The Role of Wild Rodents in the Transmission of *Schistosoma mansoni* in Brazil

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1. Introduction

The control of schistosomiasis still represents an important challenge for public health services around the world. Despite the success of schistosomiasis control programs in certain regions in reducing the prevalence and the intensity of infection, the global estimation of human cases has not changed. Schistosomiasis is an expanding, chronic parasitosis that affects about 200 million people in the world, and about 700 million people live in endemic areas (Who, 2010).

In Brazil, where this endemicity is caused only by *Schistosoma mansoni*, morbidity control has been favored by the use of Oxaminiquine and Praziquantel (Barbosa et al., 2008; Coura & Amaral, 2004; Lambertucci et al., 2000; TDR, 2005) and by an increase in sanitary sewer availability and medical assistance in the past few decades (Brasil, 2009). However, schistosomiasis still affects millions of people in Brazil (Katz & Peixoto, 2000). In 2010, there were diagnosed cases in 22 of the 27 federal units in Brazil, and the mortality between 1990 and 2008 oscillated around 500 deaths per year (Brasil, 2011a), which is more than the mortality observed for dengue and malaria during the same period (Brasil, 2011b). Despite considering schistosomiasis a rural endemicity in Brazil, there are frequent reports of the disease in urban areas in several localities (Barbosa et al., 2000; Barbosa et al., 2001; Graeff-Teixeira & Moraes, 1999; Guimarães & Neto, 2006; Guimarães et al., 1990; Guimarães et al., 1993; Kats et al., 1993; Mott et al., 1990; Soares et al., 1995). The greatest difficulty for schistosomiasis control is in transmission interruption because the occurrence of re-infection is frequent (Coura & Amaral, 2004), there are numerous favorable areas for the emergence and re-emergence of the parasistosis, and there is an evident expansion of the endemic areas (Brasil, 2010; Coura & Amaral, 2004; Graeff-Teixeira, 2004). This situation makes schistosomiasis a transmissible disease with a persistent profile in Brazil (Brasil, 2010).

Schistosomiasis transmission is favored under certain ecological, sociological, socio-economic, cultural, political and historical conditions existing in Brazil. Among them, we highlight the following: 1. Poverty and low economic development in many endemic areas (Katz & Peixoto, 2000); 2. Inadequate residential and environmental sanitation in rural and peri-urban areas (Barbosa et al., 1996; Silva, 1985); 3. Wide distribution of the mollusk intermediary hosts (Brasil, 2008); 4. Migrations, induced exodus and other permanent or transitory population movements (Coura & Amaral, 2004; Silva, 1985); 5. Absence of, scarcity of or inadequate health education programs (Schall et al., 2008); and 6. The complexity of the transmission processes with their multiple variables (Barbosa et al., 1996; Gazzinelli & Kloos, 2007; Martins Jr. & Barreto, 2003).

2. Small mammals naturally infected by *S. mansoni*

Schistosoma mansoni probably speciated from rodent schistosomas (*S. rodahini*) and is associated with the evolution of the first hominids (Després et al., 1992; Morgan et al., 2003; Morgan et al., 2005). Subsequently, *S. mansoni* became a parasite of wild rodents, and the presence of naturally infected wild rodents has become a complicating factor for control programs in endemic areas.

The presence of non-human definitive hosts increases the complexity of the epidemiologic situation of schistosomiasis in Brazil and constitutes one of the major problems for disease control because there is an overlap in the geographic distribution of the disease endemicity and the wild rodents potentially able to act as reservoirs.

In 1928, Cameron was the first to register a wild mammal naturally infected by *S. mansoni*: the African monkey introduced in the Antilles, *Cercopithecus sabaus*. Based on infection experiments carried out in rodents, he suggested the possibility of their participation in infection transmission, predicting complications in schistosomiasis control strategies. The first reports of naturally infected wild rodents were in the 1950s in Africa (Kuntz, 1952) and in Brazil (Amorim, 1953; Barbosa et al., 1953). At that time, Amorim (1953) emphasized the importance of animals with aquatic or semi-aquatic habits in the natural maintenance of *S. mansoni*. Among several wild and sinantropic rodent species found to be naturally parasitized in Brazil (*Oxymycterus* sp., *Necromys lasiurus*, *Akodon* spp., *Sooretamys* spp., *Calomys* spp., *Proechimys* sp., Cavia aperea, *Rattus rattus* and *Rattus norvegicus*), the species of the genera *Nectomys* and *Holochilus* are the most important and are generally considered wild reservoirs due to their semi-aquatic habits, wide geographic distribution and tolerance of human presence (Rey, 1993).

