Bancroftian filariasis in a Philippine village: clinical, parasitological, immunological, and social aspects

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The distribution and effects of Bancroftian filariasis in 535 inhabitants of a Philippine village were investigated. Clinical, parasitological, immunological, and socioeconomic assessments were made. A history of acute lymphatic inflammation and the presence of inguinal lymphadenopathy were common. Lymphatic obstructive disease, defined as leg oedema, hydrocele, or an epididymal cyst, was more common in men than in women and increased progressively with age. The prevalence and intensity of microfilaraemia rose with age in males, whereas the prevalence but not the intensity of infection increased with age in females. The prevalence of immunological responsiveness, as assessed by skin reactivity to microfilarial antigen and serum antibodies to adult filarial worms, increased with age in both males and females. There was no relationship between either microfilaraemia or obstructive disease and the ability to work or to have children, but both were more common in heads of household with the lowest socioeconomic score. The epidemiological factors that may have contributed to these findings are discussed.

Bancroftian filariasis is one of the major helminth diseases of mankind. Wuchereria bancrofti occurs widely throughout the tropics and subtropics, infecting an estimated 250 million people (1). While many people living in endemic areas have patent infections, clinical disease is found only in a smaller and often unknown proportion of the population. Nevertheless, considerable morbidity may be produced by acute inflammatory reactions around worms in the lymphatics and by the effects of chronic lymphatic obstruction. Cross-sectional studies in the past have yielded considerable information (2–7), but there is a continuing need to investigate populations in different endemic areas. In this way, the relationships between prepatent infection, patent infection, and overt disease may be determined and related to environmental factors. Furthermore, the clinical and socioeconomic significance of filariasis in a community needs to be defined more clearly.

Little is known about the dynamics of filarial infection in human populations unaffected by control measures (1). Information needs to be gathered concerning the number of new infections that occur during a given period, the variations in microfilaraemia levels with time, and the relationship between the intensity of microfilaraemia and the subsequent development of filarial disease. Since filariasis is a chronic infection, this information can only be provided by long-term investigations; it is against such knowledge that the relative effectiveness of various control measures such as vector control, mass chemotherapy, and perhaps immunization can be compared (1).

This study was undertaken in an attempt to shed light on some of these problems. A small, isolated village in an area endemic for Bancroftian filariasis, and which had not been the subject of
a mass chemotherapy campaign, was surveyed. This paper analyses the baseline clinical, parasitological, immunological, and socioeconomic data.

METHODS

Location and subjects

The study was undertaken in a village in the Province of Catanduanes, a small island off the southeastern tip of Luzon. The village (barrio) of Paraiso lies in hilly terrain about 300 m above sea level and 30 km by dirt road from the main town of Virac. The houses stretch out for 5 km in a winding valley along the Bato river. Most dwellings are near the road, which follows the course of the river, and are constructed of wood and bamboo with a roof of thatched palm leaves. The houses are not screened and most of the inhabitants do not use mosquito nets. There is no electricity or waste disposal system, although a number of households pump water from the river. The staple foods are rice, fish, coconut, and banana. Most of the children attend the village school. The principal occupation is the cultivation of the plantain abaca (Musa textilis) from which Manila hemp is made; the plots of abaca are often a considerable distance from the houses and men may stay overnight in their plantations.

The village had been visited approximately 10 years previously by a team from the Philippines Department of Health. At that time, W. bancrofti microfilaraemia was found in approximately 10% of the population by means of finger-prick. In view of its isolation, the relative stability of the population, and the fact that diethylcarbamazine has never been available, Paraiso seemed a suitable location for a longitudinal study. The proposed project was explained to the barrio captain (mayor) and councillors. Once approval had been obtained, the nature of the investigation was explained to the villagers and most of them agreed to participate. Each house in the barrio was visited and numbered, a census taken, and a map drawn. Investigations were then undertaken systematically, beginning at one end of the barrio and finishing at the other.

Clinical studies

The protocol used for the clinical history and examination was substantially that recommended by the World Health Organization (1). The major additions to this protocol were measurements of the circumference of each leg midway between the knee and the ankle and the scrotal contents of postpuberal males. Early-morning urine specimens were tested for protein using Albuslitx reagent strips (Ames Co., Elkhart, Indiana, USA).

