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LYMPHATIC FILARIASIS

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David T. Dennis, M.D., MPH

May 1991

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The blue square shows a microfilaria in an egg as it begins to elongate to form one of the sheathed microfilariae that circulate in the blood of a person with filariasis. The other symbols depict essential components of vector-borne disease control: the environment, communities and research.
Author

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Executive Summary

More than 91 million people are infected with the parasites that cause lymphatic filariasis and an estimated 905 million live in areas where the disease is endemic. Any one of three species of filarial nematodes, *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*, can cause filariasis. They are transmitted to human hosts by a number of mosquitoes of the genera *Culex*, *Aedes*, *Mansonia* and *Anopheles*.

Bancroftian filariasis, which is caused by *W. bancrofti*, is the most widespread form of the disease. The largest number of people at risk and infected live in India, China and Indonesia, but filariasis is an important problem in several other Asian countries and a number of Pacific island groups. Foci of the disease are also found in Egypt and most African countries, several Caribbean islands, and in limited areas of Central America and northern South America. Brugian filariasis occurs primarily in Southeast Asia and China. The incidence of bancroftian filariasis is increasing in urban areas as a result of overcrowding and poor sanitation.

The infective stage of the parasite enters a human host when an infected mosquito takes a blood meal. Adult worms mature, mate and reside in the nodes and vessels of the lymphatic system, causing changes that result in restricted flow of lymph. The worms may live for 10 years or more. During that time, the symptoms caused by their presence may range from inapparent to grossly incapacitating.

Recurrent fevers and inflammation of lymph nodes and vessels, sometimes accompanied by transient swelling of the limbs, are usually the earliest signs of the disease. Later symptoms include scrotal swelling and permanent swelling of the limbs caused by collections of fluid in cells, tissues, or body cavities. The best-known symptoms of filariasis are the grossly swollen, thick-skinned limbs characteristic of long-standing infections, a condition called elephantiasis.

Humans are the only reservoir for *W. bancrofti* and *B. timori*, but *B. malaya* is also found in monkeys and domestic cats.

Lymphatic filariasis control has been attempted through mass or selective treatment of human populations to reduce the parasite reservoir, vector suppression and control, and promotion of personal protection. These methods are usually applied in combination.

Control of the mosquitoes that transmit filariasis may be combined with efforts to control other vectors of human disease, particularly in rural areas. The necessary logistical support required for effective vector control is lacking in most endemic areas. In some areas of
southern India, community participation has been used to control filariasis by reducing vector breeding sites.

The most common approach to reducing transmission and morbidity has been selective or mass treatment with diethylcarbamazine (DEC). Results of field trials suggest that ivermectin, a semi-synthetic drug used as an animal filaricide and now as a treatment for onchocerciasis, is a promising alternative to DEC for use in community-based filariasis control programs.
1. Introduction

Filariasis is one of the most dramatic and debilitating disease groups of the tropics. Although it has been the subject of considerable study, filariasis is still poorly understood, widely prevalent and difficult to control. It has been targeted by the World Health Organization (WHO) as one of the six neglected tropical diseases requiring special efforts in research and training. A disease of the economically disadvantaged and underserved, filariasis affects the rural poor as well as increasing numbers of people living in crowded urban areas with poor sanitation and housing.

Filariasis is caused by infection with thread-like roundworms of the order Filarioidea. Eight species are parasites of humans, and six of these (Wuchereria bancrofti, Brugia timori, Brugia malayi, Loa :a, Onchocerca volvulus and Mansonella streptocerca) are recognized pathogens transmitted by mosquitoes or biting flies.

Three of these disease-producing species, W. bancrofti, B. malayi and B. timori, are called lymphatic filariae because the adult forms live in the lymphatic vessels and nodes of humans and, in some cases, animal hosts. Infection with W. bancrofti is also called bancroftian filariasis. Brugian and timorian filariasis are common synonyms for parasitism with B. malayi and B. timori, respectively. Lymphatic filariasis is often equated with elephantiasis, which is one of the more startling late-stage manifestations of the disease.

