Selective Primary Health Care: Strategies for the Control of Disease in the Developing World. VII. Filariasis

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At least 250 million people throughout the world are infected with filariae, and the number of such persons is increasing. Three species infect humans: Wuchereria bancrofti, Brugia malayi, and Brugia timori. The peak of microfilarial density in the blood usually occurs nocturnally. Transmission of filariasis is remarkably inefficient. In an endemic area, ~100,000 mosquito bites yearly are required for production of each new case of microfilaraemia. Only a small proportion of those infected suffer any ill effects from these worms. Clinical filariasis can present with acute inflammation such as lymphangitis and lymphadenitis and with chronic lymphatic obstruction such as hydrocele and lymphedema of the limbs. Measures available for potential control include the widespread usage of mosquito nets, vector control, and chemotherapy with diethylcarbamazine. Unfortunately, the efficacy of the first of these is untested and the latter two are inadequate. More research is required on vector control, assessment of new drugs, and the development of vaccines.

Filariasis is one of the major helminthic infections of humans. Although there are a number of filarial parasites, including Loa loa, Onchocerca volvulus, Mansonella ozzardi, and Dipetalonema perstans, only the three lymphatic-dwelling filariae that infect humans, Wuchereria bancrofti, Brugia malayi, and Brugia timori are considered in this paper. It has been estimated that ~250 million people throughout the world are infected with filariae, and the number of such persons is undoubtedly increasing [1]. Nevertheless, only a small proportion of these people suffer ill effects from infection with these worms. Since filariae are transmitted by mosquitoes, ecologic factors are of immense importance in affecting the vectors themselves and their interactions with humans [2]. Measures available for the potential control of filariasis include those directed against the intermediate host and those that attack the parasite itself.

Understanding the Problem

Biology. After a human is bitten by an infected mosquito, infective larvae enter the lymphatics and migrate within them to the vicinity of the draining lymph nodes, where the larvae mature during the next few months into thread-like adult worms 5-10 cm long. The fertilized females discharge large numbers of microfilariae, which pass via the lymphatics into the bloodstream. When microfilariae are ingested in the mosquito's blood meal, they unsex in the insect's stomach, penetrate its thoracic muscles, where they undergo two molts, then migrate to the proboscis and are ready to infect the next person who is bitten. This process takes approximately two weeks. The number of infective larvae per mosquito usually is small (fewer than five). Although mosquitoes have remained infective for up to 10 weeks under experimental conditions, their life-span in nature is much shorter, and it is probable that most mosquitoes are responsible for transmission of larvae to only one person.

A number of characteristics of these worms profoundly influence the distribution and transmission of filariasis. These include periodicity, infectivity for vectors, infectivity for definitive hosts, and reproductive behavior.

In many filarial infections there is a cyclical surge of microfilariae into the peripheral blood [3]. For most patients with bancroftian filariasis, periodicity is nocturnal, the peak microfilarial density occurring at approximately midnight. In patients infected with W. bancrofti in the South Pacific, however, a diurnal subperiodicity is seen;
microfilariae circulate for 24 hr, the greatest numbers occurring at midday. Microfilariae of one strain of *B. malayi* are nocturnally periodic, whereas those of the other strain are nocturnally subperiodic, i.e., microfilariae are present in the blood for 24 hr, but the numbers are greater at night. Filariasis can only be maintained in a community if microfilariae appear in the blood—and are thus accessible to mosquitoes—when vectors bite in abundance.

Within the *W. bancrofti* complex, there are a number of physiologic forms, which differ in their capacity for development in various mosquito vectors [3]. For example, urban strains of *W. bancrofti* are transmitted more efficiently by *Culex quinquefasciatus*, whereas rural strains are highly adapted to transmission by anophelines. Thus, not only must microfilarialemia occur when mosquito biting is maximal, but the parasite must have the intrinsic capacity to mature in that vector.

Humans are the only significant reservoirs of *W. bancrofti*. Periodic *B. malayi* is primarily a human infection, whereas the subperiodic form has been found in a number of monkeys; in domestic, wild, and civet cats; and in pangolins as well as in humans [4].