Parasitological studies

A preliminary study was undertaken of several persons known to have microfilaraemia. Finger-prick specimens were taken 4-hourly and the nocturnal periodicity of W. bancrofti microfilaraemia confirmed. Thereafter, blood samples were taken between 21 h 00 and 03 h 00. Samples were obtained by venepuncture from adults and from as many children as possible. One ml of anticoagulated blood was passed through a Nuclepore 5-μm pore filter 25 mm in diameter in a Swin-Lok holder (Nuclepore Corporation, Pleasanton, California, USA), washed twice with water, fixed with methanol, mounted on a glass slide, and stained with Giemsa solution (1). In small children in whom venepuncture was impossible for a variety of reasons, two 20-μl blood smears were taken by the finger-prick method and stained as described before. Early-morning urine specimens were examined for microfilariauris by passing 10 ml of urine through a Nuclepore filter and staining as before.

Immunological studies

Immediate skin hypersensitivity to filarial antigens was measured as described previously (8). In brief, 1 μg of Brugia malayi microfilarial antigen in 0.1 ml of physiological saline was injected intradermally. The size of the wheal 15–20 min later was compared to that induced by the same volume of saline injected intradermally. In children under 10 years of age, 0.5 μg of antigen in 0.05 ml of saline was given intradermally.

Serum samples were collected for measurement of antifilarial antibodies and transported to the USA. Adult worm antibodies were measured by fluorescence as described previously (9).

Socioeconomic studies

An attempt was made to relate microfilaraemia and clinical disease to several personal, social, and economic indices. Each person over the age of 15 years was asked whether he or she had been able to work on the previous day. Each man was asked whether he had genital or leg swelling that he considered interfered with his comfort or ability to work. Married couples were asked, independently, if the husband had genital swelling inter-
fearing with sexual intercourse. Procreative ability was determined by recording the number of live and still births. The heads of each household were asked the following questions in the hope that they might give some indication of economic status and social standing: do you own a house, land, a vehicle, or a radio?; do you have plumbing?; how many water buffalo do you own?

RESULTS

There were 555 inhabitants of the village living in 78 households and the population distribution was typical of that found in a rural area in a developing country. There were 355 persons aged 1 year or more and it was these that were studied.

Clinical studies

Clinical examinations were conducted on 97% of the study population. A history of acute lymphangitis or lymphadenitis was obtained from 57% of the males and 46% of the females. Approximately 25% of the children under 6 years of age had a history of acute lymphatic inflammation; the percentage of persons with such a history rose progressively until the middle-to-late teens, after which it remained constant (Fig. 1). Sixty per cent of persons claimed to have had an attack within the previous year.

Acute lymphatic inflammation was not encountered, but inguinal lymphadenopathy, often very marked, was found in 47% of males and 22% of females; the peak prevalence was in children between the ages of 5 and 10 years (Fig. 2). The percentage of men in different age groups with inguinal lymphadenopathy remained fairly constant, but it was more prevalent in older women than younger women. Axillary lymphadenopathy was relatively uncommon, being found in approximately 10% of the population; the highest prevalence (20%) was in those between the ages of 11 and 15 years. Cervical lymphadenopathy was even less common, the greatest prevalence being in children under 10 years of age (Fig. 2).

Eight men and six women had mild to moderate lymphoedema of the lower limbs; it was most marked pretibially. Their ages ranged from 25 to 76 years. The swelling was asymmetrical, with at least a 1-cm difference in the midcalf circumference in eight patients. No patient had other conditions, such as congestive cardiac failure or liver disease, that might have accounted for leg oedema. No patient had gross elephantiasis. Four men with leg lymphoedema had a concurrent hydrocele and one had an epididymal cyst. Of those with lymphoedema, 64% gave a history of acute lymphatic inflammation and inguinal lymphadenopathy was noted in 50% of those examined.

