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Population Ecology of Intestinal Helminth Infections in Human Communities

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Population ecology of intestinal helminth infections in human communities

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The distribution of worm burdens in human populations is a major determinant of both the dynamics of transmission and the level of community morbidity. The distribution exhibits convexity with host age, which appears to correlate with exposure in the young age-classes but not in adults, and may be evidence for the development of an acquired immune response. The distribution between individuals is typically overdispersed. Individuals are predisposed to high (or low) intensity of infection and to a correspondingly high (or low) rate of acquisition of infection. A major epidemiological question is whether this reflects individual differences in environmental exposure or susceptibility. Environmental studies that have observed clustering of intense infection in particular households are supportive of either mechanism. Individual host behaviours that predispose to infection have an overdispersed distribution and may alone, or as compounding factors, generate the observed distribution of infection intensity. Factors such as host nutrition and physiology may modify host immune-responsiveness and hence susceptibility. Preliminary evidence suggests correlates between infection intensity and HLA class II antigens, and tentatively implies a genetic factor in susceptibility. These findings suggest that further understanding of the relative importance of environmental factors and resistance to the acquisition of intense infection is dependent upon a multidisciplinary approach to epidemiological field study.

Introduction

Gastrointestinal helminthiases are among the most prevalent and widespread of chronic human infections. Estimates vary as to the number of cases, but all agree that a least a quarter of mankind is currently infected with one or more species of gut parasitic worm (Peters 1978; Warren & Mahmoud 1984; Bundy & Cooper 1988*a*).

Fortunately, only a minority of these infections are associated with serious disease. The clinical effect of gastrointestinal helminthiasis is dependent upon the number of worms harboured by the host; the intensity of infection, not merely the presence of infection. In general, only those individuals who have acquired large worm burdens will develop serious disease. This does not imply that helminthiases are unimportant in human public health – the minority of cases with disease number in the tens of millions – but does suggest that an understanding of the ecology of helminth disease is dependent upon an understanding of the factors that determine the intensity of infection. The necessity for quantifying infection is peculiar to the study of helminthiases; for most microparasitic infections (Protozoa, viruses and bacteria) infection is an all-or-nothing event and there is consequently more direct correspondence between infection and disease.

The intensity of infection also has important implications for the study of helminth

transmission dynamics. The five major genera of gastrointestinal helminths (*Ascaris*, *Trichuris*, *Schistosoma* and the hookworms, *Ancylostoma* and *Necator*) differ in their mode of infection but share a common characteristic of macroparasites; there is no multiplication within the host, and thus each worm is the result of a separate infection event. The individual worm is the unit of transmission and transmission rate is therefore a function of the intensity of infection. This again is fundamentally different from microparasites, in which a single successful infection leads to colonization of the host, which is thereafter the principal unit of transmission (Anderson & May 1979).

Because the intensity of infection plays such a major role in both the pathogenesis and transmission dynamics of gastrointestinal helmiths, an understanding of the ecology of infection and disease is dependent upon an understanding of the occurrence and causation of intense infection. Two factors are clearly of central importance: the extent to which a host is exposed to infection and the ability of the host to resist invasion (Bradley & McCullough 1974; Warren 1973). This paper assesses the relative importance of these factors in determining the observed patterns of infection intensity in human communities. The approach is generalised to include the schistosomes and hookworms, although the major focus is on *Ascaris lumbricoides* and *Trichuris trichiura*, two parasites that are not only the most ubiquitous of the gastrointestinal helminths but also the most neglected in biomedial research.

Infection intensity and host age

Observed patterns in human communities

A child living in an endemic area is likely to be infected with *A. lumbricoides* or *T. trichiura* before five years of age and to be continuously reinfected for the rest of his or her life. Studies of communities with endemic infection typically show a very rapid, monotonic rise in infection prevalence in the child age-classes, followed by stable and high prevalence values throughout adulthood (figure 1*a*). Age-prevalence profiles for schistosomes and hookworms are essentially similar to these, although the peak prevalence is attained at a later age and there is often a decline in schistosome prevalence in the adult age-classes.

For most gastrointestinal helminths the prevalence of infection attains a stable asymptote with age. The age–intensity profiles, in contrast, exhibit marked convexity. The intensity of *A. lumbricoides* and *T. trichiura* infection reaches a maximum value in 5–10-year-old children and declines in adulthood (figure 1*b*). In schistosomes, maximum intensity is attained in the teenage classes (figure 4*b*). The data for the age–intensity profile of hookworms are inconclusive, as both asymptotic and convex patterns have been described (Behnke 1987). The most reliable data – those based on anthelminthic expulsion and direct counting of worm burdens – suggest that the age-profile for hookworm intensity is convex and essentially similar to those of the other geohelminths (Hill 1926).

These observations, which have been made in a wide range of geographical areas with differing levels of parasite endemicity, indicate that similar proportions of adults and children are infected with helminths but the adults harbour fewer worms.

