

A 13-year follow-up of treatment and snail control in an area endemic for *Schistosoma mansoni* in Brazil: incidence of infection and reinfection

M.F.F. de Lima e Costa,¹ R.S. Rocha,² P. Coura Filho,² & N. Katz²

The incidences of Schistosoma mansoni infection and reinfection were investigated in an endemic area of Brazil (Peri-Peri, State of Minas Gerais) where chemotherapy and snail control had been used for 13 years (1974–87). Two cohorts were followed: the first consisted of 584 individuals with no evidence of infection at entry (infection cohort), and the second comprised 296 individuals who were treated and did not eliminate eggs 8–12 months afterwards (reinfection cohort). The incidence of infection (per 100 person-years) decreased from 7.5 in 1974–77 to 3.6 in 1986–87, and that of reinfection from 21.3 in 1974–77 to 3.7 in 1986–87. Calendar period, age at risk, and sex were independently associated with both infection and reinfection, while a heavy S. mansoni egg count prior to treatment (≥ 500 epg (eggs per gram of stools)) was independently associated with reinfection. The geometric mean number of eggs after treatment among those reinfected (47 epg) was approximately half that among those infected for the first time (81.5 epg). Age at risk had the greatest effect on both infection and reinfection. The rate ratios of infection and reinfection were 3 to 6 times higher among individuals younger than 20 years than among those aged ≥ 25 years, even after adjusting for confounders. This suggests the existence of a strong protective effect with increased age (because of biological and/or environmental factors) for both infection and reinfection.

Introduction

The impact of treatment for *Schistosoma mansoni* infection in endemic areas or of treatment together with snail control has often been evaluated in terms of the prevalence and intensity of the infection (11, 12, 17, 22). The incidence of the infection (first detectable infection) has rarely been considered in this respect (8, 24), and reinfection (infection after treatment) has usually been examined in the absence of a control group (10, 11, 14, 22, 24–26).

The effect of population-based treatment on the incidence of *S. mansoni* infection is still controversial. In one study, in St. Lucia, chemotherapy alone reduced the annual incidence in children over four treatment campaigns in areas of high and low transmission (8). In contrast, in Kenya, the incidence of

the infection increased slightly a year after treatment in an area of high transmission (24). Snail control reduced the incidence of infection among children in Egypt (4) and St. Lucia (19).

Follow-up studies in endemic areas of Brazil (10, 11, 14, 22) and Kenya (24) have reported that reinfection with *S. mansoni* occurs more frequently in children than adults. In the above-mentioned study in Kenya (24), the incidence of reinfection over a 12-month period decreased with age but the incidence of infection did not; the decrease was not accounted for by differences in water contact habits. This Kenyan study appears to be the only one that has examined *S. mansoni* reinfection using for comparison an uninfected control group, and it illustrates how some aspects of the incidence of *S. mansoni* infection and of reinfection are still not properly understood.

The present study forms part of the evaluation of a schistosomiasis *mansoni* control programme carried out in an endemic area of Brazil over a period of 13 years. Population-based chemotherapy and mollusciciding were the control strategies used (12).^a The focus of this article is the incidence of *S. mansoni* infection and reinfection in this area.

¹ Department of Preventive and Social Medicine, Universidade Federal de Minas Gerais, Av. Alfredo Balena 190, 30130, Belo Horizonte, Minas Gerais, Brazil. Requests for reprints should be sent to Dr de Lima e Costa at this address.

² Centro de Pesquisas "Rene Rachou", Fundação Oswaldo Cruz, Belo Horizonte, Minas Gerais, Brazil.

Reprint No. 5374

Materials and methods

Schistosomiasis control programme in Peri-Peri

Study area and snail control. Detailed descriptions of the study area and control strategies used have been reported previously (12).^a Briefly, Peri-Peri, where the study was carried out, is a village in the Capim Branco Municipality of the State of Minas Gerais (south-east Brazil), situated 61 km from the state capital, Belo Horizonte. Two streams flow through Peri-Peri and are used by the population for irrigation, swimming, bathing, and for washing clothes and utensils.

From 1974 to 1987 snail surveillance was performed in these streams at 2–6-month intervals (mean number of surveys, 5.8 ± 2.0 per year); the snails collected were examined in the laboratory for infection with *S. mansoni*. The streams were treated with niclosamide every time snails, infected or non-infected, were found (mean number of treatments, 5.3 ± 1.8 per year; mean weight of niclosamide used, 6.9 ± 4.1 kg per year). Only *Biomphalaria glabrata* were infected.^a The proportion of infected *B. glabrata* decreased from 14.3% in 1974 to 1.8% in 1987 (Table 1).

