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Wuchereria bancrofti Filariasis in French Polynesia: Age-Specific Patterns of Microfilaremia, Circulating Antigen, and Specific IgG and IgG4 Responses According to Transmission Level

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Abstract—Chanteau S., Glaziou P., Plichart C., Luquiaud P., Moulia-Pelat J. P., N'Guyen L. and Cartel J. L. 1995. *Wuchereria bancrofti* filariasis in French Polynesia: age-specific patterns of microfilaremia, circulating antigen, and specific IgG and IgG4 responses according to transmission level. *International Journal for Parasitology* 25: 81–85. The age-specific patterns of microfilaremia, Og4C3 antigenemia, anti-*Brugia malayi* IgG and IgG4 were assessed in 3 villages of low, medium and high transmission level for *Wuchereria bancrofti* filariasis. The prevalence rates for each of the 4 markers were clearly age dependent and their patterns strongly associated with the transmission level. The antigenemia prevalence rate was consistently higher than the microfilaremia prevalence rate, in all age groups. The prevalences of anti-*B. malayi* IgG and IgG4 responses were very similar and much higher than those of microfilaremia or antigenemia. Antibody responses reached the plateau at an earlier age and at a higher prevalence with increased intensity of transmission. For all the markers, the prevalence rates were significantly higher in males than in females.

Key words: Bancroftian filariasis; age pattern; microfilaremia; Og4C3 antigenemia; anti-*Brugia malayi* IgG4; *Wuchereria bancrofti.*

INTRODUCTION

The age distribution of *Wuchereria bancrofti* infection, as indicated by peripheral blood microfilaremia surveys, is remarkably consistent throughout a wide geographical range (Sasa, 1976). Typically, both prevalence and intensity rise steadily to a maximum in the 15–25 years age-class, and then decline in adulthood. The trends of the gain and loss of infection in a community with a high or low transmission potential are unlikely to be similar to those in a stabilized or changing epidemiological context. Human exposure to infective stage larvae (L3) is associated with a broad spectrum of clinical, parasitological and immunological outcomes, and the relative importance of the underlying determinants of the age distribution of infection are not known. Here we describe the age-specific patterns of subperiodic Bancroftian filariasis in 3 Polynesian villages (low, medium and high transmission levels), using two direct markers (microfilaremia and anti-

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Table 1 — Demographic data of the 3 villages studied

Villages	Number individuals blood sampled (%)*	Age range (years)	Males (%)	Females (%)
Moerai	196 (90)	10–85	97 (52)	89 (48)
Afareaitu	1027 (99)	5–84	518 (50.5)	509 (49.5)
Opoa	627 (86†)	10–86	345 (55)	282 (45)
Total	1840	5–86	960 (52)	880 (48)

* Percentage of the population in the age range.
† 128 individuals aged 10–14 years of whom 35 (27%) were blood sampled, and 593 individuals aged 15 or more of whom 592 (99.5%) were blood sampled.

genemia) and two indirect immunological markers (anti-*B. malayi* IgG and IgG4) of infection.

MATERIALS AND METHODS

This study involved 3 villages in French Polynesia: Moerai (Rurutu island in the Australes Archipelago), Afareaitu and Opoa villages (respectively in Moorea and Raiatea islands in the Society Archipelago). Venous blood samples for determination of parasitemia and serology were collected at day time, from all consenting individuals older than 10 years in Moerai and Opoa villages, and older than 5 years in Afareaitu village. The demographic data are reported in Table 1. The global microfilaremia prevalence rate was 1% in Moerai (very low transmission), 6.6% in Afareaitu (medium transmission) and 21.5% in Opoa (high transmission). The transmission level as measured by the proportion of infected parous female mosquitoes *Aedes polynesiensis* was 0% in Moerai village (Rivière, Chanteau, Séchan, Thirel & Tuhiti, 1985) and 9.7% in Opoa village (Cartel, N'Guyen, Moulia-Pelat, Plichart, Martin, Manuellan & Lardeux, 1992). Data on vectors was not available for Afareaitu village.

