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Control of lymphatic filariasis in a hunter-gatherer group in Madang Province

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SUMMARY

Diethylcarbamazine (DEC) has been successfully administered to millions of people in established villages and towns, but little or no information exists on the use of this drug to control lymphatic filariasis in isolated seminomadic groups. We have studied the impact of biannual single-dose mass treatment to control filariasis in the Hagahai, an isolated hunter-gatherer, shifting horticulturist group in the fringe highlands of Papua New Guinea. Despite low treatment coverage, 6 mass treatment rounds significantly reduced the overall prevalence of infection with *Wuchereria bancrofti*, by antigen detection assay, from 55% before treatment to 34% after treatment. Obstructive filarial disease in the form of elephantiasis or hydrocele was not observed among the indigenous population. *Anopheles* species accounted for 91% of human-biting mosquitoes collected in the area. A total of 1126 mosquitoes were caught and dissected individually but none was infected with third-stage larvae (L3). Our findings support the phenomenon of facilitation, which predicts that *Anopheles*-transmitted lymphatic filariasis can be interrupted by mass chemotherapy alone in areas of low vector density and low transmission intensity as observed in the Hagahai.

Introduction

Lymphatic filariasis is a major cause of clinical morbidity and an impediment to socioeconomic development in 96 endemic countries where 1.1 billion people are at risk and 128 million are infected or diseased (1). For nearly 50 years diethylcarbamazine (DEC) has been the drug of choice for this disease and community-wide chemotherapy has been proposed as a practical and effective strategy for its control (2). DEC has been successfully administered to millions of people in established villages and towns. However, we are not aware of any study describing mass treatment for filariasis control in seminomadic, hunter-gatherer groups. In his global survey of the epidemiology and control of human filariasis, Sasa (3) made no mention of the infection in isolated, seminomadic groups.

The Hagahai are a recently contacted group of seminomadic hunter-gatherers living in the fringe highlands of Madang Province in Papua New Guinea (PNG). When, in 1983, Baptist missionaries first walked into Hagahai territory, local newspapers carried stories of the discovery of ‘lost tribes’ (4). Scientific patrols that followed reported a relatively high degree of isolation, immunological naivete and severe disease stress (5,6). A parasitological survey conducted in 1991 revealed that lymphatic filariasis caused by *Wuchereria bancrofti* was highly endemic in the Hagahai territory (7). In 1993 biannual single-dose mass treatment with DEC was started to control the disease. This paper describes the results of entomological and serological studies carried out in November 1996 to determine the impact of 3 years of mass DEC treatment on lymphatic filariasis prevalence.

Materials and Methods

Study area

The study was carried out in the Hagahai territory located on the north side of the Yuat

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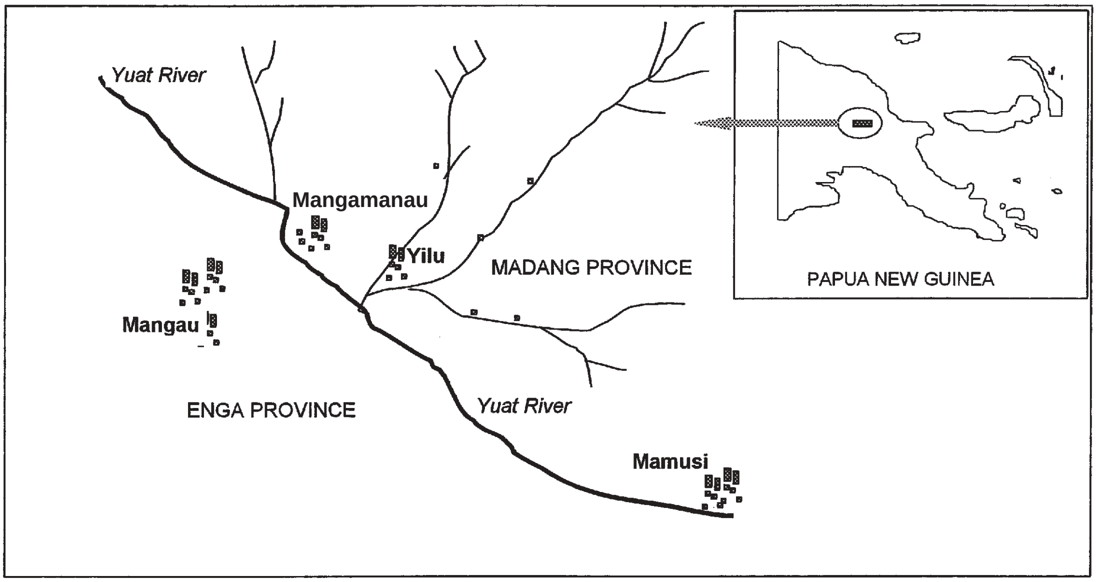

Figure 1. Map of the Hagahai region.

