Mem. Inst. Oswaldo Cruz, Rio de Janeiro, Vol. *87*, Suppl. IV, 175-182, 1992

CROSS-SECTIONAL AND EVOLUTIVE STUDIES OF SCHISTOSOMIASIS MANSONI IN UNTREATED AND MASS TREATED ENDEMIC AREAS IN THE SOUTHEAST AND NORTHEAST OF BRAZIL

JOSÉ RODRIGUES COURA; MARIA JOSÉ CONCEIÇÃO*; MOZART LIMA DOS SANTOS*; ZÉLIA GOES DE MENDONÇA** & RAIMUNDO NONATO MARTINS CUTRIM***

Departamento de Medicina Tropical, Instituto Oswaldo Cruz, Av. Brasil 4365, 21045-900 Rio de Janeiro, RJ, Brasil *Universidade Federal do Rio de Janeiro **Universidade Federal da Paraíba ***Universidade Federal do Maranhão

Cross-sectional and evolutive studies on schistosomiasis mansoni were carried out before and after mass treatment in the endemic areas of Capitão Andrade and Padre Paraiso, state of Minas Gerais, Riachuelo, state of Sergipe, Alhandra, state of Paraiba, and Aliança, Alegre and Coroatá, lowland of the state of Maranhão, Brazil, in the last eighteen years.

The studies included clinical and fecal examination by the Kato-Katz quantitative technique, skin test for Schistosoma mansoni *infection, evaluation of man-water contact and other epidemiological investigations such as infection rate and dynamic of the snail population.*

Results showed: (1) Higher prevalence of S. mansoni *infection, greater egg load elimination and higher and earlier morbidity of the chronic forms of the disease in the southeast areas of Capitão Andrade and Padre Paraiso; (2) The incidence of hepatosplenic form is higher in some family clusters, in whites and mulattos in all the endemic areas but develop earlier in the southeast; (3) The prevalence and morbity of schistosomiasis are decreasing both in the mass treated northeast and in the untreated southeast areas; (4) The mass treatment reduces rapidily the prevalence of the infection and the morbidity of the disease but can not control it because of the frequent reinfections due to the intensity of man-water contact.*

Key words: schistosomiasis mansoni – mass treatment – evolutive studies

The evolutive pattern of schistosomiasis mansoni in Brazil is not yet completely defined. Cross-sectional and evolutive studies in endemic areas and experimental investigations have shown that the principal risk factors for development of the infection by *Schistosoma mansoni* towards the severest forms of the disease are related to: (1) Intensity of primary infection and frequency of reinfections; (2) Association with malnutrition, alcoholism and virus hepatitis and (3) Familial determinants linked to race and possibly to sex (Coura et al., 1982, 1983, 1984; Conceição & Coura, 1978, 1979, Menezes & Coura, 1979; Santos & Coura, 1986; Katz & Zicker, 1975; Kloetzel, 1963a, 1964; Prata & Bina, 1968; Prata & Schroeder, 1967; Cardoso, 1953; Prata, 1988; Tavares-Neto & Prata, 1989a, b, 1990).

Studies carried out in some endemic areas in Brazil have shown that the specific chemotherapy for schistosomiasis either in individual or in mass treatment reduces the severity of its clinical forms and also that mass treatment can temporarily reduce the prevalence of the infection (Kloetzel, 1963b; Bina, 1977; Santos, 1978; Katz et al., 1978, 1980). However, because of frequent reinfections in endemic areas, mass treatment, even when repeated several times can not completely control schistosomiasis (Katz et al., 1978; Coura et al., 1980, 1987; Prata et al., 1980; Santos & Coura, 1986; Cutrim, 1987).

This work aims to revise the evolution of schistosomiasis in some mass treated and untreated endemic areas we have studied in the southeast and northeast of Brazil during the last eighteen years.

METHODOLOGY

One to several cross-sectional studies for schistosomiasis were carried out in some en-

demic areas in the states of Minas Gerais, Sergipe, Paraíba and Maranhão, before and after mass treatment. The sectional studies included clinical and fecal examination, skin test for *S. mansoni* infection, evaluation of man-water contact and other epidemiological investigations such as infection rate and dynamics of the snail population.

Areas, populations and procedures – (1) Capitão Andrade, Minas Gerais – Population initially studied, 1,234 persons. Cros-sectional studies in 1973, 1974, 1979 and 1983, before mass treatment. Mass treatment in 1983 and post treatment evaluation in 1984 and 1987. (2) Padre Paraiso, Minas Gerais – Population initially studied, 1,709 persons. Cross-sectional studies in a representative sample of the population in 1976, followed by treatment of a selected group of 436 infected patients compared with a placebo control group of 427 patients. Follow-up in the first year at 4, 8 and 12 months and ten year later (1987). (3) Riachuelo, Sergipe – Population studied, 850 persons by a cross-sectional of this sample in 1977. No follow up until to now. (4) Alhandra, Paraíba – Population initially studied, 915. Cross-sectional studies in 1979, after one mass treatment and in 1982 and 1987 after several mass treatments. (5) Aliança, Alegre and Coroatá in the western lowland of Maranhão – Population studied, 829. Follow-up from 1977 to 1987 after 13 mass treatments in Aliança, 11 in Coroatá and 4 in Alegre.