Study population and stool examination. The population studied was defined by an annual house-to-house census of everyone living within a mapped area. Each household member was provided with an identifiable container (name or mark-coded in cases of illiteracy) for collecting stool samples. Two smears of a stool sample from each subject were examined using the Kato–Katz method (9). The number of *S. mansoni* eggs per gram of stools (epg) for each individual was calculated by multiplying by 24 the arithmetic mean of the number of eggs in two slides. A survey of the entire population was carried out annually. From 1974 to 1987, the village population ranged from 622 (1974) to 598 (1987). The prevalence of *S. mansoni* infection decreased from 43.5% in 1974 to 4.4% in 1987, and the geometric mean number of eggs among those infected, from 281 epg (SD = 4.4) to 147 epg (SD = 2.9), respectively.^a Table 1 shows the coverage for stool examinations and the prevalence of infection during the study period.

Table 1: Proportion of infected snails, stool coverage examinations, prevalence of *Schistosoma mansoni* infection, and treatment coverage with oxamniquine in Peri-Peri, by year, 1974–87^a

	% of snails infected ^b	% of population:		
		Examined ^c	Infected ^d	Treated ^e
1974	14.3	95.8	43.5	84.9
1975	0.0	86.5	27.5	76.4
1976	0.0	50.0	27.7	—
1977	4.7	77.4	21.6	85.7
1978	0.0	79.1	14.3	—
1979	0.2	88.8	22.7	89.7
1980	1.7	80.0	20.6	20.2
1981	0.0	78.5	17.7	89.2
1982	0.2	82.4	9.6	47.7
1983	0.2	80.4	9.0	—
1984	0.0	81.7	15.2	85.3
1985	3.4	83.6	11.4	100.0
1986	0.0	78.6	6.0	100.0
1987	1.8	91.8	4.4	100.0

^a Treatment campaigns were not conducted in 1976, 1978, and 1983.

^b Relative to the number of snails examined.

^c Relative to the number of inhabitants.

^d Relative to the number examined.

^e Relative to the number infected.

Population-based treatment. All individuals eliminating *S. mansoni* eggs in stools (for the first or any subsequent time) were eligible for treatment with oxamniquine (20 mg/kg body weight for those aged 0–14 years and 15 mg/kg for those aged ≥ 15 years). Treatment was administered after the patient (or relative/guardian for those aged <15 years) had given verbal consent; pregnant women were not treated until after they had delivered. The drug was administered in the presence of a physician at a district government health centre. Treatment campaigns were conducted annually, except in 1976, 1978, and 1983. The effect of treatment was assessed in the course of annual surveys conducted 8–12 months after treatment. These surveys and chemotherapy campaigns were carried out from April to October. Treatment coverage is shown in Table 1.

The control programme was divided into two phases: the first phase (1974–83) was conducted by a team from Rene Rachou Research Centre, while the second phase (1984–87) was conducted by a health team from the district government. The team for the second phase (nurse, technician, and physician) was trained by the team from the first, and the work was carried out under the supervision of one of the

^a Coura Filho, P. [Evaluation of a municipal programme to control schistosomiasis mansoni in Peri-Peri (Capim Branco), Minas Gerais, Brazil]. Master's thesis. Belo Horizonte, Universidade Federal de Minas Gerais, 1990, p. 147 (in Portuguese).

authors (P.C.F.). Quality control of the stool examinations performed by the two teams showed 98% agreement in relation to the presence or absence of *S. mansoni* eggs.^b

Present follow-up study

Study design. The study was designed to examine the incidences of infection and reinfection as well as the factors associated with each of these events. Individuals were eligible for the study if they satisfied the following conditions: presented no evidence of previous treatment for schistosomiasis at entry; had been living in the study area for at least two consecutive years; and were treated by the research team.

Two cohorts of individuals were followed: the first consisted of those with no evidence of infection at entry (infection cohort); and the second comprised those who received treatment for the first time and did not eliminate eggs when examined 8–12 months after the treatment (reinfection cohort). Individuals entered the study over the period 1974–86; for the infection cohort, entry was the first time individuals were examined; for the reinfection cohort, entry was when the effect of treatment was assessed. Individuals in the infection cohort transferred to the reinfection cohort after becoming reinfected and receiving subsequent treatment (112 subjects transferred in this way during the study period).

The incidence of infection was determined from the first presence of *S. mansoni* eggs in stools after a previously negative stool examination, while the incidence of reinfection was measured from the first presence of *S. mansoni* eggs after a negative examination 8–12 months following treatment. A total of 20 of the study individuals missed a stool examination between a negative and a positive result; in these instances it was assumed that infection/reinfection occurred at the mid-point between the non-missing observations.