Filariasis tends to be insidious, stable and endemic. The infection has a prolonged incubation period and affects people of all ages. In endemic communities, infection and acute disease often begin in early childhood, but symptoms are most prevalent and severe among young adults.

a. Symptoms

The stages of lymphatic filariasis in humans may be categorized as asymptomatic, acute and chronic. During the asymptomatic stage, microfilariae may or may not circulate in the blood. The acute stage is accompanied by attacks of fever and inflammation of lymph nodes and vessels, with intermittent swelling of limbs and the scrotal sac. The presence of maturing larvae and adult worms causes lymphatic vessel to dilate and later thicken, which can result in restricted flow of lymph and accumulations of fluid in skin, subcutaneous tissues and body spaces. Swelling and cell
proliferation may proceed to the grossly swollen legs and genitalia known as elephantiasis, but elephantiasis is not an inevitable consequence of chronic filariasis.

In people who have a hypersensitivity to microfilariae, host immunological reactions to the filariae can produce an asthma-like condition known as tropical pulmonary eosinophilia (TPE), which may result in bouts of wheezing and coughing at night and shortness of breath.

b. Biogeography

Lymphatic filariasis is found throughout much of the tropics and subtropics between latitudes 40° North and 30° South. The range of the most prevalent form, bancroftian filariasis, circles the globe within this zone (Map 1). The endemic range of brugian filariasis, on the other hand, is limited to Asia, from India in the extreme west to Korea in the northeast. Timorian filariasis occurs only on the small volcanic islands of southeastern Indonesia surrounding the Savu Sea (Map 2).

c. Agents

The life cycles of each of the lymphatic filariae are essentially the same (see life cycle, p. 7). In a vertebrate host, adult worms mature and mate in the lymphatic vessels and nodes. Sheathed embryos, or microfilariae, are released into the lymphatic system and find their way into the blood. From the capillaries, they may be taken up in the blood meal of a suitable mosquito vector.

In the mosquito, microfilariae develop into infective larvae in eight to 12 days. These infective forms exit through the mouthparts of the mosquito onto the skin of a human host when the insect feeds. Larvae enter the skin through the puncture wound left by the mosquito and migrate to the lymphatics, where they mature to the adult stage after one to two months.

The prepatent period, when filarial worms mature and mate, may be prolonged, but lasts six to 12 months under favorable conditions. The female worm produces as many as 50,000 microfilariae in a day and may continue to do so for five to eight years.
Map 1. Global Distribution of Bancroftian Filariasis

Prepared by the Vector Biology and Control Project
Source map: World Health Organization, 1990
Map 2. Distribution of Brugian and Timorian Filariasis

The biological variants of lymphatic filarial parasites may be distinguished by the rhythmic patterns of microfilarial circulation in the peripheral blood of infected people. These patterns have evolved as adaptations to the biting habits of vector species. Where night-biting mosquitoes are the vectors, microfilariae are nocturnally periodic, reaching peak density in the blood between 10 pm and 4 am and slowly declining in density, disappearing during the daytime. The density of the circulating microfilariae is about 25 to 50 times greater at the peak of the daily cycle than at the nadir. Microfilariae are usually sequestered in the lungs when they are not circulating in the blood.
Life Cycle of Filarial Worms

Mosquito ingests microfilariae during blood meal

Microfilariae develop into infective larvae in 8-12 days

Infected person

Sheathed embryos called microfilariae are released into lymphatic system and enter the blood stream

Infective larvae enter human host through bite wound

Worms mature in about 9 months and mate in lymph vessels and nodes

Mature worms cause obstructions of the lymph system, leading to swelling and sometimes elephantiasis
The microfilariae of the subperiodic forms can be found in the peripheral circulation at all times but have slight diurnal or nocturnal fluctuations in density, depending upon the parasite strain. In some areas of the Pacific where filariasis vectors are daytime-biting Aedes, the parasites have developed diurnal subperiodicity. All urban forms of W. bancrofti and most rural forms are nocturnally periodic.

d. Vectors

There are a variety of vector-parasite combinations and great differences in the efficiency of transmission between one combination and another. The vector of bancroftian filariasis in urban and semi-urban areas worldwide is Culex quinquefasciatus, a primarily domestic mosquito that breeds in open sewers, drains and pits, contaminated pools and ponds, and other polluted waters. This mosquito also transmits bancroftian filariasis in crowded rural areas where domestic sanitation is poor.

