The public health importance of *Ascaris lumbricoides*

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SUMMARY

Numerous studies have shown that anthelminthic treatment can be effective in improving growth rates when given to malnourished children with ascariasis. Recent investigations have also indicated that *Ascaris* infections can affect mental processing in some school children. Poor socio-economic conditions are among the key factors linked with higher prevalences of ascariasis, as are defaecation practices, geophagia, cultural differences relating to personal and food hygiene, occupational necessity, agricultural factors, housing style, social class and gender. Chemotherapy is currently the major tool used for the strategic control of ascariasis as a short-term goal. In the long term, improvements in hygiene and sanitation are thought to aid long-term control considerably. Targeted treatment, especially when aimed at schoolchildren, has been a major focus of recent control efforts in some areas. Universal treatment reaches more people and thus decreases further aggregate morbidity, especially in nutritionally vulnerable preschool-age children. Selective treatment requires technical effort to identify heavily infected individuals; acceptance by the community may vary in less educated populations when some individuals receive treatment and others do not. Child-targeted treatment may be more cost-effective than population treatment in reducing the number of disease cases and, in high transmission areas, expanding coverage of a population can be a more cost-effective strategy than increasing the frequency of treatment.

Key words: *Ascaris lumbricoides*, child growth, cognitive performance, chemotherapy control strategies, cost effectiveness.

INTRODUCTION

PUBLIC HEALTH RELEVANCE AND RECENT GLOBAL ESTIMATES

Ascaris lumbricoides is a remarkably infectious and persistent parasite that infects a quarter of the world's population (Pawlowski & Arfaa, 1984; Crompton, 1994). It has been widely recognized that ascariasis plays a major role in the aetiology of childhood malnutrition (Crompton, 1992). Global numbers of infections have been estimated to be 800–1000 millions (Walsh & Warren, 1979), and more recently about 1400–1500 millions (Chan *et al*. 1994; WHO, 1996*a*). De Silva, Chan & Bundy (1997*a*) calculated, using sensitivity analysis of theoretical models of parasite distributions, approximately 1300 million infections globally. In order to calculate updated estimates of possible associated morbidity, epidemiological studies have developed methods for estimating the relationship between prevalence and mean intensity and potential morbidity which incorporate age classes and geographical heterogeneity (Chan *et al*. 1994). These estimates are based on empirical data and chosen to be relatively conservative. According to these estimates, the morbidity associated with *A. lumbricoides* infection amounts to approximately 120–220 million cases, 8–15 % of the total number infected (Albonico, Crompton & Savioli, 1999).

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EPIDEMIOLOGY

Geographic distribution, prevalence and intensity

An estimated 73 % of *A. lumbricoides* infections are present in Asia, while about 12 % are located in Africa and 8 % in Latin America (Peters, 1978). However, human ascariasis is cosmopolitan, with infection occurring in both temperate and tropical environments. In Africa, for example, the prevalence is low where the climate is arid but high where conditions are wet and warm (Crompton & Tulley, 1987; Prost, 1987) as these are ideal for egg survival and embryonation.

Poor socio-economic conditions are linked with higher prevalences of ascariasis. About one third of the population in the cities of some developing countries live in slums and shanty towns where the prevalence and intensity of *A. lumbricoides* is significantly increasing due to favourable conditions of transmission (Crompton & Savioli, 1993). Generally, the poorer the quality of housing and community services, the more likely *A. lumbricoides* will persist and flourish (Holland *et al*. 1988). *Ascaris* infections may cluster in certain households, with heavier infections being recorded from households with more family members (Forrester *et al*. 1988; Asaolu *et al*. 1992). Kightlinger, Seed & Kightlinger (1998) found that aggregations of *A. lumbricoides* in children in Madagascar were associated with housing style, ethnicity and agricultural factors. Other factors contributing to infection include defaecation practices (Haswell-Elkins, Elkins & Anderson, 1989) and

geophagia (Wong, Bundy & Golden 1988) but also cultural differences relating to personal and food hygiene (Haswell-Elkins *et al*. 1989; Kan, Guyatt & Bundy 1989), occupational necessity (Chandiwana, Bradley & Chombo, 1989), social class (Machado *et al*. 1996) and gender (McCullough, 1974; Cross *et al*. 1975; Arfaa & Ghadirian, 1977; Shield, Scrimgeour & Vaterlaws, 1980; Harinasuta & Charoenlarp, 1980; Cabrera & Valeza, 1980; Kightlinger *et al*. 1998; Hall *et al*. 1999).

Prevalence is defined as the number of egg-positive cases in a population whereas intensity is the mean number of worms per person (Crompton, 1994). From an epidemiological perspective, prevalence can be regarded as a rather inaccurate measure of a community's ascariasis burden compared to that of intensity. Prevalence values for geographical regions or countries are still useful however, for defining the public health significance of a problem, for determining health priorities and highlighting the need for control (Crompton, 1994; Walsh & Warren, 1979), and also for estimating the number of doses of anthelminthic drugs required.

Knowledge of the intensity of *A. lumbricoides* infection is important not only in terms of morbidity (Pawlowski & Davis, 1989) but also in terms of the dynamics of infection, particularly on the presence of heavily infected individuals and the consequences of disease (Anderson & May, 1991). A key feature of the biology of helminth infections is that the occurrence of disease is related to the intensity of infection. A few worms tend to be asymptomatic but as more worms are acquired, signs and symptoms of disease are more likely to occur (Bundy *et al*. 1990). Intensity is also important with regard to the effective implementation and monitoring of control programmes (WHO, 1987). Practical considerations determine that, in general, faecal egg counts have to be used as measures of intensity despite their variability, rather than direct counts of total worms harboured per host. The occurrence of disease is not just related to the number of worms in the host, but is likely also to be related to duration of infection and to the host's background health status (Albonico *et al*. 1999).

Diagnosis of infection

Intensity is best, but least frequently, measured directly by counting the number of worms passed in the stools after anthelminthic treatment (Croll & Ghadirian, 1981). The presence of *Ascaris* eggs in stool samples in contrast is determined with a direct smear technique or quantified using the Kato Katz or other quantitative methods (Thienpont, Rochette & Vanparijs, 1986; WHO, 1992). Egg counts give an indirect measure of the intensity of infection and are expressed as epg (eggs per gram of faeces). It is assumed that a greater faecal egg count usually indicates the presence of a greater number of sexually mature female *A. lumbricoides* worms in the infected individual (Crompton, 1994). However, difficulties may arise when interpreting faecal egg counts since density-dependent constraints on fecundity may disguise the true number of worms present (Hall, 1982; Keymer, 1982; Thein Hlaing *et al*. 1984; Holland *et al*. 1989; Forrester & Scott, 1990). In general, however, egg counts are usually consistent with worm burden (Forrester & Scott, 1990). Because the Kato Katz method is relatively sensitive, quick, inexpensive and simple to perform, stool sampling and examination offers the best method for the standard investigation of the epidemiology of *A. lumbricoides* in humans (Crompton, 1994; WHO, 1985*a*).

Morphology and life history

The morphological characteristics of *A. lumbricoides* are summarized in Table 1. *Ascaris* is the largest of the common nematode parasites of man and has a relatively simple life cycle (Fig. 1). One female worm has the potential to produce over 200000 eggs per day (Sinniah, 1982). Eggs are passed in the faeces in the unembryonated state (Stephenson & Holland, 1987). It is estimated that 10^{14} eggs pass daily into the global environment (WHO, 1981). Egg survival, once infective, is variable up to a period of 15 years (WHO, 1967; Krasnonos, 1978; Storey & Phillips, 1985) but most are thought to be destroyed soon after passage, although many will embryonate to produce second stage larvae if provided with adequate moisture, oxygen and shade (Crompton, 1994).

Humans contract ascariasis by ingestion of embryonated eggs through faecal contamination. Because the eggs are invariably sticky, they may be found adhering to utensils, furniture, money, fruit, vegetables, door handles and fingers in endemic areas (Kagei, 1983). In a study of 51 Jamaican children (aged 7–12 years) living in 2 children's homes, Wong *et al*. (1991) estimated that the mean rate of ingestion of *Ascaris* eggs was 9–20 per year. A comparison between estimated exposure and observed worm burdens suggested that between 12% and 90% of eggs ingested developed into adult worms. As infective eggs can occur in the air and household dust, there is risk of exposure by simply inhaling and swallowing in hyperendemic areas (WHO, 1967; Bidinger, Crompton & Arnold, 1981; Kroeger *et al*. 1992).