Information about treatment administered by someone other than a member of the research team was carefully investigated by interview. If such treatment had been received, we checked the drug and dosage used; only if both coincided with the prescribed schistosomicides in Brazil were recipients considered to have been treated. A total of 13 participants from both cohorts were treated by others during the study period; they were considered lost to follow-up in terms of the data for their last stool examination.

The following explanatory variables were considered: age at risk; sex; calendar period (1974–77, 1978–81, 1982–85, and 1986–87); and migration status at entry (migrants or residents). Residents were defined as those who had lived in Peri-Peri since 1974 or those who had been born in the village during the control programme. For the reinfection study, the number of eggs before treatment (12–99 epg, 100–499 epg, and ≥ 500 epg) was also considered.

Analysis of data

The data were analysed using survival and person-years approaches. Life tables were used to plot the cumulative incidence of reinfection, while Wilcoxon and log-rank tests were used to test equality over strata (18). The person-years method was used to assess the incidence rates of infection and reinfection. The strength of associations between variables was determined from the hazard ratio (rate ratio) (3, 18).

The independent effect of all the variables was assessed using the Poisson regression. All the variables examined in the univariate analysis were used to construct the infection and reinfection regression models. Any interactive effect between age and the number of eggs before treatment on the risk of reinfection was examined under the multiplicative model in the Poisson regression. The statistical significance of associations in the univariate and in the multivariate analyses was assessed by the log-likelihood ratio statistic (3, 5). Mantel-Haenszel summary estimates were used to adjust the overall rate ratios of reinfection/infection for age (3).

To compare frequencies, medians and log-means, respectively, we used χ^2 , Wilcoxon rank, and Student's *t* tests (1, 6). The analysis was carried out using EGRET (21), SAS (20), and person-years software packages.^c

Results

Study population

From 1974 to 1987, 1147 individuals lived in Peri-Peri. Of these, 881 (77%) met the inclusion criteria for the study, and 768 (87.1%) took part. A total of 77 were excluded because they eliminated *S. mansoni* eggs after treatment and 36 were excluded because they were not examined when the effect of treatment

^b See footnote a, p. 198.

^c Coleman, P.P. et al. *Person-years (PYRS): a FORTRAN program for cohort study analysis*. Lyon, International Agency for Research on Cancer. Unpublished report No. 89/006.

was assessed. The nonparticipants were similar to those in the reinfection cohort with respect to age (median age at entry, 13 and 15 years, respectively; $P = 0.159$), sex ($P = 0.110$), and time of entry to the study (89% and 84%, respectively, entered between 1974 and 1981; $P = 0.200$). The geometric mean number of *S. mansoni* eggs before treatment among the cohort participants 126.5 epg (SD = 4.4) was similar to that among the non-participants whose stools were not examined after treatment (133.0 epg (SD = 4.1); $P = 0.842$); however, the geometric mean number of eggs before treatment among those non-participants who continued to eliminate eggs after treatment was higher (239.9 epg (SD = 3.8)) than that of the cohort participants ($P < 0.001$).

Of the 584 participants in the infection cohort, 177 infected during the study period, 164 were lost to follow-up, and 243 were uninfected at the study cut-off in 1987 (median age at entry: 8.0 years, 15.5 years, and 8.0 years for those infected, lost to follow-up, and who withdrew, respectively). Of the 296 participants in the reinfection cohort, 110 reinfected during the study period, 93 were lost to follow-up, and 93 were uninfected at the study cut-off (median age: 10.5, 16.0, and 20.0 years, respectively).

Losses to follow-up were not sex-dependent and were more frequent among those who entered the study between 1974 and 1981 in both cohorts (81% and 76% of losses in the infection and reinfection cohorts, respectively). Losses to follow-up were as follows in the infection and reinfection cohorts: treatment by others (7 cases and 6 cases, respectively); refusal to continue participating in the study (40 and 26 cases, respectively); and migration or death (117 and 61 cases, respectively).

Descriptive results, univariate and multivariate analyses

The incidence rates of *S. mansoni* infection decreased from 7.5 per 100 person-years in 1974–77 to 3.7 in 1986–87. The incidence of reinfection decreased from 21.3 per 100 person-years in 1974–77 to 3.7 in 1986–87. The overall incidence of reinfection was higher (10.2 per 100 person-years) than that of infection (6.6 per 100 person-years) in the crude analysis (rate ratio of reinfection and infection: 1.6; 95% confidence interval (CI): 1.2, 2.0). When adjusted for age, the ratio of the incidences of reinfection and infection was at the borderline of significance (adjusted rate ratio: 1.3; 95% CI: 1.0, 1.7).

The results of the univariate analysis of factors associated with infection and reinfection are shown in Table 2: infection was associated with calendar period, age and sex; reinfection was associated with

calendar period, age, sex, migration status, and number of *S. mansoni* eggs before treatment.