Hydrocele was found in 20 men, whose ages ranged from 27 to 70 years; bilateral hydroceles were present in three men. The size of the hydroceles varied, the largest, in a 41-year-old man, being
Fig. 3. The prevalence of lymphatic obstructive disease, defined as leg oedema, hydrocele, or an epididymal cyst, in relation to age and sex.

34 × 26 cm. Two men had been operated on previously for hydrocele. Acute inflammation was seen in association with the hydrocele or in the seminal cord in four men. Seventy percent of the men with hydrocele gave a past history of acute genital inflammation and 65% reported previous acute inflammation in the groin. Inguinal lymphadenopathy was seen in 70% of these patients and 20% had concurrent lymphoedema of the legs.

Four men had an epididymal cyst several centimetres in diameter and one of these had concurrent lymphoedema of the legs. Epididymal thickening was noted in two men and thickening of the seminal cord in six men. A total of 28 men had a genital abnormality.

Any person with either leg lymphoedema, hydrocele, or an epididymal cyst was classified as having obstructive filariasis; 33 persons had one or more such manifestations. Disease was more common in men than in women and rose progressively with age, reaching a peak of 58% in males 60 years of age or more and 14% in females 50 years of age or more (Fig. 3).

The first 100 persons examined were tested for proteinuria: 98 were negative, one had a protein concentration of 30 µg/dl, and the other had a protein concentration greater than 1000 µg/dl.

Parasitological studies

Examinations for *W. bancrofti* nocturnal microfilaraemia were carried out in 86% of the population. Two 20-µl smears were taken from each of 131 children; all were negative. One ml of blood was taken from each of 328 persons aged 6 years or more and examined by Nuclepore filtration; 46 males (37%) and 28 females (17%) were positive. Only persons who were examined by Nuclepore filtration are included in the subsequent analysis. The prevalence rose progressively with age, beginning with an infection rate of about 15% in those aged 5–10 years and reaching a peak of 67% in males in the sixth decade and 29% in females in the seventh decade of life (Fig. 4). The intensity of infection, expressed as the geometric mean number of microfilariae per ml of blood, did not change with age in women but increased with age in men (Fig. 5).

There was no relationship between the presence or absence of microfilaraemia and either a history of acute lymphatic inflammation (25% vs 19%) or the presence of inguinal lymphadenopathy (21% vs 23%). Similarly, microfilaraemia was present in 36% of males with obstructive disease compared with 35% of men without such disease. There was an insufficient number of females with obstructive disease for analysis.

The first 100 persons examined were tested for the presence of microfilariae in the urine; none were found.
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**Fig. 5.** The intensity of *W. bancrofti* nocturnal microfilaraemia, expressed as the geometric mean number of microfilariae per ml of blood, in relation to age and sex.

**Immunological studies**

Immediate hypersensitivity skin test reactions to 1 μg of *B. malayi* microfilarial antigen were measured in 90% of the study population. When an antigen-induced wheal twice the area of that of the saline control was considered a positive reaction, the proportion of those with a positive reaction rose progressively from about 25% in 1–2-year-olds up to the age of 10 years, after which a constant proportion of about 90% of those tested showed a positive reaction (Fig. 6). The age at which half of those tested gave a positive reaction was approximately 2.5 years. When a wheal three times the area of the saline control was considered positive, the number of those with a positive reaction was slightly reduced.

Fluorescent antibodies against adult worms were measured in sera from 241 persons aged 6 years or more; 76% were positive in a dilution of 1 in 8 or more. As in the skin test, the proportion of those with positive reactions rose progressively with age, albeit at a slower rate (Fig. 7). Approximately 45% of serum samples obtained from children between the ages of 6 and 10 years were positive and the proportion rose to nearly 60% of children in their early teens. Thereafter, the prevalence in males and females diverged; most men had serum antibodies by their late teens but it was not until the age of 30 that the prevalence in women equalled that in men. Thereafter, approximately 90% of men and women had detectable fluorescent antibodies against adult worms.