Studies of reinfection suggest that the age-dependence of intensity is a function of the rate of acquisition of infection. When a population in a *T. trichiura* endemic area is successfully treated with an anthelmintic, the subsequent rate of reacquisition of infection exhibits marked age-dependency (figure 2); the children in the 5–10 age-class are reinfected more rapidly than

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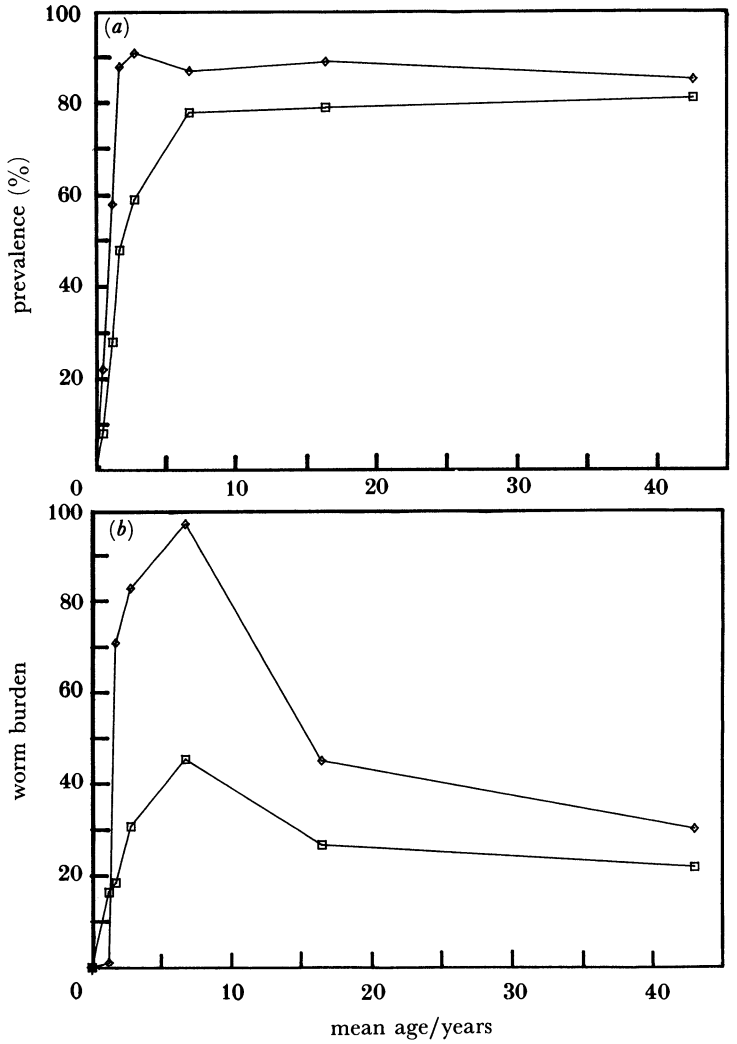

FIGURE 1. The age-dependency of prevalence (*a*) and intensity (*b*) of *T. trichiura* (◇) and *A. lumbricoides* (□) infection. Prevalence rises monotonically in childhood and attains a stable asymptote in adulthood. Intensity profiles are convex, attaining a maximum value in the 5–10 year age-class and declining in adulthood (*A. lumbricoides* worm burdens × 7) (modified from Bundy *et al.* 1987*b*).

the adults. Age-dependency in reinfection has also been shown for *A. lumbricoides* (Cabrera 1981), and the schistosomes, *Schistosoma mansoni* and *S. haematobium* (Wilkins *et al.* 1987; Bensted-Smith *et al.* 1987).

The intensity of infection is determined by the rate of acquisition of new infections and the rate of loss of existing infections. The observed age-dependency of infection intensity and reinfection rate may, therefore, be due to enhanced exposure in children, reduced susceptibility in adults, or some combination of both processes.

Age and exposure

Exposure to infection with the geohelminths *A. lumbricoides* and *T. trichiura* has proved difficult to quantify. Infection can only occur via ingestion of infective eggs, either directly with contaminated soil or indirectly with contaminated food (Pawlowski 1984). In many endemic