After those pioneering studies, several authors proposed investigating the participation of animals in the transmission cycle of mansonic schistosomiasis in the wild. Martins et al. (1955) evaluated schistosomiasis infection in *N. squamipes* in Belo Horizonte and Jabuticabas (MG) and found that they were naturally infected by *S. mansoni* with a prevalence of 26.1%. Rodrigues & Ferreira (1969) captured *N. squamipes* rodents naturally infected in São Paulo State, where they found new endemic human foci of the parasitosis. Bastos et al. (1984) captured *N. squamipes* in Maranhão State and reported that 70,6% of animals were parasitized. Silva & Andrade (1989) observed that *N. squamipes* had an important role in the maintenance of schistosomiasis in the rural area of Planalto (BA) because human prevalence was 3.26%, whereas rodent prevalence was 47%. Veiga-Borgeaud et al. (1986) found a high prevalence of *S. mansoni* in *H. brasiliensis* (currently *H. sciureus*) in swampy areas in Maranhão State. Picot (1992) confirmed the ability of the rodents *N. squamipes* and *H. brasiliensis* to eliminate viable eggs in feces in natural conditions.

Some other studies carried out in Africa and other countries of the Americas also investigated the importance of mammals as *S. mansoni* reservoirs. Borda & Rea (2006) observed *H. brasiliensis* (probably *H. vulpinus*) eliminating viable eggs in feces in Corrientes province, Argentina, and completing the transmission cycle in laboratory conditions. Sene et al. (1997) compared human and murine isolates of *S. mansoni* from Senegal in seven enzyme systems using isoeletric focusing. Rodent species studied were *Arvicanthis niloticus* and *Mastomys huberti*. They found no significant variation between human and rodent isolates. In the same region of Senegal, Duplantier & Sene (2000) investigated the importance of six rodent and one insectivore species as reservoir hosts of *S. mansoni*. Only *A. niloticus* and *M. huberti* were found infected with prevalence about 5%. They concluded that those rodents participate in the schistosomiasis transmission, but the human population is the main source of infection. Recently, Hanelt et al. (2010) examined the extent to which wild mammals acted as reservoirs of *S. mansoni* in Kenya. They found five murids and one shrew species infected with schistosomes (*S. manoni, S. bovi, S. rodhaini* and *S. kisumuensis*). The prevalence of *S. mansoni* in the reservoir populations was low (1.5%), however, the host could perpetuate snail infections and favor renewed transmission to humans.

In the 1980s, Théron, Pointier and Morand (Théron, 1984; Théron, 1985; Théron & Pointier, 1985; 1995; Morand et al., 1999) conducted the only study that incontestably demonstrated that in a wild focus, only the rodent *Rattus rattus* was responsible for schistosomiasis cycle maintenance, and in a semi-urban focus, both rodents and humans were equally responsible for the parasite cycle. Concerning the shedding pattern of cercariae, the same authors observed a late shedding pattern for wild focus mollusks, an early pattern for the urban focus, and a variable shedding pattern for the semi-urban focus. These results are in accordance with the epidemiologic context of each focus, as the late shedding patterns of cercariae relate to the crepuscular/nocturnal activity of rodents, confirming the adaptive value of the shedding patterns with the intermediary and definitive host populations involved in local transmission (Théron et al. 1992). The irrefutability of the conclusions is due to a unique characteristic of the study area: the occurrence of each species of the definitive hosts of *S. mansoni* (murine and human) separated in two distinct sub-areas and existing concomitantly in another one. This situation is very unusual and difficult to find.

The role of mammals in the schistosomiasis transmission was also investigated for *S. japonicum*, especially in China. He et al. (2001) studied the host-parasite relationships between *S. japonicum* and rodents, domesticated animals and simians and found that domesticated animals appeared to be the most important animal hosts in the transmission of *S. japonicum* infection, since they are very abundant. Rudge et al. (2009) compared the genetic differentiation of *S. japonicum* among habitat types and host species in China using microsatellite markers. They found strong genetic differences between habitat types, but little among host species, indicating high levels of parasite gene flow across species, what complicates the infection control. Lu et al. (2010) also investigated the role of small rodents and some domestic animals in the transmission of *S. japonicum* in six areas of China of different habitats over two years. The highest parasite prevalence was observed in rodents in a hilly region, whereas in marsh areas, bovines were considered as the main reservoirs.

3. The most important species of reservoir: Water-rats

The geographic distribution of the genera *Nectomys* in Brazil, which contains two species, is much wider than the distribution of mansonic schistosomiasis; nevertheless, they are

coincident in several regions. Studies of the participation of these rodents in schistosomiasis only mention *N. squamipes*, except for Bastos et al. (1982, 1984), who reported naturally infected *Nectomys squamipes amazonicus* (currently *Nectomys rattus* (Pelzen (1883)).
The water-rat *Nectomys squamipes* (Sigmodontinae) occurs in the Atlantic Forest, Rio São Francisco and Paraná Basins, and in small basins of Eastern Brazil below São Lourenço da Mata, Pernanbuco State, embracing the South, Southern and part of the Northeast regions (Fig. 1). *Nectomys rattus* occurs in the Paraná-Paraguai and Amazonic Basins and in small basins of Eastern Brazil from São Lourenço da Mata to the Amazon River (Fig. 1) (Bonvicino et al., 2008).