**Socioeconomic studies**

There was no relationship between the ability to work on the previous day and microfilaraemia levels: 95% of persons with microfilaraemia were able to work while 86% of those without micro-
Table 1. The number of live-born children of women and men in different age groups compared with the presence or absence of microfilaraemia

<table>
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<th>Age group (years)</th>
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<td>Number of persons (mean ± SD)</td>
<td>Number of persons (mean ± SD)</td>
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<td>Females</td>
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Filariaemia did so. Similarly, there was no relationship between ability to work on the previous day and the presence of obstructive disease; 96% of persons with obstructive disease were able to work compared with 89% of those without such disease. Fourteen percent of adult males admitted, on direct questioning, that they had genital or leg swelling that interfered with their comfort or their ability to work.

Nine percent of married men claimed that they had genital swelling that interfered with sexual intercourse. Seventeen percent of women said that their husbands had genital swelling interfering with sexual intercourse, but in almost one fifth of these cases no abnormality was found on examination of the husband.

There was no relationship between the presence or absence of microfilariaemia in men or women and the number of their live-born children (Table 1). Similarly, there was no relationship between obstructive disease in men and the number of their live-born children (Table 2).

The heads of households were analysed according to a number of socioeconomic indicators. Ninety-two percent of such men owned their house and 98% did not possess a vehicle. These two indices were therefore discarded as being nondiscriminatory. Forty-five percent of men owned their land, 21% owned one or more water buffalo, 35% owned a radio, and 46% had household plumbing. A positive answer to each of these questions was given a score of 1 and the total score, ranging from 0 to 4, was calculated for each man. The number of persons in each score group with a history of acute lymphatic inflammation, inguinal lymphadenopathy, microfilariaemia, and obstructive disease is shown in Table 3. There were no significant differences in age distribution in each score group. There was no relationship between score and a history of acute lymphatic inflammation or the presence of inguinal lymphadenopathy. There was, however, a significantly greater prevalence of microfilariaemia in men with a score of 0 compared with the rest (P = 0.042, Fisher's Exact Test). Similarly, there was a significantly higher prevalence of obstructive disease in men with a score of 0 compared with the rest (P = 0.007, Fisher's Exact Test).

DISCUSSION

Since filarial worms do not multiply within the human host but do live for many years (10), the worm burden is determined by the intensity and duration of exposure to infective larvae and the resistance of the host to maturation of the worms. Whether or not an infection becomes patent, with the appearance of microfilaraemia, presumably depends on the presence of male and female worms in the same place at the same time. The observations of Hairston & de Meillon (11) suggest that many people living in endemic areas harbour infective larvae or adult worms without fulfilling
the conditions necessary for mating. Further support for this concept is given by an analysis of the immunological and parasitological findings in the village we studied.

Immunological studies may provide the best index of exposure to infection with *W. bancrofti*. Although 90% of adult men and women had such evidence of infection, whether by skin testing or the detection of adult worm antibodies in the serum, only 37% of men and 17% of women had patent infections. The prevalence of positive skin test reactions rose progressively with age. This trend has been found by other investigators using *Dirofilaria immitis* antigen (6, 12, 13). In some of the latter studies, however, the maximum positivity rate was reached at a later age; furthermore, the proportion of persons showing a positive reaction was often smaller than we observed. These variations may reflect different epidemiological patterns in the villages studied or a lower sensitivity of *D. immitis* antigen compared with *B. malayi* antigen (8).

There have been few studies of serum antibodies against filariae in populations in areas endemic for filariasis. We found that the serological responses followed a pattern similar to that of skin test reactions. The proportion of people with serum antibodies to adult worms rose progressively with age and more rapidly in males than in females. This contrasts with the observations of Yong (14), who employed a test for fluorescent antibodies against fragments of *W. bancrofti* microfilariae; he did not find any relationship with age, approximately 50% of all those studied from the age of 5 years onwards having detectable antibodies. In our study, we found that there was delay in the age at which the maximum frequency of positive reactions was seen when serology was compared with skin testing. This may indicate that the former test is slightly less sensitive. In any event, it is evident that a longer exposure increases the chances of receiving sufficient infective bites to produce a detectable immunological response.

The prevalence of microfilaraemia, like the presence of a positive immunological response, rose progressively with age. A similar pattern has been encountered in some investigations (2, 4, 7, 15) but not in others (3, 6, 16). We found little difference in the prevalence of microfilaraemia between boys and girls, but thereafter microfilaraemia was approximately twice as common in males as in females. This difference in microfilaraemia rates between the two sexes has also been seen in some studies (15, 16) but not in others (2–4, 6).