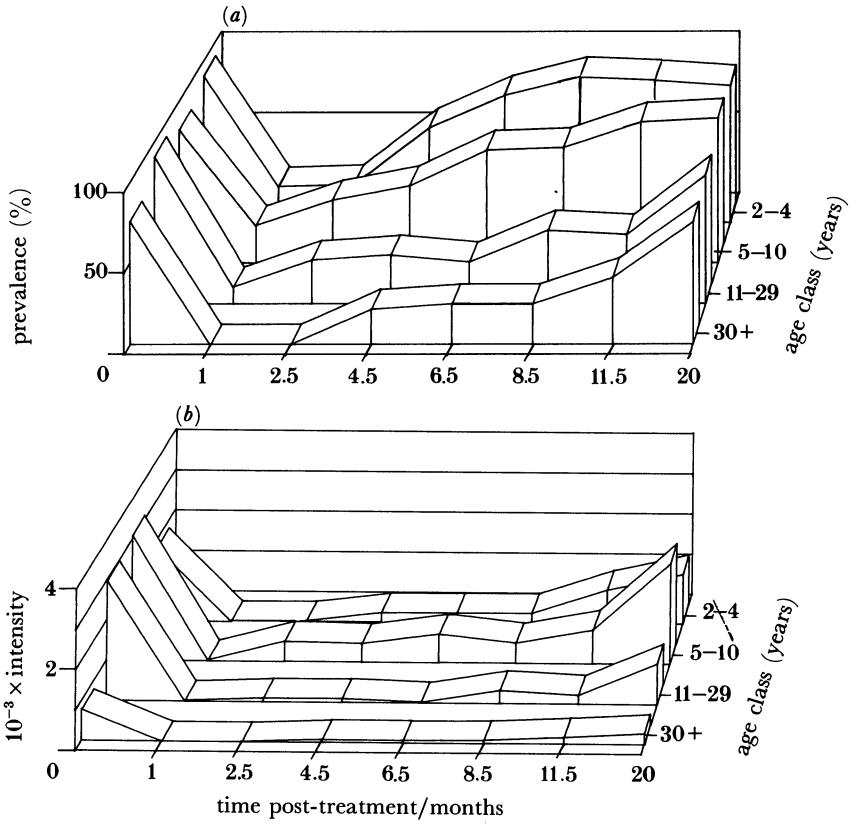

FIGURE 2. Age-dependent rate of reinfection with *T. trichiura*. Initial infection was assessed at time 0 and the population treated with an anthelmintic. The rate of reinfection was then monitored over a 20 month period following treatment. A minimum of 30 individuals were examined in each age class at each time point. The rate of increase in prevalence (*a*) is more rapid than that of intensity (*b*). The child age-classes reacquire infection more rapidly than do adults (data from Bundy *et al.* 1988).

areas the ubiquitous practice of geophagia, the most common form of pica (Halstead 1968), appears to provide a major route of infection (Larivière *et al.* 1965; Cooper & Bundy 1988). Intense infection with toxocariasis and trichuriasis are both statistically associated with a reported history of deliberate soil eating (Glickman *et al.* 1981; Gilman *et al.* 1983).

A method has recently been developed for assessing the degree of soil ingestion by measuring the amount of soil-derived silica excreted in stool; the proportion of silica in stool is directly correlated with the quantity of soil ingested, and hence the extent of geophagia practised (Wong *et al.* 1988). By using this method, the relation between age and geophagic behaviour in an endemic community has been assessed (figure 3*b*). The results indicate that the mean proportion of silica in the stools of children exceeds the level attributable to dietary sources, whereas in adults average stool silica levels are largely attributable to diet. This suggests that children directly ingest soil and are potentially exposed more frequently to geohelminth infection than are adults. Comparison with the pattern of *T. trichiura* intensity in the population studied (figure 3) indicates that intensity rises with increasing practice of geophagia, and declines as geophagia decreases. This association does not imply that soil-eating is the only route of infection – adults are continuously reinfected in the apparent absence of geophagia – but does suggest that the childhood peak in infection intensity may be related to exposure linked to behaviour.

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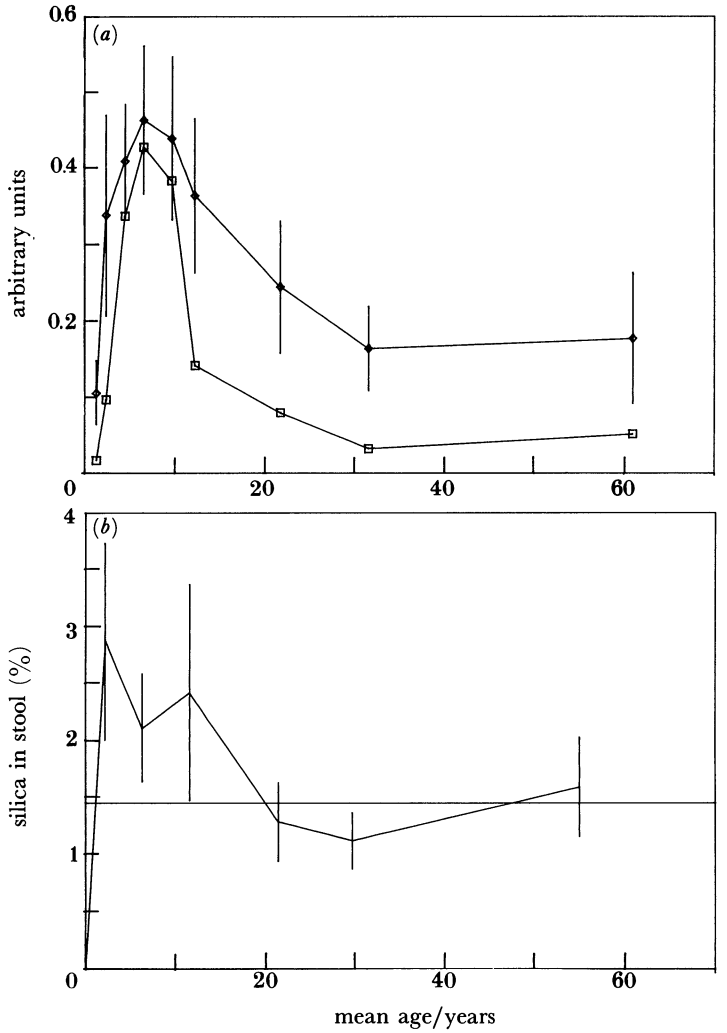

FIGURE 3. (*a*) Age-dependency of *T. trichiura* infection intensity (□) and *T. trichiura*-specific IgG antibody responses (◇). Antibody level rises as intensity increases and declines as intensity decreases. (*b*) Age-dependency of geophagic behaviour as assessed by the proportion of silica in stool. The horizontal line represents a normative silica level owing to the diet (Wong *et al.* 1988). Children have higher levels of stool silica than adults, whose silica levels are largely attributable to dietary sources. The level of silica, and presumably geophagic behaviour, corresponds with the parameters shown in (*a*), which were measured in the same population.