Fig. 1. Geographic distribution of the genera *Nectomys* in Brazil. Source: Bonvicino et al., 2008

N. squamipes is a semi-aquatic rodent, inhabiting streamside and swampy areas. It feeds primarily on insects, arthropods, snails and girinos found in the water and on fruits. Its activity is crepuscular and nocturnal (Fig. 2) (Ernest & Mares, 1986).
This species is undoubtedly the most important non-human, definitive host of *S. mansoni* in Brazil. The characteristics and studies that have proven its importance will be presented here along with the text.

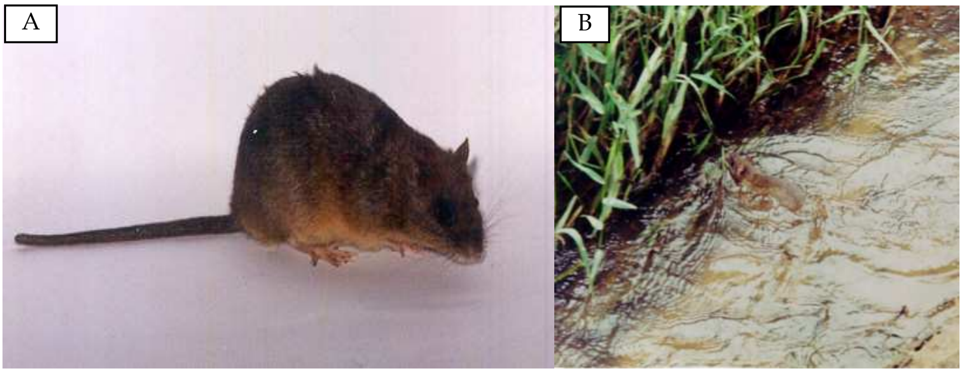

Fig. 2. *Nectomys squamipes*. A - Source: Cibele R. Bonvicino. B – Source: LABPMR

The genera *Holochilus* (Rodentia, Sigmodontinae) has four species occurring in Brazil: *H. brasiliensis*, *H. sciureus, H. chacaris* and *H. vulpinus* (Bonvicino et al., 2008). *H. sciureus* was formerly classified as *H. brasiliensis* (Wilson & Reeder, 2005). Only *H. sciureus* and *H. brasiliensis* occur in endemic areas of schistosomiasis in Brazil, the former occurring in the North region, part of the Northeast and north of the Middle-West, and the latter present from the Southeast to the South (Fig. 3).

These species live near streams and rivers or swampy and flooded areas. They are commonly found in humid fields, mostly in agricultural areas such as sugar cane, rice, corn and cotton plantations, and in vegetable gardens (Massoia, 1974; Ozanan, 1969). They are terrestrial and nocturnal, feeding on aquatic herbaceous vegetation and grass (Emmons & Feer, 1997). Outbreaks in population sizes called "ratadas" (Giovannoni et al., 1946) may occur, causing the species to become agricultural pests.

The potentiality of *Holochilus* sp. to act as wild reservoir of *S. mansoni* was demonstrated by their ability to eliminate viable eggs in feces in a natural environment (Dias et al., 1978) and by their ability to complete the parasite cycle without human presence in semi-natural conditions, using *Biomphalaria glabrata* as an intermediary host (Carvalho et al., 1976).

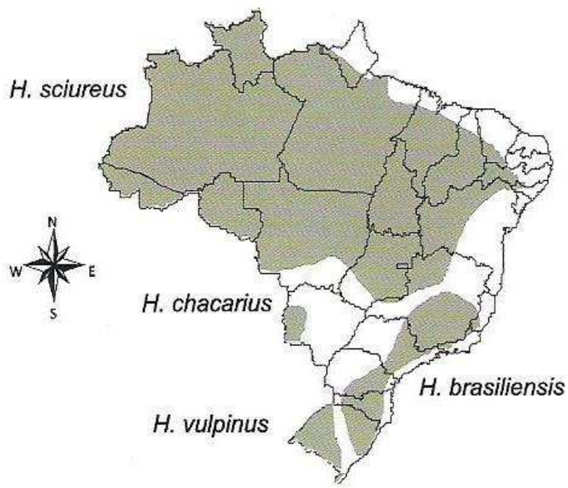

Fig. 3. Geographic distribution of the genera *Holochilus* in Brazil. Source: Bonvicino et al., 2008

4. Laboratory experiments: Water-rats as alternative experimental models for schistosomiasis studies

Several experimental studies have been carried out with the rodents *Nectomys* and *Holochilus* that proved that they can be considered alternative experimental models for studies of *S. mansoni* infection. They are highly susceptible to *S. mansoni* infections, easily handled and adapted to captivity conditions (D'Andrea et al., 1996). Here, we summarize the main results of the most relevant experimental studies on this theme.

Carvalho (1982) studied the pathology of schistosomiasis infection on *N. squamipes* and observed that most of the animals did not present with severe pathology and lesions due to the infection, suggesting a certain compatibility in the parasite-host relation.