As with most parasitic helminths, adult filariae cannot multiply within the human host. Adult worms may produce myriads of microfilariae, but these latter forms can develop further only within mosquito vectors. Thus, the number of adult worms in each person is limited by the number of infective larvae introduced into the body. It has been observed that in such circumstances the distribution of worms in the population frequently is overdispersed; i.e., most people have the lightest worm burdens while the smallest proportion of people have the heaviest infection [5]. This type of distribution almost certainly happens in filariasis; it is not possible to assess the numbers of adult worms, but the densities of microfilariae in peripheral blood, which probably reflect numbers of adult worms, often do follow such a pattern (figure 1).

The individual. Immunologic indications of infection develop long before the appearance of microfilarialemia or clinical evidence of disease [6]. In general, circulating microfilariae are nonpathogenic, and persons with microfilarialemia may or may not have clinical evidence of disease.

Clinical filariasis may be grouped into two broad categories. Acute inflammatory filariasis probably occurs when a worm located in a lymphatic moults or dies. The onset of such lymphangitis or lymphadenitis may precede the appearance of microfilaraemia. Obstructive filariasis with hydrocele or lymphedema of the limbs results when inflammation and subsequent fibrosis around worms in lymphatics are sufficiently marked so as to impede the flow of lymph. Many persons with advanced disease become amicrofilaremic.

**The population.** *W. bancrofti* is distributed widely throughout the tropics and subtropics; *B. malayi* is restricted to parts of Southeast Asia and adjacent regions, whereas *B. timori* occurs focally in the eastern Indonesian archipelago.

Patterns of filariasis in humans vary in different geographic areas [6-18]. The prevalence of microfilaraemia usually increases with age. In some regions prevalence plateaus in early adult life; in other places it rises steadily with age. Similarly, the intensity of microfilaraemia may increase progressively with age, or a plateau effect may be
noted. In some locations rates of microfilaremia are similar for the two sexes, while in others, higher prevalences are found in males.

The age and sex distribution of acute filariasis is obscure because lymphangitis and lymphadenitis have a multiplicity of causes, and thus it is difficult to be certain of a filarial etiology. For chronic filariasis, however, a reasonably consistent correlation has been found between the prevalence of obstructive disease and advancing age. Generally the prevalence of obstructive disease is higher in males, but this simply may reflect the tendency for men to develop hydroceles. The severity of illness clearly varies from one endemic area to another. Acute lymphatic filariasis is painful and unpleasant. Chronic filariasis is rarely a lethal disease, although lymph stasis predisposes to secondary bacterial infections, which may occasionally be fatal. Large hydroceles may impair both sexual gratification and fertility. Gross edema of the legs may impair mobility and the ability to work, with resultant poverty and malnutrition.

Correlation between the prevalence and intensity of microfilaremia and the risk of clinical obstructive disease is reasonably strong. This relation is indicated in figures 2–4 which show similar trends in the prevalence of microfilaremia with respect to age, intensity, and the presence of obstructive disease in men and women in a Filipino village. These trends presumably indicate that those with the heaviest worm burdens are most at risk of developing clinical disease.

Vectors of filariae include *Aedes*, *Anopheles*, *Culex*, and *Mansonella* species. The species occupy extremely diverse ecologic niches. Their breeding sites, host preferences, and favored times and location of biting vary enormously. For example, the culicine mosquitoes, which constitute the majority of vectors of filariae that affect humans, include day-biting bush mosquitoes of the *Aedes pseudoscutellaris* group and the night-biting and house-haunting *C. quinquefasciatus*.

The transmission of filariasis is remarkably inefficient. Hairston and De Meillon [19] first drew attention to this by showing that bites by 15,500 mosquitoes carrying infective larvae of *W. bancrofti* were necessary for production of each new case of microfilaremia in Rangoon. Furthermore, <1% of mosquitoes carried infective larvae. Under these circumstances transmission occurred only because the average number of mosquito bites per person per year was almost 100,000 and the average number of infective larvae received per person per year was >1,000.
These findings have been substantiated in a number of other studies in other parts of the world [20–28], although those investigations that did not employ filter concentration techniques may have underestimated low-grade microfilaremias and thus slightly overemphasized the inefficiency of transmission. The intensity of transmission is often a little higher in urban than in rural areas, but in all cases transmission is inefficient.