The relation between exposure, host age and schistosome infection has been more thoroughly examined. The infective stage is a skin-penetrating larva that occurs in fresh water, and exposure to infection is assumed to be related to the duration and frequency of contact with infective water bodies. Measuring this form of exposure is fraught with practical difficulties and is subject to the errors intrinsic to studies of human behaviour. Preliminary descriptive studies indicated that water-contact rates were maximal in the same age-class in which maximum infection intensity was attained (Dalton & Pole 1978), and were interpreted in an analogous manner to the relation between geophagia and geohelminth infection (figure 4). More recent analytical studies suggest a different conclusion. Individuals within an endemic population who have similar rates of water contact do not all acquire the same intensity of infection after treatment, but instead exhibit a trend for the reinfection rate to decrease with increasing age (Wilkins *et al.* 1987; Butterworth *et al.* 1985).

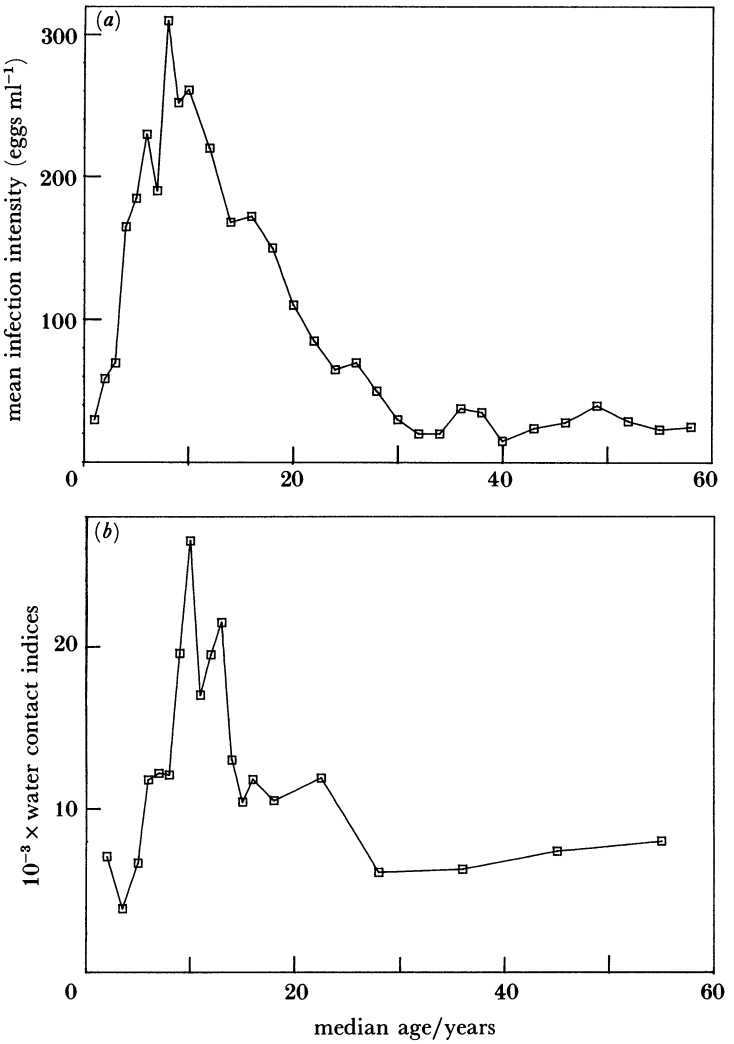

FIGURE 4. (*a*) Age-intensity profile of *S. haematobium* in Tanzania. There is a marked correspondence between infection intensity and exposure, as assessed in (*b*) (data from Bradley & McCullogh (1973)). (*b*) Age-dependency of exposure to schistosome infection as assessed by water-contact indices. Rates of water contact are maximal in the younger age-classes (data from Tingley *et al.* 1987 cited in Anderson 1987).

Thus it would appear, for the schistosomes at least, that age-dependency in exposure cannot alone account for the observed decline in infection intensity in adults. This may suggest that host resistance to infection increases with past exposure to infection and hence age.

Age and resistance to infection

Convex age–intensity profiles are likely to arise if rates of parasite establishment and survival decrease in a manner related to the hosts' accumulated past experience of infection (Anderson & May 1985*a*). An effective acquired immune response would therefore provide an appropriate mechanism for the development of age-dependent resistance.

Detailed immuno-epidemiological studies of *A. lumbricoides* and hookworm have not as yet been undertaken, although the mechanisms of the immune response have been the subject of elegant investigation in animal models (see, for example, Kennedy *et al.* 1987; Pritchard 1986), and in individual human patients (Ogilvie *et al.* 1978).

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Characterization of the human immune response to *T. trichiura* has only recently been attempted, following extensive investigation of congeneric *T. muris* in mice (reviewed by Wakelin (1982)). The murine parasite evokes a rapid and effective response from the host, typically resulting in expulsion before the worm achieves maturity. This model has few ecological parallels with the human host–parasite interaction, but its elucidation has contributed to understanding of the human immune response. Studies of immunoprecipitation of [^{35}S]methionine-labelled *T. muris* E/S antigen by IgG antibody in *T. trichiura* human infection sera have suggested that sera from adults precipitate a narrower range of antigens than sera from children (Roach *et al.* 1988). A *T. trichiura* antigen ELISA has recently been developed to examine this response (Bianco *et al.* 1988). Sera from individuals living in an endemic area show marked age-dependency in antibody levels: antigen-specific IgG levels rise in childhood and decline in adulthood (figure 3*a*). The increase and decrease in IgG closely mirrors the changes in both infection intensity and exposure to infection, as assessed by geophagic behaviour. This is good evidence for the existence of a human humoral immune response to *T. trichiura*, but unconvincing evidence of its efficacy.