In our study, the intensity of microfilaraemia did not change with age in women but a greater intensity of infection was seen in older than in younger men. Several other studies have also shown increasing intensities of infection with age (3, 6). Sajidiman et al. (16) found that, although the intensity of microfilaraemia was greater in men than in women, it did not change with age. Other investigators have found neither a relationship between intensity of microfilaraemia and age nor any difference between the two sexes (4, 15).

The variations noted in these different studies emphasize the importance of local epidemiological factors in determining the patterns of transmission in a given community. A number of factors may be conceived as influencing microfilaraemia levels. First, the number of microfilariae released is presumably proportional to the number of fertilized
female worms. Second, the host inflammatory reaction to adult worms may wall them off and prevent microfilariae escaping into the lymphatics and thence into the peripheral circulation. Third, it is possible that the development of antibodies hastens the removal of microfilariae from the blood. It seems unlikely that host reactivity or the production of antibodies differs much between males and females. It is probable, therefore, that the increased prevalence and intensity of microfilaraemia results from a greater worm burden.

The pattern of events that we observed, i.e., similar immunological and parasitological indices in boys and girls, the increased frequency of adult worm antibodies in young men, and the greater prevalence and intensity of infection in men compared with women, may be explained by the characteristics of the vector and the social habits of the population. The major vector of *W. bancrofti* in the Bicol region of the Philippines is *Aedes poecilus* (17). This mosquito breeds in water accumulations in the axils of plants, particularly abaca but also banana and *Pandanus*. It has a restricted flight range but is extremely anthropophilic, biting indoors and outdoors and by day as well as by night. There is little difference in the life styles of boys and girls but, once they reach their teens, their habits differ markedly. The major occupation of men is the growing and stripping of abaca, which is grown in plantations often a considerable distance from the houses, and the men spend a considerable proportion of their day working in these areas and may even sleep there overnight. Women, on the other hand, spend more of their time closer to the houses where the mosquito density is lower. Although all the villagers are bitten by mosquitos, it is probable that the intensity of exposure is greater among men working in close proximity to the breeding sites in the abaca. It is likely, therefore, that these men have increased worm loads and that these account for the higher prevalence of microfilaraemia and greater intensity of infection. A further conclusion that can be drawn from these observations is that little immunity is induced by prior exposure to filarial worms in this population.

Although it has not yet been proved, clinical disease may be more prevalent in persons with greater worm burdens. The likelihood of an inflammatory reaction around a worm is increased when more worms are present. Similarly, more episodes of inflammation should lead to increased fibrosis and lymphatic obstruction. Persons with obstructive disease did indeed have a longer history of lymphangitis or lymphadenitis, and inguinal lymphadenopathy was found more frequently. Furthermore, a rough parallel is seen between microfilaraemia and obstructive disease. First, both microfilaraemia and obstructive disease were more commonly found in men than in women and second, like microfilaraemia, the prevalence of obstructive disease increased with age. These features are consistent with the concept that older people, especially males, have greater worm burdens and an increased chance of developing signs of lymphatic obstruction. While the prevalences of microfilaraemia and obstructive disease increased *pari passu* in the population at large, they did not necessarily do so in the individual patient. In these instances, other factors such as the walling off of worms or the production of antibodies may play important roles.

It is difficult to find meaningful indices of the socioeconomic significance of filariasis. The presence of asymptomatic microfilaraemia or clinical disease did not affect ability to work; however, the efficiency of that work was not measured. Neither microfilaraemia nor clinical disease had any effect on procreation, but this is not surprising since clinical disease usually becomes apparent after the child-bearing years. Similarly, it is difficult to measure the quality of life. A number of adult males felt that they had obstructive disease that interfered either with their comfort, their ability to work effectively, or with their sexual performance. It is interesting that when a crude index of socioeconomic status was used, heads of households with the lowest scores had a greater chance of having both microfilaraemia and clinical disease. Although it is possible that filariasis interfered with their earning capacity and reduced their socioeconomic status, it seems more likely that these men, by being unable to employ help in the plantations or diversify their interests, spent more time working with abaca and were thus more exposed to infective mosquitos.

