found in skin	Culicoides	Probably monkeys	Cutaneous edema and elephantiasis
Mansonella ozzardi	None	Culicoides	Man	?Hydrocele and lymph gland enlargement
Onchocerca volvulus	None, found in skin	Simulium	Not proved	Nodular Ophthalmic

CHART 1.—Epidemiologic and clinical differences among filarial infections of man.

20. Singapore
21. Tonga
22. Territory of Papua and New Guinea
23. Trust Territory of the Pacific Islands
24. Viet Nam
25. Western Samoa

Altogether, some 50 people attended the seminar.

COMPARISON OF MALARIA AND FILARIASIS CONTROL. A comparison of filariasis control with the early history of malaria control shows the first measures applied against malaria to be concerned with the control of mosquitoes. These involved multiple types of drainage, spraying with oil and paris green. Subsequently, numerous other insecticides were applied against both larvae and adults. Much of the success in malarial control came from the fact that most species of anopheline mosquitoes were domestic, and usually rested in houses or buildings. This made spraying practical for control against adults.

When eradication programs became the rule, malariologists were faced with the problem of resistance to insecticides. At this time, they added surveillance and drug control to their armamentarium, and now include such measures in their regular programs. In areas where identical species of anopheline mosquitoes transmit both malaria and filariasis, e.g., *Anopheles gambiae* in Africa and *Anopheles farauti* in New Guinea, combined control programs are being considered.

Parasite	Adult Worm			Microfilaria	
	Length of Female	Location in Tissue	Time to Mature	Sheath	Tail Nuclei
Wuchereria bancrofti	Periodic, 70-100 mm. Sub-periodic 60-77 mm.?	Lymph nodes	About 12 months	Yes	
Brugia malayi	42-55 mm.	Lymph nodes	About 3 months or less	Yes	
Loa loa	50-70 mm.	Subcutaneous tissue	Possibly 1 year	Yes	
Acanthocheilonema perstans	70-80 mm.	Pleural, Peritoneal or Pericardial cavities	Not known	No	
A. streptocerca	?	Connective Tissue	Not known	No	
Mansonella ozzardi	65-80 mm.	Body Cavities	Not known	No	
Onchocerca volvulus	35-50 mm.	Subcutaneous nodules	About 12 months	No	

CHART 2.—Differences among filarioidea of man.

In filariasis control, it is recommended that mass treatment with diethylcarbamazine be administered first, thus diminishing microfilaria rates and densities, which reduces potential transmission immediately. Mosquito control is begun simultaneously, or as soon after as possible.

MOSQUITO CONTROL. Most mosquitoes which transmit malaria belong to the genus *Anopheles,* while most mosquitoes which transmit filariasis belong to one of the four genera, *Anopheles, Culex, Aedes* and *Mansonia.* The bionomics and breeding places of the many species belonging to these four genera make mosquito control for filariasis a highly specialized and expensive problem, albeit one of great importance.

DRUG CONTROL. Although arsenical and antimonial drugs, when first used for filariasis, showed promise, difficulties have often occurred during their administration and reluctance has developed concerning their use in control or mass-treatment programs.

Diethylcarbamazine, a non-toxic drug, introduced by Hewitt *et al.* in 1947, gave much promise and has been tested extensively in many parts of the world.

The writer has been closely associated with two filariasis control programs in the South Pacific, in which diethylcarbamazine has been used, the first in French Polynesia and the second in American Samoa. The motion picture film, "The Control of Subperiodic Filariasis in Polynesia" illustrates the major aspects of the problem in this area. During this study, filariasis control was based primarily on a mass-treatment regimen with