In contrast to other gastrointestinal helminths, studies of the immune response to schistosome infection in man and other animals are legion (recently reviewed by Colley (1987) and Capron (1987)). There is unquestionable evidence of a human immune response to schistosome infection. There is also persuasive epidemiological evidence of the development of reduced susceptibility in adulthood (recently reviewed by Butterworth & Hagan (1987)). However, immunological correlates with the apparently enhanced resistance in adults have not been demonstrated, and the existence of an effective acquired immune response to schistosome infection in humans is not established (Colley *et al.* 1986; Roberts *et al.* 1987).

It has been suggested with regard to the schistosomes – and the suggestion applies equally to the other helminths considered here – that if an effective immune response exists, it is slow to develop and provides only partial protection (Wilkins *et al.* 1984*b*). It is apparent from sero-epidemiological evidence, however, that an immune response is rapidly evoked; it is its effective expression that only slowly becomes apparent. The existence of blocking antibodies or some other form of parasite-mediated immuno-modulation (Butterworth *et al.* 1987; Pritchard 1986) is a biologically attractive explanation for this anomaly. It is an explanation that accords with the intense selection pressure on host and parasite during a co-evolutionary period that, in the case of trichuriasis and schistosomiasis, has extended over several millennia.

Resistance versus exposure

Whatever the uncertainties in interpreting the effects of host age on infection intensity it is clear that, for the geohelminths and schistosomes at least, the younger age-classes have the highest rates of exposure and the least resistance to infection. For what is likely to be most of the population in most endemic areas it appears that exposure is the major determinant of infection intensity.

This brings into question the relative significance to the ecology of the worms of an adult host population that may be partly resistant to infection, but that is also relatively unexposed. Wilkins *et al.* (1984*b*) suggest that host resistance may have a dramatic effect on the intensity of adult infection: the population over 25 years of age reacquires an intensity of *S. haematobium* infection at a rate that is one thousandth that of 5–8-year-old children, a difference that may be an order of magnitude greater than the disparity in levels of water contact. This large

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difference is also revealed by comparing estimates of the force of infection in observed steady-state profiles of age–intensity (Anderson & May 1985*b*). The ratio between the force of infection in children and adults appears to be approximately 360:1 for *S. haematobium* (data from Wilkins *et al.* 1984*a*), and between 180:1 and 600:1 for *S. mansoni* (data from Hiatt (1976); Bartholomew *et al.* (1981)). Published indices of water contact suggest a much smaller difference in exposure between these two age-classes, a ratio in the range 4–10:1 (Tingley *et al.* (1987) cited in Anderson (1987); Kvalsvig & Schutte (1986)). A similar comparison cannot be made for the geohelminths as adequate exposure data are unavailable at present.

The epidemiological evidence suggests that the intensity of adult infection with schistosomes is significantly reduced by resistance factors. Whether these factors include acquired immunity has yet to be determined.

Infection intensity and the individual host

The distribution of infection intensity between individuals

Comparison between age-classes clearly shows population variation in infection intensity. Age is not the only source of variation, however, because comparison within any age-class reveals considerable individual heterogeneity in worm burden. Whichever of the gastrointestinal helminths is considered, it is observed that the distribution of worm burden is highly overdispersed (Anderson & Medley 1985); most individuals have a few worms, whereas a few hosts harbour disproportionately large worm burdens (figure 7*a*). These few heavily infected individuals – the 'wormy persons' described by Croll & Ghadirian (1981) – are simultaneously at highest risk of disease and the major source of environmental contamination.

A series of recent studies suggests that individuals are predisposed to a high or low intensity of infection; the size of the worm burden reacquired after successful treatment is positively associated with the intensity of infection before treatment (figure 5). This association has been shown by community-based studies of all the major gastrointestinal helminths of humans

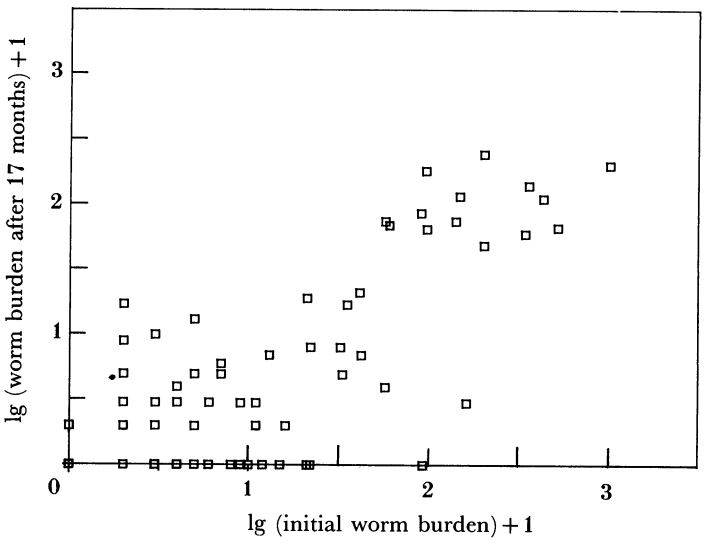

Figure 5. Predisposition to *T. trichiura* infection. A comparison between initial worm burden (determined by anthelmintic expulsion) and the worm burden acquired during 17 months of re-exposure to infection (data from Bundy (1986)).