Kawazoe & Pinto (1983) showed that the rodent *Holochilus brasiliensis* was able to eliminate viable eggs of *S. mansoni* in semi-natural conditions, but it was not able to complete the parasite transmission cycle if the intermediary host was *B. tenagophila*. However, they suggested that this rodent could have an important role in the eggs' dissemination in areas where the intermediary host was *B. glabrata*, even without the presence of parasitized humans.
Rodrigues-Silva (1988), Rodrigues-Silva et al. (1991) and Souza et al. (1992) evaluated the role of the rodents as natural hosts and as experimental models for schistosomiasis. They observed that naturally and experimentally infected animals presented tissue lesions in several organs similar to those found in mice. Based on these results, Rodrigues-Silva suggested that this rodent could be an alternative experimental model for schistosomiasis studies.
Rodrigues-Silva (1988) and Rodrigues-Silva et al. (1992) affirmed the importance of *N. squamipes* as a maintainer of the parasite cycle once the rodent proved to be a compatible or permissive host. This was demonstrated by the high infection duration and the elimination of viable, fertile and infective eggs for mollusks. *N. squamipes* is easily re-infected because the first infection facilitates the entrance of a new worm burden for the organism (Maldonado Jr. et al., 1994), assuring the elimination of viable eggs during the entire lifetime of the rodent (Costa-Silva, 2000).
Silva & Andrade (1989) studied naturally infected *N. squamipes* rodents and observed soft tissue lesions, and, despite the fact that the rodents exhibited a highly resistant immunopathology, the parasite seemed to suffer little interference with its oviposition and the number of egg eliminated.
Ribeiro et al. (1998) and Souza et al. (1992) showed that *N. squamipes* presented with a high rate of recovered worms even when infected with a low number of cercariaes, suggesting compatibility between *N. squamipes* and *S. mansoni*.
Picot (1992) showed that in semi-natural conditions, *N. squamipes* was able to close the transmission cycle of *S. mansoni* and to eliminate highly infectious, viable eggs.
Maldonado Jr. et al. (1994) evaluated the resistance of *S. mansoni* infection in *N. squamipes* by successive experimental infections, comparing the total number of worms recovered from re-infections with a control group. They concluded that previous infections did not reduce infectivity.
Ribeiro et al. (1998) evaluated the susceptibility of the rodents *N. squamipes* and *N. rattus* to *S. mansoni* infection, concluding that both species are highly susceptible to *S. mansoni* infection. *N. squamipes* presented 80% positivity after experimental infection and *N. rattus* presented 71%. They also demonstrated that the latter species was also able to complete the parasite cycle in laboratory conditions.
Costa-Silva (2000) observed that *N. squamipes* was susceptible to several *S. mansoni* strains, confirming its potential to act as a natural reservoir in some endemic areas and its utility as an experimental model for morphologic studies of *S. mansoni*.
Martinez et al. (2008) compared biological characteristics of four *S. mansoni* strains using *N. squamipes* as the experimental model. They concluded that this rodent was susceptible to different strains because the rodent did not present differences in biological parameters of infection when the different strains were compared.

5. A long term empiric study about the role of rodent reservoirs in Brazil

The first references of schistosomiasis in Sumidouro Municipality, Rio de Janeiro State, were related to studies carried out in 1959. S. Camargo (unpublished data) made the first

malacologic survey in 1962 in order to confirm the autochthony of the disease. By that time, the streams in the localities of Pamparrão, Porteira Verde and Boa Ventura were considered to be transmission foci due to the occurrence of infected snails (data recovered by Silva, 2004).
The first long-term study on schistosomiasis epidemiology in Sumidouro began in 1977 in the locality of Porteira Verde (Carvalho, 1982). The author observed that *S. mansoni* infection rates in *N. squamipes* were constant even after chemotherapy intervention in the human population and suggested that the rodent could be considered a potential natural reservoir of the disease in the region. The initial human *S. mansoni* prevalence varied between 11.2% and 17.4%. After treatment, it was reduced to 6.9% in the human population, whereas in the rodents, it was 48.2%.
Those findings on *N. squamipes* infection by *S. mansoni* in Sumidouro clearly showed the need to develop long-term studies to evaluate the role of this rodent in local transmission dynamics. With this goal in mind, a prospective survey on rodents and snails and a preliminary parasitological census in the human population were performed in 1990, thus creating the basis for the research on schistosomiasis in subsequent years. Below, we give a brief description of the project, with information on the methods, the main results and the conclusions on the schistosomiasis context in Sumidouro and, especially, on the role of rodents in the local transmission of *S. mansoni*.