Parasitemia expressed as the number of microfilaria (mf) per ml of blood, was determined by the filtration of 1 ml of EDTA venous blood through a Nucleopore membrane (pore diameter = 3 μm). The specific circulating Og4C3 antigen, expressed in arbitrary Units/ml (U/ml), was measured by sandwich ELISA (More & Copeman, 1990), according to the manufacturer's recommendations (JCU Tropical Biotechnology, Queensland, Australia). Antigen Og4C3, previously shown to be excreted mainly by adult worms, was thus used as a direct marker of infection in the present study (Chanteau, Moulia-Pelat, Glaziou, N'Guyen, Luquiaud, Plichart, Martin & Cartel, in press). The detection of anti-*B. malayi* (anti-BMA) IgG and IgG4 by ELISA was performed according to Lal & Ottesen (1988). Anti-BMA IgG results were expressed in arbitrary Units/ml (U/ml), according to a high titered standard reference pool of sera, and anti-BMA IgG4 results in μg/ml according to a calibrated standard serum determined by depletion analysis. The threshold for anti-BMA IgG was 600 U/ml (specificity 89% and sensitivity 96%), and for anti-BMA IgG4 of 4 μg/ml (specificity 89% and sensitivity 94%) (Chanteau, Plichart, Spiegel, Martin & Cartel, 1991).

RESULTS

Age specific patterns of Mf density, circulating Og4C3 antigen, and levels of anti-BMA IgG and IgG4 in populations according to intensity of transmission

The global prevalence rate and the mean value of each marker, according to the village studied, are shown in Table 2. Estimation of the intensity of transmission given by the mean microfilaremia density, confirmed the low, medium and high levels of transmission in Moerai, Afareaitu and Opoa villages, respectively. Figure 1 displays, according to the village, the age-specific prevalence rates of microfilaremia, antigenemia and specific IgG and IgG4. The prevalence rates for each of the markers were clearly age dependent and their trends strongly associated with the transmission level. In all villages studied, the age prevalence of antigenemia was consistently higher than microfilaremia. Concerning anti-BMA IgG and IgG4, their age dependent prevalence rates were very similar and much higher than the microfilaremia and antigenemia prevalence rates.

Table 2 — Global prevalence rates and mean values of microfilaremia, antigenemia, anti-BMA IgG and anti-BMA IgG4 in the 3 villages studied

Prevalence rate	Moerai	Afareaitu	Opoa
Microfilaremia	1%	6.6%	21.5%
(mean* Mf/ml)	(5)	(142)	(361)
Antigenemia	1.1%	20.4%	41.3%
(mean* U/ml)	(223)	(643)	(1958)
Anti-BMA IgG	9.7%	51.1%	92.9%
(mean* titer)	(999)	(1802)	(4623)
Anti-BMA IgG4	11.3%	45.3%	87.6%
(mean* titer)	(11)	(25)	(69)

* Geometric mean values among positive individuals.

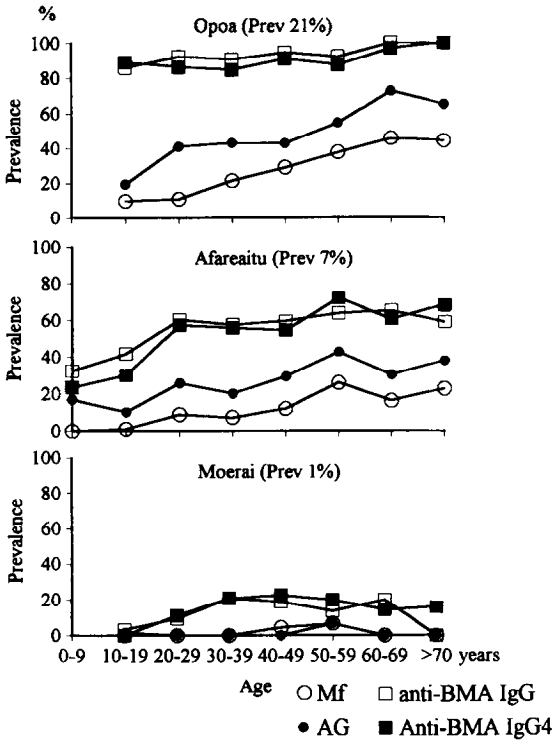

Fig. 1. Age-specific prevalences of microfilaremia, antigenemia, anti-BMA IgG and IgG4 according to the village.

The antibody plateau was reached at an earlier age and was higher with increased intensity of transmission. The Og4C3 antigen test was positive for 94.5% of the Mf+ individuals, 46% of anti-BMA IgG+ and 51% of anti-BMA IgG4+ subjects.

Age specific patterns of Mf density, Og4C3 antigen, anti-BMA IgG and IgG4 according to sex

The age-specific patterns according to sex were analysed for Afareaitu and Opoa villages, since the number of inhabitants in Moerai village was too small. The prevalence rates of all of the markers were significantly higher in males than in females (<0.001), as shown in Fig. 2 for Afareaitu village. A similar observation was made for Opoa village (results not shown).

