

Bancroftian filariasis: house-to-house variation in the vectors and transmission — and the relationship to human infection — in an endemic community of coastal Tanzania

R. T. Rwegoshora^{*}, P. E. Simonsen[†], D. W. Meyrowitsch[‡],
M. N. Malecela-Lazaro[§], E. Michael[¶] and E. M. Pedersen[†]

^{*}National Institute for Medical Research, Amani Medical Research Centre, P.O. Box 81, Muheza, Tanzania

[†]DBL — Institute for Health Research and Development, Jaegersborg Alle 1 D, 2920 Charlottenlund, Denmark

[‡]Institute of Public Health, Department of Epidemiology, University of Copenhagen, Øster Farimagsgade 5, P.O. Box 2099, 1014 Copenhagen, Denmark

[§]National Institute for Medical Research, P.O. Box 9653, Dar es Salaam, Tanzania

[¶]Department of Infectious Diseases Epidemiology, Imperial College School of Medicine, Norfolk Place, London W2 1PG, U.K.

Received 4 April 2006, Revised 12 May 2006,

Accepted 15 May 2006

The house-to-house variation in *Wuchereria bancrofti* vector abundance and transmission intensity, and the relationship of these parameters to human infection, were investigated in an endemic community in coastal Tanzania. Vector mosquitoes were collected in light traps set up in 50 randomly selected households once weekly for 1 year. They were identified, dissected and checked for filarial larvae. Vector densities and transmission potentials varied markedly between households, both for all vectors combined and for the individual vector species (*Anopheles gambiae* s.l., *An. funestus* and *Culex quinquefasciatus*), even between households located close to each other. The variation in vector abundance was probably mainly attributable to differences in the distance to breeding sites, to specific household features likely to ease mosquito entry and hiding, and to the number of household inhabitants. Household annual biting rates (ABR) correlated positively with household annual transmission potentials (ATP), indicating that intense vector biting led to a high transmission intensity. Intriguingly, however, the human filarial-infection status (as indicated by microfilaraemia or circulating filarial antigenemia) did not differ significantly between households with relatively high and lower ABR or ATP. Possible reasons for this result include the long time required for *W. bancrofti* infection to establish in humans, human behaviour affecting exposure, the sharing of mosquito populations between households, and differential susceptibility of humans to infection. The marked heterogeneity in exposure between households, and the lack of immediate relationship between transmission and detectable human infection at household level, should be taken into account when considering the transmission pattern of lymphatic filariasis.

Bancroftian lymphatic filariasis results from infection with the mosquito-borne parasitic nematode *Wuchereria bancrofti*. It affects more than 115 million people in Africa, Asia, America and the Pacific, and is a major

cause of morbidity (Michael and Bundy, 1997; Simonsen, 2003). The results of several studies on bancroftian filariasis in coastal East Africa have shown that the human infection and disease burden vary considerably from one community to the other within the same endemic area (White, 1971; Wijers, 1977; McMahon *et al.*, 1981; Meyrowitsch *et al.*, 1995; Simonsen *et al.*,

Reprint requests to: R. T. Rwegoshora.
E-mail: rrwegoshora@nimr.or.tz; fax: +255 27 2641320.

1995; Wamae *et al.*, 1998; Mukoko *et al.*, 2004). In a study recently carried out in a community of high endemicity and another of low endemicity, both in coastal East Africa, it was found that the much higher intensity of transmission and rates of human infection and disease seen in the highly endemic community were clearly associated with considerably higher vector densities (Simonsen *et al.*, 2002; Rwegoshora *et al.*, 2005), and that the differences in level of endemicity appeared to result primarily from differences in the mosquito breeding habitats in the two communities.

At any one time-point, the quality, abundance and location of vector breeding habitats, and the resulting intensity of transmission, also often differ within individual communities, as has been demonstrated in other water-related, vector-borne infections such as malaria (Manga *et al.*, 1993) and schistosomiasis (Booth *et al.*, 2004). Different parts of a single community may have different elevations, different water tables, different distances to rice fields, ponds and streams, and different densities of pit latrines, cesspits and other polluted water bodies. The different ecological requirements of the three vectors of *W. bancrofti* in East Africa (*Anopheles gambiae* s.l., *An. funestus* and *Culex quinquefasciatus*) also mean that the relative abundance of each vector species may vary from one part of the community to the other. When it comes to the micro-

epidemiological household level, additional factors, such as the characteristics of the houses and their inhabitants, may affect transmission and infection. The aims of the present study were to investigate the differences in vector density between different households within Masaika, the high-endemicity community studied by Rwegoshora *et al.* (2005), and then determine to what extent these differences were reflected in differences in transmission and human infection.

