Epidem. Inf. (1987) 98, 65–71
Printed in Great Britain

Predisposition to *Trichuris trichiura* infection in humans

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(*Accepted 8 September 1986*)

SUMMARY

The study examines the distribution of *Trichuris trichiura* infection in a village community in St Lucia, West Indies. The infection intensity of the same age-stratified population was assessed (by drug expelled worm burden and faecal egg count) at the initiation of the study, and after 17 months of reinfection following treatment. The frequency distribution of worm numbers per person was similar at both periods of sampling. There was a significant correlation between the initial infection intensity of an individual, and the intensity acquired by the same individual following the 17 month period of reinfection. This relationship was observed in a broad range of host age classes. The study provides firm evidence that individuals are predisposed to heavy (or light) *T. trichiura* infection.

INTRODUCTION

Trichuris trichiura infection is one of the most prevalent geohelminthiases in many areas of the tropical world (Peters, 1978). Intense infections involving a thousand or more worms initiate a severe clinical syndrome (Kuori & Valdes Diaz, 1952; Jung & Beaver, 1951; Ramsey, 1962). Recent studies indicate that this syndrome represents one extreme of a clinical spectrum related to infection intensity: more moderate worm burdens being associated with mucoid dysentery and growth-stunting (Gilman *et al.* 1983; Cooper & Bundy, 1986; Cooper, Bundy & Henry, 1986).

As part of a continuing investigation of the epidemiology of trichuriasis we have described the population distribution of *T. trichiura* worm burdens in an endemic community (Bundy *et al.* 1986). In the present investigation we examine the population distribution of worm burdens reacquired by the same community following a single treatment intervention.

MATERIALS AND METHODS

The study was conducted in the village of Anse-la-Raye (population 2500) situated on the Caribbean coast of the island of St Lucia. The demographic and

Table 1. *The overall prevalence and mean intensity (worm burden) of* T. trichiura *infection in a village population at the start of the study and after a 17-month period of reinfection following chemotherapy*

(All subjects examined after reinfection had also been examined before treatment.)

		Intensity	
Study	Prevalence % (n)	Mean worm burden (n)	k
Initial	71·7 (244)	54·2 (106)	0·428
17-month reinfection	66·3 (104)	23·9 (75)	0·405

clinical characteristics of the village are described elsewhere (Bundy *et al.* 1986; Cooper & Bundy, 1986).

Two faecal specimens were collected 7 days apart from an age-stratified sample ($n = 244$) of the population (see Bundy *et al.* 1986, for details of the sampling protocol). Each specimen was examined in duplicate using the Kato thick smear technique, and the mean density of *T. trichiura* eggs per gram of stool (EPG) determined.

All infected individuals were offered mebendazole therapy (100 mg b.i.d. × 3 days: VERMOX, Janssen Pharmaceutica, Belgium). Total 24 h stools were collected for 3 days post-treatment from a randomly selected subsample of infected persons recruited from each age class ($n = 106$). The number of *T. trichiura* worms expelled by chemotherapy was determined and assumed to be an estimate of the total worm burden in that individual (Bundy *et al.* 1985*a*; Bundy *et al.* 1985*b*). The efficacy of treatment was confirmed by Kato thick smear examination of stool specimens collected 30 days post-treatment.

The mean weight of stool passed/individual/day was estimated from the weights of the three consecutive 24 h stool collections. The product of this value and the mean EPG of the individual provided an estimate of the number of *T. trichiura* eggs deposited/individual/day (EPD).

The rate of reinfection of the population was then monitored by monthly coprological examination of an age-stratified sub-sample. After 17 months the prevalence and intensity of *T. trichiura* infection approached pre-treatment levels.

Duplicate stools were again examined from an age-stratified population sample, EPG estimated and mebendazole therapy offered to all infected individuals. Where possible, 3 × 24 h post-treatment stools were collected from the same individuals as were examined during the first intervention. Total *T. trichiura* worm burden and EPD at the time of the second intervention were estimated.

The infection intensities (estimated from worm burden, EPG and EPD) of the same subjects at the start of the study and after the 17-month period of reinfection were compared using Kendall's Rank Correlation test. The worm burden data were re-examined after being standardized about the means of three age classes (0·5–2 years ($n = 26$); 3–12 years ($n = 23$); and > 13 years ($n = 26$)) using the formula $y = (x - \bar{x})/s$, where: y = the age-standardized worm burden; x = observed worm burden; $\bar{x}$ = mean worm burden for that age class; s = standard deviation for that age class.