Antigen and antibody prevalences in the 10–14 years age class according to global Mf prevalence rates

Since the plateau of antibody prevalence was reached at a different age and level depending on the transmission level, the prevalence rates for specific age groups of children differed among the villages. Figure 3 shows the strong correlation between specific IgG and IgG4 prevalence rates in the 10–14-year-old group, and global microfilaremia prevalence rates. Of the IgG4 positive individuals, 78.5% were also IgG positive.

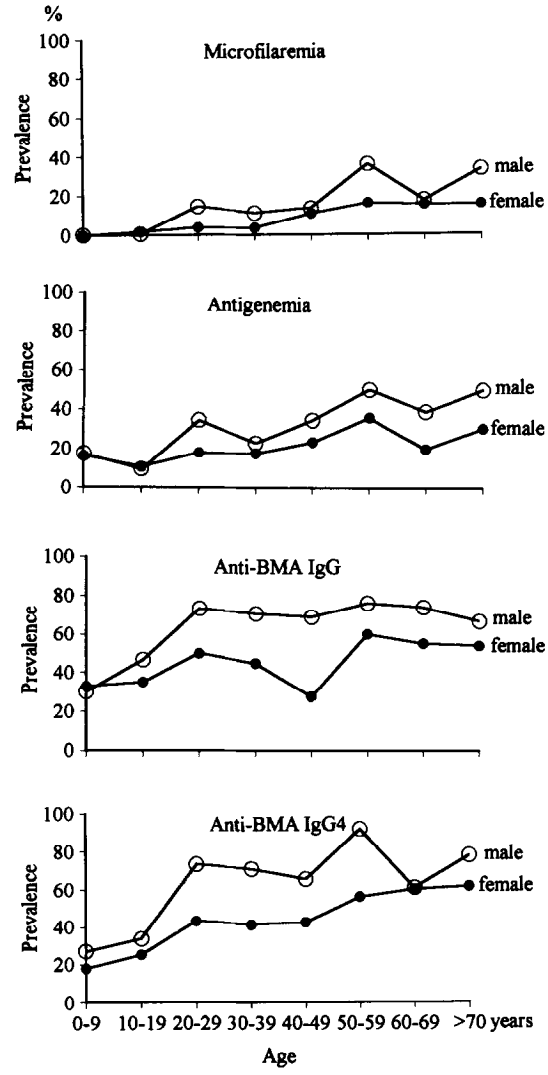

Fig. 2. Age-specific prevalences of microfilaremia, antigenemia, anti-BMA IgG and IgG4 according to sex in Afareaitu village (Mf prevalence 6.6%).

DISCUSSION

The dynamics of acquisition of Bancroftian filariasis in man are not well understood and are probably related to the intensity and the age of exposure. In French Polynesia, an extensive and effective control programme based on mass prophylaxis by DEC, implemented in 1950, has reduced the mean parasitological prevalence rate from 30% to less than 2% in the early 1980s (Pérolat, Guidi, Rivière & Roux, 1986). Today, due to variable compliance to

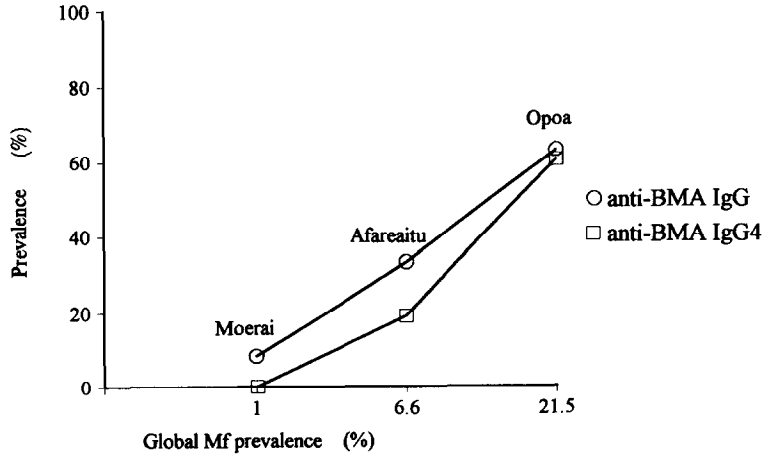

Fig. 3. Anti-BMA IgG and IgG4 seroprevalences in the 10–14 years age class according to the global microfilaremia prevalence in the population.