MATERIALS AND METHODS

Study Community

Masaika is a rural village located along the gravel road between Muheza and Pangani, approximately 25 km inland from the Indian Ocean, in the Pangani district of the Tanzanian region of Tanga. At the start of the study, in July 1998, Masaika had 285 households and 950 inhabitants aged ≥ 1 year, the prevalence of *W. bancrofti* microfilaraemia was 24.9%, and the prevalence of circulating filarial antigenaemia was 52.2% (Simonsen *et al.*, 2002). The houses in Masaika are scattered but fall into four natural clusters that are isolated from each other by pieces of land without houses. Moving from west to east, the first cluster, Mlimani, is located on a hilltop, with most houses concentrated on the northern side of the road. The next cluster, Bondeni, is a small lowland settlement. Then follows Godauni, which is located on elevated ground, and has most houses on the northern side of the road. Finally, Mbugani is a lowland stretch running eastward of the village. The distance along the road from the first to the last village house is about 3.4 km. At the time of the study, all four clusters had small rice fields at their periphery, and dugout wells for domestic water were located in or near the fields. The majority of houses had mud walls and were thatched with dried coconut leaves. Some houses had pit latrines. A seasonal stream passed close to Mlimani.

Entomological Surveillance

A longitudinal entomological survey was carried out in 50 randomly selected houses for 1 year, from July 1998 to June 1999, as described by Rwegoshora *et al.* (2005). Briefly, in each selected house, a battery-operated CDC light trap was placed, on one night each week, beside an occupied bed provided with an un-impregnated mosquito net. The traps were turned on at 18.00 hours and off at 06.00 hours. Mosquitoes

were collected from the traps in the morning, knocked down with ethyl acetate, sorted and identified to species by morphology. Live female mosquitoes were dissected so that they could be checked for infection with larvae of *W. bancrofti*. To cross-check the results of the initial examinations, the fresh smears of the specimens found positive for filarial larvae and those of 20% of the specimens found negative were stained in Mayer's acid haemalum and later re-examined.

To identify the main breeding sites for the vectors, different water bodies within and around the community were searched for mosquito larvae by use of dippers. The larvae collected were identified to species by morphology. The presence of water and/or of mosquito breeding in each pit latrine observed was checked by dropping a stone into the pit and noting whether or not a splash of water was heard and whether or not adult mosquitoes emerged from the pit.

Examination of the Human Population

All villagers aged ≥ 1 year were registered in a house-to-house survey shortly before the population was examined in July 1998. All the adult villagers who gave their oral informed consent and all the younger villagers (aged 1–14 years) whose parents or guardians gave consent for them to be investigated were given a clinical examination, for the chronic manifestations of lymphatic filariasis, and were then checked for microfilaraemia and *W. bancrofti*-specific circulating filarial antigens (CFA), as described by Simonsen *et al.* (2002). Fingerprick blood samples (100 μ l) were collected from them at night, between 21.00 and 24.00 hours, and checked for *W. bancrofti* microfilariae (mff) using the counting-chamber method. A 5-ml sample of venous blood was also collected from each subject, immediately after the collection of the fingerprick sample, and allowed to clot so that the serum could be separated

off and tested for CFA in a commercial ELISA (TropBio, Townsville, Australia).

Data Analysis

Only data from the houses used for mosquito sampling, known as the 'catching' houses, are included in the present analyses. The entomological indices of annual biting rate (ABR) and annual transmission potential (ATP) were calculated as described by Rwegoshora *et al.* (2005). Household ABR and ATP in houses with high and low mosquito densities were compared statistically in Mann-Whitney *U*-tests, and prevalences of human infection (as indicated by microfilaraemia or CFA) were compared in χ^2 tests. The levels of correlation between household ABR and ATP were explored by the calculation of Pearson's correlation coefficients (*r*) and determining the corresponding *P*-values in Student's *t*-tests. A *P*-value of < 0.05 was considered indicative of a statistically significant difference or correlation.

