Lymphatic Filariasis in the Philippines

Michael Kron, E. Walker, L. Hernandez, E. Torres and B. Libranda-Ramirez

Lymphatic filariasis caused by Wuchereria bancrofti and Brugia malayi is endemic throughout most of the southern half of the Philippine archipelago. Economic and manpower shortages prior to 1996 made it difficult to acquire new prevalence data and vector control data concurrently from all provinces. Nevertheless, analysis of cumulative prevalence data on filariasis indicates the persistence of filariasis in each of the three major island groups – Luzon, Visayas and Mindanao – including 45 out of 77 provinces. Here, Michael Kron and colleagues summarize the prevalence data, and review host, parasite and vector characteristics relevant to the design and implementation of disease control initiatives in the Philippines planned for the year 2000.

The Philippine Island archipelago contains 7100 islands covering 298 000 km², and has a population of approximately 73 million. Filariasis was first described in the Philippines more than 90 years ago, and over the past 50 years has been reported from most provinces south of central Luzon¹ (Fig. 1). In 1959, the first survey of microfilaria prevalence (Mf prevalence) included 18 provinces and revealed a mean prevalence of 8.8%. In 1960, 43 of the 63 existing provinces were shown to be endemic for the disease, leading to the creation of the National Filariasis Control Program (NFCP) in 1963. In 1987, governmental reorganization placed the NFCP under the Communicable Disease Control Service, Department of Health, sharing a general service budget with other communicable disease control programs; in 1996, however, a separate budget was finally allotted to the NFCP. Case-finding activities and accomplishment reports for the NFCP originate in its implementing arms – the provincial Filariasis Control Units (FCUs). Although filariasis is a reportable disease in the Philippines, funds for active surveillance are limited and FCU prevalence surveys are not always obtained in the same villages. Thus, the true incidence of infection and disease is still unknown in most areas.

Prevalence of infection and clinical disease

In 1984, it was estimated that approximately 20 million people were at risk of lymphatic filariasis (LF) in the Philippines. Analysis of disease surveillance data from 1960–1996 (Table 1) concluded that filariasis is now endemic in 45 out of 77 provinces²³. Twelve new provinces have been created since 1960. Two provinces, Marinduque (Region 4) and Sarangani (Region 11) became endemic after 1963. By WHO criteria⁴, 38 provinces are defined as having a low prevalence of the disease (<5%), and six as having a moderate prevalence (5–10%). In 1993, only two provinces – Marinduque and Sulu – met the criteria for high prevalence (>10%). In Marinduque⁵, a previously nonendemic area, 22.4% of people aged 40–49 years and 13.6% of all ages (n = 1349) were microfilaremic. Other provincial Mf prevalence rates range from 0.02% (Cebu) to 10.08% (Sulu).

These percentages are believed to be inaccurate and potentially gross underestimates for several reasons. First, the data include prevalence studies from more than five years ago. Second, FCUs do not always have the resources to collect night-time blood in areas where nocturnally periodic Wuchereria bancrofti exists. Third, FCUs still use thick blood films to identify Mf, and thus define a case of filariasis based only on positive blood films. A study of 143 subjects in 1994 from a moderate prevalence village by three diagnostic regimens – Giemsa-stained thick blood smears, nucleopore filtration of anticoagulated blood (the gold standard) and acridine orange-stained blood⁶ – indicated that the use of thick blood smears systematically misses at least 10% of positive samples.

Prior to 1990, health statistics only included persons with Mf in blood, ignoring the existence of acutely or chronically infected microfilarial endemic areas. Two cross-sectional data collections began in 1994 to attempt to quantitate filarial disease using both Mf prevalence and physical or historical evidence of chronic disease. Studies in rural Mapaso and Anog Sorsogon (n = 518) revealed that common acute clinical manifestations of filariasis are fever and local lymphatic inflammation (lymphadenitis or lymphangitis). Men develop chronic hydrocele with or without chyluria⁸–¹⁰. In the 518 individuals surveyed, 80% of cases of Mf were in people aged 15–69 years, and there was a distinct male to female predominance of almost 3:1 based on blood smears; 22% had physical evidence of chronic filarial disease in the absence of Mf, and another 17.5% demonstrated active Mf⁸. Therefore, the true prevalence of acute and chronic filariasis may be double the current estimates.

Parasite and vector species

Two species of filaria are known to exist in the Philippines. Nocturnally periodic W. bancrofti is the predominant organism. Nocturnally subperiodic Brugia malayi has been reported from seven provinces. Four provinces – Davao Oriental, Palawan, Eastern Samar and Sulu – have both species. Brugia malayi was first confirmed in 1964 from Palawan in a survey of 314 natives from nine villages; 33.1% were positive for Mf and eight cases were mixed infections with W. bancrofti.