This study was conducted with the agreement of the Ministry of Health (St Lucia), the St Lucia Medical Association and the Anse-la-Raye Community

https://doi.org/10.1017/S0950268800061719 Published online by Cambridge University Press

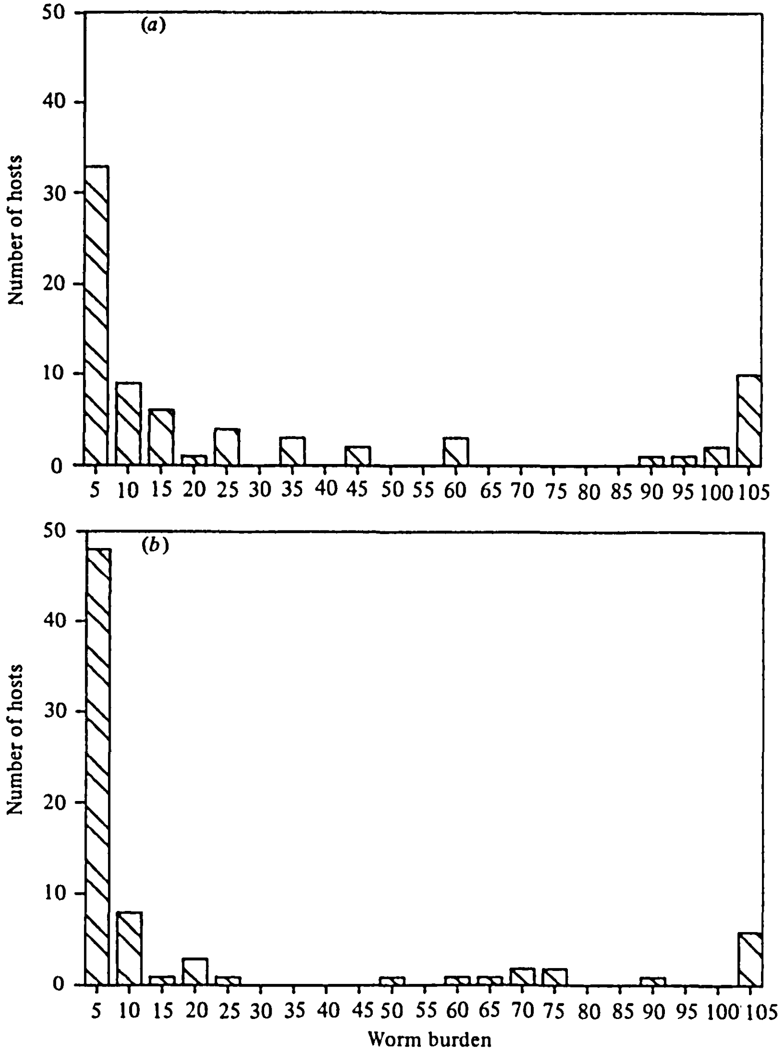

Fig. 1. Frequency distribution of *Trichuris trichiura* worm burdens, assessed by anthelmintic expulsion (*a*) at the initiation of the study; (*b*) after a 17-month period of reinfection following treatment.

Association. Permission was received from the individuals concerned, or in the case of children, their legal guardians.

RESULTS

Table 1 shows the frequency distribution of *T. trichiura* worm burdens within the village population before the first treatment, and after 17 months of reinfection. It is apparent that a 17-month period of natural reinfection was sufficient for the prevalence and intensity of infection to rebound to approximately pre-intervention levels.

The distribution of *T. trichiura* worm-burdens in an age-stratified sub-sample of the population was markedly overdispersed (Fig. 1*a*). Re-examination of the