Social and economic changes may profoundly influence the prevalence and severity of filariasis, either by altering the presence and numbers of vectors or by modifying the contact between people and mosquitoes. Deforestation and the establishment of rice plantations in Africa have resulted in an increase in the numbers of anopheline vectors [29]. Similarly, the construction of dams, ditches, ponds, lakes, and reservoirs of various kinds as well as excavations related to road and railway developments may increase mosquito densities. One of the most important of these effects has been the appearance and spread of C. quinquefasciatus in urban areas [30]. In places where there is virtually no sanitation, domestic waste water accumulates in the vicinity of houses and in badly drained channels, becomes polluted, and provides conditions favorable for mosquito breeding. Inadequate rubbish collection results in a litter of empty cans, tires, coconut shells, and other discarded materials in which water collects and mos-
quitoes breed. Consequently, filariasis is a disease primarily of the poorer classes in both rural and urban areas.

Four different epidemiologic patterns of filariasis have been described [23, 31–33]: first, high rates and densities of microfilaremia and many clinical signs of disease, indications of stable transmission in an area of high endemicity; second, high rates and densities of microfilaremia and few clinical signs of disease, indications of either the recent importation of filariasis or an increase in transmission; third, low rates and densities of microfilaremia and many clinical signs of disease, indications of either the emigration of young people with microfilaremia or a decrease in transmission; and fourth, low rates and densities of microfilaremia and few clinical signs of disease, indications of stable transmission in an area of low endemicity.

Points of Attack

The three major routes of attack on filariasis are (1) the direct attack on the parasite with anthelmintic drugs, (2) the destruction of mosquitoes by elimination of breeding sites and the use of insecticides, and (3) the limitation of biting of humans by mosquitoes by use of impediments to human-mosquito contact. In many areas various combinations of these measures have been tried [33–35]. Unfortunately, the costs, merits, and disadvantages of these various approaches have been poorly researched until recently and are ill understood. If effective vaccines are eventually developed, they may offer a further means of control.

Methods of Attack

Chemotherapy

Diethylcarbamazine has a microfilaricidal action but only limited macrofilaricidal activity, particularly against W. bancrofti. Since this drug reduces the numbers of circulating microfilariae, it ought to lessen filarial transmission. The effects of mass administration of this drug have been assessed in a number of endemic areas [36–48]. In addition, a few studies have combined the mass administration of diethylcarbamazine with measures of vector control [49–53]. In these latter circumstances, it is difficult to assess the relative contributions of
diethylcarbamazine therapy and vector control. Nevertheless, there is no doubt that the administration of diethylcarbamazine reduces the prevalence and intensity of microfilaria. Before consideration of whether this effect is worthwhile, however, two questions need to be answered—what should be treated, and what is the best treatment regimen?

In most of the studies cited above, investigators treated whole populations, irrespective of whether individuals had clinical evidence of filariasis or whether microfilaria was demonstrated. The reasons for this type of coverage have been discussed in a review by the Indian National Filaria Control Programme [54]. If everyone had not been treated, examination of the night blood of every member of the community would have been necessary—a daunting task. Furthermore, a single examination of blood frequently fails to detect infected persons, particularly if concentration techniques are not used. Finally, carriers of microfilaria are often asymptomatic and are unlikely to present themselves for blood examination. In these circumstances treating the entire population is more practical, ensures greater cooperation, and is probably cheaper than treating only the infected population. The results of treatment can be assessed merely by following a small sample of people. This view has been substantiated by Sasa et al. [50]. Those authors found that the reduction in prevalence of microfilaria was greater in villages in which the whole population was treated with diethylcarbamazine than in those villages in which only microfilaremic persons were treated. They did concede, however, that selective administration may be better in areas of extremely low endemicity.