When eggs hatch in the duodenum, the larvae migrate through the liver, lungs and upper alimentary tract. When they reach the small intestine they mature into adult worms (Thein Hlaing, 1993). Many of the larvae are destroyed on their journey through the host as they are lost in inappropriate tissues (Stephenson & Holland, 1987). The cycle

Table 1. Morphological and life history characteristics of *Ascaris lumbricoides*

Characteristic	Observation
Adult lifespan	1–2 years
Adult worm size range	
Male	150–300+mm long; 2–4 mm wide
Female	200–350+mm long; 3–6 mm wide
Ascaris egg dimensions	60–70 μm long; 40–50 μm wide
Embryonation duration	10–14 days at 30±2 °C; 45–55 days at 17±1 °C
Fecundity	134, 462–358, 759 eggs/female/day
Tissue migration	
Small intestine to liver	2–8 days post infection
Liver to lungs	7–14 days post infection
Lungs to small intestine	14–20 days post infection
Normal location of adult worms	jejunum
Prepatent period	67–76 days; 67 days in children < 4 years

Based on information from Beaver *et al*. (1984); Sinniah (1982); Stephenson & Holland (1987); Pawlowski & Arfaa (1984); Yoshida (1919); Nichols (1956); Takata (1951); Akamatsu (1959); Anderson (1982).

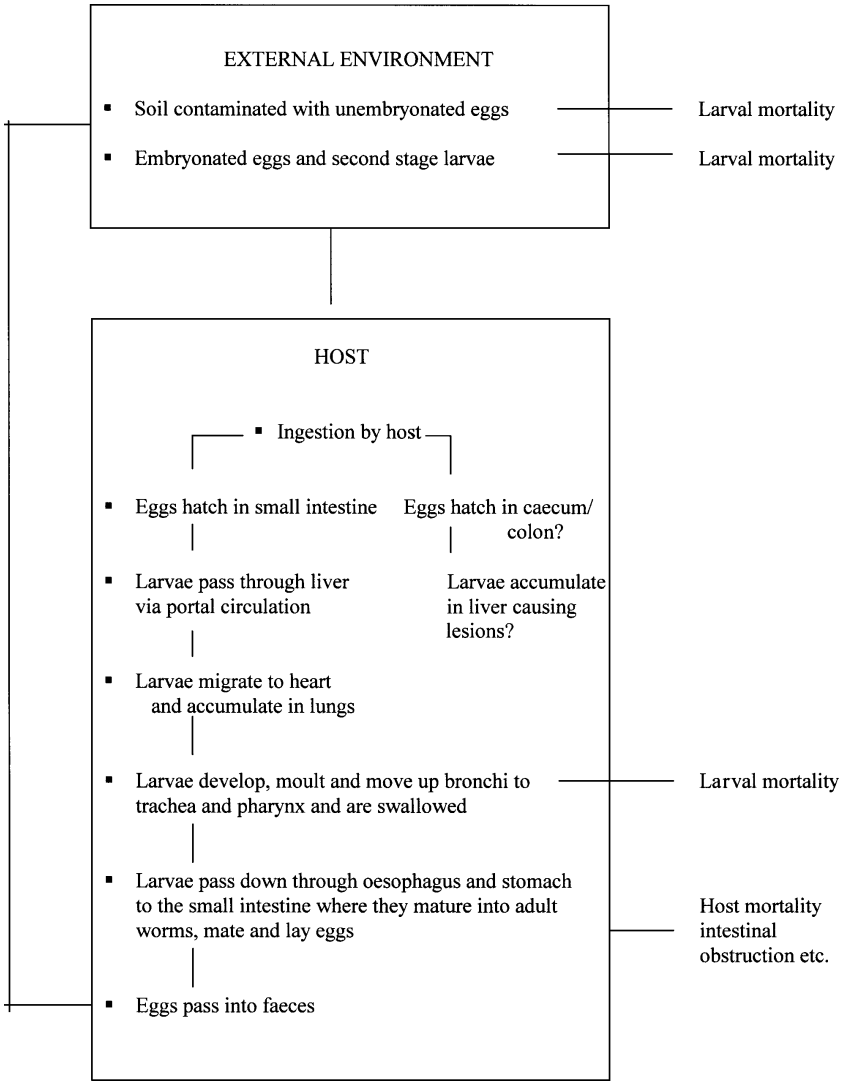

Fig. 1. Life history of *Ascaris lumbricoides* based on Crompton (1994) and Murrell *et al*. (1997).

from ingestion of eggs to the production of fertilised eggs by mature *A. lumbricoides* takes 2–3 months (Vogel & Minning, 1942) (Fig. 1). Adult worms can survive for 1–2 years and female worms can generate eggs for a period of one year although some may continue as long as 20 months (Hobo, 1956).

The widely held concept of the migratory pattern of *A. lumbricoides* in humans derives primarily from experiments employing abnormal hosts such as guinea pigs, mice and rats as hosts (Grove, 1990). However, Murrell *et al.* (1997) have demonstrated that *A. suum* L_2 larvae in the pig host penetrate the mucosa of the caecum and colon *en route* to the liver, rather than doing so in the jejunum of the small intestine as is widely described. This finding raises important questions as to whether these two species share similar migratory and development patterns in their hosts, and may suggest that the potential for liver damage in humans is greater than is currently regarded.

Uncertainty exists as to whether or not *A. lumbricoides* from humans and *A. suum* from pigs are the same species, and the possibility of cross infection with *A. suum* cannot be ruled out (Lysek, 1967; Galvin, 1968; Beaver, Jung & Cupp, 1984; Anderson, 1995), particularly in endemic regions where pigs and humans live in close proximity to one another, or where the excreta of both humans and pigs are used as a fertiliser (Peng *et al.* 1996). Evidence from Central and North America indicates that, genetically, the two parasite populations appear to be reproductively isolated (Anderson, Romero-Abal & Jaenike, 1993). In contrast, Peng *et al.* (1998) found no significant heterogeneity in the genetic composition of the *Ascaris* infra-populations in both humans and pigs, perhaps because of agricultural practices in China, which include the use of nightsoil (human faeces and urine) as fertiliser on food crops that have resulted in a random distribution of alleles within the parasite populations over time.

Population biology

Intensity peaks in the 5 to 15-year-olds and declines markedly in adults. Adults continue to be infected as they age but their worm burdens are significantly lower than those of children. Explanations for this difference likely hinge on a combination of socio-environmental and immunological factors (Crompton, 1994). Exposure to repeated infection with *A. lumbricoides* during early life may induce some level of protective immunity. Re-infection studies show that when people have been kept free of infection through regular use of anthelminthic drugs, the prevalence of the infections may increase above the pre-treatment value after treatment ceases, perhaps because resistance to the infection has been weakened or because of lack of stimulus from resident worms (Crompton, 1994).

In addition, individuals can show statistically significant correlations in numbers of worms harboured after several rounds of treatment (Holland *et al.* 1989). People (especially children) with heavy or light worm loads, either as a group or as individuals, tend to re-acquire, respectively, heavy or light intensities of infections in terms of epg or worm number per individual (Thein Hlaing *et al.* 1987). This phenomenon, termed predisposition, is widely recognized; however, not all individuals will return to the same infection intensity after treatment. Evidence as to the underlying mechanisms responsible remains elusive. The numbers of *Ascaris* worms within a host population are not normally distributed but follow an aggregated or overdispersed frequency distribution (Holland *et al.* 1989). This means that most hosts will harbour few or no worms while a small proportion of hosts will carry heavy worm burdens. Heavily infected individuals are more at risk from morbidity and mortality and also act as significant contributors of potentially infective stages in the environment.