There are four mosquito vectors of filariasis in the Philippines, based on surveys within 19 provinces. *Wuchereria bancrofti* is transmitted by either *Aedes polycilus* or *Anopheles minimus flavirostiris*\(^{11–13}\). Vector competence studies have shown that *Culex quinquefasciatus*, although present in endemic areas, is a poor vector for *W. bancrofti*\(^{14,15}\). In a survey of 50 municipalities, *Ae. polycilus* was collected in 76%\(^{16}\). Brugian filariasis is transmitted in the Philippines by *Mansonia uniformis* and *Mansonia bonnea*\(^{17}\). Domestic cats were once suggested as a reservoir of *B. malayi*\(^{1}\) but no scientific studies have been published that confirm this theory. Twenty-nine provinces reported undefined species of filaria in their populations.

Municipalities within the Bicol peninsula region of south-eastern Luzon (public health Region 5, Table 1) have been one of the most highly endemic areas for bancroftian filariasis. Villages (barangays) of average population size 700–1000 can be found throughout the region, and terrain varies considerably, from low mountains to volcanic lakes and large rivers. Rain falls throughout the year, with particularly heavy rains during the monsoon months of November to January. One of the primary agricultural products of this region is the abaca plant (*Musa textilis*), which is cultivated for production of Manila hemp. Larvae of *Ae. polycilus* utilize the water-filled leaf axils of abaca as breeding sites (Fig. 2). *Aedes polycilus* larvae also dwell in leaf axils of other plants, such as banana (Saba variety: *Musa sapientum*), taro (*Colocasia*), and screwpine (*Pandanus*). However, the extensive plantings of abaca underneath a tall canopy of coconut palms create the conditions for large populations of *Ae. polycilus* to occur.

Several biological characteristics of *Ae. polycilus* contribute to its capacity to facilitate transmission of *W. bancrofti*\(^{16}\). *Aedes polycilus* has a high human blood index (<70%), that is it preferentially seeks human hosts over animals both indoors and outdoors; furthermore, it has a high rate of survival in nature, and is highly permissive for development to infective-stage larvae. The average number of bites from this species per person per night in the Bicol region ranges from tens to hundreds. During biennial abaca harvests, men traditionally leave their villages and establish temporary camps within thickets of abaca, where biting rates are assumed to be considerably greater than those in peridomestic surroundings. This sociological phenomenon could explain in part why men have a higher infection rate for *W. bancrofti* than do women. In areas of the Philippines where *W. bancrofti* occurs but abaca is not grown, such as Palawan, the probable vector is *Anopheles flavirostris*, which is also the principal vector of malaria.

**Social and economic impact**

Disease perception and understanding of effective preventive measures is limited in rural provinces. Local populations consider elephantiasis to have various causes\(^{18}\), including standing too long in cold water, heavy lifting and punishment by forest demons. Severe, debilitating scrotal and other chronic disease may be looked upon as an almost inevitable part of the aging process. However, acute filariasis in the young can result in community reactions ranging from ridicule and shunning to silent acceptance.
The occupations associated with high Mf counts involve significant nocturnal outdoor activity – for example, farmers and plantation or field workers. For decades in the Philippines, a clear relationship has been known between the prevalence of bancroftian filariasis and the density of cultivation of abaca plants. In Sorsogon and Mindanao, Mf prevalence is threefold higher in municipalities with dense abaca cultivation (>1600 hectares) than in areas with less abaca (<100 hectares). Therefore, bancroftian filariasis in the Philippines should be thought of as a true occupational disease.

Precise indicators of the economic impact of filariasis and formal case-control studies for risk assessment in the Philippines are nonexistent. What is the best measure of the economic impact of filariasis? How many acute filarial infections constitute a serious national problem? From a historical perspective, it is interesting to recall that after an estimated 10,000 US servicemen in World War II developed acute filarial disease, an all-out effort by US pharmaceutical companies resulted in the discovery of diethylcarbamazine.

Most existing clinical databases on filariasis in the Philippines do not include the occupation of those infected. No correlation between hospitalization rates or medical treatment and pathology due to filariasis has been published for the country. However, extrapolating from recent comprehensive cross-sectional studies in Sorsogon may give some indication of the economic impact in rural areas. For example, the duration of acute filarial disease (lymphadenitis) in Sorsogon averaged 4–5 days, but occasionally persisted up to 90 days, with up to 60 days lost from work. Personal expenses incurred during episodes of acute filarial lymphadenitis or fever ranged up to 1000 pesos (US$25), excluding wages from the days lost from work. In communities where average wages are measured in hundreds of pesos per month, the economic loss due to filariasis can be considerable. If 10% of the wage earners of rural village (n = 500) experienced only one attack of incapacitating filarial lymphadenitis each year, this translates into a loss of about 2% of the total yearly income of the village. Given 20 million Filipinos living in filariasis endemic regions and the recurrent nature of acute filarial adenitis, the overall economic impact on rural economies can be staggering. If NFCP estimates of prevalence were correct at around 645,232, then each year if each person (per capita yearly wage US$3000) lost 5 days wages (1/50th of an average working year), the resulting total economic loss becomes US$38,713,920.