Diethylcarbamazine has been given in a range of doses with a variety of schedules. The findings of Sasa et al. [50] are representative of the observations of most authors. If a short course, e.g., 5 mg/kg daily for 10 days, is given, microfilarial density is rapidly reduced within a few days, but the effect is not sustained. When the same quantity of drug is given in divided doses over an extended period, the decrease in microfilarial density is much slower but eventually reaches the same level and lasts much longer than with the short-course regimen. Alternatively, an intensive short course may be given for rapid reduction in the number of microfilariae and then smaller doses can be given at wider intervals for achievement of a persistent reduction in prevalence and intensity of microfilaria. This schedule was used in a number of studies in which the drug was given only to those persons shown to be persistent carriers [43–45, 53]. Whereas this may be practicable in intensive studies of small groups of people, it is simpler to administer diethylcarbamazine repeatedly, irrespective of its effectiveness in the individual, to the whole population in large control programs for the reasons outlined earlier.

A reasonable regimen that achieves a sustained effect is the treatment of each person in the endemic area with a single dose of 5 mg of diethylcarbamazine/kg at monthly or bimonthly intervals. Unfortunately, such a protocol is difficult to administer on a mass scale. Since highly developed systems for the delivery of health care are not available in most endemic areas, the effectiveness of medicating salt with diethylcarbamazine has been evaluated [55, 56]. Although this method may be of value in small, closed communities or in endemic areas where there are no alternative sources of salt, its efficacy in large-scale operations is doubtful [57].

Given that the appropriate population in an endemic area is receiving the optimal regimen of diethylcarbamazine, costs and benefits must be analyzed by consideration of the toxicity of diethylcarbamazine, the effectiveness of the program, and the cost of administering the drug.

Toxic reactions to diethylcarbamazine are frequent, occurring in 25% to almost 100% of the people treated [39, 41, 43, 44, 51, 53, 58]. Systemic reactions including fever, chills, headache, and myalgias are the most common. These reactions usually begin within a few hours of administration and last a day or two. Smaller numbers of people have local reactions, with adenolymphangitis. Some patients complain of gastrointestinal upsets such as nausea and vomiting, while others may develop urticarial eruptions [44]. These reactions occur more commonly during the first course of treatment and are more frequent in patients with high microfilaria counts. Whereas these adverse effects may be endured by sick people desiring to be cured, most persons treated in a control campaign are not conscious of any disability due to the disease. Since word of these toxic reactions spreads rapidly, it may be difficult to persuade asymptomatic members of the popu-
lation to take the drug, particularly in large campaigns in which the people and health workers are not well known to one another [57]. These problems are compounded when patients have concurrent onchocerciasis, since reactions to onchocercal microfilariae increase the toxicity of diethylcarbamazine [58].

The effectiveness of diethylcarbamazine may be assessed in terms of the changes in the number of microfilariae in humans, the number of infective larvae in mosquitoes, or by alterations in the frequency and severity of the clinical manifestations of filariasis.

Both the prevalence of microfilaremia and the mean density of circulating microfilariae are greatly reduced by the drug. When the effects of mass administration of diethylcarbamazine in small communities are considered, the general pattern observed in the short term is a decrease in the number of cases of microfilaremia by \( \approx 80\% \) and in a decrease in the mean density of circulating microfilariae by \( >90\% \) [36, 37, 39–41, 43, 44, 51, 52]. In contrast, the effects of treatment on filarial transmission have been less clear; some investigators find a marked decrease in the number of mosquitoes with infective larvae [48, 52, 53], while others have observed little change [46].

Despite these encouraging observations, the long-term impact of mass administration of diethylcarbamazine or the impact of large-scale programs, is limited. Three examples will be cited. Burnett and Mataika [40] have recorded the course of filarial infections in a Fijian population given two courses of diethylcarbamazine six months apart. The prevalence of microfilaremia decreased by 78\%, from 12\% to 2.7\% of the population, and the mean microfilarial density decreased by 91\%, from 4.5 to 0.36 microfilariae per 20 \( \mu \)l of blood, soon after treatment. Four years later, in the absence of any further control measures, the prevalence of microfilaremia in the population had risen to 5.5\% and the microfilarial density, to 0.50 per 20 \( \mu \)l of blood.