All the endemic areas mentioned above were initially represented in an individual map with residences, public and commercial buildings, rivers, lakes and other water collections. The principal sites of man-water contact and the stations for snail captures were also represented in the map.

The residences were numbered and the residents were registered as to name, age, sex, race and family relations. The social and economic condictions of the family were also registered. The man water contact was individually identified as frequent, very frequent and non-existent. Through an anamnesis the principal symptons and signs of schistosomiasis were registered: diarrhea, constipation, hematemesis, melena, hepatosplenomegaly, etc.

The clinical forms were identified according to the classification of Pessoa & Barros (1953) modified by Barbosa (1966), in three types: (I) Schistosomiasis infection: with or without intestinal symptoms which, if present, were moderate and not necessarily atributed to the disease. (II) Schistosomiasis-disease (Hepatointestinal): frequent intestinal symptoms, dysenteric diarrhea and hepatomegaly. (III) Schistosomiasis-disease (Hepatosplenic): very frequent intestinal symptoms, dysentery and hepatosplenomegaly with or without hematemesis and melena.

The fecal examination was performed by the Kato quantitative method modified by Katz et al. (1972) and the skin test was carried out by the Kagan et al. technique (1961), injecting 0.05 ml of *S. mansoni* antigen intradermically in the left ventral forearm, with reaction evaluated fifteen minutes later.

In Padre Paraíso, Riachuelo and Alhandra, a sample of 25% of the population was studied and in Capitão Andrade, Aliança. Alegre and Coroatá the entire population available was investigated. The map (Fig. 1) shows the localization of the areas studied.

Fig. 1: localization of the endemic areas.

Mass or group treatment were made with oxamniquine, single doses, 12.5 mg/kg for adults and 15/20 mg/kg for children.

RESULTS

A total of 5,537 persons were investigated, 1,234 in Capitão Andrade, 1,709 in Padre Paraíso, 850 in Riachuelo, 915 in Alhandra and 829 in the western lowland of Maranhão

TABLE I

Prevalence of schistosomiasis by age group in four endemic areas, determined by fecal examination and skin test (ST) in southeast and northeast Brazil

Age groups (years)	Southeast				Northeast			
	Capitão Andrade (Área 1)		Padre Paraíso (Área 2)		Riachuelo (Área 3)		Alhandra (Área 4)	
	Feces (%)	ST (%)	Feces (%)	ST (%)	Feces (%)	ST (%)	Feces (%)	ST (%)
0 – 5	16.1	25.6	14.2	18.0	5.6	10.0	6.6	5.0
6 – 10	59.1	86.2	64.7	69.5	41.5	52.1	32.1	35.7
11 – 15	73.6	85.1	86.9	88.2	77.9	77.1	64.0	52.0
16 – 20	83.4	100.0	90.3	85.1	67.9	95.2	60.0	78.2
21 – 30	83.9	70.3	80.6	97.0	73.8	90.9	78.0	97.5
31 – 40	68.8	94.4	72.3	92.0	78.9	88.8	70.3	96.2
41 – 50	75.8	96.1	67.2	91.3	80.3	93.7	50.0	95.4
+ 50	57.2	81.8	56.2	90.4	48.3	94.1	65.4	87.5
Average	60.8	80.8	63.1	78.9	50.5	75.2	46.6	59.6

TABLE II

Prevalence of schistosomiasis by age group in three endemic areas, determined by fecal examination and skin test (ST) in western lowland of Maranhão, Brazil

Age group (years)	Western lowland of Maranhão					
	Aliança (Área 5a)		Alegre (Área 5b)		Coroatá (Área 5c)	
	Feces (%)	ST (%)	Feces (%)	ST (%)	Feces (%)	ST (%)
0 – 5	7.1	4.7	1.5	0.0	0.0	4.4
6 – 10	4.0	53.0	13.1	11.4	3.1	56.2
11 – 15	3.7	88.8	23.1	52.9	29.6	85.1
16 – 20	8.6	91.3	32.6	63.6	21.4	78.5
21 – 30	9.5	95.2	28.8	65.9	23.5	76.4
31 – 40	15.3	84.6	27.5	82.1	30.0	80.0
41 – 50	10.7	100.0	25.0	69.4	0.0	77.7
+ 50	5.0	90.0	28.8	69.2	18.7	81.2
Average	7.4	69.9	21.0	46.2	12.9	55.8

– 256 in Aliança, 403 in Alegre and 170 in Coroatá.

Cross-sectional studies – The prevalence of *S. mansoni* determined by fecal examination and by skin test in Capitão Andrade, Padre Paraíso, Riachuelo and Alhandra is represented in Table I, and the one of Aliança, Alegre and Coroatá in Table II. As we can observe the prevalence of the infection in children, younger than 10 years, was higher in the southeast areas, indicating a stronger pressure of infection in these areas.