RESULTS

House-to-house Variation in ABR and ATP

Overall, 26,264 vector mosquitoes were collected during the 1-year period (12,859 *An. gambiae* s.l., 5376 *An. funestus*, and 8029 *Cx. quinquefasciatus*). Of these, 17,608 (9329 *An. gambiae* s.l., 2701 *An. funestus*, and 5578 *Cx. quinquefasciatus*) were dissected and examined for filarial infection.

The household ABR, for all vector species combined, varied widely between the 50 'catching' houses [Fig. 1(a)], with a range from 920 (house 180) to 23,353 (house 110) bites/person-year. Even houses located close to each other sometimes differed markedly. For example, houses 6 and 7 (which were only 11 m apart) had ABR of 5647 and 21,941 bites/person-year, respectively, and houses 143 and 147 (which were 31 m apart) had ABR of 6430 and 20,095 bites/person-year, respectively.

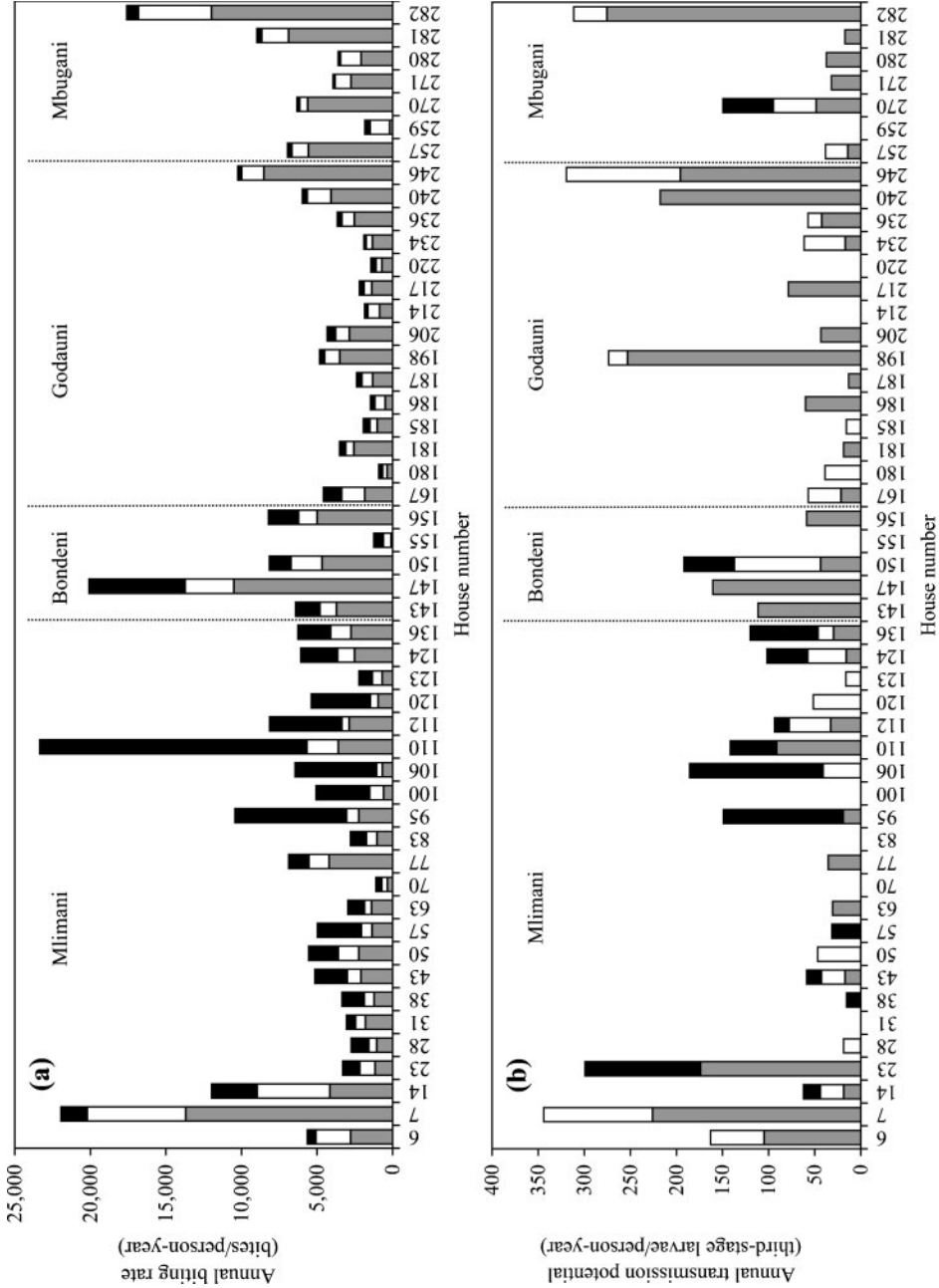


FIG. 1. Household annual biting rates (a) and household annual transmission potentials (b) for *Anopheles gambiae* s.l. (■), *An. funestus* (■) and *Culex quinquefasciatus* (□) in the four clusters of houses (Mlimani, Bondeni, Godauni and Mbugani) that form the village of Masaika.