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(Anderson 1986; Bundy & Cooper 1988*b*). A longitudinal study of *T. trichiura* confirms that this positive association reflects a direct relation between the rate of reinfection and initial infection status (figure 6). Thus in an endemic community it appears that an individual will consistently have an above (or below) average intensity of infection, although the relative magnitudes of the worm burdens will scale according to age.

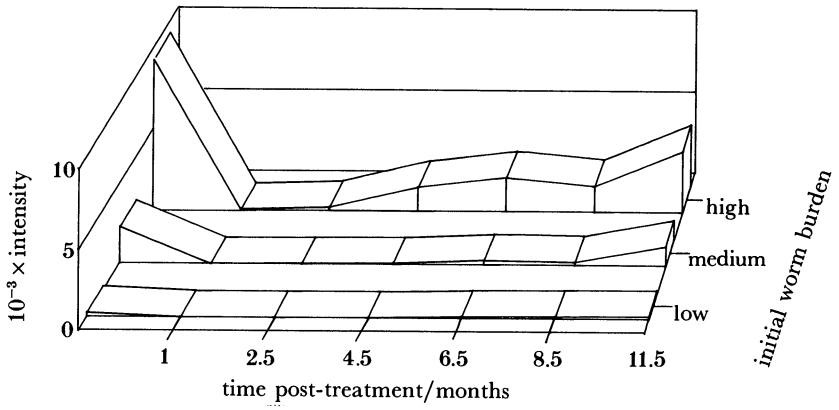

FIGURE 6. Relation between initial infection intensity and rate of reacquisition of *T. trichiura* infection. The mean worm burdens of the children (mean age 4.5 years) in each intensity class ($n = 10$) at the start of the study were: high, 295.5; medium, 36.9; low, 5.3. Initial worm burdens were determined by anthelmintic expulsion. The same cohort of children was examined at each time point, and infection intensity expressed as eggs per gram stool (EPG) (data from Bundy *et al.* 1988).

This pattern is also apparent at the family level. In endemic areas more families tend to have a majority of family members with heavy (or light) infections of *T. trichiura* and *A. lumbricoides* that would be expected by chance, whereas families with a mixture of both heavy and lightly infected individuals are less common than predicted (Chai *et al.* 1985; Forrester *et al.* 1988*a*): heavily infected individuals tend to be aggregated in families. A recent study of *A. lumbricoides* in Mexico has shown that families also exhibit predisposition to infection: a heavily infected family tends to reacquire heavy infection even after all the family members are successfully treated (Forrester *et al.* 1988*b*).

The implication of these findings is that individuals, either alone or as a family group, differ in their exposure or susceptibility to infection, and that this difference is a long-term characteristic of the individual or family.

Individual differences in exposure to infection

The spatial clustering of intense infection in families has been attributed to variation between households in level of sanitation. This explanation is not supported by the available evidence. Although it is self-evidently true that area-wide improvements in sanitation have a substantial impact on the transmission of faecal-borne infection (Henry 1981; Feachem *et al.* 1983*a*), comparison of individual households within a single community has in general failed to show any positive association between the availability of sanitational infrastructure and infection status (Feachem *et al.* 1983*b*).

This lack of correlation probably arises because the availability of sanitation facilities does not predicate their use, raising the question of the importance of individual or family hygienic

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behaviour. Assessment of the role of human behaviour in infection exposure, particularly the more personal hygienic behaviours, has rarely been attempted. Quantitative studies of one such behaviour, geophagia, indicate the rates of exposure due to soil ingestion vary considerably between individuals (Wong *et al.* 1988), and that the overdispersed distribution of the practice within a community closely mirrors observed frequency distributions of geohelminth infection intensity (figure 7), although studies have not yet sought to correlate soil ingestion rates and infection intensity. Geophagia may also be relevant at the family level because the practice has been attributed to familial characteristics, such as diet (Halstead 1968) and psycho-social factors (Singhi *et al.* 1981).

Individual behaviours appear to influence exposure to hookworm infection. In some endemic areas, communal defaecation grounds appear to act as foci for transmission (Schad