Anopheles mosquitoes transmit bancroftian filariasis in the hill forest and coastal fringe areas of Southeast Asia, the coastal plains of China, and the Pacific Islands west of longitude 170° East. Aedes polynesiensis and related species are the vectors of W. bancrofti in the island groups to the east of this line. They breed in small collections of water such as those found in crab holes, tree holes, coconut shells, and tin cans and other discarded containers. Anopheles gambiae and An. funestus are responsible for most transmission of bancroftian filariasis in rural Africa. In the Western Hemisphere, the principal vectors are Cx. quinquefasciatus and Anopheles darlingi.

In Indian and Southeast Asian locales with rice fields and open swamps, transmission of brugian filariasis is mostly through Mansonia species whose larvae and pupae breathe by attaching themselves to the roots and stems of aquatic plants. Mansonia bonnea and Ma. dives, which transmit B. malayi, breed in swamp forests and feed on monkeys and other forest mammals as well as humans. The subperiodic form of B. malayi is the only lymphatic filaria that has animal reservoirs. Leaf monkeys of the Presbytis genus are important animal reservoirs in Malaysia and Indonesia. In the hill forests of Southeast Asia and the rice-growing areas of Vietnam, China and Korea, B. malayi is vectored by anophelines. Aedes togoi, which breeds in rock holes, transmits the parasite in some coastal foci of China and Korea.
Two-thirds of the people infected with lymphatic filariasis live in India, China and Indonesia. WHO estimates that 905 million live in areas where transmission is known to occur and 91 million are infected. Because the diagnostic methods available cannot detect infection in those who have been exposed but do not have circulating microfilaremia or symptoms of the disease, the total number of people infected with filariasis is probably much higher.

The vectors of filariasis have strict ecological requirements, so the geographic distribution of the filariae is often patchy and focal. *W. bancrofti*’s numerous vectors include both urban and rural forms. The parasites that cause brugian filariasis, on the other hand, are transmitted only in rural settings.

Planned and unplanned environmental changes that increase vector breeding or bring people into new areas can also result in increased filariasis transmission. For example, dam building and irrigation for rice cultivation have resulted in increases in the filariasis vectors of the *An. gambiae* complex in Africa and in *An. barbirostris*, the vector of *B. timori*, in Indonesia. Farm workers and others whose occupations bring them into close contact with filariasis vectors are often at high risk of infection. Migration has established new foci of the disease and brought people with no immunity into endemic areas.

WHO estimates that 82 million people are infected with *W. bancrofti*, but other estimates are as high as 250 million. In Asia, bancroftian filariasis is found widely in urban and rural foci on the Indian subcontinent, Sri Lanka and Burma, and in scattered rural foci in Thailand and Indochina. It also occurs in the southern and eastern alluvial plains of China, among indigenous peoples of the hill forests of the Malayan Peninsula and northern Borneo, and in the Philippines. In Indonesia, the disease is endemic in low-lying hill forests of Sumatra, Kalimantan and Sulawesi, along the coasts of small islands east of Lombok, and in cities on the north coast of Java, particularly Jakarta.

Bancroftian filariasis is highly prevalent in low-lying areas of the island of New Guinea and in many islands of Melanesia, Micronesia and Polynesia. It also occurs throughout Polynesia, New Caledonia and the Loyalty Islands.
The second major endemic zone of bancroftian filariasis is in sub-Saharan Africa, where it is found in a patchy distribution throughout the equatorial belt between 25° North and 20° South. It is also found in urban and rural foci on East African coastal plains and offshore islands. Elsewhere in equatorial Africa, bancroftian filariasis is a rural problem. The disease is endemic in the southern Sudan, adjacent lowland Ethiopia and the Nile Delta, where it has spread to urban areas.

Bancroftian filariasis was introduced to the Western Hemisphere by the slave trade. Although its prevalence is now much diminished, it is still an important disease in Haiti, the Dominican Republic, the Guianas, and in some urban and periurban areas of coastal Brazil.