Only a few studies have attempted to explain the mechanisms behind the observed predisposition to *Ascaris* in humans. Holland *et al.* (1992) found, in a study of class I HLA antigen distribution among children predisposed to heavy, light or no infection with *Ascaris*, that individuals who remained consistently uninfected despite exposure to infection lacked the A30/31 antigen. In another study of the same group of 5–15 year old Nigerians, immunity to *Ascaris* was associated with higher levels of serum ferritin, C-reactive protein and eosinophil cationic protein, indicating an ongoing acute phase of infection or some inflammatory process (McSharry *et al.* 1999). In contrast, children who were predisposed to the infection had little serological evidence of inflammation despite their high parasite burdens. In addition, IgE antibody responses in conjunction with inflammatory processes appeared to be associated with natural immunity to ascariasis. In an important recent study, Williams-Blangero *et al.* (1999) provided evidence for a strong genetic component accounting for between 30% and 50% of the variation in *Ascaris* worm burden among over 1200 individuals from a single pedigree in the Jirel population of East Nepal.

CLINICAL FEATURES OF ASCARIASIS

The symptoms associated with migration of *A. lumbricoides* larvae through the liver and lungs have rarely been systematically studied at community level (Table 2) (Stephenson & Holland, 1987). Furthermore, studies involving the treatment of larval infections are not yet possible as there is no conclusive evidence that any anthelminthic used against intestinal ascariasis is also effective against

Table 2. Clinical features and potential nutritional outcomes associated with *Ascaris lumbricoides* infection

Stage	Event	Clinical features	Potential Nutritional Outcome
Larval migration	Migration of larvae through lungs	Pneumonitis, including: asthma cough dyspnea substernal pain	?Decreased food intake
		Conjunctivitis	–
		Convulsions	Decreased food intake
		Eosinophilia	–
		Fever	Increased nitrogen loss
		Skin rash	?Decreased food intake
Migration/oviposition	Presence of juveniles and patent adult worms in small intestine	Abdominal distension	Decreased food intake
		Abdominal pain	Decreased food intake
		Colic	Decreased food intake
		Nausea	Decreased food intake
		Vomiting	Increased nutrient loss
		Anal itching	–
		Anorexia	Decreased food intake
		Disordered small bowel pattern	?Malabsorption
		D-xylose and lactose malabsorption	Increased carbohydrate excretion
		Enterocolitis	Increased nutrient excretion
		Fat malabsorption	Increased fat excretion
		Intermittent diarrhoea	Increased nutrient loss
		Jejunal mucosal abnormalities	Malabsorption
		Protein malabsorption	Increased protein excretion
		Restlessness	–
		Vitamin A malabsorption	Increased vitamin A excretion
Complications	Migration or aggregation of adult *Ascaris* in intestine	Intestinal obstruction Intussusception Invasion of bile duct (producing cholangitis obstructive jaundice, gallstones, or liver abscesses) Acute appendicitis Acute pancreatitis Intestinal perforation Peritonitis Upper respiratory tract obstruction Volvulvus	Life-threatening illnesses which all decrease food intake and may increase nutrient requirements (due due to fever) and nutrient losses (due to diarrhoea)

Adapted from Stephenson & Holland, 1987.

the larvae in the liver and lungs (Beaver *et al*. 1984). According to Pawlowski (1978), dying larvae are thought to do more harm to their hosts than the living ones. Larval migration can lead to the onset of pneumonitis, which can include asthma, cough, substernal pain, fever, skin rash and eosinophilia (Pawlowski & Arfaa, 1984; Coles, 1985), a condition that can sometimes be fatal (Beaver & Danaraj, 1958). In contrast, clinically evident pulmonary ascariasis is said to be relatively mild and short lived, lasting about five days (Gelphi & Mustafa, 1967). Further population-based investigations of pulmonary ascariasis are required to define clearly its public health significance, in part because fever, when associated with respiratory disease, can increase urinary nitrogen loss and because respiratory infections are one of the major acute causes of death in young children in developing countries (Stephenson & Holland, 1987).

Intestinal helminths, and *A. lumbricoides* especially, can provide particularly potent stimuli for the production of IgE antibody (Jarrett & Miller, 1982). Using extracts derived from *A. lumbricoides*, bronchial challenge induced bronchoconstriction in clinically asthmatic children from helminth-endemic areas (Lynch *et al*. 1992*a*). Non-asthmatic children in such areas were later shown to respond significantly to bronochodilator inhalation, and this was reversible with anthelminthic treatment (Lynch *et al*. 1992*b*). A follow-up study of asthmatic patients in Venezuela, 23% of whom were infected at the beginning with *A. lumbricoides*, showed that regular anthelminthic treatment of 39 asthmatics with albendazole for a period of one year resulted in

significant improvement up to two years (Lynch *et al*. 1997). After two years without treatment however, the severity of asthma reverted to the initial state. In contrast, no significant changes were observed in the 50 untreated patients over the same period of evaluation. IgE antibody levels and skin test positivity to *Ascaris* exhibited a 'tendency' towards an increase among those who had received anthelminthic treatment; Lynch *et al*. (1997) concluded that this might have been because asthmatic patients were being further exposed to *Ascaris* eggs over the duration of the study.

The presence of adult worms in the small intestine is thought to be generally well tolerated although large studies of symptoms in infected communities have not yet received sufficient attention (Table 2) (Stephenson & Holland, 1987). Coles (1985) suggested that abdominal symptoms were the result of the host responding to toxins produced by the worms or to a peptide that causes the release of histamine or allergens resulting in immunopathology or a combination of these.

Most *Ascaris* infections are of a chronic form and are widely considered to significantly impair childhood nutrition, especially in areas where poor growth and ascariasis are common; the infection is most likely to affect bodily growth, fat absorption, vitamin A absorption, iodine absorption, lactose digestion, and protein absorption (Carrera, Nesheim & Crompton, 1984; Stephenson & Holland, 1987; Taren *et al*. 1987; Tomkins & Watson, 1989; Thein Hlaing, 1993; Crompton, 1994; Curtale *et al*. 1994; Tanumihardjo *et al*. 1996; Furnee *et al*. 1997). *Ascaris* infection reduces appetite (Hadju *et al*. 1996*b*; 1998), and the intestinal pathology that occurs in malnourished children includes villus atrophy and cellular infiltration of the *lamina propria* (Tripathy *et al*. 1972). Furthermore, the causal association between ascariasis and protein-energy malnutrition is substantiated by the association between the intensity of *Ascaris* infection and the degree of malnutrition (Blumenthal & Schultz, 1976; Thein Hlaing *et al*. 1991*a*).

Because intestinal infections can lead to nutritional deficiencies, they can lower the immunity that is essential for the maintenance of innate resistance and the genetically constituted immune response that police parasites (Beisel, 1982; Puri & Chandra, 1985). El-Araby, El-din & Abdou (1984) found a relationship between ascariasis and impaired cellular response in Saudi Arabian children which would suggest that either pre-existing immunodeficiencies reduce resistance or that the presence of worms has an immunosuppressive effect.

A worm expulsion study carried out with 428 children (aged 4–10 years) in southeastern Madagascar revealed that in communities where children were predominantly stunted, *A. lumbricoides* did not always aggregate in the most malnourished or immunosuppressed children (Kightlinger, Seed & Kightlinger, 1996). This, the authors concluded, suggested the independence of growth status and *A. lumbricoides* worm burden. In contrast, Thein Hlaing *et al*. (1991*a*) showed that growth gains in children were dependent on the initial worm burden: those with higher initial worm burdens had lower increments in growth rates than those with lower worm burdens. Thus, children with recurrent heavy infections are at most risk of developing some permanent growth deficit due to protein-energy malnutrition; this latter finding is what one would expect in most communities based on decades of research on malnutrition and infections (Scrimshaw & SanGiovanni, 1997).

Both adults and children experience acute life-threatening ascariasis, in which intestinal obstructions and biliary complications predominate (Table 1) (Khuroo, Zargar & Mahajan, 1990; Thein Hlaing *et al*. 1990; Chai *et al*. 1991; Chrungoo *et al*. 1992). De Silva *et al*. (1997*a*) estimated that 12 million acute cases occur each year with approximately 10000 deaths and that complications are very much more rare than faltering growth and are probably associated with higher worm burdens. These complications have a high case fatality rate (Pinus, 1985), are expensive to treat and are likely to cause frank malnutrition in those children who are not already malnourished when complications develop (Stephenson & Holland, 1987).