The results of the multivariate analysis that were significant are shown in Table 3. The association between reinfection and migration status disappeared after adjustments had been made for confounders. Calendar period, age, and sex were independently associated with both infection and reinfection, while the number of *S. mansoni* eggs prior to treatment was associated with reinfection. The rate ratios of infection were higher over the periods 1974–77 and 1978–81. The rate ratio of reinfection was higher over the period 1974–77. Males had higher risks for infection and reinfection than females. The age at risk had the greatest effect on infection and reinfection: for infection, the highest rate ratios were for the age range 10–14 years and 15–19 years (4.0 and 3.8, respectively); for reinfection, the highest rate ratios occurred in the age groups 5–9 years and 10–14 years (6.3 and 5.5, respectively).

Reinfection was more rapid and frequent among individuals who eliminated ≥ 500 epg before treatment (Fig. 1). After 12 years' participation, 81.4% of subjects who eliminated ≥ 500 epg, 50.6% of those who eliminated 100–499 epg, and 50.6% of those who eliminated 12–99 epg at entry were reinfected. Differences over strata were statistically significant ($P < 0.001$ in both Wilcoxon and log-rank tests).

Table 4 shows the rate ratios for reinfection in different age groups, according to the number of *S. mansoni* eggs before treatment. The ratios are adjusted for sex and calendar period, allowing for interaction in the Poisson regression; the model was not statistically significant ($P = 0.245$). The rate ratios of reinfection were higher among individuals who eliminated ≥ 500 epg compared with those who eliminated 12–499 epg for the age groups 15–19 years (5.6 versus 3.4) and 20–24 years (5.8 versus 1.1). For individuals aged 5–9 years and 10–14 years, rate ratios of reinfection tended to be more among those with the highest egg counts (8.3 versus 6.0 and 6.2 versus 5.4, respectively), but the confidence intervals overlapped. For those aged ≥ 25 years, the rate ratio of reinfection was similar for individuals who eliminated 12–499 epg and ≥ 500 epg.

The geometric mean number of *S. mansoni* eggs in the infected and reinfected cohorts was 81.5 epg (SD = 3.8) and 47.0 epg (SD = 3.4), respectively ($P < 0.001$); individual egg counts were 12–1320 epg in the reinfected cohort and 12–5544 epg in the infected. Fig. 2 shows the geometric mean number of *S. mansoni* eggs in the infected and reinfected cohorts, according to age; the only significant difference was for the age group ≥ 25 years ($P = 0.043$).

Incidence of infection and reinfection with *Schistosoma mansoni* in Brazil

Table 2: Incidence of *Schistosoma mansoni* infection and reinfection, according to calendar period, age group, sex, migration status, and number of *S. mansoni* eggs before treatment among those at risk of reinfection in the study area

	Infection				Reinfection			
	No. of person-years at risk	No. infected	Incidence (per 100 person-years)	Rate ratio	No. of person-years at risk	No. reinfected	Incidence (per 100 person-years)	Rate ratio
<i>Period</i>								
1974–77	707.8	53	7.5	2.1 (1.1, 3.9) ^a	258.5	55	21.3	5.7 (2.2, 14.1)
1978–81	792.6	73	9.2	2.6 (1.4, 4.7)	305.0	23	7.5	2.0 (0.8, 5.2)
1982–85	832.7	38	4.6	1.3 (0.7, 2.4)	380.5	27	7.1	1.9 (0.7, 4.8)
1986–87	365.8	13	3.6	1.0	134.1	5	3.7	1.0
			<i>P</i> < 0.001 ^b				<i>P</i> < 0.001	
<i>Age at risk (years)</i>								
0–4	522.0	16	3.1	0.8 (0.5, 1.5)	15.0	0	0.0	—
5–9	516.5	52	10.1	2.7 (1.8, 4.1)	82.5	20	24.2	7.2 (3.7, 13.8)
10–14	273.0	41	15.0	4.1 (2.7, 6.3)	155.5	33	21.2	6.3 (3.5, 11.4)
15–19	130.5	18	13.8	3.8 (2.2, 6.5)	189.6	29	15.3	4.5 (2.5, 8.3)
20–24	113.5	8	7.0	1.9 (0.9, 4.1)	162.5	12	7.4	2.2 (1.0, 4.6)
≥25	1143.5	42	3.7	1.0	473.0	16	3.4	1.0
			<i>P</i> < 0.001				<i>P</i> < 0.001	
<i>Sex</i>								
Males	1038.4	97	9.3	1.9 (1.4, 2.6)	554.1	68	12.3	1.5 (1.1, 2.3)
Females	1660.4	80	4.8	1.0	524.0	42	8.0	1.0
			<i>P</i> < 0.001				<i>P</i> = 0.025	
<i>Migration status</i>								
Residents ^c	1992.9	138	6.9	1.3 (0.9, 1.8)	956.6	104	10.9	2.2 (1.0, 5.0)
Migrants	706.0	39	5.5	1.0	121.5	6	4.9	1.0
			<i>P</i> = 0.204				<i>P</i> = 0.035	
<i>No. of eggs before treatment^d</i>								
≥500	—	—	—	—	155.1	32	20.6	2.3 (1.5, 3.7)
100–499	—	—	—	—	329.5	26	7.9	0.9 (0.6, 1.4)
12–99	—	—	—	—	593.5	52	8.8	1.0
							<i>P</i> < 0.001	

^a Figures in parentheses are the 95% confidence interval.

