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Reinfection with *Ascaris lumbricoides* after chemotherapy: a comparative study in three villages with varying sanitation

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Abstract

This study examined the effect of the 2 major means of control of *Ascaris lumbricoides*—chemotherapy and sanitation. About 200 pre-school Caribbean children living in 3 villages with varying sanitation were studied by quantitative stool examination for the presence of the eggs of helminths. Children with *Ascaris* eggs were treated with piperazine. Over a 2-year period this procedure was repeated after every 6 months of natural re-infection. Results showed that (i) the rate of reinfection was on average 20% higher than the rate of new infection; (ii) there was a highly significant correlation between the result of children's initial stool examination and that 6 months later; (iii) children with high *Ascaris* egg counts also frequently had high *Trichuris* egg counts; (iv) during the 6-month intervals, 36% of the infected children were not reinfected after treatment; the difference in reinfection rates between villages with and without sanitation was 48%. Regression analysis indicated that, after several socio-economic variables were controlled, only sanitation and crowding remained significantly associated with reinfection. The implications of these findings in formulating control strategies are discussed.

Introduction

Intestinal helminths are amongst the most common infections of human beings (PETERS, 1978). Although safe and effective drugs are available for treating them, the best way to use these drugs for the benefit of the community—rather than the individual—is yet to be determined.

Recent research on the population dynamics and transmission of helminths shows that it is essential to consider these aspects of the population biology in the design of chemotherapeutic control strategies. Three common epidemiological trends have been observed in several studies. Firstly, while high prevalence rates persist after infancy through to adulthood, heavy worm burdens are found mainly in children (ELKINS *et al.*, 1986; BUNDY *et al.*, 1987). Secondly, the distribution of worm numbers per person is highly aggregated, so that a small proportion harbour most of the parasite population and many people have few or no worms (SEO & CHAI 1979; CROLL *et al.*, 1982; BUNDY *et al.*, 1985; ANDERSON & MAY, 1985). Thirdly, individuals with high initial burdens often have the heaviest worm loads after reinfection (ANDERSON & MEDLEY, 1985; ELKINS *et al.*, 1986).

These findings emphasize the importance of studying the factors which regulate parasite intensity and reinfection in epidemiological investigations related to parasite control. Little is known of the effect of sanitation interventions on the prevalence and intensity of parasitic infections.

Previous work illustrated the rapidity with which *Ascaris* infections return to their pre-treatment prevalence rates (HENRY, 1981). The relative contributions of nutritional, behavioural, social and environmental factors to this pre-treatment rate are unknown. Using 4 sequential surveys in 3 villages with different types of sanitation, this study attempted to answer the following 4 major questions about reinfection.

1. Does the rate of reinfection of pre-school children exceed the rate of acquiring new infection?
2. What is the impact of sanitation, chemotherapy, or both together, on reinfection?
3. Are children with a high intensity of infection likely to have a high intensity after reinfection?
4. Do social, environmental or nutritional factors predispose children to reinfection with *Ascaris*?

Methods

Three areas in rural St Lucia were selected for study.

Area 1: Cul de Sac (control)

This area had 5 settlements, each with widely dispersed public water standpipes, which had been installed by the government several years before and were located at various points along the main roads. The population:pipe ratio was nearly 350:1. Pit latrines were common but of poor quality and infrequently used.

Area 2: Desruisseau (water)

This area had 3 settlements and was very similar to the control area, but each household was supplied by tap water. Each household had a pipe fitted with Fordilla valves, spring-loaded valves which closed automatically after a few seconds and discharged a fixed amount every time they were reactivated.

Area 3: Ti Rocher (water and latrine)

This area had 3 settlements and was very similar to area 2. In addition to household water supplies, each house also had a pour-flush, water-seal latrine.

These areas were similar before intervention. Pre-treatment surveys indicated no difference between the areas in the prevalence of intestinal helminths or the growth of children (HENRY, 1981).

All children less than 6 months old were located using hospital records and through local registrars. The dates of birth were reliable as many children were born in hospital, while those born at home were

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registered with the local registrar during the first week after birth. Parents of these children were invited to let their children participate in this study. Of the initial sample of 229 children, 10 dropped out over the 2 year period and, overall, the co-operation of parents in collecting stool specimens, treatment of children, and in other aspects of the study was excellent.