De Silva *et al*. (1997*b*) concluded from an analysis of published reports on *Ascaris*-induced intestinal obstruction that it constitutes the commonest acute complication of ascariasis, accounting for almost 57% of all complications. Intestinal obstruction is most frequent in children less than 10 years of age, perhaps because the peak intensity of *Ascaris* is usually in the 5–10 year age group and because the narrow intestinal lumen diameter makes under 5 year olds more vulnerable to obstruction. The incidence was on the order of 0–0·025 cases per year per 1000 population in endemic regions, was non-linearly related to the prevalence of infection, and was associated with a mean case fatality rate of over 5%.

LONGITUDINAL FIELD STUDIES OF *A. LUMBRICOIDES*-INDUCED MALNUTRITION IN CHILDREN AND ITS IMPACT ON GROWTH

One of the most important associations found in the studies reported below is that appetite improves after treatment of *Ascaris* infection in undernourished children. We expect that finding (see Table 6 showing depressed feed intakes in parasitic infections in various species, Malnutrition and Parasitic Helminth Infection, this volume), but food intakes are very difficult, labour intensive and expensive to

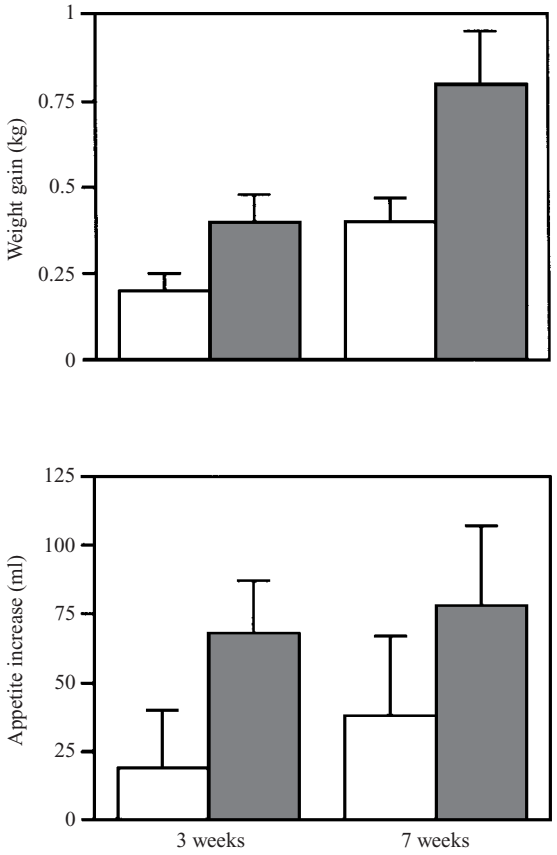

Fig. 2. Weight gain (kg) and appetite increase (ml) at 3 and 7 weeks after treatment for *A. lumbricoides* in Indonesian school boys in the pyrantel-treated (PR, shaded bars) and placebo (PL, open bars) groups. Values are means ± S.E.M., $n = 72$ at 3 weeks and 64 at 7 weeks. At baseline, there were no significant differences between groups in appetite and weight. At 3 weeks, increases in appetite and weight gain in the PR group were greater than in the PL group. (Group *t*-test *P* for difference in weight gain in kg = 0·53 and for difference in appetite increase, $P = 0{\cdot}04$). At 7 weeks, increase in appetite in the PR group was not significantly greater than in the PL group ($P = 0{\cdot}17$) but weight gain was ($P = 0{\cdot}02$). Source: Hadju *et al.* (1996*a*). Reprinted with permission from *Parasitology* (Cambridge University Press).

quantify precisely in free-living humans, especially without influencing what is eaten and are rarely measured in parasitized children. The study that demonstrates this relationship most definitively for ascariasis in children may be that of Hadju *et al.* (1996*a*), in which 6–10 year old Indonesian school boys were given pyantel pamoate (which has little or no effect on *Trichuris trichiura*) for *A. lumbricoides* infection (86% baseline prevalence); they ate significantly more of a mid-day snack offered *ad lib.* at school at 3 weeks after treatment. It was reported that their appetites were significantly better than placebo boys both 3 and 7 weeks after treatment, and they also had gained significantly more weight 7 weeks after treatment (Fig. 2). A related study, also in Indonesian schoolboys, found increased free play activity as measured by Caltrac™ accelerometers, in addition to improved appetite and growth (height-for-age Z-scores and mid upper arm circumference) 6 months after treatment for *A. lumbricoides* and *T. trichiura* infections with albendazole (Hadju *et al.* 1998). These findings are important for mental and social as well as physical development because children learn more when they are healthy and have the energy to be active. Ten intervention studies which examined the extent to which growth rates improve in undernourished *Ascaris*-infected children following anthelminthic chemotherapy are described below.

Study design, country, population, intervention, duration, and measurements

All ten studies reviewed here on childhood malnutrition were undertaken in developing countries in Asia and Africa (Table 3). The study populations were pre-school and school age children. Apart from one Kenyan study in which growth was examined in *Ascaris*-infected and non-infected groups (Stephenson *et al.* 1980*a*), the children were allocated at random to either control or treatment groups. One study however, randomised children and allocated them to one of three groups: placebo, one-dose treatment and two-dose treatments (Stephenson *et al.* 1993*a*). The anthelminthic drugs tetramisole, levamisole, albendazole and pyrantel pamoate were used in these studies; dosing frequencies used are shown in Table 3. Albonico *et al.* (1999) give a detailed profile of these and other anthelminthic drugs currently used to treat *Ascaris* infection. The study duration ranged from a minimum of 7 weeks in Indonesia (Hadju *et al.* 1996*a*) to two years in Myanmar (Thein Hlaing *et al.* 1991*a*) (Table 3). The prevalences of the various intestinal parasites observed in these intervention studies at baseline are shown in Table 4. Among the body growth indicators also measured in these studies were weight, height, arm circumference, triceps skinfold thickness, and subscapular skinfold thickness, using various reference standard populations. Details of the numbers of subjects assigned to the control and treatment groups feature in Table 5.

Statistical analyses

Most studies used paired or group Student's *t*-tests to test for comparability of control and treatment groups at baseline and to test for significant differences in growth rates between treatment and control groups following anthelminthic intervention (Stephenson *et al.* 1980*a*, 1989, 1993*b*; Thein Hlaing *et al.* 1991*a*; Adams *et al.* 1994; Hadju *et al.* 1996*a*, 1998). This same relationship was also examined using Chi-square analysis (Gupta *et al.* 1977; Gupta, 1985), analysis of variance (Stephenson *et al.* 1993*a*) and multiple regression (Willett, Kilama & Kihamia,

Table 3. Longitudinal field studies of *A. lumbricoides*-induced malnutrition in children: country of study, anthelminthic drug regime employed, and duration of follow-up

Duration follow-up (Months)	Country of study	Drug used	Frequency	Reference
12	India	Tetramisole	3 times 4-monthly	Gupta *et al.* (1977), Gupta (1985)
12	Tanzania	Levamisole	4 times 3-monthly	Willett *et al.* (1979)
3·5	Kenya	Levamisole	Single	Stephenson *et al.* (1980*a*)
6	Kenya	Albendazole	Single	Stephenson *et al.* (1989)
24	Myanmar	Levamisole	8 times 4-monthly	Thein Hlaing *et al.* (1991)
8·2	Kenya	Albendazole	Single, double	Stephenson *et al.* (1993*a*)
4	Kenya	Albendazole	Single	Stephenson *et al.* (1993*b*)
2·25	Kenya	Albendazole	Single	Adams *et al.* (1994)
1·75	Indonesia	Pyrantel pamoate	Single	Hadju *et al.* (1996*a*)
6	Indonesia	Albendazole	Single	Hadju *et al.* (1998)

Table 4. Baseline prevalence of major intestinal parasites in randomized intervention study areas

Reference	Group	*n*	*A. lumbricoides* prevalence (%)	*T. trichiura* prevalence (%)	Hookworm prevalence (%)
Gupta *et al.* (1977); Gupta (1985)	I	143	40	–	–
	N	98	46	–	–
Willett *et al.* (1979)	I	166	51	–	10
	N	175	55	–	12
Stephenson *et al.* (1989)	I	78	44	98	95
	N	72	54	97	79
Thein Hlaing *et al.* (1991*a*)	I	595	81	5	2
	N	611	83	7	1
Stephenson *et al.* (1993*a*)	I–1X	96	35	90	85
	I–2X	95	26	81	86
	N	93	32	92	88
Stephenson *et al.* (1993*b*)	I	27	44	96	96
	N	26	38	100	96
Adams *et al.* 1994	I	28	32	79	93
	N	27	26	89	93
Hadju *et al.* (1998)	I	86	93	97	–
	N	43	95	98	–
Hadju *et al.* (1996*a*)	I	36	89	100	–
	N	36	86	100	–

I, Intervention group; I–1X, Intervention 1 dose; I–2X, Intervention 2 doses; N, Non-intervention group.