^b *P*-values are for the log-likelihood ratio statistic.

^c Those who had lived in Peri-Peri since 1974 or were born in the village during the control programme.

^d No. of eggs per g of stool (epg).

Discussion

The primary objectives of the study were as follows: to assess changes in the incidence of infection and reinfection; to examine the effects of the available demographic information (age, sex, and migration status) on infection and reinfection; and to examine the effect of the number of *S. mansoni* eggs before treatment on reinfection. An additional objective was to compare the intensity of *S. mansoni* infection with that of reinfection.

The incidence of both *S. mansoni* infection and reinfection decreased over the study period. Similar demographic factors were associated with infection and reinfection. Infection and reinfection were more frequent among males; there was no association with migration status after adjustments for confounders; and age had the greatest effect on both infection and reinfection.

The risks of reinfection were higher for those aged 5–9 years and 10–14 years. This agrees with the observation that reinfection is more frequent

Table 3: Significant results in the multivariate analysis of *Schistosoma mansoni* infection and reinfection

	Rate ratio ^a	
	Infection	Reinfection
<i>Period</i>		
1974–77	1.9 (1.1, 3.5) ^b	2.9 (1.1, 7.5)
1978–81	2.5 (1.4, 4.6)	1.4 (0.5, 3.6)
1982–85	1.3 (0.7, 2.4)	1.5 (0.6, 4.0)
1986–87	1.0	1.0
<i>Age at risk (years)</i>		
0–4	0.8 (0.4, 1.4)	—
5–9	2.6 (1.7, 3.9)	6.3 (3.2, 12.4)
10–14	4.0 (2.6, 6.2)	5.5 (3.0, 10.2)
15–19	3.8 (2.2, 6.6)	3.7 (2.0, 7.0)
20–24	2.3 (1.1, 4.9)	2.0 (0.9, 4.2)
≥25	1.0	1.0
<i>Sex</i>		
Male	2.0 (1.5, 2.7)	1.7 (1.1, 2.4)
Female	1.0	1.0
<i>No. of eggs before treatment^c</i>		
≥500	—	1.7 (1.1, 2.6)
100–499	—	1.1 (0.6, 1.7)
12–99	—	1.0
	$P < 0.001^d$	$P < 0.001^e$

^a Adjusted using the Poisson regression method (final model).

^b Figures in parentheses are the 95% confidence interval.

^c No. of eggs per g of stool (epg).

^d *P*-value of log-likelihood ratio statistic (period, age and sex are included in this final model).

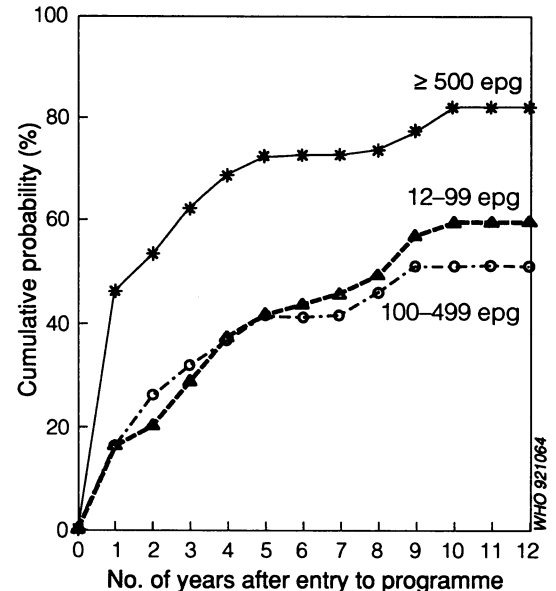
^e *P*-value of log-likelihood ratio statistic (period, age, sex, and number of eggs are included in this final model).

among under-15-year-olds (10, 11, 22, 24, 26). The risk of infection increased until 10–19 years of age and decreased thereafter. This pattern is similar to the age-prevalence curve of infection observed in most endemic areas (7, 8, 16, 24).^d The decreased incidence of infection and of reinfection among older subjects might be the consequence of reduced water contact and/or a form of resistance/immunity. Studies in Brazil and in Kenya have led to the conclusion that older people could have a form of resistance/immunity to schistosomiasis since the relationship between age and the prevalence of infection (16) or incidence of reinfection (24) could not be explained completely by differential water contact activities.