The situation is even worse when mass administration is attempted on a massive scale. Gonsalves [38] has described the campaign in Mangalore, India, which at the time of the study had a population of >1 million inhabitants. Fifty-nine percent of the population received a five-day course of diethylcarbamazine, and 69\% took the drug for at least one day. The prevalence of microfilaremia decreased by only 45\%, from 16\% to 8.8\%, and two years later had increased to 12.2\%. Similarly, the microfilarial density decreased by 76\%, from 49 to 12 microfilariae per smear, and increased to 18 microfilariae per smear after two years.

At the other end of the spectrum are the attempts to eradicate filariasis in Tahiti [52]. Despite a 10-year campaign of mass administration of diethylcarbamazine to the whole population, which was followed by repeated treatment of carriers and intensive and constant measures of vector control, filarial infection was not eliminated. Significant gains were made in the several years after the initiation of the campaign; microfilaremia rates fell from 30\% to 6\% of the population, and microfilarial density decreased from 23 to 1.5 microfilariae per 20 \( \mu \)l of blood. Eight years later little further change had occurred; 7\% of the population were still carriers, and the mean microfilarial density was 1.3 microfilariae per 20 \( \mu \)l of blood. This failure to eradicate filariasis results from the inability of diethylcarbamazine to eliminate microfilaremia in all patients [59, 60].

Since diethylcarbamazine has little effect on established disease, the effects of mass treatment on clinical filariasis can only be determined by long-term observation. A reduction in filarial transmission may be reflected in a decrease in the number of episodes of acute adenolymphangitis (which may be difficult to interpret since this condition may also be due to other infections) and by a decrease in the prevalence of obstructive disease over many years. Unfortunately, few data are available. March et al. [49] have shown, however, that during 10 years of the intensive filariasis control campaign in Tahiti, the rates of elephantiasis in males, of hydrocele, and of acute filarial lymphangitis in males older than 20 years decreased from 6.9\% to 2.2\%, 9.9\% to 3.2\%, and 36\% to 4\% of the population, respectively. Furthermore, no new cases of elephantiasis appeared during that time.

Thus, even in ideal circumstances, as in Tahiti, once the rate of filarial infection is brought down to a certain level, any further reduction becomes very difficult to achieve. Consequently, Laigret et al. [52] concluded that the slightest relaxation of control measures would lead to a renewed rise in the percentage of the population with micro-
filaremia, but provided that these rates remain below a critical level, the rates of clinical disease will continue to improve slowly.

One hundred 50-mg tablets of diethylcarbamazine can be purchased in Australia for \(~\$5.00\) (U.S.); however, the drug probably can be acquired by a developing country at a lesser price when bought in bulk. With use of this figure and on the assumption that each person is treated with a course of 5 mg of diethylcarbamazine/kg daily for seven days followed by a monthly dose for one year, then the cost is in the order of \$5.00\) for each adult. This calculation takes no account of the costs of providing the infrastructure necessary for the administration, delivery, and supervision of drug consumption, let alone of analysis of the efficacy of the campaign or of treatment of patients with adverse reactions to the drug.

Clearly, diethylcarbamazine is not a panacea; its use is associated with toxicity, and it does not eradicate microfilaremia. In an attempt to increase the effectiveness of anthelmintic therapy for filariasis, levamisole has been given alone or in conjunction with diethylcarbamazine [61]. Unfortunately, no significant improvements were noted for this combination compared with diethylcarbamazine alone. The ideal drug has not yet been found; desirable attributes include an ability to sterilize female worms permanently and the absence of any macrofilaricidal effect, thus preventing the precipitation of acute adenolymphangitis.

Vector Control

Numbers of mosquitoes may be reduced by physical measures directed against larval breeding sites or by destruction of immature or adult mosquitoes with chemicals. Since the species of vectors change from region to region, the most appropriate means of mosquito control vary widely. Frequently, a combination of control techniques is desirable.