5.1 Schistosomiasis context in Sumidouro

Sumidouro is a city of the State of Rio de Janeiro (22° 02 ' 59 " S, 42° 40 ' 29 " W), 179 km away from the state capital (Rio de Janeiro), which has a humid mesothermic climate (Fig. 4). Almost 63% of its 14920 inhabitants live in the rural area (IBGE 2010). In 2000, the Municipal HDI – (Human Development Index) was 0.712 (UNDP 2000). The work was carried out in five agricultural localities (Pamparrão, Porteira Verde, Encanto, Soledade and Volta), which had small portions of the Atlantic Forest on mountain summits and were cut by streams, small dams and irrigation ditches (Fig. 5).
In a new approach to schistosomiasis research in Brazil, different areas of scientific knowledge were adopted with an interdisciplinary perspective, an approach deemed more suitable for the situation than a multidisciplinary one, according to Almeida Filho (1997). This approach went beyond the domain of biomedical sciences, searching, for example, to understand cultural and behavioral factors that contribute to the complexity of the local schistosomiasis situation (Soares et al., 2002; Stotz et al., 2006). Thus, it was possible to understand the context of the role of rodents in the local cycle of the parasite and the situations that underlie the occurrence of schistosomiasis in the region. This was the only study with such characteristics carried out in Brazil on schistosomiasis.
Throughout the study period, the human population participated in a process that included questionnaires, interviews, focus groups, video sessions, debates, science fairs and coprology (Hoffman, Kato-Katz and other auxiliary methods, on average, 3 samples and 9 blades per person), serology (ELISA IgG and IgA; soluble extract of *S. mansoni* adults), clinical examination and treatment for all the diagnosed parasites. At the same time, the transmission foci were mapped according to the population density, dispersion and natural infection of the snail *Biomphalaria glabrata* by *S. mansoni* (Giovanelli et al., 2001). The serum samples were submitted to immunoenzymatic reactions using adult *S. mansoni* membrane soluble extract as antigen. One of the techniques used was western blotting to analyze the reactivity profile of anti-*S. mansoni* IgG antibodies. ELISAs were also carried out for anti-*S. mansoni* IgG, IgG1 and IgE.

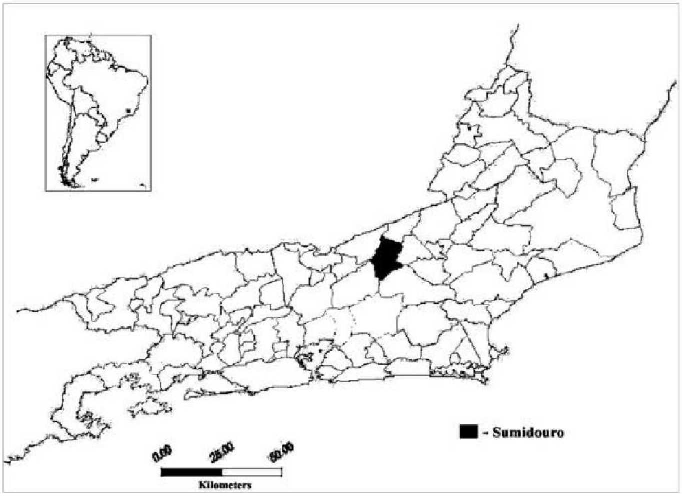

Fig. 4. Study area, indicating the Sumidouro Municipality in Rio de Janeiro State and in South America. Source: D'Andrea et. al., 2000.

Fig. 5. Human activities in the study area.

These approaches disclosed bio-ecological, socio-ecological, socio-economic, historical, cultural and behavioral peculiarities that could not explain the persistence of transmission and the recurrence of high focal prevalences and hepatoesplenomegaly cases, despite all of the investments in controlling schistosomiasis in Sumidouro since the 1960s by several research groups and institutions. Amongst these peculiarities and beyond the relevance of the presence of the water-rat as a complicating factor for the control of schistosomiasis, the precariousness of the socio-ecologic and socio-economic conditions that put the populations under different environmental risks, including schistosomiasis, was notable.

The socio-ecologic precariousness was evidenced by the observation of the following conditions in the study territory: a) leisure, residential supply, farming, and other activities dependent on water contaminated by sewers *in natura* from almost all the houses; b) proliferation of snail vectors as a consequence of overflows due to alterations in the topography by deforestation and farming activities; c) perennial and occasional foci of *B. glabrata*, with high intensities of infection by *S. mansoni*, that occurred downstream, upstream and around residences, and water bodies visited daily by wild rodents of semi-aquatic habits during foraging activities; d) blockage of water bodies due to inadequate collection and disposal of garbage; e) scarcity of health water sources due to different types of environmental contamination and increasing deforestation around the springs; f) convergence of small water bodies and larger ones used by the population of other localities for residential supply, leisure, irrigation and other activities.