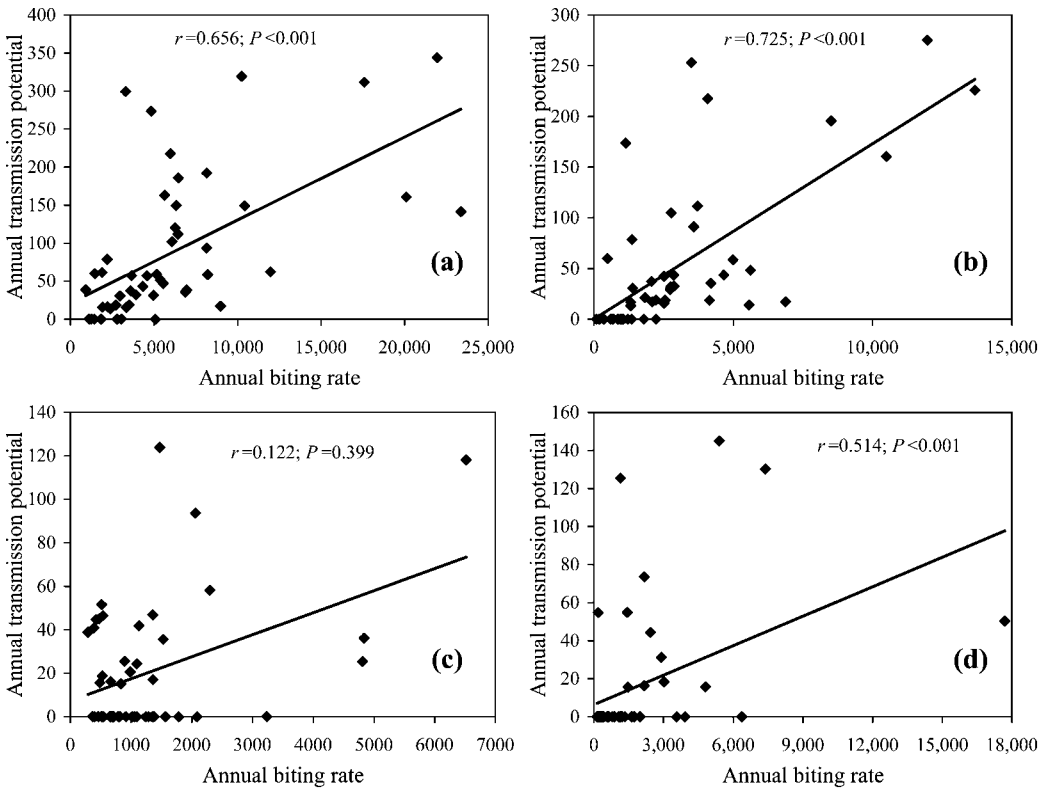


FIG. 2. Scatter plots, with regression lines, showing the relationships between annual biting rates (bites/person-year) and annual transmission potentials (third-stage larvae/person-year) in the 50 'catching' households in Masaika. The values shown are for all vector species combined (a), *Anopheles gambiae* s.l. (b), *An. funestus* (c) and *Culex quinquefasciatus* (d).

On a broad scale, household ABR for *An. gambiae* s.l. and *An. funestus* followed a similar pattern across the village (with the former generally higher than the latter), whereas the household ABR for *Cx. quinquefasciatus* were markedly higher in the western part of the village than in the eastern. Household ABR for individual vector species also sometimes differed markedly between houses located close together. Houses 95 and 110, for example, which were only 4.6 m apart, had *Cx. quinquefasciatus* ABR of 7385 and 17,688, respectively (house 110 having a pit latrine that was highly productive for *Cx. quinquefasciatus*).

Mosquitoes carrying the human-infective third-stage larvae (L_3) of *W. bancrofti* were detected in 42 of the 50 'catching' houses.