An estimated 9 million people are infected with brugian filariasis. On the Indian subcontinent, brugian filariasis is only found in Kerala State on the west coast and in a few scattered rural foci in other states. In southern Thailand and Peninsular Malaysia, it is commonly found in open swamps and rice-growing areas of the west coast and along the lower reaches of the major coastal rivers. B. malayi is endemic in the Red River Valley of Vietnam, the eastern alluvial rice-growing areas of China, and on the southern tip of the Korean Peninsula and a few offshore islands. It is widespread in some islands of Indonesia, where five to 10 million people may be at risk.

Timorian filariasis, caused by infection with B. timori, an anopheline-borne parasite closely related to B. malayi, is endemic in low-lying river and coastal strip areas of Timor, Flores, Sumba and other small islands surrounding the Savu Sea in southeastern Indonesia. Timorian filariasis is responsible for high morbidity among affected populations.

a. Urban filariasis

The incidence of bancroftian filariasis is increasing in Asian and African cities as a result of the poor sanitary conditions that often accompany rapid urbanization. Polluted water, blocked open drains, roadside ditches, broken septic tanks, and accumulation of sewage effluents all create ideal breeding habitats for Cx. quinquefasciatus, the main vector of urban filariasis. The growth of urban slums has also led to increases in bancroftian filariasis in metropolitan areas of northeastern Brazil, Guyana and the Dominican Republic.

Ironically, efforts to improve water and sanitation have actually led to increased filariasis transmission in some areas. Construc-
tion of bucket-type latrines in 14 coastal towns in Sri Lanka, for example, created new breeding areas for *Cx. quinquefasciatus* and led to active filariasis transmission. Pit latrines have had the same effect in other areas.

b. Child survival

Lymphatic filariasis is not a threat to child survival. Infection often begins in early childhood, but its effects are most severe later in life. Young children of migrants in Indonesia have developed elephantiasis, but this is unusual.

c. Economic Impact

Filariasis can result in prolonged inability to work. Because it primarily affects people of working age, it can significantly decrease productivity in highly endemic areas. Few studies have attempted to measure this effect on productivity, or to compare the cost-effectiveness of various control measures.
3. Control Measures

The limited control of filariasis that has occurred during the past 25 years has usually required costly national mass treatment and vector control programs. Efforts are underway to replace this vertical approach with methods that can be integrated into primary health care (PHC) systems. The three main control strategies -- mass or selective treatment of human populations to reduce the parasite reservoir, vector suppression and control, and promotion of personal protection -- are usually applied in combination.

a. Treatment

The drug diethylcarbamazine citrate (DEC) has been the mainstay of most national filariasis control programs since its introduction about 40 years ago. It is an inexpensive, relatively safe, effective microfilaricide that can be used in all age groups and against any of the lymphatic filariae. A single round of treatment can markedly reduce episodes of acute lymphatic inflammation. DEC treatment in the early stages of the disease can reverse lymphatic swelling, but it does not affect elephantiasis or other advanced stages of the disease.

Unpleasant side effects, such as fever, headache and lymphatic inflammation, as well as the need for a relatively prolonged treatment schedule are DEC's major limitations. Toxic reactions to the drug itself, which may include dizziness, weakness and nausea, are mild and last for a few hours. Reactions to the death of filarial parasites are longer-lasting and more severe. Destruction of microfilariae can cause high fevers, headaches, muscle and joint pain, abdominal pain, dizziness, weakness, lethargy and asthma for two to four days. Death of adult worms during or shortly after treatment may result in filarial abscesses or acute attacks of lymphatic inflammation. Fear of such reactions has deterred people from participating in treatment programs in some areas.

Most large control programs use DEC to treat all people in each community with a microfilarial rate of five percent or greater. Retreatment is usually necessary. Teams of health workers conduct pre- and post-treatment microfilarial surveys and attempt to ensure individual compliance with drug taking. Salt medicated with low doses of DEC has proved a successful control method in mainland China and offshore islands, where it was used by millions of people.
Selective treatment for microfilarial carriers is the standard method in India. It is used in many other places as a follow up to mass treatment or when the rate of microfilarial carriers in the population is low. India abandoned mass treatment of endemic communities when popular opposition developed because of reactions to treatment. This opposition is attributed to the lack of sufficient staff to develop a rapport with the community.