A questionnaire was used to collect information on socioeconomic and general household conditions. The survey included questions about the education of the mother, hygiene practices, solid waste disposal, crowding, and other matters. There was close similarity between the different areas in terms of literacy, crowding, house construction, cooking facilities, garbage disposal and the use of boiled water in infant food preparation. The infant feeding pattern was similar in the 3 areas. Quantitative water use was estimated by observation and direct measurement. Families with their own household water used it almost exclusively for all domestic purposes. Unlike pit latrines, the water-sealed latrine encouraged widespread use because it was not malodorous, did not attract flies, previous faeces were not seen, and it was easy to clean.

Anthropometry

Weight and height were measured every month: weight to the nearest 0·1 kg on scales which were regularly checked for their accuracy; length to the nearest 0·1 cm using a locally made length board. Measurements were made by the same investigator using the same instruments throughout the study. Anthropometric values were expressed as a percentage of the values given in the National Centre for Health Statistics standard (HAMILL *et al.*, 1979).

Stool collection and examinations

Fresh stool specimens were collected by field workers at the homes of all children. Repeated visits were made to collect specimens from absentees. All samples were examined quantitatively in the laboratory of the Research and Control Department using a formol-ether technique (ALLEN & RIDLEY, 1970). 4 stool examinations were made between December 1977 and August 1979, with intervals of approximately 6 months between each. Stools were collected from the same 205 children in both the first and second surveys, i.e. before and after the first interval. There were 198 pairs for the second interval, and 188 for the third. The significance of differences between results was assessed by calculating χ^2.

Deworming

Immediately after each survey, children whose stools contained the eggs of *Ascaris* were treated with piperazine phosphate. Piperazine is largely ineffective against *Trichuris*. A second stool examination was made for children who were treated and the few children who still had *Ascaris* eggs in their stools were treated again. No further specimens were examined until the next round of examination about 6 months later. None of the children showed adverse reactions to the treatment.

Results

Age and sex distribution

The distributions of *Ascaris* and *Trichuris* infections by age and sex are presented in Table 1. The rate of infection was low in the first year of life but increased in the second and third years. The increase in prevalence of *Trichuris* was steady and rapid. For *Ascaris*, which was treated, the increase in infections was not consistent. For example, between the second and third years of age the percentage of *Ascaris* infections declined in females. However, despite treatment, the overall prevalence of *Ascaris* infection was higher than that of *Trichuris*. 24% of all the samples tested were positive for *Ascaris*, 18% for *Trichuris* and 9% for both *Ascaris* and *Trichuris*.

Infection and reinfection

Table 2 shows the infection and reinfection rates

Table 1—Prevalence of helminth infections by age and sex in St Lucia, 1977-1979

Age (months)	Sex	No. of samples	Percentage infected *Ascaris*	Percentage infected *Trichuris*
0-11	M	116	3·4	0
	F	138	5·1	0·7
12-23	M	188	34·0	16·0
	F	192	32·3	18·7
24-35	M	110	36·4	35·5
	F	112	25·0	39·3
Totals	M	414	26·1	16·7
	F	442	21·9	18·3

Table 2—*Ascaris* infection and reinfection in children below 3 years examined 6·5 months after treatment

(a) Interval 1		Mean age (midway) = 10 months		
Dec. 1977-July 1978	*N*	Percentage uninfected in Dec. 77	Percentage infected in Dec. 77	Percentage of all children
− −*	151	77·0		73·7
− +	45	23·0		21·9
+ −	4		44·4	2·0
+ +	5		55·6	2·4
Total	205	100	100	

(b) Interval 2		Mean age (midway) = 16 months		
July 1978-Jan. 1979	*N*	Percentage uninfected in July 78	Percentage infected in July 78	Percentage of all children
− −	86	57·7		43·4
− +	63	42·3		31·8
+ −	23		46·9	11·6
+ +	26		53·1	13·1
Total	198	100	100	

(C) Interval 3		Mean age (midway) = 23 months		
Jan. 1979-Aug. 1979	*N*	Percentage uninfected in Jan. 79	Percentage infected in Jan. 79	Percentage of all children
− −	85	80·9		45·2
− +	20	19·1		10·6
+ −	41		49·4	21·8
+ +	42		50·6	22·3
Total	188	100	100	

*− −, never infected; − +, gained infection; + −, not reinfected; + +, reinfected.

during the 3 intervals. Four possible combinations exist: a child may have been infected at the start and at the end of the 6 months period (+ +), at the start but not at the end (+ −), at the end but not at the start (− +), or at neither the end nor the start (− −). Table 2 shows that up to 80% of children who were initially uninfected remained uninfected (− −). The exception to this high proportion was during interval 2 (i.e. mean age = 16 months), when new infections were acquired rapidly. Over half of the children treated for *Ascaris* regained the infection in about 6 months. This pattern persisted irrespective of age, indicating that initially infected children had a higher probability of being reinfected than did initially uninfected children. Nevertheless, the total number of new infections was greater than the number of reinfections at younger ages (intervals 1 and 2), but during the third interval (mean age = 23 months) reinfections were much higher in number and proportion. Over the 3 intervals, an average of 30% of uninfected children became infected, whereas an average of 50% of infected children became reinfected. The reinfection rate was similar for boys and girls in all age groups.