This estimation yields a dollar value very similar to the value derived from economic impact studies in Tamil Nadu, India where yearly lost wages due to acute filarial disease totalled US$42 million.

### NFCP agenda for the new millennium

In line with the WHO’s goal of elimination of filariasis as a public health problem, the Communicable Disease Control Service of the Department of Health and the NFCP set clinical research priorities for filariasis covering the years 1997–2002. Underlying these decisions were a number of factors.

A void was recognized in understanding the relative social and economic costs of filariasis to individuals, communities and the provincial health systems.

<table>
<thead>
<tr>
<th>Regions and provinces of the Philippines</th>
<th>Population (1996)</th>
<th>Total cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(72,676,547)</td>
<td>(645,232)</td>
<td>(0.89)</td>
</tr>
<tr>
<td>Region 1: Ilocos N., S.; La Union Pangasinan</td>
<td>4,219,604</td>
<td>196</td>
<td>0.005</td>
</tr>
<tr>
<td>Region 2: Batanes; Cagayan; Isabela; Nueva Vizcaya; Quirino</td>
<td>2,779,154</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Region 3: Bataan; Bulacan; Nueva Ecija; Pampanga; Tarlac; Zambales</td>
<td>7,361,569</td>
<td>1,757</td>
<td>0.02</td>
</tr>
<tr>
<td>Region 4: Aurora; Batangas; Cavite; Laguna; Marinduque; Mindoro Occ., Or.; Palawan; Quezon; Rizal; Romblon</td>
<td>9,810,184</td>
<td>51,705</td>
<td>0.53</td>
</tr>
<tr>
<td>Region 5: Albay; Camarines N., S.; Catanduanes; Masbate Sorsogon</td>
<td>4,644,975</td>
<td>262,484</td>
<td>5.65</td>
</tr>
<tr>
<td>Region 6: Aklan; Antique; Capiz; Guimaras; Iloilo; Negros Occ.</td>
<td>6,541,150</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Region 7: Bohol; Cebu; Negros Or.; Siquijor</td>
<td>5,450,656</td>
<td>4,331</td>
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<td>Region 8: Biliran E., N., W.; Samar N.; S. Leyte</td>
<td>3,765,778</td>
<td>57,340</td>
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<td>Region 9: Basilan; Zamboanga N., S.</td>
<td>2,919,524</td>
<td>12,512</td>
<td>0.43</td>
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<td>Region 10: Bukidnon; Camiguin; Misamis Occ., Or.; Agusan N.; Surigao N.</td>
<td>2,608,276</td>
<td>49,694</td>
<td>1.91</td>
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<td>Region 11: Davao N., S., Or.; Sarangani; S. Cotabato; Surigao S.</td>
<td>5,120,482</td>
<td>74,656</td>
<td>1.46</td>
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<td>Region 12: Lanao N.; N. Cotabato; Sultan Kudarat</td>
<td>2,155,259</td>
<td>20,232</td>
<td>0.94</td>
</tr>
<tr>
<td>ARM: Lanao S.; Maguindanao; Sulu; Tawi-Tawi</td>
<td>2,441,248</td>
<td>56,575</td>
<td>2.32</td>
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<tr>
<td>CAR: Abra; Benguet; Ifugao; Kalinga Apayao; Mt. Province</td>
<td>1,357,428</td>
<td>180</td>
<td>0.01</td>
</tr>
<tr>
<td>NCR</td>
<td>9,406,184</td>
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<td>0</td>
</tr>
</tbody>
</table>

Table 1. Regional and provincial estimation of filariasis compiled by the National Filariasis Control Program (1963–1996), based on the presence of microfilaraemia on thick blood smears.