1979; Stephenson *et al.* 1980*a*, 1989, 1993*a*, *b*). Among the identified confounding variables were socio-economic factors, health and nutritional status and the presence of other helminth infections.

RESULTS

Weight and/or weight-for-age were examined as a body growth indicator in all 10 studies. Eight of 9 using weight in kg for hypothesis testing found a statistically significant improvement in weight after treatment; in the Tanzanian study, the significant gain occurred in initially *Ascaris*-positive children in the treatment group vs. those given a placebo (Willett *et al.* (1979). Seven studies (Gupta *et al.* 1977; Gupta, 1985; Stephenson *et al.* 1980*a*, 1989, 1993*a*, *b*; Hadju *et al.* 1996*a*) also calculated percentage weight-for-age and all of them apart from Stephenson *et al.* (1980*a*; borderline $P < 0{\cdot}10$) and Hadju *et al.* 1998 ($P > 0{\cdot}10$) showed statistically significant improvements in intervention groups compared to non-intervention groups (Table 5).

Table 5. Difference in increments in growth following treatment between intervention and non-intervention groups for longitudinal field studies of ascariasis in children: weight; % weight-for-age, height, % height-for-age, % weight-for-height, % of median or *Z*-scores

			Increment in weight, height and weight for height														
References	Group	*n*	Weight (kg)	Diff.	*P*	Weight for age (% or *Z*-score)	Diff.	*P*	Height (cm)	Diff.	*P*	Height for age (% or *Z*-score)	Diff.	*P*	Weight for height (% or *Z*-score)	Diff.	*P*
Gupta *et al.* (1977, 1985)	I	74	–			3·5	−3·5	< 0·001	–			–			–		
	N	80				−0·3											
Willett *et al.* (1979)	I	273	2·08	0·2	< 0·06	–			–			–			–		
	N	273	1·92														
Stephenson *et al.* (1980*a*)	I	61	0·07 ± 0·4	0·2	< 0·05	1·6 ± 2·7	0·9	< 0·10	–			–			–		
	N	125	0·05 ± 0·5			0·7 ± 3·1											
Stephenson *et al.* (1989)	I	78	2·1 ± 0·10	1·3	< 0·0002	1·8 ± 0·29	4·5	< 0·0002	2·2 ± 0·10	0·6	< 0·0002	−0·2 ± 0·06	0·5	< 0·0002			
	N	72	0·8 ± 0·10			−2·7 ± 0·34			1·8 ± 0·29			−0·7 ± 0·08					
Thein Hlaing *et al.* (1991*a*)	I	210	3·6 ± 1·28	0·9	< 0·001				11·3 ± 2·04	0·9	< 0·001						
	N	205	2·6 ± 1·04						10·3 ± 1·77								
Stephenson *et al.* (1993*a*)	I–1X	96	3·3 ± 0·18	1·1	< 0·0001*	1·9 ± 0·36	3·3	< 0·0001*	3·8 ± 0·12	0·1	NS	−0·2 ± 0·08	0·2	NS	2·8 ± 0·36	3·1	< 0·0001*
	I–2X	95	3·1 ± 0·14	0·9		1·3 ± 0·30	2·7		3·6 ± 0·11	−0·1		−0·3 ± 0·08	0·1		2·6 ± 0·35	2·9	
	N	93	2·2 ± 0·12			−1·4 ± 0·28			3·7 ± 0·12			−0·4 ± 0·07			0·3 ± 0·30		
Stephenson *et al.* (1993*b*)	I	27	1·6 ± 0·15	1·0	< 0·0002	1·0 ± 0·42	3·0	< 0·0002	2·0 ± 0·19	0·6	< 0·003	−0·1 ± 0·13	0·5	< 0·0015	1·6 ± 0·49	2·2	< 0·0002
	N	26	0·6 ± 0·08			−2·0 ± 0·24			1·4 ± 0·08			−0·6 ± 0·28			−0·6 ± 0·28		
Adams *et al.* (1994)	I	28	1·0 ± 0·06	0·7	< 0·0002	0·30 ± 0·024Z	0·22	< 0·0002	0·9 ± 0·10	0·1	NS	0·16 ± 0·017Z		NS	0·33 ± 0·036Z	0·3	< 0·0002
	N	27	0·3 ± 0·10			0·08 ± 0·034Z			0·8 ± 0·11			0·16 ± 0·023Z	0·00		−0·03 ± 0·060Z		
Hadju *et al.* (1996*a*)	I	34	0·8 ± 0·9	0·4	< 0·02	1·5 ± 3·4	1·7	< 0·02	–			–			–		
	N	30	0·4 ± 0·4			−0·2 ± 0·3											
Hadju *et al.* (1998)	I	86	1·08 ± 0·6	0·01	NS	0·05 ± 0·2Z	0·01	NS	3·54 ± 0·9	0·10	NS	0·16 ± 0·1Z	0·06	< 0·03	−0·13 ± 0·3Z	0·03	NS
	N	43	1·09 ± 0·8			0·06 ± 0·2Z			3·44 ± 0·8			0·10 ± 0·2Z			−0·10 ± 0·3Z		

Values are means ± S.E.M. except for Hadju *et al.* (1996*a*) and Hadju *et al.* (1998) which are means ± S.D. I: Intervention group; I–1X: Intervention 1 dose: I–2X: Intervention 2 doses; N: Non-intervention group; Weight for age, Height for age and Weight for Height are expressed as % of the median of growth references or as *Z*-scores (Standard Deviation units). Diff.: Difference. *P*, *t*-test significances value; *, ANOVA Tukey honestly significant difference test significance value; NS, not statistically significant.

Table 6. Differences in increments in growth following treatment between intervention and non-intervention groups in longitudinal field studies of ascariasis in children: triceps skinfold thickness, triceps skinfold thickness for age (%), arm circumference, arm circumference for age (%), subscapular skinfold thickness and subcapular skinfold thickeness for age, % median or *Z*-scores