Schistosoma mansoni egg load elimination in the studied population in Capitão Andrade, Padre Paraíso, Riachuelo and Alhandra can be seen in Table III and that in Aliança, Alegre and Coroatá in Table IV. The mean egg load was higher in the population of the southeast areas, confirming the stronger pressure of infection mentioned above.

The clinical forms of schistosomiasis in Capitão Andrade, Padre Paraíso, Riachuelo and Alhandra are represented in Fig. 2 and that ones in Aliança, Alegre and Coroatá in Fig. 3. As we can observe that the severest forms of the disease occurred in the endemic areas of the southeast, which correlate with the prevalence of the infection and with the egg load elimination. The prevalence of the hepato-

TABLE III

Median of number of eggs of *Schistosoma mansoni* per g of feces by age group determined by Kato-Katz technique in four endemic areas in southeast and northeast, Brazil

Age groups (years)	Southeast		Northeast	
	Capitão Andrade (Área 1)	Padre Paraiso (Área 2)	Riachuelo (Área 3)	Alhandra (Área 4)
	Eggs/g feces	Eggs/g feces	Eggs/g feces	Eggs/g feces
0 – 5	138	46	46	72
6 – 10	253	333	69	192
11 – 15	391	782	69	168
16 – 20	322	874	115	180
21 – 30	207	299	92	408
31 – 40	264	333	92	276
41 – 50	207	149	69	180
+ 50	172	138	69	216
Average	244	391	77.6	211

TABLE IV

Median of number of eggs of *Schistosoma mansoni* per g of feces by age group, determined by Kato-Katz technique in the western lowland of Maranhão, Brazil

Age groups (years)	Western lowland of Maranhão		
	Aliança (Área 5a)	Alegre (Área 5b)	Coroatá (Área 5c)
	Eggs/g feces	Eggs/g feces	Eggs/g feces
0 – 5	312	24	0
6 – 10	36	50	24
11 – 15	24	43	132
16 – 20	168	219	48
21 – 30	60	63	90
31 – 40	48	56	585
41 – 50	60	226	0
+ 50	48	43	48
Average	94.5	90.5	115.8

splenic form was 5.8% in Capitão Andrade, 4.4% in Padre Paraíso and 2.4% in Riachuelo and in Alhandra. In Aliança and Coroatá the hepatosplenic form was not observed. Unexplainingly 7.6% of hepatosplenic forms was found in Alegre. All the 15 patients with hepatosplenic form found in this locality were older than 20 years, males, hunters or fishermen with very frequent water contact that could perhaps explain this clinical form.

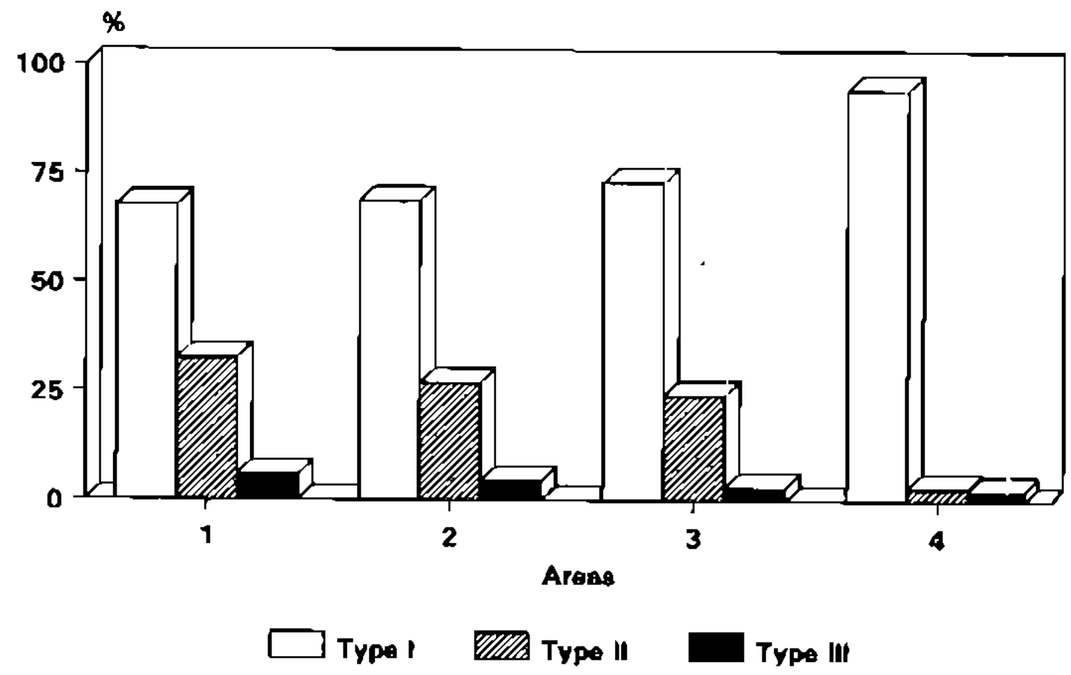

Fig. 2: clinical forms of schistosomiasis.