The modifications of the physical environment that are most appropriate in any particular area are dependent on the habits of the major vector or vectors. In urban areas \textit{C. quinquefasciatus}, which breeds in polluted water, is extremely important. This mosquito can be controlled by avoiding the use of open drains for sewage and sullage, or, if these are absolutely necessary, by prevention of stagnation in them by frequent cleaning and flushing, together with mosquito-proofing of septic tanks and pit latrines and clearance of vegetation from waste-stabilization ponds [30]. In areas where swamp-breeding mosquitoes such as \textit{Mansonella} and \textit{Anopheles} species act as vectors, the drainage of swamps and the conversion of land for agricultural use may be very effective [62]. In Tahiti, where \textit{Anopheles polynesiensis} is the vector, mosquito breeding sites, such as empty bottles, cans, and coconut shells, were cleared for 100 meters around every household [49]. Despite intensive measures in these various situations, however, it frequently is impossible to eradicate the vectors, although a substantial reduction in mosquito numbers may be feasible.

Larvae or adults may also be controlled by chemicals. The former are the preferred target for control of \textit{C. quinquefasciatus}. Petroleum oil may be added to mosquito-breeding sites, where it kills larvae by interfering with their respiration. Organophosphate insecticides such as temephos, malathion, chlorvinphos, chlorpyrifos, and diazinon are lethal to mosquito larvae at extremely low concentrations; these chemicals are fairly expensive but remain effective for several weeks in polluted, stagnant water so that frequent treatment is not necessary. Large-scale urban trials have shown very substantial suppression of adult biting populations as a result of prolonged application of these agents, although the evolution of resistance to these insecticides is creating problems (reviewed in [30]). Such reductions in mosquito numbers may be expected to result in a decrease in filarial transmission, as indeed was observed by Kolstrup et al. [48], who noted a 93\% decrease in the number of infective mosquito bites per person. On the other hand, Rao et al. [18] were unable to demonstrate any significant reduction in filariasis, although this may have reflected a larviciding program that was inadequate as a result of practical difficulties.

In areas where \textit{Anopheles} species are major vectors of filariasis, house spraying with residual chlorinated hydrocarbon insecticides such as DDT (chorophenothane), chlordane, and dieldrin may

\(^1\) J. E. McMahon, “Chemotherapy with Diethylcarbamazine with Levamisole in Bancroftian Filariasis,” manuscript in preparation.
be effective. Indeed, control of filariasis has been a welcome by-product of some malaria eradication campaigns [63]. Similarly, in Liberia, where villages were sprayed with DDT every six months for two years, transmission of infective *W. bancrofti* larvae was reduced by >90%, and the microfilarial density fell, although the microfilaremia rate remained unaltered [45, 46]. Unfortunately, resistance to residual insecticides is becoming widespread and is limiting the efficacy of these measures. Furthermore, pollution of the environment with insecticide may have undesirable consequences.

Petroleum oil and insecticides are expensive. It is possible to estimate the expense of purchasing and administering these chemicals. For example, a 10-year spraying program in India was calculated to cost $3.00 (U.S.) per capita annually compared with $0.50 per person annually for a two-year antilarval campaign [47]. It is much more difficult, however, to evaluate the costs of environmental sanitation. Such sanitary programs may be relatively simple, such as removal of waste containers and filling ditches and pits in which mosquitoes breed. In other areas, however, extremely expensive water-supply and waste-disposal systems may need to be installed.

New techniques for mosquito control are being developed. These include biological control with fish that eat larvae and with various mosquito predators, pathogens, and parasites. Genetic control may be achieved with the use of sterile flies. Vector mosquitoes may be displaced competitively by the introduction of nonvector species. These measures are not yet applicable for control of filariasis in developing countries but may become feasible in the future.

**Comparison of Chemotherapy and Vector Control**

Several studies have appeared recently in which the effectiveness of filariasis control by administration of diethylcarbamazine or by vector control have been compared.