Reference	Group	*n*	Triceps skinfold thickness (mm)	Diff.	*P*	Triceps skinfold thickness for age (% or *Z*-score)	Diff.	*P*	Arm circum. (cm)	Diff.	*P*	Arm circum. for age (% or *Z*-score)	Diff.	*P*	Subscapular skinfold thickness (mm)	Diff.	*P*	Subscapular skinfold thickness for age (% or *Z*-score)	Diff.	*P*
Stephenson *et al*. (1980*a*)	I	61	2·0±0·9	2·9	< 0·0005	21·7±9·7	32·1	< 0·0005	–			–			–	–				
	N	125	−1·1±1·2			−10·4±13·4			–			–	–				–			
Stephenson *et al*. (1989)	I	78	1·0±0·08	1·2	< 0·0002	9·4±0·87	12·7	< 0·0002	0·7±0·05	0·5	< 0·0002	1·7±0·24	2·9	< 0·0002	0·9±0·07	1·2	< 0·0002	11·8±1·32	21·3	< 0·0002
	N	72	−0·2±0·08			−3·3±0·77			0·2±0·05			−1·2±0·28			−0·3±0·08			−9·5±0·08		
Stephenson *et al*. (1993*a*)	I–1X	96	2·0±0·11	1·8	< 0·0001*	17·0±0·98	16·5	< 0·0005*	0·8±0·05	0·5	< 0·0001*	0·8±0·05	0·5	< 0·0001*	1·8±0·09	1·4	< 0·0001*	23·7±1·19	21·3	< 0·0001*
	I–2X	95	2·0±0·12	1·8		17·1±0·94	16·5		0·7±0·05	0·4		0·7±0·05	0·4		1·9±0·11	1·5		26·2±1·53	23·8	
	N	93	0·2±0·08			0·5±0·79			0·3±0·04			0·3±0·04			0·4±0·08			2·4±1·25		
Stephenson *et al*. (1993*b*)	I	27	1·0±0·09	1·0	< 0·0002	10·2±1·04	11·6	< 0·0002	0·3±0·06	0·3	< 0·0002	−0·0±0·33	1·5	< 0·0005	1·0±0·09	1·0	< 0·0002	17·1±1·67	18·1	< 0·0002
	N	26	−0·0±0·10			−1·4±1·19			−0·0±0·05			−1·5±0·23			0·0±0·07			−1·0±0·36		
Adams *et al*. (1994)	I	28	1·0±0·13	0·8	< 0·0002	0·37±0·051Z	0·28	< 0·0002	0·6±0·07	0·3	< 0·0002	0·40±0·045Z	0·24	< 0·0002	0·9±0·10	0·8	< 0·0002	0·82±0·092Z		
	N	27	0·2±0·09			0·09±0·035Z			0·3±0·05			0·16±0·037Z			0·0±0·18			0·04±0·129Z	0·78	< 0·0002
Hadju *et al*. (1998)	I	86	0·98±1·5	0·28	0·15	0·22±0·6Z	0·03	0·30	0·62±0·6	0·29	< 0·01	0·07±0·4Z	0·14	< 0·02	–			–		
	N	43	0·70±1·3			0·19±0·5Z			0·33±0·7			−0·07±0·5Z			–			–		

Values are means±S.E.M. except for Hadju *et al*. (1998) which are means±S.D.: I, Intervention group; I–1X, Intervention 1 dose; I–2X, Intervention 2 doses; N, Non-intervention group; Triceps skinfold for age; Arm circumference for age and Subscapular skinfold for age are expressed as % of the median of growth references or as *Z*-scores. *P*, *t*-test significance value; ANOVA Tukey honestly significant difference test significance value; NS, Not statistically significant; Diff.: Difference.

Stephenson *et al*. (1989, 1993*a*, 1993*b*), Thein Hlaing *et al*. (1991*a*), Adams *et al*. (1994) and Hadju *et al*. (1998) measured height in their studies and it was only Stephenson *et al*. (1993*a*) and Adams *et al*. (1994) who did not find a statistically significant result. Three of the five studies which examined height for age (% of median or Z-scores) found significant improvement at follow-up. Four studies, Stephenson *et al*. (1993*a*, *b*), calculated weight-for-height; 3 of those reported statistically significant differences (Table 5). Stephenson *et al*. (1989; 1993*a*, *b*), Adams *et al*. (1994) and Hadju *et al*. (1998) assessed arm circumference and arm circumference-for-age in their studies and found them to be significantly improved after treatment (Table 6).

When triceps skinfold thickness was investigated (Stephenson *et al*. 1980*a*; 1989; 1993*a*, *b*; Adams *et al*. 1994; Hadju *et al*. 1998), it was found in 4 of 5 studies to be highly statistically significantly associated with improved growth in children. Subscapular skinfold thickness was measured by Stephenson *et al*. (1989; 1993*a*, *b*) and Adams *et al*. (1994) and was shown to be highly statistically significant in each case ($P < 0{\cdot}0005$, Table 6). A multiple regression analysis by Stephenson *et al*. (1980*a*) also revealed that *A. lumbricoides* infection was by far the most important of 37 possible health, nutritional and socio-economic variables in explaining the differences in skinfold thickness observed both before and after treatment. In three studies where children were found to be infected with a variety of helminths, decreases in intensities, including those of *Ascaris*, *Trichuris trichiura* and hookworm, were significant predictors of growth improvement in multiple regression analyses (Stephenson *et al*. 1989; 1993*a*, *b*).

A. LUMBRICOIDES AND COGNITIVE PERFORMANCE IN CHILDREN

In 1993, Connolly & Kvalsvig stated there was a good deal of evidence linking malnutrition with the impairment of cognitive function but that there was a paucity of data indicating a causal link between it and parasitic illness. However, some studies have implicated *Ascaris* infections in impairments of mental processing in some school children.

Kvalsvig, Cooppan & Connolly (1991), for example, carried out two studies in Natal, near Durban in South Africa to consider the link between infection, malnutrition and impaired cognitive function. Of the 276 children in the survey, some were infected with a combination of *A. lumbricoides*, *Schistosoma* spp., *T. trichiura*, and hookworm. In the first study, children were given tests of information processing and perceptual speed before and after treatment with a single dose of 500 mg of mebendazole. The pattern of results was consistent with the hypothesis that parasitic infection combines with nutritional deficits to impair the efficiency of cognitive processes. However, there were some confounding variables, and the single drug treatment reduced but did not eliminate the parasites. A second study removed the confounding variables of age and nutrition and employed a more comprehensive drug treatment programme. A memory task and a test of sustained attention were administered. Parasitic status showed a significant association with poor performance on the attention task, but no association was observed with educational attainment or memory function.

Later, Watkins, Cruz & Pollitt (1996) carried out a similar study of the effects of deworming with albendazole on indicators of school performance in 246 rural Guatemalan children, aged 7–12 years. Ninety-one percent of children harboured A. lumbricoides, and 82% had *T. trichiura*; they were randomly assigned to treatment and control groups at 0 and 12 weeks in a double blind study. Albendazole successfully reduced the prevalence of *Ascaris* but it was less successful against *Trichuris* at the 400 mg dosage used. The treated children were largely free of *Ascaris* for at least 6 months, but during that period, no improvement in reading, vocabulary or attendance was observed.

More recently, Hadidjaja *et al*. (1998) conducted a study with 336 children (aged 6–8 years) in northern Jakarta, Indonesia among whom the prevalence of *A. lumbricoides* was 58%. The objective of the study was to investigate the effect of treatment with mebendazole and health education on nutritional status and cognitive function. The children were divided into five groups: Group 1 was given the anthelminthic mebendazole, group 2 was provided with health education, group 3 was given both the anthelminthic and health education, group 4 was given a placebo, and group 5 consisted of children whose stools tested negative for *Ascaris* eggs. After intervention, a mean prevalence of 41% was found. Approximately 80% of the children showed good scores for nutritional status in the pre- and post-treatment data, and only a small percentage (0·9–16·2%) showed mild or moderate malnutrition. No significant difference in pre- and post-treatment nutritional status was observed. However, cognitive test results indicated that the group treated with mebendazole showed significant improvements in learning ability, concentration and eye-hand coordination 5 months post-treatment.

A. LUMBRICOIDES AND ANTHELMINTHIC CONTROL STRATEGIES

Approaches to control strategies

The main elements in planning anthelminthic con-

trol programmes are epidemiology, targets, chemotherapy, health education, sanitation, monitoring and evaluation (Albonico *et al*. 1999). According to the WHO (1985*b*), these elements should be integrated into the prevailing system of primary health care and must be based on multisectoral collaboration. Control programmes cannot be planned, implemented or sustained without recent and reliable information on the infections of interest, the people at risk and the associated morbidity. Geographical distribution, seasonality and re-infection rates of helminth infection are also crucial elements to consider in well-planned control programmes (Albonico *et al*. 1999).