Like the ABR, the overall and vector-species-specific household ATP differed considerably between the houses [Fig. 1(b)]. Although *An. gambiae* s.l. and *An. funestus* contributed to transmission in all parts of the village, *Cx. quinquefasciatus* contributed to transmission mainly in the western part of the village. In general, transmission was most intense (i.e. ATP were highest) in houses with high ABR, and the overall household ATP were significantly positively correlated with the overall household ABR ($P<0.001$; Fig. 2). The *An. gambiae* s.l. and *Cx. quinquefasciatus* household ABR were also significantly correlated with the corresponding household ATP ($P<0.001$ for each) but this was not the case for *An. funestus* ($P=0.4$).

Relationship between Household Vector Density, Transmission and Human Infection

To examine the relationship between vector density, transmission intensity and human filarial-infection status at household level, the 'catching' houses were divided into two groups of approximately equal size, of households with ABR of >5000 bites/person-year ($N=24$) and households with lower ABR ($N=26$). The mean numbers of vector mosquitoes collected (in total and of each vector species) were significantly higher in the high-ABR households than in the low-ABR households (see Table). Similarly, the mean household ABR and mean household ATP were also significantly higher in the high-ABR households than in the low-ABR households. While no transmission was recorded in 26.7% of the low-ABR houses, this was only the case for 4.2% of the high-ABR houses. Moreover, the mean number of inhabitants aged ≥ 1 year was significantly higher in the high-ABR houses than in the low-ABR (4.3 and 3.5 individuals, respectively).

The differences seen in biting and transmission levels were not clearly reflected in

the human filarial-infection status (see Table). Although individuals aged ≥ 15 years in the high-ABR houses were more likely to be microfilaraemic than their counterparts in the low-ABR houses (with prevalences of 38.5% and 29.1%, respectively), the difference was not statistically significant, and there was practically no difference in prevalence of CFA between these two groups (63.5% and 63.6%, respectively).

DISCUSSION

Houses are important sites of contact between humans and night-biting mosquitoes and are regarded as the main sites for transmission of many mosquito-borne human pathogens, including *W. bancrofti* in some areas of its distribution. In East Africa, for example, the microfilariae of *W. bancrofti* have a nocturnal periodicity and the three species of vector mosquitoes (*An. gambiae* s.l., *An. funestus*, *Cx. quinquefasciatus*) take most of their bloodmeals at night. Household variations in vector density, transmission and human infection have

TABLE. The densities of the mosquitoes that act as vectors of *Wuchereria bancrofti*, and the levels of transmission and human infection status in houses with annual biting rates (ABR) above 5000 bites/person-year (range=5075–23,353) and below 5000 bites/person-year (range=920–4973)

	High-ABR houses	Low-ABR houses	P
No. of houses	24	26	
NO. OF MOSQUITOES COLLECTED AND (MEAN NUMBER/HOUSEHOLD)			
All three vector species	20,079 (836.6)	6185 (237.9)	<0.001
<i>Anopheles gambiae</i> s.l.	9749 (406.2)	3110 (119.6)	<0.001
<i>An. funestus</i>	3795 (158.1)	1581 (60.8)	<0.001
<i>Culex quinquefasciatus</i>	6535 (272.3)	1494 (57.5)	<0.001
Mean ABR/house (bites/person-year)	9471	2777	<0.001
Mean annual transmission potential/per house (L_3 inoculated/person-year)	130.4	46.1	<0.001
No. and (%) of houses without detected transmission	1 (4.2)	7 (26.9)	–
No. inhabitants aged ≥ 1 year and (mean number/house)	103 (4.3)	90 (3.5)	0.046
NO. INHABITANTS AGED ≥ 15 YEARS			
Present	56	60	–
With microfilaraemia/examined, and (% microfilaraemic)	20/52 (38.5)	16/55 (29.1)	0.31
With CFA/examined, and (% antigenaemic)	33/52 (63.5)	35/55 (63.6)	0.99

L_3 , Human-infective, third-stage larvae of *W. bancrofti*; CFA, circulating filarial antigen.