The socio-economic conditions contributed to the complexity of schistosomiasis control by exposing the population to psycho-social and chemical risks, given that irregularities and excesses in pesticide use were common in local agricultural production, with strong consequences for human and environmental health. The historical approach of schistosomiasis in Sumidouro showed the following: a) since the 1960s, there were cases of severe collateral effects from medicine, failures of sanitation, as well as environmental and material injuries after the use of moluscicides for snail control; b) in addition to these low quality of life, poverty, lack of good life quality perspectives, alcoholism and other factors that stimulate pessimism and inaction turned part of the communities against the diagnosis and treatment of schistosomiasis, as well as against the methodologies of sanitation and snail control suggested by the public powers and by the researchers; c) these refusals increased the limitations of coprological diagnosis that contributed to uncertainty in the real number of infected people; d) these facts demand the adoption of a wide range of measures, such as methodologies to understand the needs of the population and to make people understand schistosomiasis transmission and the serological techniques used for diagnosis (Gonçalves et al., 2005; Soares et al. 2002).

In this complex context, schistosomiasis transmission to the human population occurred in home backyards and for other reasons (occupational, recreational and occasional), with high ratios of non-treatment due to migration, refusal or medical precaution and with a high prevalence in specific groups (men and farm workers).

To simplify the comprehension of key aspects of the relevance of rodents' participation in schistosomiasis transmission in Sumidouro, the next section will describe each phase of the study concerning *N squamipes*.

5.2 Eco-epidemiologic monitoring - The rodent as a focus transmission biological indicator – Pamparrão and Encanto localities

Long-term monitoring of the ecology and parasitology of the water-rat *Nectomys squamipes*, together with an epidemiologic study of the human population, was carried out in two localities in Sumidouro Municipality, at different times: in Pamparrão from 1991 to 1996, and in Encanto from 2001 to 2006. In both localities, a capture-mark-recapture study of small mammals was conducted. Trappings were conducted along streamsides, which is the habitat of the rodent (Fig. 6). Stool and serologic diagnostics were performed on the rodents. Human populations were also diagnosed and treated. With this design, we obtained results that have enabled us to raise the small mammal fauna of the area (D'Andrea et al., 1999), understand the pattern of population dynamics of the water-rat (Bonecker et al., 2009; D'Andrea et al. 2007; Gentile et al. 2000) and its habitat use (Gentile & Fernandez 1999), understand aspects of the relationship between *S. mansoni* and *N. squamipes* (D'Andrea et al. 2000; Gentile et al., 2006), and adapt procedures and techniques to local particularities.

In Pamparrão, which is a low endemicity area, the population dynamic study of the water-rat showed that it reproduced throughout the year, predominantly during the rainy periods. The population size also increased during and after rainy periods and was related to survival rather than population outbreaks (Fig. 6) (Gentile et al., 2000).

The habitat preference study showed that *N. squamipes* preferred areas of dense herbaceous vegetation near the ground as well as courses and water bodies (Gentile & Fernandez 1999).

In the parasitological survey, the high prevalence and parasitic burden confirmed that *N. squamipes* was highly susceptible to infection by *S. mansoni*. Three factors were related to the level of infection of the rodent: human sewage contamination in the home range of the rodents, local snail abundance and the movement pattern of rodents between transmission sites. The *S. mansoni* infection rates in snails was generally very low throughout the study area, except for some isolated sites where concentrated infected specimens were found with infection rates ranging from 10 to 25%. The level of *S. mansoni* infection in rodents increased with the proximity to human habitations, which was also related to the level of infection in humans. There was no correlation between population size and the *S. mansoni* infection rates in the rodents (Fig. 7).

Fig. 6. A general view of a transect capture site of the water-rats. Source: LABPMR.

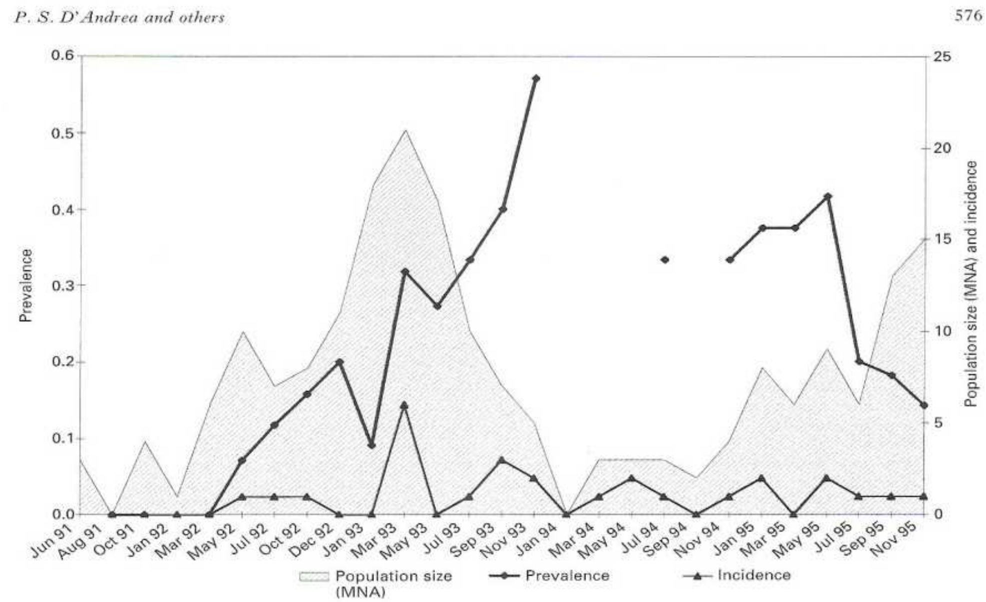

Fig. 7. Population parameters of the *Nectomys squamipes* in Pamparrão, Sumidouro, Rio de Janeiro State, Brazil. Source: D'Andrea et al., 2000.