In parts of Kerala State, India, malayan filariasis has been controlled by various regimens and combinations of repeated residual spraying with hexachlorocyclohexane with or without diazinon for up to 10 years, larvicidal treatments with temephos and Baytex (generic name: fenthion), for two years, and single administration of diethylcarbamazine to either the whole population or to microfilarial carriers; a final comparison area has had no organized control measures [47]. Microfilaremia rates were reduced to a similar degree with either residual spraying or administration of diethylcarbamazine on a mass scale or to carriers only. Little further improvement was found in microfilaremia rates when spraying and chemotherapy were combined, although the microfilarial density (presumably in persistent carriers, although this is not clearly stated in the text) was reduced further when both control techniques were used together. Disease rates were comparable with all methods of control. Larviciding was ineffective. It was calculated that a single round of diethylcarbamazine treatment cost about the same as residual spraying every three months for two years.

In an area of Liberia, West Africa, where bancroftian filariasis is endemic, the effects of two mass treatments with diethylcarbamazine were compared with semiannual spraying with DDT for two years or with a combination of both measures in different villages [45, 46]. Diethylcarbamazine reduced the microfilaremia rate and the microfilarial density but did not reduce the rate of transmission. The microfilaremia rate did not decrease with DDT spraying, but the microfilarial density was reduced as was vector density and transmission of new infections. To achieve improvement in all these parameters, a combination of both methods was necessary.

In a region in Tanzania endemic for bancroftian filariasis, mass treatment with diethylcarbamazine over six months was compared with larviciding of pit latrines with chlorpyrifos for control of *C. quinquefasciatus*, plus or minus simple environmental measures [48]. Each control technique was similarly effective; marked decreases in the number of infective bites per person occurred in all areas.

In conclusion, a flexible approach is required; the method used depends on the transmission pattern in the area under consideration. Administration of diethylcarbamazine and vector control, in these studies at least, seem to be equally efficacious. The relative costs of the two techniques will vary depending on the complexity and costliness of the measures necessary for vector control. A combination of both approaches may be beneficial in some endemic areas, but even so, eradica-
tion of filariasis is unlikely, and these programs may need to be maintained indefinitely in order to keep filarial infection under control.

**Limitations of Human-Mosquito Contact**

Interactions between humans and mosquitoes usually decrease as socioeconomic conditions improve. This pattern results both from a reduction in the number of mosquitoes after the elimination of breeding sites and from an increase in various impediments to contact between mosquitoes and humans. As housing standards improve, mosquito-proofing measures such as screens on windows and doors commonly are incorporated. Even where these are not present, wealthier populations may be able to afford mosquito nets for use while sleeping. As a consequence—and without and direct effort being made—filariaisis may be controlled or even eradicated in areas where predominant vectors are indoor-biting species.

This has occurred in both small and large regions. For example, improved housing led to a regression of filariasis on the island of Réunion, where mud huts with thatched roofs and tiny windows were replaced by bigger houses with sheet-metal roofs and larger windows [29]. Similarly, in a rural area of Java, the development of a well-organized irrigation system and the conversion of swamps into rice fields resulted in a reduction of breeding sites for *Mansonina* mosquitoes and a subsequent decrease in filariasis [62]. On a grander scale, the bancroftian filariasis that once was endemic in northeastern Australia and southeastern United States has disappeared spontaneously *pari passu* with improved socioeconomic circumstances [64].

While improved standards of living are desirable, they are unlikely to occur to any significant degree in many developing countries where filariasis is endemic. It is too much to expect mosquito-proofed dwellings, but it may be possible to introduce the widespread usage of mosquito nets at night. Such a measure would seem appropriate in filarial areas in which transmission occurs at night as a consequence of the nocturnal periodicity of most *W. bancrofti* and *B. malayi* infections.