been reported commonly in relation to malaria (Gamage-Mendis *et al.*, 1991; Manga *et al.*, 1993; Ribeiro *et al.*, 1996; Gunawardena *et al.*, 1998; Ghebreyesus *et al.*, 2000), with distance to breeding sites and quality of house construction identified as the major causes. The results of other studies have indicated that microfilaraemia and the clinical manifestations of lymphatic filariasis may vary considerably between households within the same community (Joseph, 1971; Wijers and Kiilu, 1977; Baruah and Rai, 2000; Kumar *et al.*, 2004). In the present study, household variation in the densities of the vectors of *W. bancrofti*, and its consequences for transmission and human infection, were explored within a highly endemic community. A marked variation in household biting density was observed, both overall and for the individual vector species, even between houses located close to each other. The many scattered *Anopheles* spp. breeding sites in and around Masaika made it difficult to assess the role of distance — between such sites and the study households — in the household abundance of the anopheline vectors. *Culex quinquefasciatus*, on the other hand, were particularly abundant in the two western clusters, which had many wet pit latrines. Their biting densities, moreover, varied considerably between some closely located houses as a result of differences in proximity to a single, highly productive, pit latrine.

As poorly constructed houses are likely to provide many holes and openings for mosquito entry and hiding, the way in which each study house was constructed also probably affected the densities of the mosquito vectors of *W. bancrofti* in that house, as reported before (Wijers and Kiilu, 1977; Baruah and Rai, 2000; Terhell *et al.*, 2000). A third factor affecting the densities of the vectors in each household may have been the number of household inhabitants, as the combined body odour from many people may attract more mosquitoes than the body odour from just one or a few people

(Burkot, 1988; Vanamail *et al.*, 1989; Knols *et al.*, 1995). In this respect, it was interesting to note that the high-ABR households were generally larger, in terms of the number of people in the household, than the low-ABR households.

The level of *W. bancrofti* transmission (as indicated by the number of mosquitoes carrying L_3) also varied markedly from house to house. The variation in the magnitude of the ATP generally followed that of the ABR, and there was a clear correlation between the household ATP for all vectors combined and the corresponding ABR. Marked house-to-house variations in filarial transmission have been reported before, and attributed mainly to differences in house construction affecting mosquito abundance (Wijers and Kiilu, 1977; Joseph, 1971; Baruah and Rai, 2000; Kumar *et al.*, 2004). As mentioned above, however, it is likely that the distance to the vector breeding sites and the number of inhabitants also play an important role. Overall, the factors responsible for both ABR and ATP at the household level appear to be closely related to the wealth status of the households.

When the 'catching' houses were divided into those with high and low ABR, there was — as expected — significantly more transmission in the former group than the latter. Intriguingly, however, the proportion of adults (aged ≥ 15 years) with detectable filarial infection (microfilaraemia and/or circulating filarial antigenaemia) did not differ significantly between these two groups of houses. One reason could be that the establishment of a human infection with *W. bancrofti* that is detectable (as microfilaraemia and/or circulating filarial antigenaemia) is the result of cumulative exposure over a long period of time. Unlike the incidence of malaria, which represents current exposure, the incidence of detectable filarial infection is generally the result of many years of exposure. In addition, it takes the L_3 inoculated into a human by a vector at least 8–12 months to mature and begin producing mff (Southgate, 1992; Simonsen,

2003). The time factor is thus important when considering the link between transmission and detectable infection in filariasis, and vector densities, or even transmission intensities, observed over a 1-year period should not be expected to have an immediate effect on detectable infection in humans. The fact that both ATP and the prevalence of microfilaraemia were higher (although not significantly) in the high-ABR houses than the low-ABR, whereas CFA prevalences in the high- and low-ABR were almost identical, indicates that transmission intensity is more a reflection of human microfilaraemia than *vice versa*.

Other factors might have contributed to the lack of an observed relationship between transmission intensity and (detectable) human filarial infection. Year-to-year seasonal variations in the number of temporary breeding sites and the distances between such sites and households, for example, may modulate the transmission pattern of *W. bancrofti* in time and space. Over short or longer periods, human behavioural and occupational factors may have led to other exposure patterns than those observed in the present study. With the closeness of houses, some sharing of vector populations between households may be another factor contributing to the lack of a relationship between household vector indices and human filarial-infection status. Finally, humans may also differ in susceptibility to (detectable) filarial infection, as indicated by the results of several previous studies (Ottesen *et al.*, 1981; Terhell *et al.*, 2000; Choi *et al.*, 2003).