The population of the parasite did not regulate the host population and did not affect the longevity of the animals. Parasitism did not affect the survival of the rodents, who continued to eliminate viable eggs of the parasite throughout their lifecycle, as shown in the laboratory. In general, the infection did not seem to reduce the fitness (survival rates, reproduction and movement) of the rodents. The presence of infected animals in locations removed from areas contaminated by human feces and the observation of rodent movement suggested that the rodent is capable of carrying *S. mansoni* to non-transmission sites and may introduce the parasite into new areas, creating new foci and complicating disease control (D'Andrea et al., 2000).

In the Encanto locality, where schistosomiasis present at a medium endemicity, another phase of the study was conducted over four years to evaluate the effects of chemotherapy treatment in the infected human population on the rate of rodent infection and to compare diagnostic methods. During this phase, we also studied the population dynamics of the rodent *N. squamipes*, the infection rate of schistosomiasis on the water-rat populations and its change over time, and different methods for *S. mansoni* diagnosis (Bonecker et al., 2009; Gentile et al., 2006).

The population dynamics of *N. squamipes* were in accordance with other studies and with the Pamparrão study, where the reproduction of the animals occurred throughout the year but primarily during rainy periods, a trend that is related to the close association of this rodent to resources found in water (Ernest & Mares, 1986; Gentile et al., 2000). These animals reproduce opportunistically so that reproduction is triggered by resource availability according to rainfall pattern (Gentile et al., 2000), resulting in rapid population increases with higher survivorship a few months after the rainy periods, and young individuals are primarily observed in those periods (Fig. 8). The rodents showed no potential for outbreaks or for becoming agricultural pests (Bonecker et al., 2008).

There was a positive correlation between the prevalence rates estimated by the two methods of diagnosis; however, the coprological method underestimated the rate of *S. mansoni* infection in rodents at about 35%, mainly when prevalence was low. The two methods showed the same trends over time. Therefore, diagnosis by the serological method was more appropriate for assessing rates of *S. mansoni* infection in rodents, especially when the intensity of infection was low (Gentile et al., 2006).

The abundance of *N. squamipes* was related to rainfall, which, in turn, had a direct influence on the rates of *S. mansoni* transmission in rodents. *S. mansoni* prevalence was negatively correlated with rainfall at a delay of four months, and the highest prevalence rates were observed during periods of lower abundance in the rodent population, which occurred at the end of the dry season. The incidence of the parasite in the rodent population did not show a seasonal pattern. Serologic conversion was observed in five animals monitored over time. There was no difference regarding the sex of the infected and uninfected animals (Gentile et al., 2006).

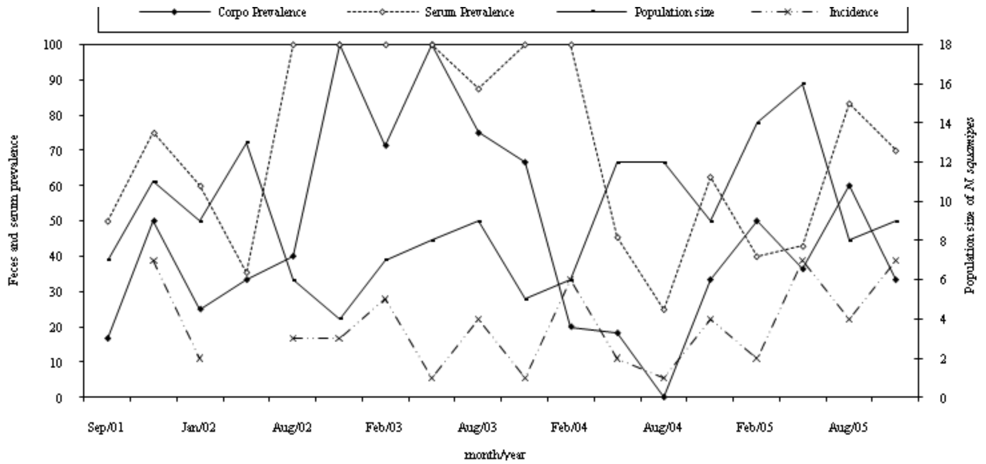

Fig. 8. Prevalences and incidences of *Schistosoma mansoni* in *Nectomys squamipes* and rodent population sizes over four years at Encanto, Sumidouro, Rio de Janeiro State, Brazil. Source: Gentile et al., 2006.