The risk of reinfection was higher than that of infection among children aged 5–9 years and 10–14 years (RR = 6.3 versus 2.6 and 5.5 versus 4.0,

^d See footnote a, p. 198.

Fig. 1. Cumulative incidence of *Schistosoma mansoni* reinfection at various years after entry to the programme, according to the number of eggs before treatment (12–99 epg, 100–499 epg and ≥500 epg). These failure estimates are based on data provided by all 296 subjects in the reinfection cohort. The differences over strata were statistically significant ($P < 0.001$ in both Wilcoxon and log-rank tests).



respectively). An increased risk of reinfection relative to infection in these age groups has also been reported by Sturrock et al. (24), and needs further investigation.

The influence of the pretreatment intensity of *S. mansoni* infection on reinfection is controversial.

Table 4: Rate ratios for reinfection, according to age group and number of *Schistosoma mansoni* eggs before treatment^a

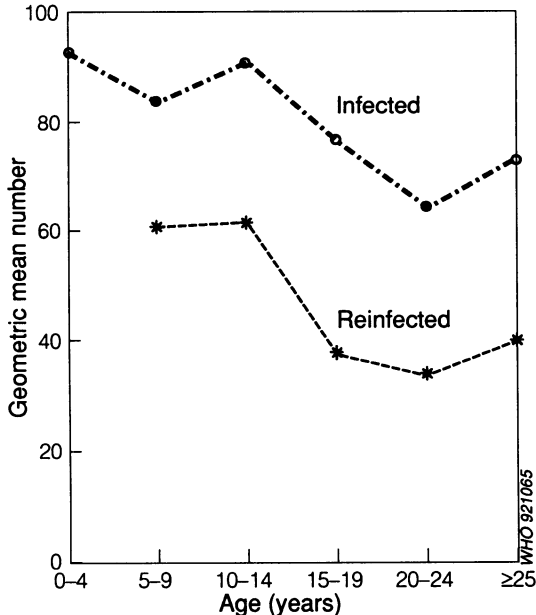
Age at risk (years)	Rate ratios at egg levels: ^b	
	12–499	≥500
5–9	6.0 (2.9, 12.5) ^c	8.3 (3.0, 23.1)
10–14	5.4 (2.8, 10.3)	6.2 (2.3, 16.6)
15–19	3.4 (1.6, 6.9)	5.6 (2.5, 12.6)
20–24	1.1 (0.4, 3.0)	5.8 (2.3, 14.6)
≥25	1.0	1.0 (0.2, 4.2)

^a Rate ratios were adjusted for sex and period, allowing for interaction in the Poisson regression method (*P*-value of log-likelihood ratio statistic on 4 degrees of freedom = 0.245).

^b No. of eggs per g of stool (epg).

^c Figures in parentheses are the 95% confidence interval.

Fig. 2. Geometric mean number of *Schistosoma mansoni* eggs when infection or reinfection was detected, according to age at that time. The only statistically significant difference between the infected and reinfected was for those aged ≥ 25 years ($P = 0.043$).



Two studies in Kenya have reported a significant association between egg counts prior to treatment and after reinfection (2, 25), but no association between reinfection and pretreatment egg counts was found in another study in Kenya (23). In our study, a heavy infection (≥ 500 egg) was a predictor of faster and more frequent reinfection. This effect persisted when the data were controlled for age, sex, and calendar period. When stratified by age group, the risks of reinfection among those most heavily infected before treatment tended to be higher in all but one age category; this effect disappeared only among those aged ≥ 25 years. Although not significant, this result indicates that age (≥ 25 years) modifies the association between heavy egg counts and reinfection.

Population-based treatment in endemic areas can reduce the intensity of *S. mansoni* infection, and a concomitant decrease in morbidity due to schistosomiasis has been ascribed to this strategy (17, 22, 27, 28)^e Follow-up studies in endemic areas have also

shown that the intensity of *S. mansoni* infection after treatment is lower than that prior to treatment, which suggests that the treatment (or any factor associated with it) has a protective effect against heavy reinfections (10, 14, 17, 24). Comparison of *S. mansoni* egg counts in the infected and the reinfected subjects in the present study indicated that the number of eggs in both cohorts varied widely, but that the overall geometric mean number of eggs for the reinfected cohort was approximately half that for the infected cohort.