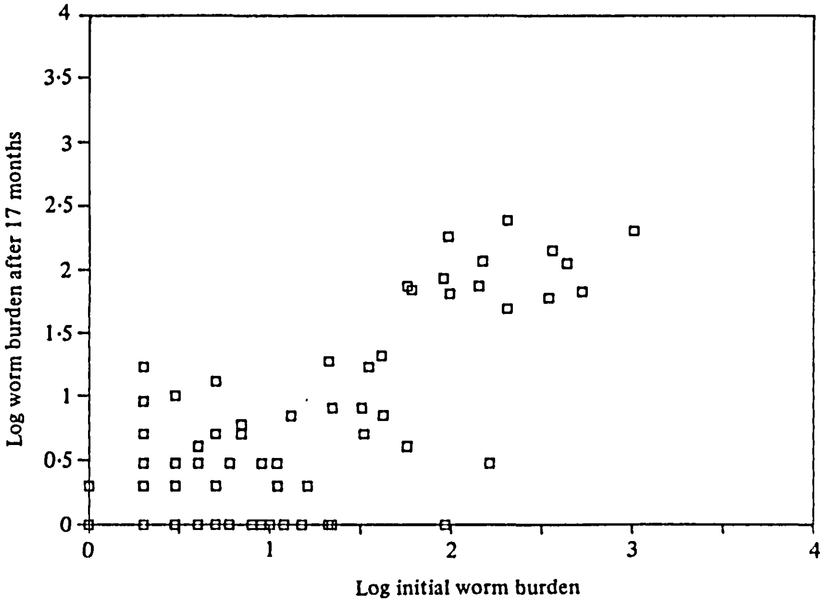

Fig. 2. Predisposition to *T. trichiura* infection. A comparison between initial worm burden (determined by anthelmintic expulsion) and the worm burden acquired by the same subjects after 17 months of reinfection.

same individuals after reinfection revealed a similarly aggregated distribution (Fig. 1*b*). The exponent of the negative binomial distribution (k), which varies inversely with the severity of aggregation, did not differ significantly between the two observations (Table 1).

Comparison of worm burdens in individual subjects at the first and second round of anthelmintic treatment revealed a significant correlation (Kendall's coefficient of rank correlation, $\tau = 0{\cdot}4333$, $P < 0{\cdot}001$, $n = 75$) (Fig. 2). Individuals who were intensely infected at the first observation tended to reacquire heavy worm burdens during the 17-month period of reinfection, while individuals who were initially lightly infected tended to reacquire light infections. This correlation remained significant when the data were standardized about the means for each age class ($\tau = 0{\cdot}6417$, $P < 0{\cdot}001$, $n = 75$), suggesting that the relationship is independent of age.

The other, indirect measures of infection intensity (EPG and EPD) also showed significant correlations between the infection intensities of the same individuals before and after reinfection: EPG ($\tau = 0{\cdot}3228$, $P < 0{\cdot}001$, $n = 102$); and EPD ($\tau = 0{\cdot}4433$, $P < 0{\cdot}001$, $n = 87$) (Fig. 3).

DISCUSSION

The results show that the intensity of infection reacquired by an individual following treatment is significantly correlated with the intensity of infection prior to treatment. The relationship is observed whether infection is estimated directly by anthelmintic expulsion of the worm burden, or indirectly by assessing the