This study has analysed the relationships among a number of clinical, parasitological, immunological, and socioeconomic parameters. Although most individuals were probably infected early in life, it is likely that microfilaraemia, clinical disease, or both develop only after repeated infection. The environmental features determining the degree of this exposure are influenced by a number of
factors such as age, sex, and wealth. It is hoped that a further survey of this population several years from now will provide more information on the natural history of filariasis by determining the number of new infections, following levels of microfilaraemia in current patent infections, and defining which persons develop obstructive filarial disease.

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RÉSUMÉ

ASPECTS CLINIQUES, PARASITOLOGIQUES, IMMUNOLOGIQUES ET SOCIAUX DE LA FILARIOSE À WUCHERERIA BANCROFTI DANS UN VILLAGE DES PHILIPPINES

La distribution et les effets de la filariose à W. bancrofti ont été étudiés chez 535 habitants d’un village isolé des Philippines. Les enquêtes ont porté sur les manifestations cliniques de la maladie, la parasitologie, l’immunologie et, enfin, la situation socio-économique des individus concernés. Selon les indications recueillies, 51% de la population avait souffert de lymphangite ou de lymphadénite aiguës, les atteintes ayant été plus fréquentes chez les hommes et dans les groupes d’âge supérieurs. Une lymphadénopathie inguinale souvent très marquée a été constatée chez 35% de la population, avec une prévalence plus forte chez les hommes et maximale chez les enfants de 5 à 10 ans. Le lymphœdème des membres inférieurs a été noté chez 8 hommes et 6 femmes ; l’hydrocéle était présente chez 20 hommes et un kyste de l’épididyme chez 4. Les manifestations d’obstruction lymphatique ont été rencontrées plus souvent chez les hommes que chez les femmes et leur taux augmentait progressivement avec l’âge. Chez 37% des hommes dont le sang (1 ml) a été examiné par filtration, une microfilariémie nocturne due à W. bancrofti a été décelée, la proportion étant de 17% chez les femmes ; la prévalence et l’intensité de l’infection augmentaient avec l’âge chez les hommes, alors que seule la prévalence augmentait chez les femmes. La prévalence des réactions cutanées positives à l’antigène microfilarien de Brugia malayi augmentait jusqu’à la dixième année ; au delà de cet âge, une proportion constante de 90% de la population présentait une réaction. La prévalence des anticorps sériques contre les vers adultes de B. malayi augmentait également avec l’âge et des anticorps ont été décelés chez 90% des adultes. On n’a pas constaté de relation entre la microfilaraémie ou l’œdème obstructif, d’une part, et la capacité de travailler ou de procréer d’autre part. Parmi les hommes adultes, 14% se sont plaints de l’inconfort résultant de l’œdème obstructif et 9% ont déclaré que l’enflure des organes génitaux était génant pour les rapports sexuels. La microfilaraémie et l’œdème obstructif étaient plus fréquents chez les chefs de famille les moins favorisés sur le plan socio-économique, mais non la lymphadénopathie inguinale.

Les différences constatées, notamment entre la prévalence et l’intensité chez les hommes et chez les femmes, montrent l’importance de l’étude des facteurs épidémiologiques locaux, qui déterminent la dynamique de la transmission dans une collectivité donnée. Dans la région de l’étude, W. bancrofti est transmis par Aedes poecilus. Le vecteur se reproduisant dans les gains des feuilles de bananier dont les pétioles servent à fabriquer l’abaca ou chanvre de Manille — source principale de revenus des habitants — on peut considérer la filariose à W. bancrofti comme une maladie professionnelle. Bien que la plupart des individus aient sans doute été infectés dès le début de leur existence, il est probable que la microfilaraémie, les symptômes cliniques, ou les deux, ne se développent qu’à la suite d’expositions répétées à l’infection. Un nouvel examen de la population étudiée est prévu d’ici quelques années en vue d’établir un tableau plus complet de l’histoire naturelle de la filariose.

REFERENCES