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* Abbreviations: ARM, Autonomous Region of Muslim Mindanao; CAR, Cordillera administrative region; NCR, Metropolitan Manila.
There are little or no data on the epidemiology, social and economic impact of filarial disease among certain populations, such as women, children, marginalized groups, farmers, abaca workers, and indigenous and ethnic minorities. Previous mass community treatment with diethylcarbamazine by the NFCP since 1963 clearly lowered MF prevalence, but the effect in communities such as Marinduque was short-lived and deemed unacceptable. Better treatment options should be considered. Recruitment of barangay (village) captains and village-level health promoters is recognized as an integral component of all diagnosis and treatment initiatives. In community-based disease control campaigns, full participation of respected village-level leaders is the key to compliance and continuity of care. Therefore, three high priority goals were developed: (1) to establish a clearer vision of the magnitude of filariasis in the Philippines, (2) to evaluate new control strategies; and (3) to strengthen the public health structure for the prevention, control and elimination of lymphatic filariasis.

To these ends, a series of interdisciplinary public health initiatives will be implemented, beginning in spring, 2000. Combination chemotherapy with albendazole plus diethylcarbamazine will be distributed and monitored in five sentinel endemic communities in Regions 4 (Marinduque), 5 (Sorsogon), 8 (Leyte), 9 (Zamboanga del Norte) and 11 (South Cotabato). This work is supported in part by the Department of Health, the WHO and the SmithKline Beecham Albendazole Donation Program.

While the effects of chemotherapy are monitored on human and vector populations over the next three years, prospective comparisons of new diagnostic methods will take place. For example, in 1998 the NFCP working with the FCU in Barangay Tablimao, Cagayan de Oro City, conducted a pilot study of the immunochromatographic test (ICT) for filariasis on day-time blood. The ICT delivered a sensitivity of 100% under field conditions with a specificity of 96.7%, a positive predictive value of 92% and a negative predictive value of 100%. If the ICT or other new diagnostic approaches (eg. antigen detection systems, amplification of filarial DNA by PCR) are economical for large-scale implementation, they will be integrated into the public health system to monitor the effectiveness of mass chemotherapy. Also, PCR methods to detect filarial DNA will be used on pooled mosquito collections for vector incrimination studies and to monitor the impact of human chemotherapy.

Conclusion

The logistic difficulty of providing disease control services and surveillance in a nation of several thousand islands, a historical problem in quantifying the economic impact of a nonlethal disease, and the absence of a separate NFCP budget before 1996, all contribute to the persistence of lymphatic filariasis in the Philippines. Conditions still exist for the spread of filariasis into previously non-endemic municipalities. In special populations such as abaca workers, intensive interdisciplinary control efforts directed at reducing occupational exposure of infected persons to *Ae. poicilius* could have a major impact on disease transmission and lost wages. Carefully designed new public health initiatives are needed to evaluate precisely and to monitor filariasis control interventions. Specific clinical epidemiological studies are needed to confirm the perceived association of filariasis with significant social, economic and clinical outcomes.

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References


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C-type lectins (C-TLs) are a family of carbohydrate-binding proteins intimately involved in diverse processes including vertebrate immune cell signalling and trafficking, activation of innate immunity in both vertebrates and invertebrates, and venom-induced haemostasis. Helminth C-TLs sharing sequence and structural similarity with mammalian immune cell lectins have recently been identified from nematode parasites, suggesting clear roles for these proteins at the host–parasite interface, notably in immune evasion. Here, Alex Loukas and Rick Maizels review the status of helminth lectin research and suggest ways in which parasitic worms might utilize C-TLs during their life history.

C-type or Ca$^{2+}$-dependent lectins (C-TLs)* are a family of animal lectins that bind carbohydrates in a Ca$^{2+}$-dependent fashion, ranging from simple monosaccharides to complex glycoconjugates. The carbohydrate-recognition domain (CRD) of C-TLs comprises $\approx$110–130 amino acids and contains at least four perfectly conserved Cys residues that form intrachain disulphide bonds. C-TLs are usually multimodal proteins, the CRDs (of which there can be many in one polypeptide) being accompanied by collagen-like, Cys-rich and/or transmembrane domains. In addition, many C-TLs are homomultimeric, maximizing their binding capacities for ligands. The CRDs of different C-TLs adopt a similar fold (Fig. 1), first characterized in the crystal structure of the archetypal C-TL, rat serum mannose-binding protein A (MBP-A). MBP-A is found in serum as a bouquet of trimers organized around a collagenous stalk. In this milieu, it binds directly to bacterial and fungal cell surfaces and triggers the complement protein $\mathrm{Cl}q$ in an antibody-independent manner. Subsequently, co-crystallization of MBP-A and an oligomannose ligand identified the amino acid sequence of the lectin–ligand interactions.

*The term C-type lectin is usually abbreviated to CTL; however, this abbreviation is also widely used for cytotoxic T lymphocytes. We have therefore used C-TL to denote C-type lectin throughout this review.

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**Readings**


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**Reviews**

**Helminth C-type Lectins and Host–Parasite Interactions**

A. Loukas and R.M. Maizels

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