There do not seem to be any studies in which the efficacy of such a practice has been assessed. Nevertheless, it does not seem unreasonable to suppose that mass usage of mosquito nets may have considerable potential for reducing the prevalence and intensity of microfilaria and perhaps even for bringing about the ultimate eradication of filariasis. It ought to be possible to produce mosquito nets cheaply (i.e., for several dollars each) in large quantities in areas where the cost of labor is relatively low. The success of such a program, however, would depend in large measure on a well-planned concurrent educational campaign. This relatively simple approach may have much to offer, but initial pilot studies for assessment of the feasibility of production and delivery of mosquito nets, the degree of compliance in their use, together with the effects on the prevalence and incidence of microfilaria and clinical disease are urgently needed. It should be anticipated that there would be a relatively rapid decrease in transmission, as indicated by a reduction in the number of bites by infective mosquitoes, but that significant decreases in microfilaria rate, microfilarial density, and prevalence of clinical disease may take a number of years to become apparent.

**Special Problems with Subperiodic Malayan Filariaisis**

Control will be more difficult in those limited areas where subperiodic malayan filariasis is endemic. This infection is a zoonosis, and it often is impossible to control the animal reservoir. Furthermore, larvae of the vector mosquitoes attach themselves to the roots of floating water plants and inhabit vast areas of inaccessible swamp forest. Finally, these mosquitoes frequently bite outdoors at dawn and dusk. Currently, chemoprophylaxis offers the only feasible control measure.

**Summary and Conclusions**

In most developing countries, the control of filariasis has a much lower priority than do programs designed for more serious diseases such as malaria, diarrhea, and pneumonia. Consequently, the funds available for control of filariasis are likely to be limited, and a choice must be made between chemotherapy with diethylcarbamazine and vector control, or some combination of the two. Both are likely to be too expensive to make any significant impact in many countries.

Thirty years of experience with diethylcarbamazine should have taught us that this drug is not the
answer. It is relatively costly, toxic, and has not eradicated filariasis. It may be appropriate as an adjunct in small communities such as on those islands where filariasis is endemic, but it should not be the linchpin of control campaigns in larger areas.

Vector control has a lot more to offer. In addition to being useful in filariasis control, there may be a significant reduction of other insect-borne infections such as malaria, leishmaniasis, and arboviral infections. Insecticide resistance and environmental contamination may be problems, but the major difficulty is the costliness of vector control measures.

Perhaps the greatest hope for poor countries in which nocturnal transmission of filariasis occurs is the introduction and widespread usage of mosquito nets. This is likely to be relatively cheap and has the advantage of being useful for the control of other mosquito-borne infections. Unfortunately, the practicality and effectiveness of this approach remain unproved, and a plea is made for their documentation.

In summary, strategies for the control of filariasis are based on the following premises. (1) Transmission is dependent on a cyclical surge of microfilariae into the blood; in most regions, this occurs at night. (2) The intensity of infection is proportional to the number of bites by infective mosquitoes; transmission is extremely inefficient. (3) Patterns of microfilaraemia and clinical disease vary, but, in general, both appear to rise progressively with age, pari passu with increasing exposure. (4) Filariasis is spreading in regions in which socioeconomic changes have increased the numbers of vector mosquitoes. (5) Control of filariasis by mass chemotherapy with diethylcarbamazine is of limited efficacy. (6) Control of filariasis by physical and chemical measures directed against mosquitoes is effective but costly. (7) Filariasis has been controlled or eradicated spontaneously in regions in which socioeconomic standards have risen. (8) Mass usage of mosquito nets may be both economically feasible and effective in controlling filariasis in many endemic areas in developing countries; pilot studies are required urgently.

In conclusion, given the current state of knowledge, the first priority for control of filariasis should be mosquito-control measures appropriate for a given locality. The second priority should be treatment with diethylcarbamazine. In general, mass administration to the population at large is preferable to the identification and selective treatment of microfilaremic persons, although in areas of low endemicity, a case could be made for the latter. The widespread usage of mosquito nets may be the best approach, but the effectiveness of this method is not yet known. In those few regions where day-time transmission of filariasis occurs, mosquito nets clearly are inappropriate. Here reliance must be placed on measures of vector control supplemented, if financially possible, with administration of diethylcarbamazine.

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