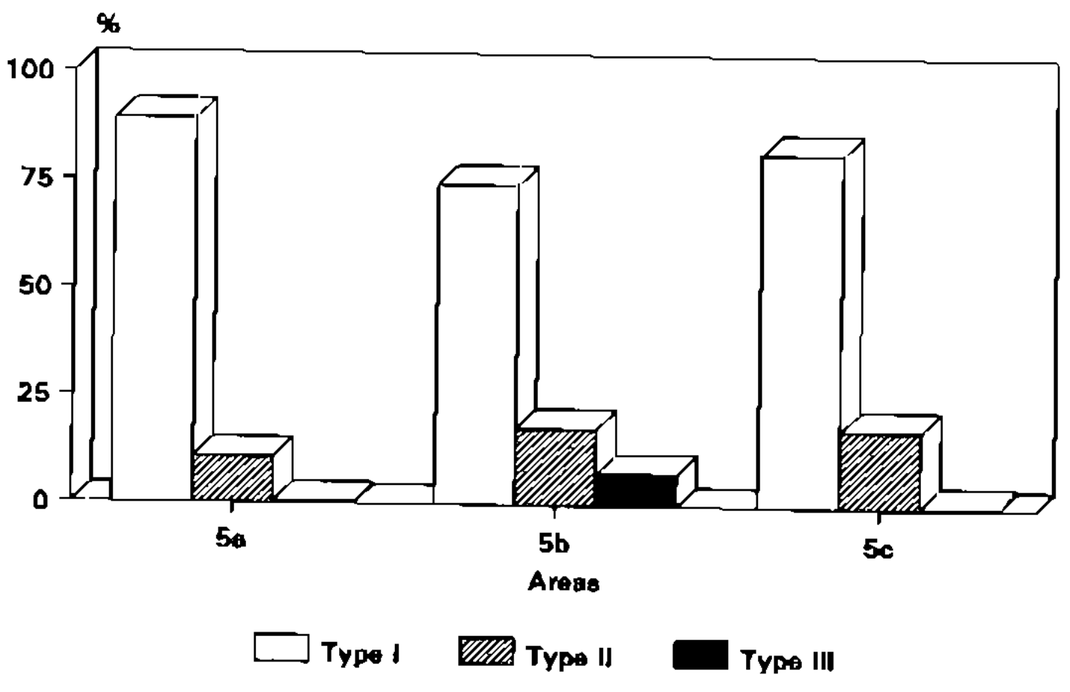

Fig. 3: clinical forms of schistosomiasis.

There was a direct correlation between the intensity of man-water contact and the prevalence of the infection, egg load elimination and severity of clinical forms, however, there was no correlation between infection rate of snails with prevalence, egg load or clinical form of the human disease. The snail found in Capitão Andrade, Padre Paraíso, Riachuelo, Alhandra, Aliança and Alegre were *Biomphalaria glabrata* and in Coroatá only *B. straminea* was found.

The great majority of hepatosplenic forms was observed in whites and mulattos; we have rarely seen hepatosplenic forms in blacks. On the other hand hepatosplenic forms where more frequent in men than women, except in Alhandra. In the southeast areas the majority of hepatosplenic forms were observed in the second decade of life while in the Northeast it occured later, from the third decade on.

Evolutive studies – (1) Capitão Andrade: the prevalence of *S. mansoni* infection without any mass treatment or other intervention measure dropped spontaneously from 60.8% in 1973 to 36.2% in 1983. In this last year we applied a mass treatment in the population and

one year later (1984) the prevalence was 16.9%. A new evaluation in 1987 showed a prevalence of 19.5% with a tendency to rise, as we can see in Fig. 4. The incidence (new cases) in this area from 1973 to 1983 was 40.3%.