In conclusion, the present study demonstrated marked variations in vector density and transmission intensity between households, even between those located close to each other. Mosquito biting obviously did not occur at random within the endemic village, and not all individuals were at equal risk of being bitten or being exposed to L_3 . Such small-area variations in the levels of contact between vectors and humans may have a profound effect on vectorial potential

(Dye and Hasibeder, 1986; Burkot, 1988). The heterogeneity in exposure detected in Masaika, and the lack of an obvious relationship between exposure and infection in humans, should be investigated further, in order to get a more complete understanding of the epidemiology of lymphatic filariasis. Such knowledge may be important for the optimal design and implementation of control programmes and for devising ways and means of monitoring the success of such programmes.

ACKNOWLEDGEMENTS. The inhabitants of Masaika and the project staff of Bombo Research Station (Tanga, Tanzania) are thanked for their commitment and co-operation. The study received financial support from the INCO-DC programme of the Commission of the European Union (via contract ERBIC 18 CT 970257) and DBL — Institute for Health Research and Development, Charlottenlund, Denmark. A research visit by R.T.R. to DBL was sponsored through a scholarship from Danish International Development Assistance (Danida). The article is published with the permission of the Director General of the National Institute for Medical Research, Dar es Salaam, Tanzania.

REFERENCES

- Baruah, K. & Rai, R. N. (2000). The impact of housing structure on filariasis. *Japanese Journal of Infectious Diseases*, **53**, 107–110.
- Booth, M., Vennervald, B. J., Kenty, L., Butterworth, A. E., Kariuki, H. C., Kadzo, H., Ireri, E., Amaganga, C., Kimani, G., Mwatha, J. K., Otedo, A., Ouma, J. H., Muchiri, E. & Dunne, D. W. (2004). Micro-geographic variation in exposure to *Schistosoma mansoni* and malaria, and exacerbation of splenomegaly in Kenyan school-aged children. *BMC Infectious Diseases*, **4**, 13.
- Bukort, T. (1988). Non-random host selection by anophelines. *Parasitology Today*, **4**, 156–162.
- Choi, E. H., Nutman, T. B. & Chanock, S. J. (2003). Genetic variation in immune function and susceptibility to human filariasis. *Expert Reviews in Molecular Diagnosis*, **3**, 367–273.