The results of the present study may have been affected to some extent by the following losses to follow-up; low sensitivity (because only one stool examination was carried out); and by excluding subjects who were still eliminating *S. mansoni* eggs or did not have a stool examination 8–12 months after treatment. Similar proportions of cases were lost to follow-up in each cohort, and both cohorts were also similar in age, sex and calendar period of entry to the study. Although losses to follow-up might have influenced the descriptive results, it is unlikely that they would have affected infection and reinfection cohorts to different extents, producing biased comparisons. The sensitivity of a single stool examination decreases with the prevalence and intensity of *S. mansoni* infection (7). In our study, adjustments for calendar period might have partially corrected the influence of low sensitivity caused by changes in the prevalence and intensity of infection. The therapeutic efficacy of oxamniquine in Brazil ranges from 65% to 72% for children and from 80% to 85% for adults (12, 13, 15, 22). In the present study the number of subjects still infected after treatment (77 of 373 treated (20.6%)) was within that expected due to the treatment inefficacy, but it cannot be excluded that some of these individuals were not reinfected. Both the reinfection cohort participants and non-participants were similar in age, sex, and period of entry to the study, but the pre-treatment intensity of infection among those who still eliminated eggs after treatment was higher than that among the cohort participants. The risk of reinfection for those who were heavily infected prior to treatment may have been underestimated in our study.

Our findings lead to the conclusions shown below.

- The incidences of *S. mansoni* infection and reinfection decreased in the study population, suggesting that changes in the transmission of schistosomiasis occurred during the control programme.
- For most of the aspects investigated, infection and reinfection patterns were similar, indicating that both are part of the same process.
- A heavy *S. mansoni* egg count before treatment

^e See footnote a, p. 198.

(≥ 500 epg) was a predictor of more rapid and frequent reinfection among under-25-year-olds.

- The overall intensity of reinfection was lower than that of infection.
- The risks of infection and reinfection varied more with age than with any other variable studied. The risks of infection and reinfection among individuals aged <20 years were 3 to 6 times greater than those among individuals aged ≥ 25 years, even after adjusting for confounders. This suggests the existence of a strong protective effect with increased age (owing to biological and/or environmental factors) for both infection and reinfection.

Acknowledgements

We thank Professor D. Bradley, Dr L.C. Rodrigues and Dr S. Barreto, for commenting on and reviewing the manuscript, and Mr R. Hayes for helpful advice.

The analysis of the data was carried out during a visiting research fellowship sponsored by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases at the Department of Epidemiology and Population Sciences, London School of Hygiene and Tropical Medicine, London, England.

Résumé

Treize ans de suivi de la lutte contre les mollusques et du traitement des infestations dans une région d'endémie de *Schistosoma mansoni* au Brésil: incidence de l'infestation et de la réinfestation

Une étude sur l'incidence de l'infestation et de la réinfestation par *Schistosoma mansoni* a été effectuée dans une région d'endémie du Brésil (Peri-Peri, Etat de Minas Gerais), où chimiothérapie et lutte contre les mollusques ont été mises en œuvre pendant 13 ans (1974–1987). Deux cohortes ont été suivies: la première comportait 584 sujets ne présentant aucun signe d'infestation au début de l'étude (cohorte d'infestation) et la seconde 296 personnes ayant été traitées et n'éliminant plus d'œufs 8 à 12 mois après (cohorte de réinfestation). L'incidence de l'infestation a diminué, passant de 7,5 pour 100 personnes-années en 1974–1977 à 3,6 pour 100 personnes-années en 1986–1987, de même que celle de la réinfestation qui est passée de 21,3 pour 100 personnes-années en 1974–1977 à 3,7 pour 100 personnes-années en 1986–1987. La période considérée, l'âge à risque et le sexe sont associés de

façon indépendante à l'infestation comme à la réinfestation, tandis qu'un nombre important d'œufs de *S. mansoni* avant le traitement (≥ 500 epg (œufs par gramme de selles)) est associé de façon indépendante à la réinfestation. La moyenne géométrique du nombre d'œufs après traitement dans la cohorte réinfestée (47,0 epg) est à peu près la moitié de celle observée dans la cohorte infestée (81,5 epg). L'âge à risque a été le facteur qui a eu le plus d'effet sur l'infestation et la réinfestation. Les proportions des taux d'infestation et de réinfestation chez les moins de 20 ans sont 3 à 6 fois plus élevées que chez les 25 ans et plus, même après ajustement des facteurs confondants. Cela laisse à penser qu'il existe un effet protecteur puissant (dû à des facteurs biologiques et/ou environnementaux) qui augmente avec l'âge pour l'infestation comme pour la réinfestation.