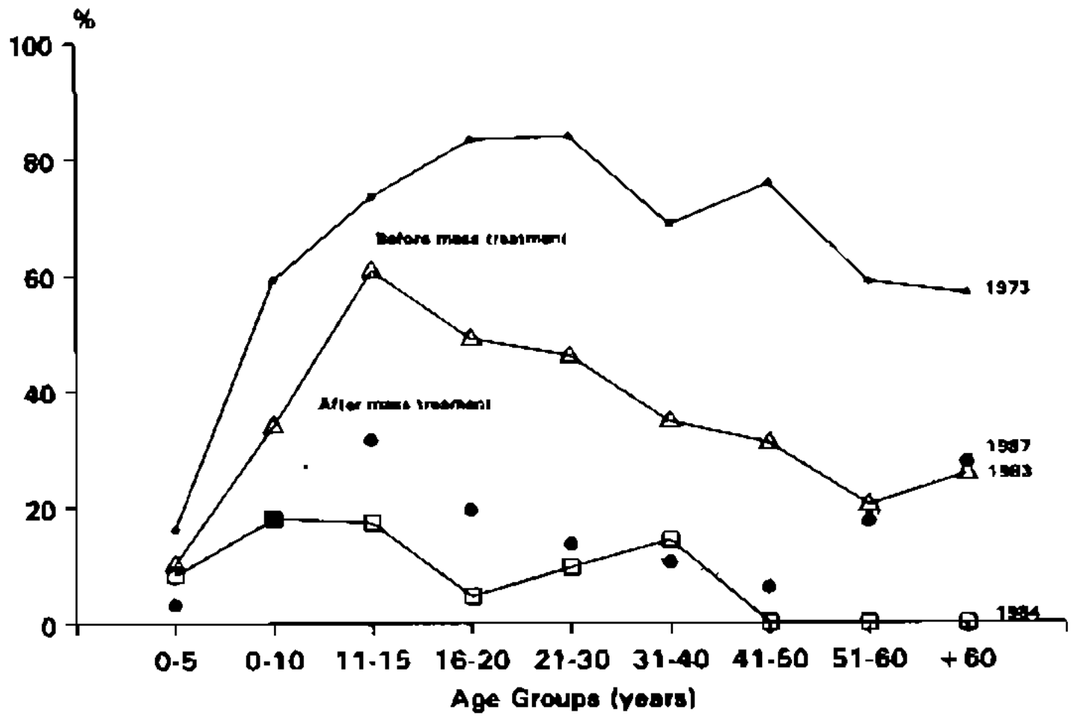

Fig. 4: prevalence of *Schistosoma mansoni* infection in Capitão Andrade, Minas Gerais, Brazil, before and after mass treatment.

Median egg load elimination in relation to clinical forms, before and after mass treatment is shown in Table V. As we can see, there was an important drop of the egg load even before the mass treatment (1973-1983) and also after treatment (1984-1987) in all clinical forms. There was no important changes in the clinical forms before treatment, but after that there was a significative reduction of the severest forms types II and III (Table VI). (2) Padre Paraíso: the prevalence of *S. mansoni* infection in the population of Padre Paraíso fell from 63.1% in 1976 to 37.7% in 1987 (Fig. 5). The group of patients treated in 1976 had a lower prevalence in 1987 (26.8%).

Median of egg load elimination in 1976 was 391 eggs per g of feces which dropped to 72 in 1987. There was also a significative reduction of the severest clinical forms, types II and III (Table VII). (3) Riachuelo: no follow-up study was performed in Riachuelo up to now. (4) Alhandra: a six years follow-up carried out in Alhandra from 1979-1985, after several mass treatments showed a reduction of prevalence from 46.6% to 25.8%. The incidence (new cases) of *S. mansoni* in this periodo was 29.8%.

Mean egg load elimination was 211 eggs per g of feces in 1979 dropping to 49 in 1985. The clinical forms in 1979 were 94.4% type I, 3%

TABLE V

Egg load median pre- and post-treatment according to the schistosomiasis clinical forms. Capitão Andrade, Minas Gerais, Brazil, 1973-1987

Clinical forms	Egg load median		
	Pre-treatment		Post-treatment
	1973	1983	1987
Type I	207	72	48
Type II	345	120	72
Type III	506	240	96

TABLE VI

Prevalence of clinical forms of schistosomiasis pre- and post-treatment in Capitão Andrade, Minas Gerais, Brazil, 1973-1987

Clinical forms	Pre-treatment		Post-treatment
	1973 %	1983 %	1987 %
Type I	67.7	66.7	73.4
Type II	32.5	27.0	22.7
Type III	5.8	6.3	3.9