River in the far western corner of the Schrader Range in Madang Province (Figure 1). Although occasional explorers and miners probably walked through Hagahai territory as early as the 1930s and several attempts were made to census them during the 1970s, these people effectively remained hidden from mission and government influence until the 1980s. In 1996 the Hagahai territory included three villages, Yilu, Mamusi and Mangamanau, around which hunting and shifting horticultural activities took place. Yilu is located about 550 m above sea level while Mangamanau and Mamusi are located near the Yuat River < 400 m above sea level. The Hagahai area and territorial groups have been described in detail by Jenkins et al. (6).

While there are still no roads or air communication (other than helicopter) to towns there is an extensive system of bush tracks and the people of the Hagahai community are not, and probably never have been, totally isolated. Yilu, Mamusi and Mangamanau villages served as treatment centres for biannual mass DEC treatment (6 mg/kg). A village health worker and two local assistants who resided in Yilu walked to the other villages to administer treatment. Walking between villages in this mountainous area sometimes lasted more than 12 hours. A total of six mass treatment rounds were conducted between June 1993 and November 1996.

Enzyme-linked immunosorbent assay (ELISA)

Post-treatment infection rates were determined using the *Wuchereria bancrofti*-specific Og4C3 antigen-capture ELISA described by More and Copeman (8). Daytime finger-prick blood samples were collected on filter paper discs. Samples were obtained from all ages and transported to our laboratories in Madang where they were processed as instructed by the suppliers of the commercially available ELISA kit (9). Filter paper discs containing blood samples were placed in elution tubes and boiled in EDTA diluent to release parasite antigens. After boiling, the samples were centrifuged at 2000 g for 15 minutes and then 50 µl aliquots of supernatant fluid were added to test wells in a 96-well microtitre plate precoated with Og4C3 monoclonal antibody. An ELISA was then performed using EDTA as negative control and seven dilutions of *Onchocerca gibsoni* antigen as positive controls. Plates were read using an ELISA plate reader at a wavelength of 414 nm. Based on optical densities of the 7 positive control samples the test samples were allocated into 8 titre groups. All test samples allocated to titre group 3 or higher were considered positive.

Before using the filter paper ELISA test to process blood samples collected in the Hagahai territory we conducted a pilot study to compare prevalence of bancroftian filariasis determined by Nuclepore filtration and filter paper-based ELISA. The pilot study involved 26 untreated people in a highly endemic village in the East Sepik Province of Papua New Guinea. Out of 1.5 ml of blood collected from each individual between 10 pm and midnight, 1 ml was processed by the Nuclepore filtration technique to determine presence of microfilaria. Thereafter, filter paper discs were soaked in the remaining blood samples for analysis by ELISA.

Sampling and processing of mosquitoes

Entomological surveys were conducted in the villages of Mangamanau, Mamusi and Yilu. Human-biting mosquitoes were caught by two adult residents using the all-night landing catch method as described by Bockarie et al. (10). Mosquitoes were captured between 1800 and 0600 hours as they attempted to feed on humans seated on benches. They were identified in the field and stored in 70% ethanol for transportation to laboratories in Madang where they were later stained for filarial parasites using Mayer's acid haemalum (11). Specimens were individually dissected to determine infection with filarial larvae. Movement between Madang and the study area was by helicopter.

Results

Prevalence of *Wuchereria bancrofti* infection and disease among the Hagahai

In the Hagahai region, we collected finger prick blood samples from a total of 262 people including 185 indigenous inhabitants and 77

TABLE 1

Prevalence of *Wuchereria bancrofti* antigenaemia in the indigenous population and recent arrivals in the Hagahai region, Madang Province

Village	Males		Females		Total	
	N	% pos	N	% pos	N	% pos
Indigenous population						
Mamusi	31	58.1	34	44.1	65	50.8
Mangamanau	20	40.0	14	35.7	34	38.2
Yilu	62	11.3	24	16.7	86	12.8
Total	113	29.2	72	33.3	185	30.8
Recent arrivals						
Mamusi	1	0.0	0	0.0	1	0.0
Mangamanau	42	57.1	34	35.3	76	47.4
Yilu	0	0.0	0	0.0	0	0.0
Total	43	55.8	34	35.3	77	46.8
Total						
Mamusi	32	56.3	34	44.1	66	50.0
Mangamanau	62	51.6	48	35.4	110	44.5
Yilu	62	11.3	24	16.7	86	12.8
Total	156	36.5	106	34.0	262	35.5

new arrivals who were born in other provinces outside the Hagahai territory. The overall prevalence of *W. bancrofti* was 35%, with males (37%) and females (34%) having similar prevalence rates (Table 1). Amongst the recent arrivals the prevalence in males (56%) was higher than in females (35%) but the difference was not statistically significant. Overall prevalence in recent arrivals (47%) was higher than in the indigenous population (31%) and the difference was statistically significant (χ^2=6.04, df=1, p=0.01). Results of a preliminary study comparing the prevalence of bancroftian filariasis determined by filtration (58%) and ELISA (77%) showed the filter paper ELISA method to be 1.3 times more sensitive than the former.