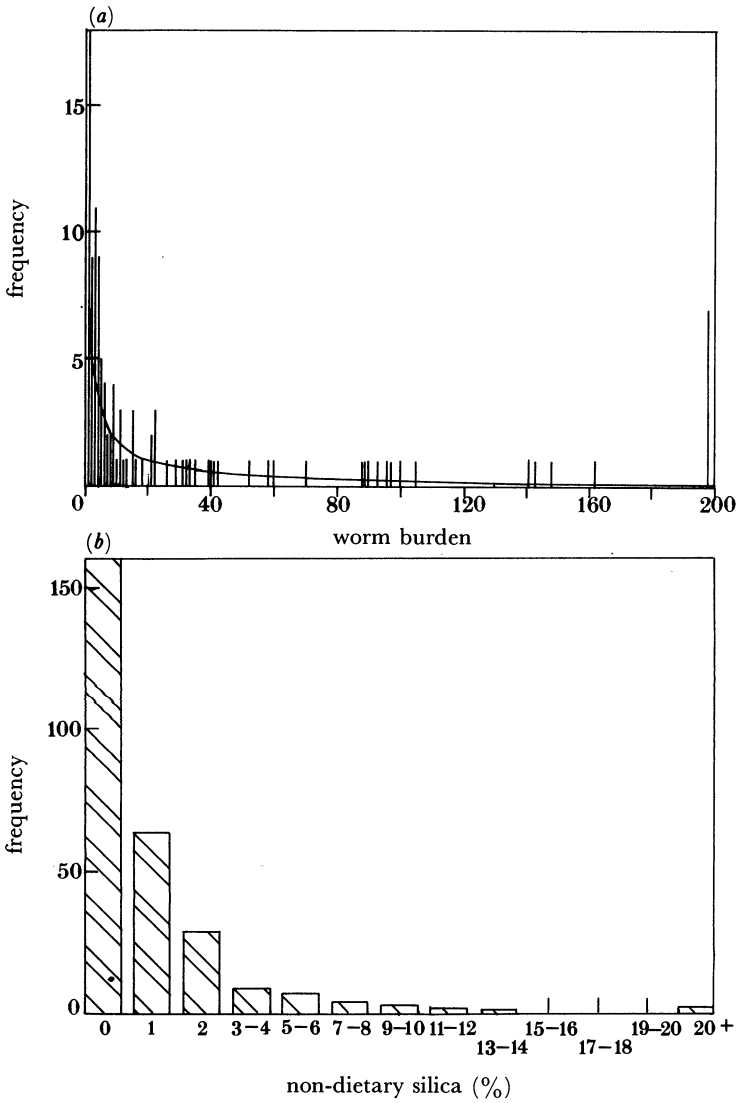

FIGURE 7. (*a*) Frequency distribution of *T. trichiura* infection intensity. The distribution is markedly overdispersed (data from Cooper & Bundy 1988). (*b*) Frequency distribution of geophagia in children as assessed by levels of silica in stool which exceed normative dietary amounts. The distribution of this exposure parameter is overdispersed and resembles that shown in (*a*) above.

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et al. 1983). Children and young adults, particularly males who disregard behavioural norms and defaecate in previously contaminated areas, have significantly higher intensities of infection (Hominick *et al.* 1987).

Studies of water-contact behaviour reveal considerable individual variation in potential exposure to schistosome infection. Within the child age-classes, the intensity of infection with *S. haematobium* appears to be related to the rate of water contact (Wilkins *et al.* 1987) although, as discussed above, the magnitude of the intensity in adults may be modified by host resistance.

The literature indicates a wealth of support, based largely on anecdotal evidence, for a central role for exposure in determining the infection intensity of an individual. There is a lack of objective evidence, however, and a particular need for more precisely quantified behavioural studies.

Individual differences in resistance to infection

In considering the role of susceptibility in the age-dependency of infection intensity the focus was on immunity acquired as a result of prior experience of infection. The resistance mechanisms involved in predisposition cannot primarily depend on acquired immunity because the evidence for predisposition suggests that it is the individuals with the greatest prior experience of infection who subsequently reacquire intense infection. Studies of susceptibility in this context, therefore, are concerned with intrinsic differences in levels of resistance between individuals. Immunological correlates with individual resistance have been demonstrated for schistosomes (recently reviewed by Colley (1987) and Butterworth & Hagan (1987)), but have not been sought for the other intestinal helminths. The focus in this section is on factors that consistently diminish (or enhance) immune-responsiveness at the individual or family level.

One candidate factor is nutritional status, which has been shown to vary both between individuals and between families. Malnutrition, whether gross or involving single nutrients, has been demonstrated to have a major impact on the human immune and inflammatory responses (Suskind 1980). Studies of animal models have shown that malnutrition may influence the ability of a host to resist gastrointestinal helminth infection. Studies of humans have primarily concentrated on the impact of infection on nutritional status; evidence for the reverse interaction is rarely sought, but may be crucial to an understanding of the role of nutrition in the ecology of infection. There is some evidence that nutrition influences human susceptibility to geohelminths. Individuals with low levels of plasma zinc, a trace element that is essential to thymus-mediated immune responses (Beisel 1982), tend to have above-average *T. trichiura* worm burdens (Bundy & Golden 1987). This may indicate that individuals or families receiving a zinc-deficient diet are predisposed to intense infection. A role for diet is also suggested by the observation that predisposition to infection is apparently not demonstrable in institutionalized populations where all the individuals receive a nominally identical diet; there is variation in individual worm burden, but no significant association between initial infection status and the intensity reacquired following treatment (Bundy & Cooper 1988*b*).

A second factor that may influence individual susceptibility is genetic control. This is a particularly attractive candidate because its influence will be long term – studies indicate that predisposition is demonstrable for periods of at least years (Schad & Anderson 1985; Bundy *et al.* 1987*a*) – and will exhibit strong familial association. Studies of mouse models have demonstrated genetic restriction of susceptibility to a range of gastrointestinal helminths and

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have mapped the restriction gene (*Ir*) to the H-2 MHC (reviewed by Wakelin (1985)). In the best-defined example, susceptibility is determined by the differential expression of class II antigens on antigen-presenting cells; antigen presented in the context of I-E products induces a T-cell response that suppresses I-A restricted T-cell proliferation (Wassom *et al.* 1987). There appears to be a parallel in immune-response mediation of human disease in *S. haematobium* infection, where HLA-DQ is epistatic to HLA-DR in controlling the response to schistosomal antigen (Hirayama *et al.* 1987).