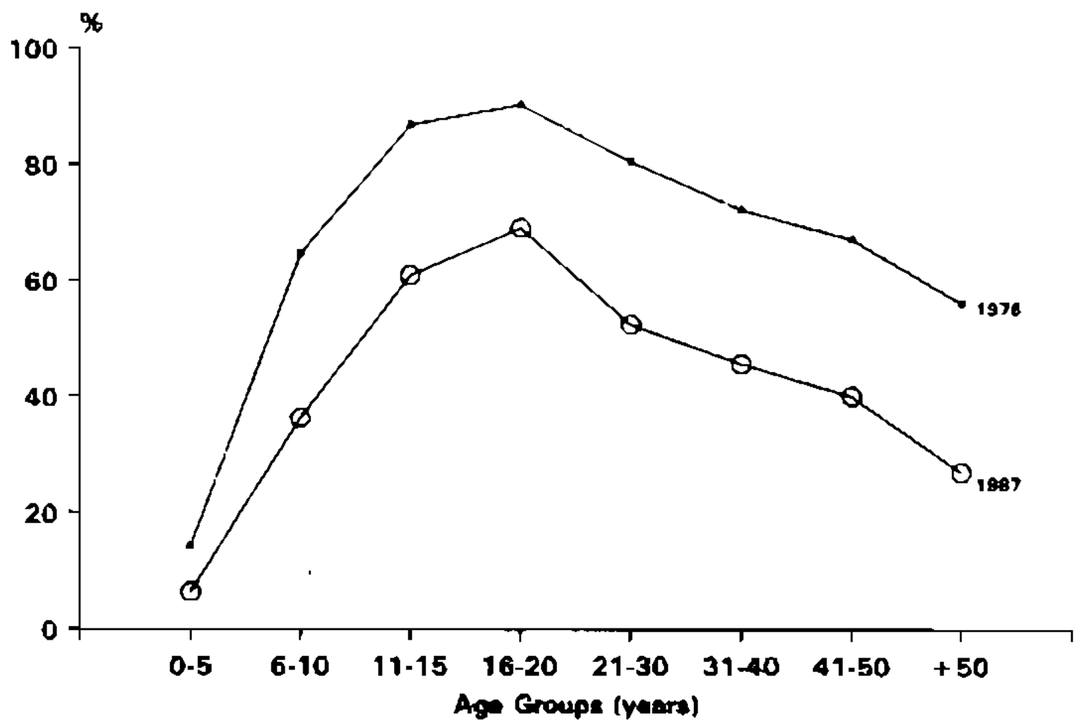

Fig. 5: prevalence of *Schistosoma mansoni* infection in Padre Paraíso, Minas Gerais, Brazil, 1976-1987.

TABLE VII

Prevalence of clinical forms of schistosomiasis in Padre Paraíso, Minas Gerais, Brazil, 1977-1987

Clinical forms	Prevalence %	
	1977	1987
Type I	68.7	87.2
Type II	26.9	9.7
Type III	4.4	3.3

type II and 2.4% type III. From 71 new infected cases seen in 1985, 88.7% had type I clinical form, 11.2% type II and none the hepatosplenic type III. (5) Western lowland of Maranhão: after 13 mass treatments in Aliança from 1977 to 1987 the prevalence of *S. mansoni* infection was reduced from 57.9% to 7.4%. In Coroatá with 11 mass treatments in the same period, the reduction of prevalence was from 69.2% to 12.9% and in Alegre, with only four mass treatments in the same period there was pratically no prevalence reduction: 22.9% to 21%.

There are no informations about the egg load elimination and distribution of clinical forms of schistosomiasis in the areas before the mass treatment. In 1987 the egg load elimination was 94.5 eggs per g of feces in the population of Aliança, 90.5 in Alegre and 115.8 in Coroatá (Table IV). The distribution of the clinical forms in the localities is shown in Table VIII. The clinical forms type II was 10.8% in Aliança, 17.9% in Alegre and 18% in Coroatá. The hepatosplenic (type III) form was not seen in Aliança and Coroatá but unexplainingly was 7.6% in Alegre.

TABLE VIII

Clinical forms of schistosomiasis in three endemic areas of Maranhão, northeastern Brazil, 1987

Clinical forms	Aliança %	Alegre %	Coroatá %
Type I	89.1	74.3	81.9
Type II	17.9	10.8	18.0
Type III	0.0	7.6	0.0

DISCUSSION

As we have shown in Table I there was an increase of the prevalence of *S. mansoni* infection both in the southeast and in the northeast areas from the first to second decade of life up to the age of 20. This fact has been observed also by other authors in Brazil (Kloetzel, 1963a; Barbosa, 1966; Prata & Bina, 1968; Katz et al., 1978) and elsewhere. In part this is thought to be due to the slow development of protective antibodies of the IgE class (Capron et al., 1977; Colley, 1987; Hagan, 1991; Dunne et al., 1991) and also to the earlier development of blocking antibodies to IgM, IgG2 and IgG4 (Damian, 1987; Dunne et al., 1987; Hagan, 1991) regulated, respectively, by secretion or suppresion of the related cytokines.

On the other hand, this work shows that the prevalence of *S. mansoni* infection in children younger than 10 was higher in the southeast than in the northeast areas, this being interpreted from the epidemiological point of view as a stronger pressure of infection in the southeast areas. However, one can argue also if the level of maternal and children protective antibodies or suppressor antibodies factors are not different from one region to another.

The median egg load elimination in our observations (Table III) was also higher in the shoutheast than in the northeast areas and there was a direct correlation between the intensity of egg burden and the severity of the clinical forms. Therefore we concluded that the egg load is one important factor, although not unique, for the severity of the disease. Familial concentration of hepatosplenic cases and the greater incidence of these cases in whites and in patients of the group A of ABO system and in sons and daughters of mother with the hepatosplenic form, suggest a polygenic inheritance for the severest form o schistosomiasis (Cardoso, 1953; Prata & Schroeder, 1967; Conceição & Coura, 1979; Tavares-Neto & Prata, 1980, 1989a, b).

The evolutive studies performed in Capitão Andrade from 1973 to 1983, before mass treatment, showed spontaneous reduction of *S. mansoni* infection as well as of the egg burden, however there was no important change in the clinical form of the disease. This fact had been also observed by Barbosa (1975) in northeast Brazil. After the mass treatment there was an abrupt reduction of the prevalence of the infection and also in the egg load; a moderate reduction of the severity of the clinical forms was also noted. The same was observed when a group of patients treated with oxamniquine was compared with other submitted to a placebo in Padre Paraíso (Santos & Coura, 1986).