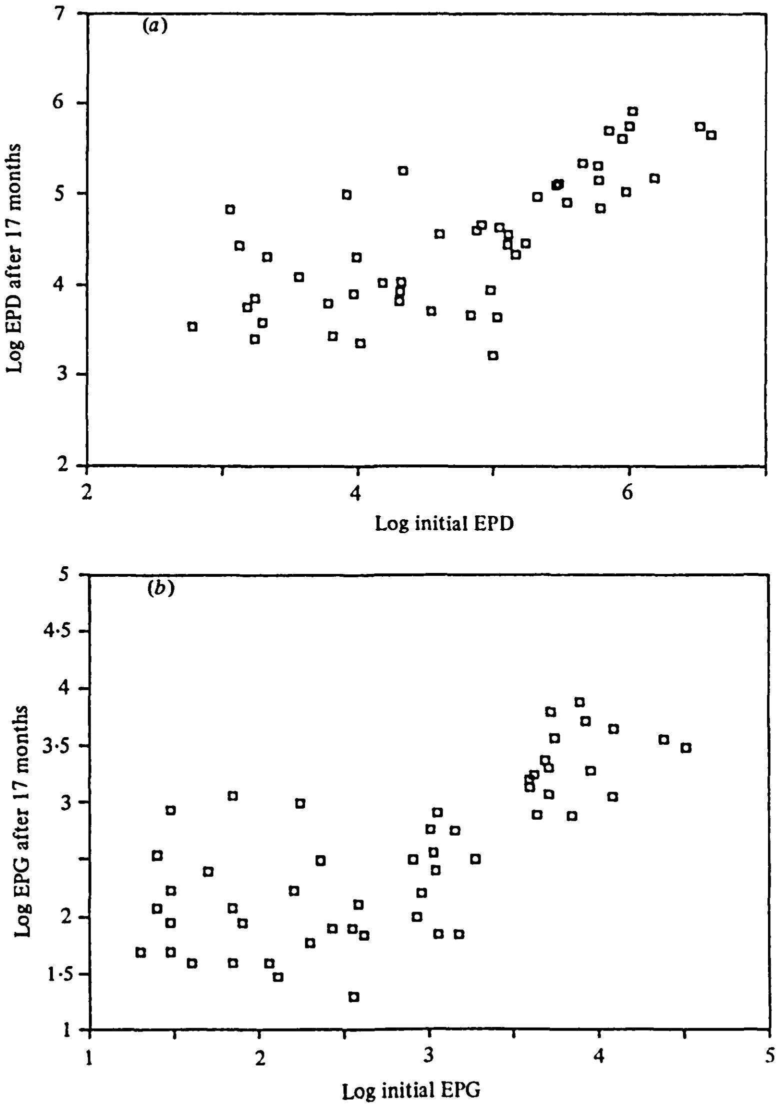

Fig. 3. Comparison between initial infection intensity and the intensity of infection acquired during 17 months of reinfection of the same individuals. (*a*) Eggs excreted/individual/day (EPD). (*b*) Eggs excreted/g stool (EPG).

density of helminth eggs in stool (EPG and EPD). These observations suggest that an individual is predisposed to heavy (or light) infection with *T. trichiura*.

In common with other geohelminths, the intensity of *T. trichiura* infection intensity has a convex relationship with host age (Sadun, 1955; Anderson & May, 1985; Bundy, 1986). Intensity tends to be low in infants and adults, and high in the child age classes. Over a period of reinfection (short with respect to host life-span) it might be expected that children would reacquire high, and adults would reacquire low, worm burdens due to differences in behavioural factors relevant to parasite transmission. A study of reinfection trends in a population of mixed age might therefore be expected to produce the observed results as a consequence of age-related differences in the rate of acquisition of infection. The present analyses, however, yield significant correlations even when the data are standardized for age, implying that predisposition of individuals to a heavy or light *T. trichiura* infection is independent of host age.

The present study of a village community with endemic trichuriasis is the first demonstration of age-independent predisposition to *T. trichiura* infection. In an earlier study of an institutionalized population we did not record significant correlations between worm burdens in children at two time points following a period of reinfection (Bundy *et al.* 1985*a*). The possible reasons for this are analysed elsewhere (Bundy & Cooper, 1986). Previous studies have demonstrated predisposition of humans to hookworm (Schad & Anderson, 1985), *Ascaris* (Croll *et al.* 1982; Anderson & Medley, 1985), and *Enterobius* infection (Haswell-Elkins, Elkins & Anderson, 1986). Indeed, predisposition to gastrointestinal nematode infection has been demonstrated by all detailed studies examining reinfection following treatment of individuals in stable communities (Anderson, 1986).

The phenomenon of predisposition argues for the existence of some determinant of parasite infection success which is associated with some characteristic or characteristics specific to an individual host. For example, some combination of individual differences in susceptibility and environmental exposure (Schad & Anderson, 1985). At present the human immune response to trichuriasis remains enigmatic (Ogilvie & De Savigny, 1982), and the effect of environmental factors has been described at the familial, but not at the individual level (Forrester *et al.* 1986). Further research is required to identify the factors responsible for the pattern reported in this paper.

The practical significance of the phenomenon of predisposition is in its relevance to control. Since heavily infected individuals suffer most morbidity (Jung & Beaver, 1951; Gilman *et al.* 1983; Cooper & Bundy, 1986) and also make the major contribution to the transmission of infection (Anderson & May, 1982, 1985), targeting treatment at individuals predisposed to intense infection could simultaneously control both infection and disease.

The practical advantages of selectively treating a few high risk individuals have long been recognized (Smillie, 1924), but the economic rationale for this approach is crucially dependent upon the cost of identifying target individuals (Warren & Mahmoud, 1976; Walsh & Warren, 1979). If predisposition to intense infection is a fixed characteristic of an individual then identifying the high risk targets in a community might become a unique, and potentially affordable activity. Understanding the factors which generate predisposition to intense helminth infection is central to the development of rational and cost-effective control strategies.

We gratefully acknowledge the Ministry of Health, St Lucia, for granting permission for the conduct of the investigations. The study was supported by the Wellcome Trust.

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