Among the indigenous population, infection prevalence was much lower in those seen in Yilu (13%) than in Mamusi (51%) and Mangamanau (38%) (χ^2=26.12, df=2, p<0.0001); for those younger than 18 years the corresponding prevalence rates were 0% (0/38), 30% (7/23) and 13% (1/8). Those people not born in the Hagahai area mostly settled in the Mangamanau area where 76 of the 77 recent arrivals were seen.

The magnitude of worm burden, assessed from the mean ELISA optical densities (ODs), was similar in infected males (0.774) and females (0.813) in the indigenous population. Similarly, there was no significant difference in the worm burden for infected males (0.678) and females (0.603) amongst recent arrivals. Overall, the indigenous population had a similar worm burden (0.791) to the new arrivals (0.653) (Kruskal-Wallis H=0.281, df=1, p=0.596). Worm burden was, however, significantly lower in Yilu (0.492) than in Mamusi (0.943) and Mangamanau (0.656) (Kruskal-Wallis H= 8.39, df=2, p=0.015). No clinical examinations were performed to determine filarial disease status but interviews with several people from the different areas revealed that two recent arrivals living in Mangamanau had elephantiasis.

Treatment coverage

Six treatment rounds were conducted between June 1993 and November 1996. Table 2 shows the treatment coverage among indigenous Hagahai who were 5 years or older when mass treatment started in 1993. Of the 154 that participated in the November 1996 filariasis survey, 102 (66%) had received DEC treatment. A slightly higher proportion of males (71%) than females (61%) were treated but the difference was not statistically significant.

The percentage of people who received one or two treatments was similar in all 3 villages; it varied from 33% in Mangamanau to 38% in Mamusi. However, very few people in Mamusi (2%) received more than two treatments. Treatment coverage was higher in Mangamanau and Yilu where the percentage of those who had received more than two treatments was 47% and 46% respectively.

Impact of mass treatment with DEC on *W. bancrofti* infection rates

The impact of DEC mass treatment on the prevalence of *W. bancrofti* amongst the indigenous population was determined by comparing the results of the present survey

TABLE 2

NUMBER OF INDIGENOUS PEOPLE (≥5 YEARS OLD) REPORTING PREVIOUS TREATMENT WITH DEC (6 MG/KG)

Village	No previous treatment (%)	1 or 2 previous treatments (%)	>2 previous treatments (%)	Total
Mamusi	32 (60.4)	20 (37.7)	1 (1.9)	53
Mangamanau	6 (20.0)	10 (33.3)	14 (46.7)	30
Yilu	14 (19.7)	24 (33.8)	33 (46.5)	71
Total	52 (33.8)	54 (35.1)	48 (31.2)	154

with the pretreatment prevalence of 42% (44/106) obtained in 1991 by Desowitz et al. (7). The 1991 infection prevalence was based on night blood samples, from people 6 years and older, determined using the Nuclepore filtration technique. In 1996, after six mass treatment rounds, the overall prevalence of *W. bancrofti*, determined by ELISA, had reduced to 34% (53/154) in the same age group but the difference was not significant. However, from the ratio of microfilaria positives to antigen positives (1:1.3) obtained during the pilot study we estimated a pretreatment antigen prevalence of 55%, which was significantly higher than the post-treatment prevalence (χ^2=14.7, df=1, p=0.00013). The gender-specific prevalence rates in the present survey were 33% (32/98) for males and 38% (21/56) for females but the difference was not statistically significant.

Only 55 of the 106 people who participated in the 1991 survey were identified in the present survey. Amongst these the pretreatment prevalence of microfilaraemia (63%) was significantly higher than the post-treatment prevalence of antigenaemia of 26% (χ^2=16.23, df=1, p=0.000056).