References

1. Armitage, P. & Berry, G. *Statistical methods in medical research*. Oxford, Blackwell Scientific Publications, 1987.
2. Bensted-Smith, R. et al. Evidence for predisposition of individual patients to reinfection with *Schistosoma mansoni* after treatment. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **81**: 651–654 (1985).
3. Breslow, N.E. & Day, N.E. *Statistical methods in cancer research: the analysis of cohort studies*. Lyon, International Agency for Research on Cancer, 1987 (IARC Scientific Publications No. 82).
4. Farooq, M. et al. The effect of area-wide snail control on the endemicity of bilharziasis in Egypt. *Bulletin of the World Health Organization*, **35**: 369–375 (1966).
5. Holford, T.R. The analysis of rates and of survivorship using log-linear models. *Biometrics*, **36**: 229–306 (1980).
6. Hollander, M. & Wolfe, D.A. *Nonparametric statistical methods*. New York, Wiley, 1973.
7. Jordan, P. & Webbe, G. *Schistosomiasis epidemiology, treatment and control*. London, Heinemann, 1981.
8. Jordan, P. et al. Evaluation of chemotherapy in the control of *Schistosoma mansoni* in Marquis Valley, Saint Lucia. *American journal of tropical medicine and hygiene*, **31**: 103–110 (1982).
9. Katz, N. et al. A simple device for quantitative stool thick-smear technique in schistosomiasis mansoni. *Revista do Instituto de Medicina Tropical de São Paulo*, **14**: 397–400 (1972).
10. Katz, N. et al. Re-infection of patients in schistosomiasis mansoni endemic areas after specific treatment. I. Influence of age and worm burden. *Revista do Instituto de Medicina Tropical de São Paulo*, **20**: 273–314 (1978).
11. Katz, N. [Experiences with large-scale chemothera-

- py to control schistosomiasis in Brazil]. *Revista do Instituto de Medicina Tropical de São Paulo*, **22**: 40–51 (1980) (in Portuguese).
12. **Katz, N. et al.** [Control of schistosomiasis in Peri-Peri (Minas Gerais) by means of repeat clinical treatment and application of molluscicides]. *Revista do Instituto de Medicina Tropical de São Paulo*, **22**(suppl. 4): 203–211 (1980) (in Portuguese).
 13. **Katz, N. & Rocha, R.S.** Double-blind clinical trial comparing praziquantel with oxamniquine in schistosomiasis mansoni. *Revista do Instituto de Medicina Tropical de São Paulo*, **24**: 310–314 (1982).
 14. **Kloetzel, K.** A rationale for the treatment of schistosomiasis mansoni, even when reinfection is expected. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **61**: 609–610 (1967).
 15. **Lambertucci, J.R. et al.** A double-blind trial with oxamniquine in chronic schistosomiasis mansoni. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **76**: 751–755 (1982).
 16. **Lima e Costa, M.F.F. et al.** Water-contact patterns and socioeconomic variables in the epidemiology of schistosomiasis mansoni in an endemic area in Brazil. *Bulletin of the World Health Organization*, **65**: 57–66 (1987).
 17. **Mahmoud, A.A.F.** Effect of targeted mass treatment on intensity of infection and morbidity in schistosomiasis mansoni. *Lancet*, **1**: 849–851 (1983).
 18. **Miller, Jr, R.G. et al.** *Survival analysis*. Wiley, 1981.
 19. **Prentice, M.A. et al.** Reduction in transmission of *Schistosoma mansoni* by a four-year focal mollusciciding programme against *Biomphalaria glabrata* in Saint Lucia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **75**: 789–798 (1981).
 20. **SAS Institute.** *SAS technical report: P179 additional SAS/Stat Procedures. Release 6.03*. Cary, 1988.
 21. **Statistics and Epidemiology Research. EGRET: Upgrade document: changes from previous versions**. USA, 1990.
 22. **Sleigh, A.C.** Manson's schistosomiasis in Brazil: 11-year evaluation of successful disease control with oxamniquine. *Lancet*, **1**: 635–637 (1986).
 23. **Sturrock, R.F. et al.** Observations on possible immunity to reinfection among Kenyan schoolchildren after treatment for *Schistosoma mansoni*. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **75**: 363–371 (1983).
 24. **Sturrock, R.F. et al.** Immunity after treatment of human schistosomiasis mansoni. III. Long-term effects of treatment and retreatment. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **81**: 303–314 (1987).
 25. **Tingley, G.A. et al.** Predisposition of humans to infection with *Schistosoma mansoni*: evidence from the reinfection of individuals following chemotherapy. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **82**: 448–452 (1988).
 26. **Wilkins, H.A.** Reinfection after treatment of schistosome infections. *Parasitology today*, **5**: 83–88 (1989).
 27. WHO Technical Report Series No. 738, 1985 (*The control of schistosomiasis: report of a WHO-Expert Committee*).
 28. WHO Technical Report Series No. 830, 1993 (*The control of schistosomiasis: second report of the WHO Expert Committee*).