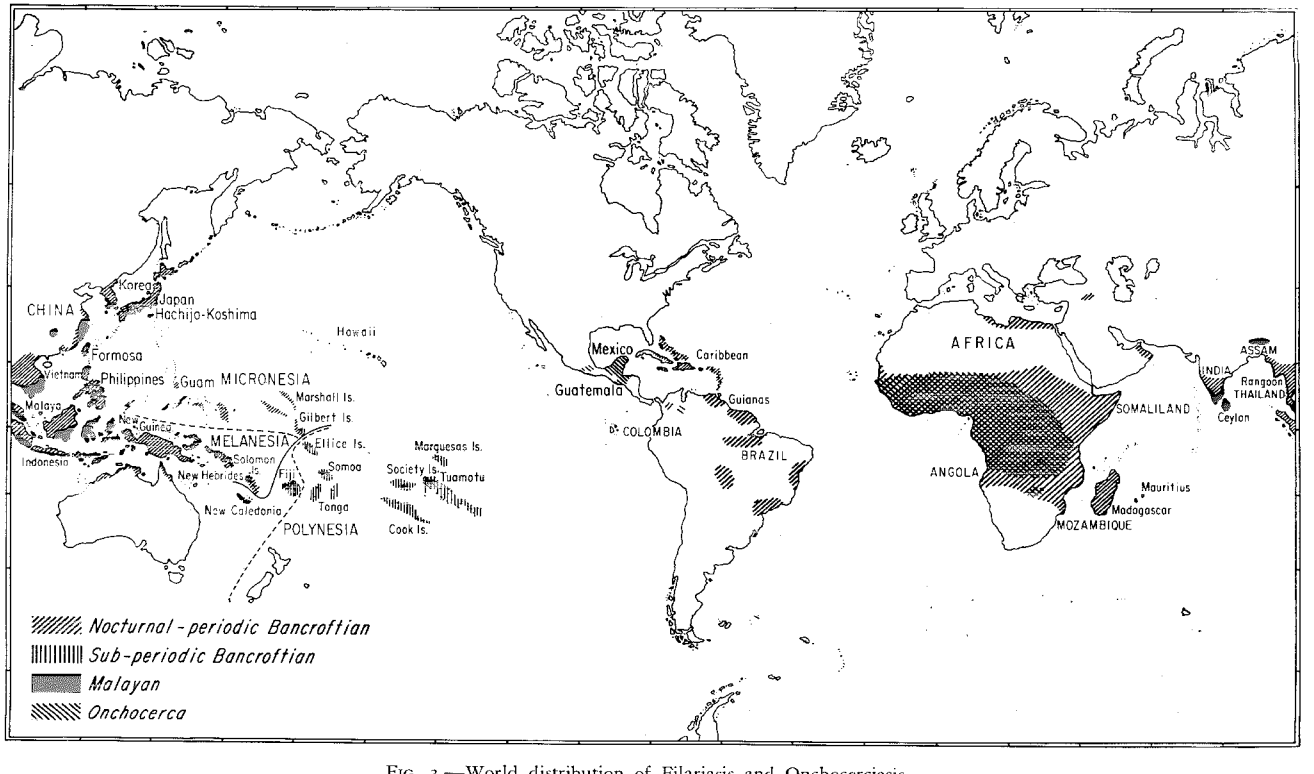

FIG. 3.—World distribution of Filariasis and Onchocerciasis.

a minimum of 12 doses of 6 mg per kg of body weight, i.e., a total of 72 mg per kg of body weight of diethylcarbamazine, to the whole population.

Three main systems of spacing the administration of the 12 doses of diethylcarbamazine have been used in the two programs: (1) once a day for six days then once a month for six months, (2) once a day for six days, rest six months, then repeat once a day for six days, and (3) once a month for 12 months. The first follow-up blood survey is recommended one year after the last treatment. Theoretically, each person who shows microfilariae in annual follow-up blood surveys begun one year after the close of diethylcarbamazine treatment is retreated with a standard regimen of diethylcarbamazine.

Sanitation procedures and clean-up of mosquito breeding places within and around each home in Tahiti for a radius of 100 yards was recommended on a volunteer basis and is supervised by an instruction and inspection team. In American Samoa, clean-up is performed on a village basis with weekly collection by trucks of garbage, cans, bottles, etc., that might serve as breeding places for mosquitoes.

Prior to control in Tahiti, as shown by Beye *et al.* (1952 and 1953), the microfilaria rates per rural district ranged from 25 percent to 43 percent, with an average rate of 32 percent. The average microfilaria count per 20 cmm of blood per person in these districts was 32 and per carrier was 80, the latter with a range from a low of 41 to a high of 118.

