

- Journal of Tropical Medicine and Hygiene*, **29**, 554–558.
- Piessens, W. F., Hoffman, S. L., Ratiwayanto, S., Piessens, P. W., Partona, F., Kurniawan, L. & Marwofo, H. A. (1983). Opposing effects of filariasis and chronic malaria on immunoregulatory T lymphocytes. *Diagnostic Immunology*, **1**, 157–260.
- Ravindran, B., Satapathy, A. K., Das, M. K., Patnaik, N. M. & Subramanyam, V. R. (1990). Antibodies to microfilarial sheath in Bancroftian filariasis—prevalence and characterization. *Annals of Tropical Medicine and Parasitology*, **84**, 607–613.
- Richard, G., Barbara, L. & Antony, S. (1991). The involvement of TNF- α , IL-1, and IL-6 in immune response to protozoan parasites. *Parasitology Today*, **12**, 13–16.
- Rooth, I. B. & Björkman, A. (1992). Suppression of *Plasmodium falciparum* infections during concomitant measles or influenza but not during pertussis. *American Journal of Tropical Medicine and Hygiene*, **47**, 675–681.
- Schmidt, L. H. & Esslinger, J. H. (1981). Course of infections with *Plasmodium falciparum* in owl monkeys displaying microfilaremia. *American Journal of Tropical Medicine and Hygiene*, **30**, 5–11.

- Schuurkamp, G. J., Matango, M., Kereu, R. & Napil, J. (1987). Malaria, splenomegaly and filariasis in the Ok Tedi area of the Star Mountains, Papua New Guinea: three years after residual DDT spray. *Papua New Guinea Medical Journal*, **30**, 219–300.
- Taverne, J., Tavernier, J., Fiers, N. & Playfair, J. H. L. (1987). Recombinant tumour necrosis factor inhibits malaria parasites *in vivo* but not *in vitro*. *Clinical and Experimental Immunology*, **64**, 1–4.
- Yan, Y., Inuo, G., Akao, N., Tsukidate, S. & Fugita, K. (1997). Down-regulation of murine susceptibility to cerebral malaria by inoculation with third stage larvae of the filarial parasite *Brugia pahangi*. *Parasitology*, **114**, 333–338.

Received 15 May 1996; revised 28 July 1997; accepted for publication 29 July 1997

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (1998) **92**, 23–24

Short Report

Parental infection confounded with local infection intensity as risk factors for childhood microfilaraemia in bancroftian filariasis

N. D. E. Alexander^{1,2}, J. W. Kazura³, M. J. Bockarie⁴, R. T. Perry^{3,5}, Z. B. Dimber⁵, B. T. Grenfell² and M. P. Alpers¹
¹Papua New Guinea Institute of Medical Research, P. O. Box 60, Goroka, Papua New Guinea; ²Department of Zoology, Downing Street, Cambridge, UK; ³Division of Geographic Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA; ⁴Papua New Guinea Institute of Medical Research, P. O. Box 378, Madang, Papua New Guinea; ⁵Papua New Guinea Institute of Medical Research, P. O. Box 400, Maprik, Papua New Guinea

Keywords: filariasis, *Wuchereria bancrofti*, risk factors, children, Papua New Guinea

The propensity of children to develop patent *Wuchereria bancrofti* infection (LAMMIE *et al.*, 1991), the qualitative nature of filarial antigen-specific T cell reactivity (STEEL *et al.*, 1994), and the likelihood of developing acute adenolymphangitis (WARTMAN, 1947), have all been proposed as being influenced by maternal infection during gestation. Collectively, these studies suggest that offspring of microfilaraemic (mf+) mothers have an increased susceptibility to patent infection and reduced severity of disease manifestations compared with children born of uninfected (mf-) mothers. The intensity of transmission is an important determinant of the microfilaria (mf) carrier rate, and may be heterogeneous even within small geographical areas (SOUTH-GATE, 1992). Detailed residence data in an area endemic for *W. bancrofti* in East Sepik Province, Papua New Guinea (KAZURA *et al.*, 1984) allowed us to examine the extent to which maternal mf status independently accounts for the observed relationship between parental and childhood infection status. Recent ento-

mological surveys of several geographically distinct clusters of households in this 100 km² area demonstrated marked variability of annual transmission potential, with a range of 31 to more than 2000 infective larvae per person per year (BOCKARIE *et al.*, 1996).

As part of a prospective study to evaluate the efficacy of single annual doses of chemotherapy to control bancroftian filariasis (KAZURA *et al.*, in press), a parasitological survey of approximately 2000 residents of the Dreikikir area was conducted in 1993, before administration of antifilarial medication. Amongst those evaluated for mf levels (by Nuclepore[®] filtration of 1 mL of night blood samples) were 288 children aged 4–10 years, the mothers of 261 of them and the fathers of 210. Analysis of mf status among these groups using Mantel-Haenszel χ^2 statistics and Cornfield confidence intervals (Epi Info version 6, Centers for Disease Control, Atlanta, Georgia, USA) showed that both children of mf+ mothers and those of mf+ fathers had a higher risk of being mf+ compared with offspring of mf- parents (Table).