- Dye, C. & Hasibeder, G. (1986). Population dynamics of mosquito-borne diseases: effect of flies which bite some people more frequently than others. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **80**, 67–77.
- Gamage-Mendis, A. C., Carter, R., Mendis, C., Dezoysa, P. K., Herath, P. R. J. & Mendis, K. N. (1991). Clustering of malaria infections within an endemic population: risk of malaria associated with the type of housing construction. *American Journal of Tropical Medicine and Hygiene*, **45**, 77–85.
- Ghebreyesus, T. A., Haile, M., Witten, K. H., Getachew, A., Yohannes, M., Lindsay, S. W. & Byass, P. (2000). Household risk factors for malaria among children in the Ethiopian highlands. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **94**, 17–21.
- Gunawardena, D. M., Wickremasinghe, A. R., Muthuwatta, L., Weerasingha, S., Rajakaruna, J., Senayaka, T., Kotta, P. K., Attanayake, R., Carter, R. & Mendis, K. N. (1998). Malaria risk factors in an endemic region of Sri Lanka, and the impact and cost implications of risk factor-based interventions. *American Journal of Tropical Medicine and Hygiene*, **58**, 533–542.
- Joseph, A. (1971). Studies on the pattern of distribution of filarial carriers in a seaport in Kerala. *Indian Journal of Public Health*, **15**, 103–108.
- Knols, B. G., de Jong, R. & Takken, W. (1995). Differential attractiveness of isolated humans to mosquitoes in Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **89**, 604–606.
- Kumar, D. V. R. S., Krishna, D., Murty, U. S. & Sai, K. S. K. (2004). Impact of different housing structures on filarial transmission in rural areas of southern India. *Southeast Asian Journal of Tropical Medicine and Public Health*, **35**, 587–590.
- Manga, L., Fondjo, E., Carnevale, P. & Robert, V. (1993). Importance of low dispersion of *Anopheles gambiae* (Diptera: Culicidae) on malaria transmission in hilly towns in South Cameroon. *Journal of Medical Entomology*, **30**, 936–938.
- McMahon, J. E., Magayuka, S. A., Kolstrup, N., Mosha, F. W., Bushrod, F. M., Abaru, D. E. & Bryan, J. H. (1981). Studies on the transmission and prevalence of bancroftian filariasis in four coastal villages of Tanzania. *Annals of Tropical Medicine and Parasitology*, **75**, 415–431.
- Meyrowitsch, D. W., Simonsen, P. E. & Makunde, W. (1995). Bancroftian filariasis: analysis of infection and disease in five endemic communities of north-eastern Tanzania. *Annals of Tropical Medicine and Parasitology*, **89**, 653–663.
- Michael, E. & Bundy, D. A. P. (1997). Global mapping of lymphatic filariasis. *Parasitology Today*, **13**, 472–476.
- Mukoko, D. A. N., Pedersen, E. M., Masese, N. N., Estambale, B. B. A. & Ouma, J. H. (2004). Bancroftian filariasis in 12 villages in Kwale district, Coast province, Kenya — variation in clinical and parasitological patterns. *Annals of Tropical Medicine and Parasitology*, **98**, 801–815.
- Ottesen, E. A., Mendell, N. R., McQueen, J. M., Weller, P. F., Amos, D. B. & Ward, F. E. (1981). Familial predisposition to filarial infection — not linked to HLA-A or -B locus specificities. *Acta Tropica*, **38**, 205–216.
- Ribeiro, J. M. C., Seulu, F., Abose, T., Kidane, G. & Teklehaimanot, A. (1996). Temporal and spatial distribution of mosquitoes in an Ethiopian village: implications for malaria control strategies. *Bulletin of the World Health Organization*, **74**, 299–305.
- Rwegoshora, R. T., Pedersen, E. M., Mukoko, D. A., Meyrowitsch, D. W., Masese, N., Malecela-Lazaro, M. N., Ouma, J. H., Michael, E. & Simonsen, P. E. (2005). Bancroftian filariasis: patterns of vector abundance and transmission in two East African communities with different levels of endemicity. *Annals of Tropical Medicine and Parasitology*, **99**, 253–265.
- Simonsen, P. E. (2003). Filariasis. In *Manson's Tropical Diseases*, 21st Edn, eds Cook, G. C. & Zumla, A. pp. 1489–1526. London: W. B. Saunders.
- Simonsen, P. E., Meyrowitsch, D. W., Makunde, W. H. & Magnussen, P. (1995). Bancroftian filariasis: the patterns of microfilaraemia and clinical manifestations in three endemic communities of northern Tanzania. *Acta Tropica*, **60**, 179–187.
- Simonsen, P. E., Meyrowitsch, D. W., Jaoko, W. G., Malecela, M. N., Mukoko, D. N., Pedersen, E. M., Ouma, J. H., Rwegoshora, R. T., Masese, N., Magnussen, P., Estambale, B. B. A. & Michael, E. (2002). Bancroftian filariasis infection, disease, and specific antibody response patterns in a high and a low endemicity community in East Africa. *American Journal of Tropical Medicine and Hygiene*, **66**, 550–559.
- Southgate, B. A. (1992). Intensity and efficiency of transmission and the development of microfilaraemia and disease: their relationship in lymphatic filariasis. *Journal of Tropical Medicine and Hygiene*, **95**, 1–12.
- Terhell, A. J., Houwing-Duistermaat, J. J., Ruiterman, Y., Haarbrink, M., Abadi, K. & Yazdanbakhsh, M. (2000). Clustering of *Brugia malayi* infection in a community in south Sulawesi, Indonesia. *Parasitology*, **120**, 23–29.
- Vanamail, P., Subramanyan, S., Das, P. K., Pani, S. P. & Bundy, D. A. P. (1989). Familial clustering in *Wuchereria bancrofti* infection. *Tropical Biomedicine*, **6**, 67–71.
- Wamae, C. N., Gatika, S. M., Roberts, J. M. & Lammie, P. J. (1998). *Wuchereria bancrofti* in Kwale district, coastal Kenya: patterns of focal distribution of infection, clinical manifestations and

- anti-filarial IgG responsiveness. *Parasitology*, **116**, 173–82.
- White, G. B. (1971). Studies on transmission of bancroftian filariasis in north-eastern Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **65**, 819–829.
- Wijers, D. J. B. (1977). Bancroftian filariasis in Kenya. I. Prevalence survey among adult males in Coast Province. *Annals of Tropical Medicine and Parasitology*, **71**, 313–331.
- Wijers, D. J. B. & Kiilu, G. (1977). Bancroftian filariasis in Kenya III. Entomological investigations in Mamburi, a small coastal town, and Jaribuni, in rural area more inland (Coast province). *Annals of Tropical Medicine and Parasitology*, **71**, 347–359.