The total dose of DEC administered is more important than the schedule of treatment. Weekly, monthly, or even biannual doses can be effective. Widely spaced doses are logistically simpler to administer and often more acceptable than the usual single or divided doses of 4 to 6 mg/kg for 14 to 21 days. Although doses higher than 8 mg per kg are associated with unpleasant side effects, China has employed single doses as high as 20 mg per kg without harmful effect. It is generally accepted that a total dose of DEC equaling 72 mg per kg body weight administered over several days or even weeks is optimal.

WHO has supported a major effort in new drug development during the past decade. Ivermectin (Mectizan®), which has been used as an animal filaricide and most recently as a treatment for onchocerciasis, looks promising for bancroftian filariasis control. Results of a number of studies show that this drug, which can be given as a single dose, suppresses microfilarial densities quickly and for at least six months. Side effects from the death of microfilariae are similar to those seen with DEC, but ivermectin treatment does not result in the more serious side effects caused by the death of adult worms. Although it does not appear to kill adult worms, ivermectin may combine the advantages of clearing microfilariae and suppressing the reproductive ability of adult worms without causing filarial abcesses.

b. Vector control

There are three widely used methods of vector control: chemical, biological and environmental. These measures reduce mosquito breeding sites, control vectors at their breeding sources, and interrupt transmission by adult mosquitoes.

Larviciding polluted breeding sites and sanitary engineering at the municipal and household level are the most important methods of controlling the Culex vectors of bancroftian filariasis. Resistance to chlorpyrifos, fenthion and temephos is developing rapidly in many areas, but a number of new pyrethroid com-
pounds have shown considerable promise as larvicides against *Culex*. Most of these agents, however, are too expensive to be used widely for routine control. Source reduction and larviciding of tin cans, old tires, coconut husks and other *Aedes* breeding sites are used with minimal effect to control filariasis in the South Pacific.

Indoor spraying of residual insecticides is effective against many of the anopheline vectors of bancroftian and brugian filariasis. Spraying to control malaria has reduced *W. bancrofti* transmission in Melanesia, Malaysia and Togo, and has completely eliminated bancroftian filariasis in the Solomon Islands.

Control programs in India and on the west coast of Malaysia have had limited success in controlling periodic *B. malayi* by draining open swamps and controlling water plants in swamps, ditches and ponds where *Mansonia* mosquitoes breed. Environmental management has not demonstrated a practical role in the control of subperiodic forms, however, because they are maintained in leaf monkeys and other animal reservoirs of infection.

Biological control is an ecologically sound method of vector control. A fish, *Poecilia reticulata*, has helped reduce *Culex* in polluted breeding sites, but it is more effective in less contaminated sites. *Gambusia* fish have been used effectively against mosquitoes breeding in rice fields. A great advantage of using fish as a method of control is that it can be done at the village level. Larvicidal bacteria, such as *Bacillus thuringiensis* var. *israeliensis* and *B. sphaericus*, show considerable promise, but have not proven practical on a wide scale to date.

Historically, oil was used against *Culex* larvae in India. Organophosphorus insecticides have replaced oil as larvicides. In Pondicherry, the emphasis has been on environmental management through community participation. Limited success in suppressing the vectors of brugian filariasis has been achieved in the coastal belt of Kerala State, India, by controlling the growth of *Pistia* and *Eichornia* plants in ponds. These plants are used to manufacture a prepared fiber for rope-making called coir, which is the major industry in the area.

Expandable polystyrene beads have been used to control *Cx. quinquefasciatus* breeding in privies and cess pits in Zanzibar and Dar es Salaam. The beads are expanded in boiling water and applied to form floating layers that deny mosquitoes access to the water to lay their eggs. If eggs or larvae are already present, these layers interfere with larval respiration and the emergence
of the final larval stage. Study results from Dar es Salaam suggest that a treated pit will remain mosquito-free for at least five years unless the pit floods. Given the success of these trials in East Africa, expandable polystyrene beads appear to be a promising tool for urban filariasis control.