Table. Influence of parental infection status and local infection intensity on *Wuchereria bancrofti* infection in children aged ten years or less

	Proportion microfilaraemic	Odds ratio ^a Unadjusted	Adjusted ^b
Maternal microfilaraemia			
Yes	79/182 (43.4%)	1.99 (1.08–3.67)	1.40 (0.77–2.60)
No	22/79 (27.8%)	P=0.018	P=0.28
Paternal microfilaraemia			
Yes	66/144 (45.8%)	2.88 (1.42–5.90)	1.86 (0.93–3.87)
No	15/66 (22.7%)	P=0.0014	P=0.09

^a95% Confidence interval in parentheses.

^bAdjusted for local infection intensity.

To investigate the possible effect of local transmission intensity on these findings, the community microfilarial load (CMFL; geometric mean number of mf per mL plus one; REMME *et al.*, 1986) was calculated, based on those persons aged 11 years or more living in the same 90 geographically-defined hamlets as the children. When the logarithm of CMFL was used as a second predictor in a logistic regression (S-PLUS for Windows[®] version 3.3, Statistical Sciences UK Ltd, Oxford, UK), the effects of parental infection were substantially reduced in terms of both odds ratios and statistical significance (Table). The logarithm of the local CMFL was highly significant in each case ($P<0.001$). The odds ratio for maternal infection has some sensitivity to sam-

Address for correspondence: Neal Alexander, Papua New Guinea Institute of Medical Research, P. O. Box 60, Goroka, EHP 441, Papua New Guinea.

pling variability in the CMFL, but 'bootstrap' resampling (EFRON & TIBSHIRANI, 1993) of the mf levels within each hamlet indicated that this was only moderate: among 2000 bootstrapped datasets, 95% of the odds ratios lay between 1.35 and 1.73.

These data suggest that local transmission intensity is a significant source of heterogeneity and a confounding variable in determining the propensity of children to develop patent *W. bancrofti* infection. The report by LAMMIE *et al.* (1991) does not contain information on geographical variability of mf densities or entomological measures of transmission, although RACCURT *et al.* (1988) reported that suburban residents of the same region had a median mf intensity of 19.1 per 20 mm³ of blood, compared to 8.8 in the city. The interquartile range of the hamlet CMFL in the current study was 11–77 mf/mL.

Finally, it should be noted that our observations do not disprove maternal mf status as a risk factor for childhood infection (adjusting for local mf intensity weakened but did not remove the positive association) or the propensity to develop lymphatic pathology, as suggested by studies in experimental animals (KLEI *et al.*, 1986). Rather, the current findings underscore the importance of transmission intensity as one of multiple host and ecological factors that may affect the burden of infection and disease due to *W. bancrofti* at a population level.

Acknowledgements

We thank the people of Urat and Urim for giving their blood. The study was supported by a grant from the Tropical Diseases Research programme of the World Health Organization (F30/181/67). Bryan Grenfell was supported by the Wellcome Trust.

References

- Bockarie, M., Kazura, J., Alexander, N., Dagoro, H., Bockarie, F., Perry, R. & Alpers, M. (1996). Transmission dynamics of *Wuchereria bancrofti* in East Sepik Province, Papua New Guinea. *American Journal of Tropical Medicine and Hygiene*, **54**, 577–581.
- Efron, B. & Tibshirani, R. (1993). *An Introduction to the Bootstrap*. New York: Chapman and Hall.
- Kazura, J. W., Spark, R., Forsyth, K., Brown, G., Heywood, P., Peters, P. & Alpers, M. (1984). Parasitologic and clinical features of bancroftian filariasis in a community in East Sepik Province, Papua New Guinea. *American Journal of Tropical Medicine and Hygiene*, **33**, 1119–1123.
- Kazura, J., Bockarie, M., Alexander, N., Perry, R., Bockarie, F., Dagoro, H., Dimber, Z., Hyun, P. & Alpers, M. P. (in press). Transmission intensity and its relationship to infection and disease due to *Wuchereria bancrofti* in Papua New Guinea. *Journal of Infectious Diseases*.
- Klei, T. R., Blanchard, D. P. & Coleman, S. U. (1986). Development of *Brugia pahangi* infections and lymphatic lesions in male offspring of female jirds with homologous infections. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **80**, 214–216.
- Lammie, P. J., Hitch, W. L., Walker Allen, E. M., Hightower, W. & Eberhard, M. L. (1991). Maternal filarial infection as risk factor for infection in children. *Lancet*, **337**, 1005–1006.
- Raccurt, C. P., Lowrie, R. C., jr, Katz, S. P. & Duverseau, Y. T. (1988). Epidemiology of *Wuchereria bancrofti* in Leogane, Haiti. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **82**, 721–725.
- Remme, J., Ba, O., Dadzie, K. Y. & Karam, M. (1986). A force-of-infection model for onchocerciasis and its applications in the epidemiological evaluation of the Onchocerciasis Control Programme in the Volta River basin area. *Bulletin of the World Health Organization*, **64**, 667–681.
- 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.
- Steel, C., Guinea, A., McCarthy, J. S. & Ottesen, E. A. (1994). Long term effect of prenatal exposure to maternal microfilaraemia on immune responsiveness to filarial parasite antigens. *Lancet*, **343**, 890–893.
- Wartman, W. B. (1947). Filariasis in American armed forces in World War II. *Medicine*, **26**, 334–394.

Received 11 July 1997; accepted for publication 7 August 1997