The incidence of *S. mansoni* reinfection was around 4 to 5% a year both in mass treated and in the untread areas.

Our final conclusions are: (1) The prevalence of the infection, the egg load and the morbidity of schistosomiasis are higher and develop earlier in the Southeast endemic areas; (2) The incidence of hepatosplenic form is higher in some family clusters, in whites and mulattos and it develops earlier in the

southeast areas; (3) The prevalence and morbidity of schistosomiasis are decreasing both in the mass treated northeast and in the untreated southeast; (4) The mass treatment reduces rapidily the prevalence of the infection and the morbidity of the disease but can not control it because of the frequent reinfections.

ACKNOWLEDGEMENTS

To Dr Leonidas de Mello Deane for the revision of the language.

REFERENCES

BARBOSA, F. A. S., 1966. Morbidade da esquistossomose. *Rev. Bras. Malariol. D. Trop., Número Especial, 1:* 3-159.

BARBOSA, F. S., 1975. Control of Schistosomiasis: A perspective. *Brasília Médica, 11:* 93-100.

BINA, J. C., 1977. *Influência da terapêutica específica na evolução da esquistossomose mansoni.* Thesis, Univ. Fed. Bahia, 97 p.

CAPRON, M.; CAMUS, D.; CARLIER, Y.; FIGUEIREDO, J. F. M. & CAPRON, A., 1977. Immunological studies in human schistosomiasis. II. Antibodies cytotoxic for *Schistosoma mansoni* schistosomules. *Am. J. Trop. Med. Hyg., 26:* 248-253.

CARDOSO, W., 1953. A esquistossomose mansônica no negro. *Med. Cirurg. Farm., 202/203:* 89-95.

COLLEY, D. G., 1987. Dynamics of the human immune response to schistosome, p. 101-123. In R. A. Thompson *Recent advances in clinical immunology,* Vol. 1. Churchill Livingstone, London.

CONCEIÇÃO, M. J. & COURA, J. R., 1978. Morbidade da esquistossomose mansoni em uma comunidade rural de Minas Gerais. *Rev. Soc. Bras. Med. Trop., 12:* 97-103.

CONCEIÇÃO, M. J. & COURA, J. R., 1979. Ocorrência familiar de esplenomegalia esquistossomótica em uma área rural de Minas Gerais. *Rev. Soc. Bras. Med. Trop., 13:* 17-20.

COURA, J. R.; ARGENTO, C. A.; CONCEIÇÃO, M. J.; LEWIS, E. M.; SANTOS, M. L. & MAGALHÃES, P., 1980. Experiências de campo com oxamniquine oral no tratamento da esquistossomose mansoni. *Rev. Inst. Med. trop. S. Paulo, 22* (Suppl. 4): 77-84.

COURA, J. R.; CONCEIÇÃO, M. J.; MENEZES, A. P.; SANTOS, M. L. & MENDONÇA, M. Z. G., 1983. Morbidade da esquistossomose mansoni no Brasil. II. Estudo em quatro áreas de campo nos Estados de Minas Gerais, Sergipe e Paraíba. *Mem. Inst. Oswaldo Cruz, 78:* 1-11.

COURA, J. R.; CONCEIÇÃO, M. J. & PEREIRA, J. B., 1984. Morbidade da esquistossomose mansoni no Brasil. III. Estudo evolutivo em uma área endêmica no periodo de dez anos. *Mem. Inst. Oswaldo Cruz, 79:* 447-453.

COURA, J. R.; MENDONÇA, M. Z. G. & MADRUGA, J. P., 1987. Tentativa de avaliação do Programa Especial de Controle da Esquistossomose (PECE) no Estado da Paraíba, Brasil. *Rev. Soc. Bras. Med. Trop., 20:* 67-76.

COURA, J. R.; QUEIROZ, G. C.; FLORÊNCIO, C. G.; ARGENTO, C. A.; COUTINHO, S. G.; FIGUEIREDO, N.; WANKE, B. & CAMILLO-COURA, L., 1982. Morbidade da esquistossomose mansoni no Brasil. I. Estudo de 4.652 casos observados no Rio de Janeiro de 1960 a 1979. *Mem. Inst. Oswaldo Cruz, 77:* 69-88.

CUTRIM, R. N. M., 1987. *Aspectos clínicos-epidemiológicos da esquistossomose mansoni em três localidades da Baixada Ocidental Maranhense.* Thesis. Instituto Oswaldo Cruz, 107 p.

DAMIAN, R. T., 1987. The exploitation of host immune responses by parasites. *J. Parasitology, 73:* 3-13.

DUNNE, D. W.; BUTTERWORTH, A. E.; FULFORD, A. J. C.; OUMA, J. & STURROCK, R. F., 1991. Human IgE responses to *Schistosoma mansoni* and reinfection after treatment. Abstract. 15, Intern. Symp. on Schistosomiasis, Recife, Brazil, 20-25 Oct.