A recent study has sought an association between HLA antigen frequencies and intensity of infection with *A. lumbricoides* and *T. trichiura* in a Caribbean population (Bundy *et al.* 1988). Comparison of class II antigen frequencies between a short series ($n = 40$) of subjects who are either uninfected (resistant?) or heavily infected (susceptible?), reveals higher frequencies of DQw2 antigen in the uninfected population. This is of potential relevance to susceptibility to gut parasites because HLA-DQ antigens in general appear to be associated with restriction of cytotoxic T-cells (Navarrete *et al.* 1985), and DQw2 in particular is a marker for coeliac disease (Sachs *et al.* 1986), a disease whose pathology appears to be related to gut-associated T-cell hyper-reactivity (Ferguson & MacDonald 1977). A longer series of class I antigen frequencies ($n = 126$) reveals a statistically significant assocation between B14/Bw65 antigen and intense infection with either parasite. This antigen is uncommon (0–6%) in comparable populations, and in the present study was found only in the heavily infected sub-population. It is a marker for a haplotype associated with IgA deficiency (Dawkins *et al.* 1983) and therefore a potential candidate for enhanced susceptibility to luminal parasites. It should be stressed, however, that these studies are preliminary and the associations demonstrated are tentative at present. They indicate that genetic determinants may be of considerable relevance, but further assessment of expression products is required before any firm conclusions can be drawn.

Resistance versus exposure in the individual

This is a subject that, undeservedly, has attracted much less research interest than the study of acquired resistance. There is now a substantial body of evidence that suggests that infection intensity varies considerably between individuals, and that individuals are predisposed to acquire high or low levels of infection. There is also convincing evidence that individuals differ in their exposure and susceptibility to infection, and suggestive evidence for causal mechanisms. The relative importance of exposure and resistance, however, will remain enigmatic until studies are conducted that assess exposure and resistance simultaneously for the same individuals.

Prospects

Human parasite ecology is entering a new phase of development. Extensive descriptive field studies, from the seminal observations of Stoll, Cort, Otto and others in the Americas in the 1920s and 1930s to the excellent recent work in Southeast Asia, have provided a good picture of epidemiological patterns. Recent developments in the molecular biology and immunology of parasites have provided clear insights into the underlying mechanisms. What is now necessary is to bring these together in analytical studies of infection in endemic communities: to develop an equal partnership between field study and the best of recent laboratory-based studies.

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Some studies of this type have already been undertaken notably by Butterworth and colleagues in Kenya and Wilkins and colleagues in the Gambia – and have demonstrated the value of this approach. The only convincing evidence of acquired resistance to schistosome infection is epidemiological, providing the *raison d'être* for an army researching into the mechanisms of schistosome immunology, and a platoon involved with the other gastrointestinal helminths. It is careful longitudinal field work that has demonstrated the phenomenon of predisposition, with its major implications for the pattern of disease and infection.

Analytical field studies will not be simplistic. They will require careful design if their results are not to be open to the criticism, often justifiably applied to field analyses, that they are based on outmoded theory, are inadequately controlled and, most commonly, involve an inadequate sample size.

Human field studies, particularly of such chronic infections as the helminthiases, are difficult to organize, expensive to maintain and constrained by ethical and political considerations. The long period of study necessary for longitudinal analysis of infection and reinfection exacerbates these difficulties, not least because the studies depend for their success on factors outside the control of the experimenters, including the long-term compliance of a population who may not perceive any immediate benefit. Many of the data sets presented here represent the single result of several years of field study and an equally long preliminary period of discussion and negotiation. Once initiated, such studies are difficult to modify and usually impossible to repeat in the same population.

These constraints have encouraged an understandable conservatism, but the need for human studies that direct rather than follow research trends argues for iconoclasm in their design. Analytical field work will require the incorporation of new research areas and the development of new research tools. The only direct evidence for acquired resistance to infection is a mismatch between the intensity of infection observed and that predicted on the basis of exposure. Such evidence is crucially dependent on the accuracy of exposure assessment, yet the study of factors determining infection exposure is an almost non-existent area of research. Field research may also need to broaden its approach. Despite extensive studies, there is little evidence of immunological correlates with resistance, perhaps indicating that other age-dependent factors of relevance to resistance, such as nutrition and physiology, are deserving of closer attention. A multi-disciplinary approach may also be relevant to future studies of the phenomenon of predisposition. The term predisposition encompasses effects that may result not only from differences in individual immune-responsiveness, but also from individual differences in behaviour, nutrition, physiology and genetic characteristics. Future field studies will need to take at least some of these factors into account.

In conclusion, the available evidence allows a description of the ecology of gastrointestinal helminthiasis in humans but not of the controlling mechanisms. An understanding of these factors is not only of academic interest. The reasons why children are more heavily infected than adults, and why some individuals consistently exhibit more severe symptoms of disease than others in the community, are fundamental to the control and clinical management of human infection.

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