c. Personal protection

Protective clothing, repellents, pyrethrin coils, bed nets, avoidance of mosquito-biting environments and improved housing are common-sense tools for reducing exposure to filarial infection. Concerted promotion of their use, however, has been largely ignored. People tend to adopt measures to avoid nuisance mosquitoes to the extent that their finances allow, and there is a strong correlation between infection and low socioeconomic status. Impregnation of nets with long-acting pyrethrin compounds is being field-tested extensively for malaria control, and might also prove effective for filariasis control.

d. Vaccines

There are no vaccines for lymphatic filariasis. Epidemiological studies strongly suggest that naturally-acquired protective immune responses occur, but these responses are incomplete and develop only after many years of exposure. The mechanism of protective immunity is very poorly understood.

e. Analysis of control efforts

Each of the major strategies for the control of lymphatic filariasis (vector control, reduction of infection in the human reservoir, personal protection) has significant financial, logistical and technological limitations. In many places, the use of all three methods has fallen short of expectations.

Some countries and regions have made considerable progress in controlling filariasis during the past 30 years. In Japan, where an estimated 1 million people had infection or disease at one time, environmental sanitation and an intense campaign of mass chemotherapy have essentially eliminated filariasis. The same has been true of Taiwan and its offshore islands. Bancroftian filariasis is no longer a public health problem in peninsular Malaysia,
and China's integrated control programs also may be or the way to reducing filarial infection below one percent.

Most other endemic countries have had very limited success in controlling filariasis because of technical difficulties and lack of resources, as the summaries below illustrate. Little is known about the extent of the disease in Africa, where few control efforts have been attempted. The growing problem of bancroftian filariasis in overcrowded cities poses new challenges for control.

India

India provides a classic example of the failure of a vertical program based on eliminating infection and interrupting transmission. An estimated 35 million people are infected and 300 million live in filariasis-endemic zones. People have not accepted DEC treatment, and larviciding cannot make up for failed sewage systems in cities and omnipresent collections of wastewater in rural areas. The population is so vast and rapidly expanding that disease control programs do not have the trained manpower or the other resources necessary to reach the majority of those exposed.

India is developing a horizontal approach to controlling filarial disease through early detection and treatment of clinical filariasis within the PHC framework. Because DEC is widely available at small pharmacy shops at low cost and without prescription, education campaigns could promote self-diagnosis and treatment in addition to the use of the village health worker system.

China

Chinese programs combining mass treatment and community-based environmental sanitation have controlled filariasis over large areas, with more than 90 percent cooperation from the populations involved. This approach relies heavily on public health education, political will and a strong organization of health workers reaching down to the community level. It may eliminate filariasis as a public health problem in China in the foreseeable future.

Indonesia

In the third major endemic area in Asia, Indonesia, vertical filariasis control programs have been successful in a few areas. A village-based approach has shown considerable promise.
Health education is followed by weekly administration of DEC by village workers through heads of households. Subsequent acute attacks of filariasis are reported and treated immediately. This system has been implemented only on a small, experimental scale and must be incorporated into the national primary health care program to be fully successful.

Malaysia

Endemic bancroftian filariasis has been essentially eliminated in peninsular Malaysia as a result of malaria control and environmental sanitation programs. Trained teams located in endemic areas have used mass and selective treatment, vector suppression, and education to control brugian filariasis. Infection with the periodic form has been brought below three percent in most of the country. Because of the continuing reservoir of infection in leaf monkeys and other forest mammals, the subperiodic form has been more difficult to control with traditional drug treatment programs. Rising socioeconomic conditions, however, have resulted in improved personal protection and have greatly reduced the public health impact of this disease in all but scattered remote areas.

South Pacific

Micronesia and Polynesia were long recognized as areas with high rates of elephantiasis and infection with bancroftian filariasis. Repeated mass treatment programs, combined with educational efforts on reducing peridomestic breeding sites of *Aedes* vectors, have significantly reduced infection and disease on all major islands. Transmission continues at low levels in most areas, however, requiring continuing surveillance and repeated treatment at widely spaced intervals. Community nurses, teachers and women's committees have been the backbone of community treatment programs in Samoa.

In the Solomon islands, bancroftian filariasis has been eliminated by malaria control program activities aimed at the vector of both diseases, *An. punctulatus*. Since the *punctulatus* group transmits filariasis in the Papuan region, indoor residual spraying may show similar gains elsewhere.