Entomological surveys

Entomological surveys produced a total of 1126 mosquitoes in Mamusi, Mangamanau and Yilu where human-biting rates were 117, 20 and 9 bites/person/night respectively. The majority of the mosquitoes (91%) were *Anopheles* species but only 175 (17%) of the 1021 anopheline mosquitoes were identified as members of the *Anopheles punctulatus* complex: *An. farauti* (38 mosquitoes) and *Anopheles punctulatus* (137 mosquitoes). *Anopheles karwari* was the most common mosquito, accounting for 75% of all mosquitoes caught (Table 3). Other species caught were *Culex annulirostris* (14 mosquitoes), *Culex* spp. (7 mosquitoes), *Armigeres* spp. (60 mosquitoes) and *Aedes* spp. (24 mosquitoes). All mosquitoes caught were individually dissected but none was found to contain infective larvae (L3).

Discussion

The filter paper-based Og4C3 ELISA, which detects circulating *W. bancrofti* antigen, was used successfully to determine post-treatment filariasis endemicity in a very remote area in Madang Province. Previous studies on the effect of mass treatment on filariasis endemicity in Papua New Guinea have been based on examining whole blood samples for the presence of microfilariae (12-14). This is the first report of the use of the filter paper-based ELISA method to monitor the impact of treatment. Although several researchers in Africa have raised concerns about the sensitivity and reliability of this method (15,16) our study showed it to be a simple, sensitive and effective tool for monitoring the

TABLE 3

TOTAL NUMBER OF MOSQUITOES CAUGHT IN THE HAGAHAI VILLAGES OF MAMUSI, MANGAMANAU AND YILU

Species	Number caught			
	Mamusi	**Mangamanau**	**Yilu**	**Total**
Anopheles farauti	36	1	1	38
An. karwari	844	2	0	846
An. punctulatus	44	81	12	137
Culex annulirostris	0	6	8	14
Culex spp.	3	1	3	7
Armigeres spp.	4	16	40	60
Aedes spp.	2	14	8	24
Total	933	121	72	1126

effect of treatment. The fact that circulating antigen may persist after the death of adult worms means that the true prevalence of active infection after treatment is likely to be even less than that shown by this method, or any other that measures antigenaemia. The simplicity and convenience of collecting daytime finger-prick blood may have contributed to the high turnout of 262 people during the post-treatment survey compared to 106 in the pretreatment survey when venous blood was collected between 10 pm and 1 am.

Despite the remoteness of the area and the seminomadic way of life of the Hagahai people, treatment coverage was comparable to what has been reported for community-wide ivermectin treatment for onchocerciasis control in established villages in Burundi (17) and Sierra Leone (18). The overall post-treatment antigen prevalence of 35% was lower than the microfilarial carrier rates for many endemic areas in Papua New Guinea: for example, microfilarial carrier rates in 14 communities in the East Sepik Province ranged from 32% to 85% (14). It was, however, high compared to other endemic areas in the world (1). In the present study the prevalence rates in males and females were similar, which is contrary to what Desowitz et al. (7) reported for their pretreatment survey in the same area in 1991 when the microfilaria rate was significantly higher in males. The discrepancy between the pre- and post-treatment results may be due more to the fact that in the present study a more sensitive parasite detection method was used since there was no gender difference in compliance with treatment.

Obstructive filarial disease in the form of elephantiasis or hydrocele was not observed among the indigenous Hagahai population during the present survey. However, two people from Enga Province had elephantiasis. The pattern of infection and disease tends to suggest that filariasis was recently introduced into the Hagahai area from Enga Province. According to Desowitz et al. (7), who also failed to observe filarial disease in the Hagahai in 1991, Hagahai oral history tells of lymphatic manifestations that could be of filarial origin but this condition is reported to have occurred in the groups living at the lower altitudes near the border with Enga Province.

The *An. punctulatus* group of mosquitoes were more common in the villages of Mangamanau and Mamusi, where filariasis was more endemic, than in the less affected village of Yilu, suggesting that they may be the main vectors in the Hagahai region. The low endemicity of filariasis in the high altitude areas near Yilu (13%) compared to the low altitude areas of Mamusi (50%) and Mangamanau (45%) may be partly explained by the high treatment coverage in the Yilu area. Other possible explanations could be the low human-mosquito contact in this village compared to the other two and the influx of infected people from Enga Province into the low altitude areas.

Failure to find infective filarial larvae in mosquitoes caught in the present study may be attributed to the interruption of transmission following mass treatment with DEC. One single-dose mass treatment in a highly endemic area in the East Sepik Province almost interrupted transmission in two villages where the prevalence of filariasis was similar to pretreatment rates in the Hagahai (14). Our findings support the phenomenon of facilitation which predicts that *Anopheles*-transmitted lymphatic filariasis can be interrupted by mass chemotherapy alone in areas of low vector density and low transmission intensity as observed in the Hagahai.

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