Experimental areas receiving diethylcarbamazine and control areas with neither diethylcarbamazine nor mosquito control were compared as follows:

A. Microfilariae in blood surveys.

The results of blood surveys in experimental areas may be reported either by recording microfilaria rates and average counts in (1) the total population of the area, which furnishes an epidemiologic base line for clinical and blood surveys and for comparison with larval rates in mosquito surveys; or (2) only in those carriers who have received a complete regimen of a standard treatment. This selected group provides information concerning chemotherapeutic results. The following observations were apparent:

a. There was no reduction in microfilaria rates nor in microfilaria counts when no drug was administered.

b. Results reported by procedure (1), above, showed a decline in microfilaria rates to 2.5 percent by the first year after the close of treatment with average microfilaria counts per 20 cmm of blood of less than one. In areas receiving no further treatment, the average rate had increased to 7.5 percent during the third year; however, with average microfilaria counts still less than one. In areas where recurrent positives, detected by annual follow-up blood surveys, were routinely treated with diethylcarbamazine, the follow-up microfilaria rates held at 3 percent or less, thus indicating that the results are dependent upon the thoroughness of the treatment. Procedure (2), above, for two groups of carriers, one with a pre-treatment average microfilaria count of 61 per 20 cmm of blood who received twelve doses of diethylcarbamazine, totaling 72 mg per kg of body weight, and the other with a pre-treatment average count of 56, who received a total of 152 mg per kg in 26 doses, gave the following results three years after the treatment: The first showed a microfilaria rate of 24 percent with an average microfilaria count of 1.8, and the second showed a rate of 13 percent with an average microfilaria count of 0.2. It will be noted that the group receiving the greater amount of drug showed the lower microfilaria rate and count.

B. Infective stage larvae in mosquitoes.

The infective stage larva rate of *Wuchereria bancrofti* in naturally infected mosquitoes in two areas, when checked each three months for two years before control, was 3.1 percent with a low of 1.2 percent and a high of 8.7 percent. Three years after the first round of mass-treatment with diethylcarbamazine, the rate in these two areas was less than 0.5 percent.

C. Clinical manifestations.

The prevalence of elephantiasis and hydrocele in four rural villages in American

Samoa in 1962 is compared with reports by Dickson (1943) and Murray (1948), from surveys made when the U.S. Navy was in charge of medical and public health activities. There was little change in the rates from 1943 to 1962, a period of 19 years, during which control measures were not instituted.

In contrast, Laigret *et al.* (1965) in Tahiti, where an island-wide filariasis control program was in progress during a 12-year period from 1953 to 1965, report appreciable reductions in both elephantiasis and hydrocele.

PROBLEMS AND CONCLUSIONS. The success of a control program against filariasis is directly proportional to the thoroughness with which it is executed. Several important problems in the use of diethylcarbamazine as a chemotherapeutic control measure should be emphasized: (1) The number of people excused from mass-treatment campaigns for health reasons. (2) The number of people refusing to take the drug. (3) The speed with which the new microfilaria carriers who migrate to a given area are adequately treated. (4) The recurrent microfilaria positives, as compared with pre-treatment positives. The higher the pre-treatment density, the greater the likelihood of recurring microfilaremia. See Ciferri and Kessel (1965).

Reports listed in the References, together with current information, show that adequate administration of diethylcarbamazine will result in marked lowering of microfilaria rates and densities in man, infective-stage larval rates in mosquitoes, and in clinical filariasis rates, to the point where the disease is no longer the severe public health problem previously experienced. Even so, at least in areas of highest microfilaria densities, as found in Tahiti before filariasis control, eradication has not been reported.

In a few regions, notably those with lowest microfilaria rates and densities, as in certain areas of Japan and in the Austral Islands, interruption of transmission may have been attained. Where this can be confirmed, studies leading to filariasis eradication programs are indicated.

An additional important problem remains, as found in control of any infectious disease, i.e., improvement of currently used therapeutic agents and methods. Diethylcarbamazine, the safest and most generally used drug, may require several administrations to eliminate recurrence of microfilariae. With its continued use, one must practice perseverance by repeated administration.

To increase efficiency in present control measures and advance to successful eradication programs, attempts should be made (1) to improve drugs now in use and to discover more efficient ones, (2) to improve insecticides and methods of vector control, and (3) to enhance public health education.

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