Africa

Filariasis control programs have been poorly developed in Africa. Vector control and DEC administration programs conducted by rural health center and village health unit staff
have reduced filariasis infection in rural parts of the Nile Delta. In coastal East Africa, a highly endemic region, research has shown that combinations of larviciding, simple environmental procedures and chemotherapy could markedly reduce transmission. Recent research in East Africa has shown promising results using polystyrene beads to control vector breeding in conjunction with DEC treatment of the populace. Only limited efforts at lymphatic filariasis control have been conducted elsewhere in Africa.

**Latin America and the Caribbean**

There also have been no concerted national efforts to control filariasis in the Western Hemisphere. Better environmental sanitation, suppression of *Anopheles* by antimalarial campaigns, and greater use of personal protection resulting from improved socioeconomic conditions have all contributed to the gradual reduction in filariasis in some areas of the Americas. On the other hand, the prevalence of bancroftian filariasis is increasing in the urban slums of northeastern Brazil, Guyana and the Dominican Republic. Transmission is apparently unchanged in Haiti.
4. Current Research

a. Diagnosis

Current research in filariasis diagnosis is primarily directed at developing and improving immunologic methods for detecting infection in people living in endemic areas who have been exposed, but who may have no symptoms or circulating microfilariae. With the techniques available, it is impossible to determine whether these people are infected.

Specific needs for improved immunodiagnosis include: 1) the ability to diagnose infection in people who do not have detectable microfilaremia; 2) the ability to quantify worm burdens in infected persons and to assess the effectiveness of treatment; 3) definition of epidemiologic factors, such as intensity of infection and duration of infection; and 4) a better understanding of the biology of the parasite.

Major research advances in immunodiagnosis during the past few years have made it possible to develop tests for detecting parasite antigens. *Brugia* and *Wuchereria* species have been reared in laboratory animals in suitable quantities to harvest antigens and *Brugia* species have been cultured *in vitro* up to the pre-adult stages. These discoveries have led to the development of tests that are sensitive and reliable in detecting infection in people with microfilaremia, even at times of the day when parasites are not normally found in the blood. Extraordinarily specific immunologic discrimination of species and strains of parasites is now possible using DNA probes.

Most recently, researchers have cultivated *B. malayi* to maturity *in vitro*, producing adult worms that mate and reproduce. This achievement will facilitate studies of the biochemistry and immunology of filariasis, production of monoclonal antibodies, and drug and vaccine testing.

b. Chemotherapy

Field studies of varying regimens and methods of delivering antifilarial drugs continue. Earlier studies suggested that ivermectin had no effect on adult worms because it eliminated microfilariae only temporarily. A more recent study in Haiti showed that a higher dose of ivermectin (400 μg/kg over two days instead of one 200 μg/kg
dose) preceded by a 20 μg/kg dose to clear the blood of microfilariae was as effective as a 12-day course of DEC and had fewer side effects. A double-blind controlled trial in July 1990 showed that a single dose of 400 μg/kg of ivermectin was well tolerated by filariasis patients. WHO is sponsoring multicenter clinical trials to compare this combination of a low clearing dose and a single high dose of ivermectin with other regimens of ivermectin and DEC. More research is needed to determine whether distribution of single high-dose ivermectin in communities would be feasible and to gain a better understanding of how ivermectin works against adult worms.

Other drugs under study include ivermectin, a derivative of DEC, and furapyrimidone, a new drug being tested in China. Single doses of CGP 2037, a benzothialide derivative, have reduced the number of microfilariae of several parasite species, including *B. malayi*, in the rodent *Mastomys natalensis*.

The types of drug action being tested include chemotherapy, suppressive treatment and prophylaxis. Recent studies of *Brugia* infections in leaf monkeys show that DEC acts as a prophylaxis by preventing the development of fourth- and fifth-stage larvae into adult forms. Field trials of DEC as a prophylactic agent in Indonesia and India have not produced conclusive results.

c. Vaccine development

The major focus of filariasis vaccine research in recent years has been to develop protective responses in animals against challenge with infective-stage larvae and other early developing larval stages. Another focus has been the development of immunologic responses against the microfilarial stages, which might be useful in reducing the reservoir of infection.