DUNNE, D. W.; FULFORD, A. J. D.; BUTTERWORTH, A. E.; KOECH, D. & OUMA, J. A., 1987. Human antibody response to *Schistosoma mansoni:* Does antigen directed, isotype restriction result in the production of blocking antibodies? *Mem. Inst. Oswaldo Cruz, 82* (Suppl. IV): 101-104.

HAGAN, P., 1991. Recent advances on immunity to human schistosomiasis. Abstract. 14, Intern. Symp. on Schistosomiasis, Recife, Brasil.

KAGAN, I. G.; PELLEGRINO, J. & MEMORIA, J. M. P., 1961. Studies on standartization of intradermal test for the diagnosis of Bilharzias. *Amer. J. Trop. Med. Hyg., 10:* 200-207.

KATZ, N.; CHAVES, A. & PELLEGRINO, J., 1972. A simple device for quantitative stool thick-smear technique in schistosomiasis mansoni. *Rev. Inst. Med. Trop. S. Paulo, 14:* 397-400.

KATZ, N.; ROCHA, R. S. & PEREIRA, J. P., 1980. Schistosomiasis control in Peri-Peri (Minas Gerais, Brazil) by repeated clinical treatment and molluscicide application. *Rev. Inst. Med. Trop. S. Paulo, 22* (Suppl. 4): 84-93.

KATZ, N. & ZICKER, F., 1975. Correlation between symptomatology and intensity of *Schistosoma mansoni* infection in inhabitants from endemic areas in Minas Gerais State, Brazil. *Brasilia Médica, 11:* 55-59.

KATZ, N.; ZICKER, F.; ROCHA, R. S. & OLIVEIRA, V. B., 1978. Reinfection of patients in a schistosomiasis endemic area after specific treatment. I. Influence of age and worn burden. *Rev. Inst. Med. Trop. S. Paulo, 20:* 273-278.

KLOETZEL, K., 1963a. Some quantitative aspects of diagnosis and epidemiology in schistosomiasis mansoni. *Am. J. Trop. Med. Hyg., 12:* 334-347.

KLOETZEL, K., 1963b. Sobre a conveniência da quimioterapia em população em contínuo contacto com os focos (Nota prévia). *Rev. Inst. Med. Trop. S. Paulo, 5:* 106-110.

KLOETZEL, K., 1964. Natural history and prognosis of splenomegaly in schistosomiasis mansoni. *Am. J. Trop. Med. Hyg., 13:* 541-544.

MENEZES, A. P. & COURA, J. R., 1979. Estudo seccional sobre a esquistossomose mansônica no município de Riachuelo, Estado de Sergipe. *Rev. Soc. Bras. Med. Trop., 13:* 1-15.

PESSOA, S. B. & BARROS, P. R., 1953. Notas sobre a

epidemiologia da esquistossomose mansônica no Estado de Sergipe. *Rev. Med. Circ. S. Paulo, 13:* 147-154.

PRATA, A., 1988. O papel da consangüinidade na esquistossomose hepatosplênica em certas áreas endêmicas. Editorial. *Rev. Soc. Bras. Med. Trop., 21:* 45-46.

PRATA, A. & BINA. J. C., 1968. Development of hepatosplenic form of schistosomiasis (A study of 20 patients observed during 5 year period). *Gaz. Med. Bahia, 68:* 49-60.

PRATA, A.; BINA, J. C.; BARRETO, A. C. & ALECRIM, M. G., 1980. Attempt to control the schistosomiasis transmission by oxamniquine in an hyperendemic locality. *Rev. Inst. Med. Trop. S. Paulo, 22* (Suppl. 4): 65-72.

PRATA, A. & SCHROEDER, S., 1967. A comparison of whites an negroes infected with *Schistosoma mansoni* in a hyperendemic area. *Gaz. Med. Bahia, 67:* 93-98.

SANTOS, M. L., 1978. *Esquistossomose mansoni. Estudo da morbidade e interferência da terapêutica específica em uma área endêmica*. Thesis, Univ. Fed. Rio de Janeiro, 97 p.

SANTOS, M. L. & COURA, J. R., 1986. Morbidade da esquistossomose mansoni no Brasil. IV. Evolução em pacientes tratados e seus controles. *Mem. Inst. Oswaldo Cruz, 81:* 53-60.

TAVARES-NETO, J. & PRATA, A., 1989a. Family ocorrence of schistosomal hepatosplenomegaly and maternal effect. *Rev. Soc. Bras. Med. Trop., 22:* 13-18.

TAVARES-NETO, J. & PRATA, A., 1989b. Coeficiente de endocruzamento em portadores de esquistossomose mansônica. *Rev. Soc. Bras. Med. Trop., 22:* 45-49.

TAVARES-NETO, J. & PRATA, A., 1990. Forma hepatosplênica da esquistossomose mansônica em relação à composição racial e ao nível sócio-econômico, em Catolandia, Bahia. *Rev. Soc. Bras. Med. Trop., 23:* 37-42.