For *Trichuris*, which was untreated, the proportion of children with new infections (− +) increased rapidly and consistently. In addition, the proportion of children maintaining the infection (+ +) also steadily increased.

Chemotherapy versus sanitation

In Table 3 the 3 intervals are combined and *Ascaris* infection is compared in 3 different hygienic settings. These results show that both new infections and reinfections were lower in areas where hygiene status was good, and that a greater proportion of children remained uninfected in the better hygienic areas. For children in the control area, the probability that those infected before treatment would again be infected 6 months later was 1·9 times higher than for children who were initially uninfected (64 versus 34%, $P<0·0001$; see Table 3). In the water area it was 1·7 times higher (46 versus 27% $P<0·05$), and in the water and sanitation area it was 1·4 times higher (34 versus 24%, $P>0·1$). Table 3 also shows that after chemotherapy 64% of children regained the infection in the control area. This reinfection rate was reduced by 29% in the area with water and by a further 19% in the area with both water and latrines. Hence, during the three 6-month intervals, 36% of children found to be infected were not reinfected after chemotherapy, whereas the reinfection rate was reduced by 48% with the improved water and sanitation.

Correlation between egg counts on infection and reinfection

Throughout the study there was a highly significant association between the result of a child's initial stool examination and that 6 months later. Children who were initially infected with *Ascaris* had a higher probability of being infected at a follow-up stool examination, despite treatment, than did those who were initially uninfected. A comparison was also made of the faecal egg counts on infection and on reinfection. The intensity of infection, ranked according to the number of eggs per gram, was compared at a child's initial infection and at its subsequent reinfection. There was a significant correlation between pre-treatment and reinfection faecal egg counts for the same children. This correlation was maintained in all 3 sanitation areas, although the intensity of infection was different.

80 samples contained both *Ascaris* and *Trichuris* eggs. Egg counts for each species were ranked and correlated with each other. Children with high infestations of one species were prone to high infestations with the other ($r = 0·29$). This correlation was particularly strong in children over 2 years of age ($n = 37$, $r = 0·52$).

Social factors related to reinfection

Children in the (− −) category and the (+ +) category represented opposite states: always uninfected and always infected. These categories were used to detect any social factors which might be used to discriminate between them. Table 4 compares several variables in the uninfected and reinfected

Table 3—Comparisons of *Ascaris* infection and reinfection rates in three villages with varying sanitation (all intervals combined)

	Control		Water		Water & sanitation	
	n	%	*n*	%	*n*	%
− −*	101	(66)	112	(73)	109	(76)
− +	51	(34)	42	(27)	35	(24)
	152		154		144	
+ −	24	(36)	24	(54	20	(67
+ +	43	(64)	20	(46)	10	(33)
Totals	67		44		30	

*See footnote to Table 2

Table 4—Comparisons of social and environmental factors in the uninfected and reinfected groups during interval 3

Factors	Uninfected $n = 85$		Reinfected $n = 42$		
	Mean	(SD)	Mean	(SD)	*P*(*t*-test)
Crowding (persons/room)	2·2	(1·1)	2·6	(1·3)	<0·05
Income/person (SECC)*	49·1	(37·8)	36·2	(20·1)	<0·05
Water/person/day (litres)	18·2	(9·2)	16·7	(15·1)	NS
Family size	6·3	(2·4)	6·9	(2·6)	NS
Weight gain, kg (during interval 3)	1·1	(0·5)	1·1	(0·4)	NS
Height gain, cm (during interval 3)	4·9	(1·6)	4·9	(1·7)	NS
	%		%		$P(\chi^2)$
Water-sealed latrine present	38·8		16·7		<0·01
Resident of control area	31·8		52·4		<0·05
Mother completed primary school	44·7		37·7		NS
No organized disposal of garbage	94·1		95·2		NS

*2·6$ Eastern Caribbean Currency ($ECC) = 1$ US (1978)
NS = not significant

groups in all areas combined during interval 3. Significance tests were performed on the logarithms of these values.