Naturally acquired immunity against lymphatic filariasis develops after years of infection and is only partial. Successful vaccination against developing larval stages of the parasite has been achieved using live, irradiated, third-stage larvae in monkeys, dogs, cats, birds and mice. Protective responses are invoked by live and killed parasites, but the response is greatest to the live attenuated vaccines. The antigens providing the protective response are not yet defined.

Immunologic suppression of microfilariae is a common response to natural infection and is easily induced in the laboratory using a variety of parasite antigens. *In vitro* studies of microfilariae and third-stage larvae have been used to study immune reactions against
parasites. Although great advances have been made in understanding the immunologic aspects of host-parasite relationships, development of a practical vaccine is a distant goal.

d. Vector biology and control

Continuing studies have documented the effects of ecological changes on vector dynamics, particularly changes caused by dam building and other waterworks, forest clearing, and the deterioration of municipal sanitation in crowded urban areas. One disturbing finding is the increase in vector breeding sites in some areas as a consequence of the expansion of domestic and community water sources, which can lead to increased water storage, providing new breeding sites for *Culex* mosquitoes.

Considerable laboratory studies have been made of insect growth regulators and genetic manipulations that might be useful in biological control. Recently discovered strains of bacteria are larvicidal for vectors of lymphatic filariasis. *Bacillus sphaericus*, in particular, shows promise for control of *Cx. quinquefasciatus* because of its persistence and efficacy in polluted habitats and its potential for recycling when larvae feed on the cadavers of other larvae that have succumbed after ingesting the bacterium. Field trials of the use of expandable polystyrene beads to control *Culex* breeding in latrines and cess pits are being conducted in East Africa and Brazil.
5. Lymphatic Filariasis from the A.I.D. Perspective

In most endemic countries, filariasis control is given lower priority than control of malaria and other diseases with high mortality. Yet lymphatic filariasis can be debilitating and its control would not only eliminate morbidity, but could promote greater economic development.

Breeding sites for vectors of filariasis are found in rural and urban settings. Poorly planned urban development or rural irrigation projects can exacerbate the potential for filariasis transmission. In addition to A.I.D.'s involvement in vector and disease control efforts, pre-implementation planning in other Agency projects could help reduce the incidence of lymphatic filariasis.

a. The Horizon

New diagnostic technologies, the availability of ivermectin and improvement of alternative vector control methods will increase the potential for controlling lymphatic filariasis to acceptable levels. As PHC facilities and systems become more accessible, basic diagnosis at the local level and rapid treatment will provide sustained suppression of microfilaremia. Control could be enhanced through education programs to promote community participation in source reduction and personal protection.

Because these efforts would also reduce biting by vectors of other diseases, including malaria and arboviruses, integrated approaches could reap a double return. The Agency can promote such approaches by supporting primary health care strategies that include vector-borne disease control.

b. Future priorities

- Operational research efforts that take a multidisciplinary (medical, entomological, sociological) as well as intersectoral (health, urban planning) approach to vector control, including: engineering projects to eliminate breeding sites for *Cx. quinquefasciatus* in urban and rural settings; development of improved methods of biological control; field trials of the use of polystyrene beads and pilot studies of the effectiveness of pyrethroid-impregnated bed nets in filariasis control.
• Strengthening existing training and retraining courses for primary health care workers, technicians, medical entomologists, parasitologists, physicians and epidemiologists in countries where national control programs exist, and developing training modules on filariasis recognition, treatment and control for PHC workers.

• Involving the health sector in pre-implementation planning of preventive measures and supplementary or routine disease control activities in irrigation and other development projects.

• Developing diagnostic tools that allow for rapid surveillance and response.

• Studies of new methods of treatment, including continued field trials of ivermectin in community treatment of bancroftian and brugian filariasis, and further studies on the use of DEC-medicated.

• Promotion of diagnosis and treatment through PHC clinics as an alternative to vertical mass treatment programs and investigation of the expanded role of the private sector in drug distribution.

• Studies of village-based control programs and community participation in environmental control efforts.
6. Selected References