DEC treatment, the epidemiological situation appears as mixed zones of very low, medium and high transmission. Hygiene and sanitation in those islands, dramatically improved during the last 30 years, are among the best in the South Pacific. Gastro-intestinal nematode infections are infrequent and other parasitic infections, such as malaria and schistosomiasis, that are known to interfere with the host immune response, are absent. However, *Dirofilaria immitis,* which infects dogs and is transmitted by the same vector as *W. bancrofti,* is endemic in French Polynesia and probably influences the antibody seropositivity in humans. To minimize the serological background due to cross reactive antigens, the thresholds for anti-BMA IgG and IgG4 tests were determined in endemic normal sera and set for a specificity of 89% (Chanteau *et al.*, 1991). Concerning circulating Og4C3 antigen detection, even though the monoclonal antibody was generated against a zoonotic filaria, the test has been demonstrated to be very specific for *W. bancrofti* infection when applied to human sera (More & Copeman, 1990).

In the 3 villages studied, the prevalence rates of microfilaremia and Og4C3 antigenemia were age dependent and closely related to the intensity of transmission. In Papua New Guinea, similar results for age-specific patterns of *W. bancrofti* infection have been observed, using microfilaremia and phosphorylcholine antigen detection tests (Day, Grenfell, Spark, Kazura & Alpers, 1991). Microfilaremia prevalence and density correlated directly with prevalence rates of antigenemia and anti-BMA antibodies. However, microfilaremia confirms the existence of one or more living, mated, fecund female worms and so lacks sensitivity, owing to the long prepatent period in lymphatic filariasis, the impeded access of Mf to the blood circulation in cases of lymphatic damage and the possible suppression of microfilaremia and microfilarial production by immune mechanisms (WHO, 1984). Og4C3 circulating antigen, detected in microfilaremic and amicrofilaremic patients, was recently shown to be a better marker of infection and a possible indicator of adult worm burden (Chanteau *et al.*, in press). The observation that anti-BMA antibodies were more prevalent than Og4C3 antigen or microfilaremia suggests that only a small proportion of the persons who acquire infective larvae from mosquitoes go on to harbour adult worms (antigen positive) and even fewer patent infections (microfilaria carriers). Such a low transmission efficiency of *W. bancrofti* has been found in the Philippines, by comparing mosquito infectivity rates and parasitological prevalences in humans (Valeza & Grove, 1979).

The prevalence of microfilaremia was higher in males than females, as also reported in India (Pani, Balakrishnan, Srividya, Bundy & Grenfell, 1991), and correlated with antigen and antibody prevalences. A possible explanation is that males are more exposed to infection during outdoor activities, since *Aedes polynesiensis* is a rural vector.

Seropositivity in filariasis does not necessarily denote active infection, mainly because of persisting circulating antibodies after clearance of parasites, antibody responses to repeated exposure to infective larvae and false positives due to dog filaria cross-reacting antibodies. The higher age-specific prevalence of antibodies than of microfilaremia or antigenemia was therefore not surprising.

The association of anti-BMA IgG and IgG4 antibodies with microfilaremia and antigenemia suggests

their possible usefulness as indicators of transmission intensity in a population. In several studies, anti-filarial IgG4 antibodies were demonstrated to be more specific than IgG because the level of this isotype is remarkably raised in current filarial infections and does not participate in the response to phosphorylcholine, a common cross-reacting antigen (Ottesen, Skvaril, Tripathy, Poindexter & Hussain 1985; Kwan-Lim, Forsyth & Maizels, 1990; Egwang, Nguiri, Kombila, Duong, Richard-Lenoble, 1993). In French Polynesia, probably on account of the relative good sanitary situation, such a discriminative pattern between specific IgG and IgG4 was not observed (Chanteau *et al.*, 1991). The present study again shows similar IgG and IgG4 responses in all ages groups of the Polynesian population.

Very low adult worm loads or unisexual infections may still remain undetected by the antigen test (Chanteau *et al.*, in press) or blood microscopy. So, it is currently impossible to measure the absolute rate of acquisition of new adult filarial worm infection in man. Intensity of transmission may be estimated from the entomological parameters in vectors or, indirectly, from serological parameters in appropriate subsections of the population, such as children of a defined age-group. In our study, we selected the 10–14 year-old children in whom the antibody prevalence rates were shown to be closely related to the intensity of transmission in the village. Because it can be performed on filter paper collected blood (Chanteau *et al.*, 1991), the anti-BMA IgG test in a selected age group of children could be an epidemiological marker of the efficacy of a filariasis control program.

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