Control programmes based on sanitation aim to reduce or interrupt transmission, prevent re-infection and gradually to reduce worm loads (Wong & Bundy, 1990). However, despite the well-recognized role of effective sanitation in preventing transmission of intestinal helminths, the impact of improved water supply and sanitation intervention has not been well studied. In heavily or frequently contaminated areas, one can expect decades to elapse before improved sanitation by itself measurably decreases *A. lumbricoides* infection (Huttly, 1990). However, the use and availability of latrines combined with periodic chemotherapy enhances the reduction in intensity of helminth infection and lengthens the time-span of re-infection both in research studies (Esrey *et al*. 1991) and control programmes (Albonico *et al*. 1999). For example, one study from St. Lucia reported that prevalence of infection with *A. lumbricoides* and *T. trichiura* in children was significantly lower in areas with improved sanitary conditions, as was the re-infection rate 6 months after chemotherapy (Henry, 1988).

In the long term, the prevention and control of ascariasis will be dependent upon economic development with consequent improvements in water supplies, sanitation and health education. Due to the scarcity of resources in most developing countries, the emphasis is currently on developing more cost-effective approaches to control using available chemotherapeutic agents as a short-term goal (Savioli, Bundy & Tomkins, 1992). The optimal choice of a chemotherapy control strategy is also based upon a number of factors including ease of administration and acceptability to the target population (Holland *et al*. 1996*a*). Current helminth control programmes are focused on reducing infection load and transmission potential in order to reduce morbidity and avoid mortality associated with the disease rather than to eradicate infection (Gilles, 1985; WHO, 1987). Repeated treatment ensures that even if re-infection occurs, intensity is maintained below the level associated with morbidity (Savioli *et al*. 1992).

Crompton (1994) describes in detail four main practical and feasible approaches to developing control strategies for ascariasis: (1) A mathematical approach that attempts to identify the gaps in knowledge of how *A. lumbricoides* persists with such stability in human communities; (2) The integration of family planning, nutrition and parasite control programmes, as exemplified by the broad-reaching activities of the Japanese Organisation for International Co-operation in Family Planning and the Asian Parasite Control Organisation; (3) The establishment of primary health care infrastructures in developing countries, whose populations must endure most of the morbidity associated with ascariasis; (4) Anthelminthic drugs that provide the most rapid means of reducing the intensity of infection and thereby reducing morbidity to more tolerable levels.

Epidemiological evidence suggests that anthelminthic chemotherapy can be used in one of three ways in community control programmes: universal, targeted or selective treatment (WHO, 1996*b*), defined as follows by Anderson (1989) and Albonico *et al*. (1999). (1) Offering universal treatment to all individuals in an area of high endemicity irrespective of the age, gender, worm burdens or other social characteristic of the individuals in the affected populations. (2) Offering targeted treatment to a group within a community where the group may be defined by age, gender, religion or other social characteristics, such as primary school children. (3) Offering selective treatment based on intensity of current or past infection.

A series of studies in Nigerian villages compared the efficacy of different treatment strategies, namely universal, targeted and selective treatment with levamisole (Asaolu, Holland & Crompton, 1991). Both universal and targeted treatment of schoolchildren were identified as the most effective approaches to control both in terms of reducing intensity in a high risk group and having an effect on intensity in untreated adults. Bundy *et al*. (1990) obtained similar results in a study of children infected with both *T. trichiura* and *A. lumbricoides* (aged 2–15 years) on the island of Montserrat, in which the prevalence and intensity of both infections declined not only in the treated group, but also in the 16–25 year old group that received no treatment.

In contrast, a study of 880 people in Dhaka, Bangladesh treated with pyrantel three times at 6 month intervals (Hall, Anwar & Tomkins, 1992), revealed that nearly two-thirds of all subjects were heavily infected at least once over the 18 month period and that universal chemotherapy was a more appropriate control strategy with which to reduce the level of *Ascaris* infection in the community. The authors concluded that if treatment at rounds 2 and 3 had been provided only to those people who were heavily infected at round 1, 155 subjects would not have been treated, and that over the duration of the study these 155 subjects would have become heavily re-infected at least once.

Chemotherapy regimes

Several re-infection studies of a population group treated for *Ascaris* have indicated that re-infection rates reach the pre-control level within 6 to 12 months (Tu *et al*. 1972; Cabrera, Arambulo & Portillo, 1975; Arfaa & Ghadirian, 1977; Thazin Oo, 1977; Croll *et al*. 1982; Seo, 1983; Yodmani *et al*. 1983; Cabrera, 1984). Thein Hlaing *et al*. (1987) showed that 6-monthly chemotherapy reduced intensity in both children and adults but that 12-monthly treatment lowered intensity only in adults. In a later study Thein Hlaing *et al*. (1991*b*) observed that 3-monthly chemotherapy with levamisole gave better results in terms of both prevalence and intensity than 4-monthly and 6-monthly treatments. For the 3 chemotherapeutic regimes used in the study and provided at 3-monthly intervals targeted at children under 15 years old, (a) with and (b) without universal chemotherapy, and (c) at 2–12 years old children over a period of 2 years, all were almost equally effective in reducing the prevalence and intensity not only in target children but also in non-target adults. Similar findings were reported for 4-monthly (Cabrera & Cruz, 1983; Holland *et al*. 1996*a*) and 3-monthly (Cabrera *et al*. 1989) chemotherapeutic treatment regimes in children under 15 years of age. Other studies also reported reductions in the prevalence and intensity of ascariasis in untreated adults within communities where children have been targeted for treatment (Thein Hlaing *et al*. 1990, 1991; Bundy *et al*. 1990).

Choice of anthelminthic drug in control programmes

According to Albonico *et al*. (1999) the choice of anthelminthic drug in public health should be tailored to the local epidemiology of soil-transmitted helminth infections. This is why information should be collected on prevalence and intensity of helminth infections, the population groups at highest risk of morbidity, and the health impact of helminth infections in the community that can benefit from treatment. Furthermore, the choice of anthelminthic drug for use in a control programme depends on (1) its safety record, (2) its therapeutic effect (cure rate or efficacy), (3) its spectrum of activity, (4) local health policy, and (5) financial considerations. A key issue for the optimal use of an anthelminthic drug is to decide when and how frequently to treat the population of concern. The results of epidemiological surveys to determine re-infection rates are also useful for determining the treatment schedules (Hall *et al*. 1992).

A number of studies have compared the efficacy of various anthelminthic drugs in communities polyparasitised by soil-transmitted helminths. Hadju *et al*. (1996*b*) compared the efficacy of pyrantel and albendazole in 6–11 year old children in South Sulawesi, Indonesia who were infected with both *A. lumbricoides* and *T. trichiura*. Five hundred and seven children were assigned randomly to 4 anthelminthic groups (pyrantel or albendazole once or twice per year) and a placebo, according to gender and *A. lumbricoides* egg counts. Children with signs of severe protein malnutrition were excluded. Children received single doses of pyrantel, albendazole or placebo at baseline, 3, 6 and 12 months. During the 12-month follow-up however, only 330 children (65%) completed all exams. No important differences were noted at baseline between those children and those who completed the study. In addition, no differences were found between the five groups at baseline in prevalence and intensity of both infections. At the end of the study, both albendazole and pyrantel groups had significantly lower prevalences of *A. lumbricoides* than the placebo group ($P < 0{\cdot}05$). At the 12 month examination, the intensity of ascariasis in the twice dosed albendazole and pyrantel groups was significantly lower than the placebo group ($P < 0{\cdot}005$ and $P < 0{\cdot}0005$, respectively). The results indicated that two doses yearly of each drug were more effective than one dose yearly.

Many studies have reported highly effective single dose treatments for *A. lumbricoides*. For example Sinniah, Chew & Subramaniam (1990), Albonico *et al*. (1994) and Rahman (1996) have all observed that both albendazole and mebendazole can be very effective in eliminating *Ascaris*. Williams, Koroma & Hodges (1997) found that both levamisole and albendazole significantly reduced both the prevalence and intensity of *Ascaris*. Marti *et al*. (1996) found both ivermectin and albendazole to be just as effective. In deciding the anthelminthic of choice in the treatment of ascariasis, health planners need to consider not just the cost of available drugs but also their efficacy against other human soil-transmitted helminths such as hookworm, *T. trichiura*, and *Strongyloides stercoralis*. Infections of *A. lumbricoides* are rarely found alone in human communities (Crompton, 1994). Many of the above studies have reported mixed results in the efficacies of the drugs against these other helminth species. For example, as albendazole is effective against both the adult and ova/larval stages of hookworm, unlike pyrantel, it is therefore necessary to retreat at-risk populations more frequently with pyrantel than with albendazole (Williams *et al*. 1997). Similarly, single-dose albendazole treatment was reported to be more effective than mebendazole against hookworm (Holzer & Frey, 1987; Ismail, Premaratne & Suraweera, 1991; Albonico *et al*. 1994; Rahman, 1996). For this reason administration of more expensive drugs cannot be justified in communities in which parasitic infections besides *Ascaris* are not prevalent or are of low prevalence.