Using univariate analyses, significant differences in crowding, monthly income per head, environmental area and method of faecal disposal were found between the 2 groups. Neither the quantity of water used per head nor the growth of children was significantly different in the 2 groups. Regression analysis of these variables showed that only the method of faecal disposal and crowding were significant predictors of reinfection when the other variables were controlled.

Discussion

Intestinal helminths have a remarkable ability to maintain stable populations in their hosts despite various attempts to reduce their prevalence (ANDERSON, 1982; ANDERSON & MAY, 1982; ANDERSON & MEDLEY, 1985). New attempts to control these parasites require an understanding of the factors which put children at risk of repeated infection, especially if these same children accumulate heavy infections and also pass a disproportionate number of eggs into the community.

In this study I found that children infected with *Ascaris* were also often infected with *Trichuris*. Furthermore, for children with both infections, those with high *Ascaris* egg counts also had high *Trichuris* egg counts. This pattern was more evident when the prevalence rate was high, i.e. in older pre-school children.

This study also showed that children living in villages with poor sanitation were not only more likely to be infected initially but were also more likely to become reinfected after treatment. Furthermore, previous *Ascaris* infection did not greatly restrict the rate of reacquisition of infection. These results can be interpreted to mean that there was a consistent susceptibility to infection, or a consistently high exposure to infection, or both. This process of constant reinfection, which is responsible for the high prevalence and intensity of infections in endemic areas, is a major obstacle to rational parasite control. It appears that environmental, socioeconomic and immunological factors conjointly play important roles in this dynamic process of reinfection. Although immune responses may limit the number of parasites in the host at any one time (PAWLOWSKI, 1982) acquired immunity does not seem to be related to reinfection in an obvious and direct way. The environmental and socioeconomic factors are more commonly implicated in reinfection through contamination and spread of the parasites.

In villages close to the cohort population, detailed studies of human behaviour and of risk factors for helminth transmission have been made for schistosomiasis (DALTON, 1976; JORDAN *et al.*, 1978). These studies established that the parasite burden was directly correlated with the degree of exposure to contaminated water. My previous work shows that, within the study communities, soil-borne helminths also predictably accumulated in persons with increased exposure risks (HENRY, 1981). The present analysis indicates that reinfection is also related to increased exposure risks. These findings, reinforced by the observation that sanitation and crowding are crucially important to reinfction, suggest that behavioural and environmental factors should be key elements to be considered in the design of long-term parasite control strategies.

The high rates of *Ascaris* infection and reinfection (Table 2) expose the limitation of simple chemotherapeutic regimes as means for parasite control. Nevertheless, the results further suggest that focusing drug treatment on the wormy proportion of the population could be an attractive option, because identifying people with high faecal egg counts not only identifies those who often have repeated attacks but also those likely to be infected with other parasites. These findings imply that, in communities where reinfection rates are high, attempts should be made to reduce the high basic reproductive rate by improved sanitation and hygiene, so that the impact of chemotherapy can be enhanced. The overall impact should be made cost-effective by treating the most heavily infected individuals regularly and on a long-term basis, ensuring that the diagnostic step is also cost-effective.

The search for a vaccine against helminths such as *Ascaris* holds great potential. However, there are practical problems of creating herd immunity by vaccination for an infectious disease agent with a wide and varied antigenic spectrum (ANDERSON & MAY, 1985). This means that, for less developed countries, improved sanitation and hygiene together with selective chemotherapy still present the most attractive combination for the control of intestinal helminths in the near future.

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Short Report

Mansonella streptocerca in the Central African Republic

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A microfilaria survey was carried out in the villages of Djema, Obo and Zémio, in the eastern part of the Central African Republic. 267 people of both sexes (age range 1-100 years) were studied. Thick peripheral blood films were made from each person, dried in air, and stained in 10% Giemsa's stain for 20-30 min. Using an oil immersion objective, parasites were searched for amongst a minimum of 500 white blood cells. Blood films from 36 (13·5%) people contained *Mansonella streptocerca* microfilariae; no other microfilariae were found. *M. streptocerca* had been previously reported from man and other primates in the Congo basin (Zaire) (DUBOIS & VITALE, 1933; PÉEL & CHARDOME, 1952; VAN DEN BERGHE & CHARDOME, 1952; VAN DEN BERGHE *et al.*, 1964), but not, to our knowledge, from the Central African Republic.

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