DISCUSSION

Many studies have investigated the contribution of ascariasis to child malnutrition in spite of the difficulties in imputing causality posed by polyparasitism (Keusch & Migasena, 1982; Watkins & Pollitt, 1996). When polyparasitised hosts are dewormed with broad-spectrum drugs, it is difficult to determine the extent to which the improvements seen are due to each parasite species treated. This is one reason why further studies should be undertaken to differentiate between the pathogenic effects of individual intestinal helminth species on their hosts.

The potential mechanisms responsible for reduced growth and other developmental insults of *Ascaris* infection (described in detail by Stephenson & Holland, 1987; Taren & Crompton, 1989) function primarily via reductions in nutrient intake, and to a lesser extent, decreases in digestion, absorption and nutrient utilization (see Fig. 3 and Anorexia in Malnutrition and Parasitic Helminth Infections, this volume). However, because the relationship between ascariasis and child malnutrition is conditional and is one that depends on the interaction of multiple biomedical and behavioural factors (Cerf, Rohde & Soesanto, 1981), not every study undertaken to examine this relationship is successful in demonstrating that anthelminthic treatment can lead to improved growth. Stephenson & Holland (1987), Thein Hlaing (1993) and Watkins *et al*. (1996) have outlined other reasons why some studies have not demonstrated improved growth in children treated for *Ascaris* infection; these include: (1) Sub-optimal use of chemotherapeutic drug; e.g. see Greenberg *et al*. (1981); (2) Combination of factors including the absence of severe malnutrition in the population, relatively adequate dietary energy and protein intakes, possible low worm burdens and/or a failure to eliminate ascariasis, e.g. see Gupta & Urrutia, 1982; Kightlinger *et al*. 1996; (3) Presence of other parasites such as *Giardia lamblia* in a study area against which anthelminthic drugs such as mebendazole or piperazine are ineffective; e.g. see Gupta & Urrutia (1982); Thein Hlaing (1993); (4) Presence of other adverse environmental influences and infectious diseases, including diarrhoea and acute respiratory infections; e.g. see Ismail & Perara (1986); (5) Small sample size and insufficient time for follow-up examination, e.g. see Freij *et al*. (1979); (6) Communities where *Ascaris* prevalence is low and where there are different worm populations; e.g. see Watkins *et al*. 1996. The authors suggested that one reason why only a modest gain in weight was observed in Guatemalan children compared with the four Kenyan studies conducted within the same population (Adams *et al*. 1994; Stephenson *et al*. 1993*a*, *b*, 1989) was that hookworm infections strongly influenced the latter studies. However the populations also differed in that the Guatemalan children were stunted, showing past chronic malnutrition but little current acute malnutrition, and the Kenyan children exhibited both forms of malnutrition.

Connolly & Kvalsvig (1993) outline two broad classes of causal connection by which parasitic infection may impair cognitive function. The first involves direct action of the parasitic agent itself on the hosts central nervous system and the impact this may have on behaviour or mental processes. The second is that by causing ill-health and debilitation a parasite can indirectly restrict the activities of the host to the extent that certain intellectual skills are less readily acquired compared to others who are not affected in this way. Connolly & Kvalsvig (1993) propose the hypothesis that a general effect of parasitic infection is to limit the energy resources available to infected individuals and adversely affect motivation, emotion and patterns of social interaction, and that these in turn will affect their capacity for physical and mental work in a variety of contexts (e.g. school, home, play, work). This hypothesis clearly requires further investigation. The question of whether or not the effects are irreversible where there is gross insult to the central nervous system also needs further investigation.

According to Thein Hlaing *et al*. (1991*b*), there are two possible explanations for the substantial reductions in worm intensity that occur with age-targeted community chemotherapy. Firstly, children in the community harbour most of the total adult worm population and therefore pass most of the eggs that infect others (Thein Hlaing *et al*. 1984; Elkins, Haswell-Elkins & Anderson, 1986). Secondly, regular and repeated treatments heighten the impact of chemotherapy because of the predisposition to acquire heavy infection (in children) or light infections (in adults) of *Ascaris* (Haswell-Elkins, Elkins & Anderson, 1987; Thein Hlaing *et al*. 1987).

Since *A. lumbricoides* infections usually co-exist with other intestinal infections, compelling reasons exist for promoting control programmes aimed at soil-transmitted helminthiases generally. *A. lumbricoides* is readily expelled in response to a single oral dose of anthelminthic drugs (Crompton, 1994); this makes the results of chemotherapy an ideal focus for health education lessons about improved personal hygiene and sanitation. Since the control of such infections in developing countries requires the deployment of scarce resources, the optimal choice of treatment strategy must be based on analysis of the financial costs of each type of intervention as well as on the public health significance (Holland *et al*. 1996*b*). Albonico *et al*. (1995) highlighted the importance of data on prevalence and intensity for planning, monitoring and evaluating large-scale helminth control programmes, so that each control strategy can be tailored to the local epidemiological situation.

Results of a study in four Nigerian villages to compare the effects of universal, targeted and selective chemotherapy (Asaolu *et al*. 1991) showed that both universal and targeted treatments were the most effective regimes on the basis of a reduction of 1000 eggs per g of faeces (Holland *et al*. 1996*b*). For the number treated, the selective approach was 17 times more expensive than universal treatment. Targeted treatment was only twice the cost per person treated relative to the universal approach. The targeted approach carries other significant advantages, including the case of reaching children through attendance at school (Stephenson *et al*. 1980*b*), the reduced possibility of disrupting acquired immunity in the adult classes (Keymer & Pagal, 1990), the avoidance of concern over teratogenic effects (Bundy & Cooper, 1989) and in the way schools can greatly facilitate the administration of anthelminthic treatment as a centre for drug delivery where modern health education can also be developed and integrated with the chemotherapy (Crompton, 1994). However, because school enrolment and attendance rates can be low in some developing countries, significant numbers of children will not receive anthelminthic treatment in a targeted programme (Albonico *et al*. 1999).

In contrast, the selective approach would seem in theory to be a particularly attractive option since the use of relatively few doses of drugs would reduce costs and perhaps help delay or avoid conditions that might lead to the development of drug resistance (Crompton, 1994). In practice, however, the disadvantages of this type of treatment are that heavily infected people must be identified before they are treated and that not only are most people likely to be infected at least once over a relatively short period of repeated treatment, but a large proportion are likely to be heavily infected (Hall *et al*. 1992). Also, selectivity may cause resentment, particularly in endemic communities where the need for treatment is a general perception (Holland *et al*. 1996*b*).

The economic evaluation of control programmes in developing countries is important in part because it introduces concepts of cost analysis and gives an indication of affordability. Guyatt, Bundy & Evans (1993) undertook a cost effectiveness examination of different frequencies of universal chemotherapy using cost data from an actual control programme for *A. lumbricoides* (Bundy *et al*. 1990). Using a dynamic model of helminth infection transmission (Medley, Guyatt & Bundy, 1993), the analysis suggested that for a strategy with defined control objectives, budgetary constraints and a specific rate of transmission, it could be more cost-effective to intervene in a high transmission area than in a low transmission area. Also, the analysis showed that employing relatively long intervals between treatments offers the best results. Even though child-targeted treatment can never be more effective than treatment of the total population, Guyatt *et al*. (1995) found, in a follow-up analysis of the same data source, that because children tend to have higher intensities of infection, child-targeted treatment can be more cost-effective than population treatment in reducing the number of disease cases. Furthermore, the same analysis suggested that expanding the proportion of a population covered could be a more cost-effective approach then increasing frequency of treatment.

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