Despite the low rodent infection rate at 18 months after the chemotherapy in the human population, this treatment did not interrupt the rodent infection, as after one year, there was a resurgence in the rodent infection rate, whereas the human population prevalence was considerably reduced (from 19.3% to 4.8%). The high incidence and the serologic conversions observed in the last year of the study corroborated these data and indicated a continuous process of *S. mansoni* transmission in the area, despite the chemotherapy in the human population (Gentile et al., 2006).

5.3 The *S. mansoni* – water-rat interaction

In an another phase of the study, aspects of the parasite interaction between *S. mansoni* and *N. squamipes* were evaluated. In this study, the collected animals were examined for *S.*

mansoni and other helminth species. The abundance and intensity of *S. mansoni* in the population of *N. squamipes* were determined, as well as the degree of aggregation and the interaction with other helminths.

The distribution of *S. mansoni* in the population of *N. squamipes* was highly aggregated, and 50% of the worms were concentrated in 4.2% of the host population. Considering only the infected rodents, 11.4% of them harbored half the population of parasites (D'Andrea et al., 2000). Spatial heterogeneity and low infection rates in snails explain the patchy distribution, which restricts the foci of transmission to only a few areas.

The prevalence of *S. mansoni* on the water-rats was 34.5%, the intensity was 48.3 individuals and the abundance was 16.7. These high intensity and abundance values reflect the high susceptibility of the rodent to the parasite and the high transmissibility of the parasite in the region. In the *N. squamipes* population, *S. mansoni* was the dominant species of the helminth community. There was no antagonistic or synergistic interaction between *S. mansoni* and the other helminth species (Maldonado Jr. et al., 2006).

5.4 On a regional scale

Cross-sectional studies were conducted in other localities during the same time as the study in Encanto. In Pamparrão and Soledade, areas of low and high endemicity, respectively, animals were captured and necropsied. In Volta, an area with no human cases of schistosomiasis, a mark-recapture study of the rodents was carried out. The *S. mansoni* diagnosis was made by serological and parasitological methods and necropsy to compare the techniques and refine the diagnosis for areas of low endemicity.

At this step of the study, we observed different patterns regarding the participation of the water-rat in the *S. mansoni* transmission dynamics in each location. In Volta, the rodents were able to maintain the *S. mansoni* infection even without infected humans, at least over a short period of time. In Pamparrão, the low rodent population size and the absence of rodent infection over two years did not eliminate infection transmission, as human prevalence was 13.4%. In Soledade, a high endemic area, we observed infected rodents far from human habitations, and the human and rodent transmission cycles did not seem to be affecting each other. (Gentile et al., 2006).

Regarding the comparison of diagnostic methods, the similarity in the reactive serology profile between individuals diagnosed coprology/necropsy negative and those diagnosed coprology/necropsy positive demonstrates that serology detects recent infection, including the false negatives in coprology, because antibodies can be found after five days of infection in laboratory experiments with *N. squamipes* (Peralta et al., 2009). The low titers of antibodies in most of these samples corroborates this hypothesis.

5.5 A natural experiment on the time of activity of the water-rat

D'Andrea et al. (2002) conducted two field experiments in the location of Pamparrão with the following objectives: 1) Determine the activity pattern of *N. squamipes* and its use of the aquatic environment; and 2) Prove the occurrence of late transmission of *S. mansoni* cercariae to *N. squamipes* in natural conditions using sentinel animals. These experiments showed the occurrence of infection of *N. squamipes* by cercariae in natural conditions in daylight and twilight hours with no significant differences, demonstrated by the recovery of worms used in rodent sentinels. The observation of the occurrence of infections in rodents during their natural time of activity (at dusk) raised the possibility of an adaptative process of *S. mansoni* to different definitive hosts (D'Andrea et al., 2002). The emission peak during the day would be more related to human infection, as this is the time of greatest activity for the local people and of increased contact with contaminated water bodies, and the crepuscular peak could be related to infection in rodents, as they have twilight/nocturnal activity (Fig. 9 and Table 1) (D'Andrea et al., 2002).

	Diurnal (10 a.m. – 2 p.m.)		Crepuscular / Nocturnal (5 p.m. – 9 p.m.)	
	July	November	July	November
Number of water-rats exposed	8	6(3[a])	8	6
Number of water-rats infected	5	3	4	4
Total of adult worms recovered	14	8	8	5
Total of worms pairs recovered	3	1	3	1

Table 1. Exposure of water-rats (born in captivity) to early and late *Schisotosoma mansoni* infection and worm recoveries. [a] Water-rats died during the experiment. Source: D'Andrea et al., 2002.

Previous studies have attempted to show differences between rodents and human *S. mansoni* strains through the following factors: external morphology of adult worms (Machado-Silva et al., 1994), pathogenicity in mice (Bastos et al., 1984, Silva & Andrade 1989), compatibility with snails (Bastos et al., 1984; Dias et al., 1978), sensitivity to drugs

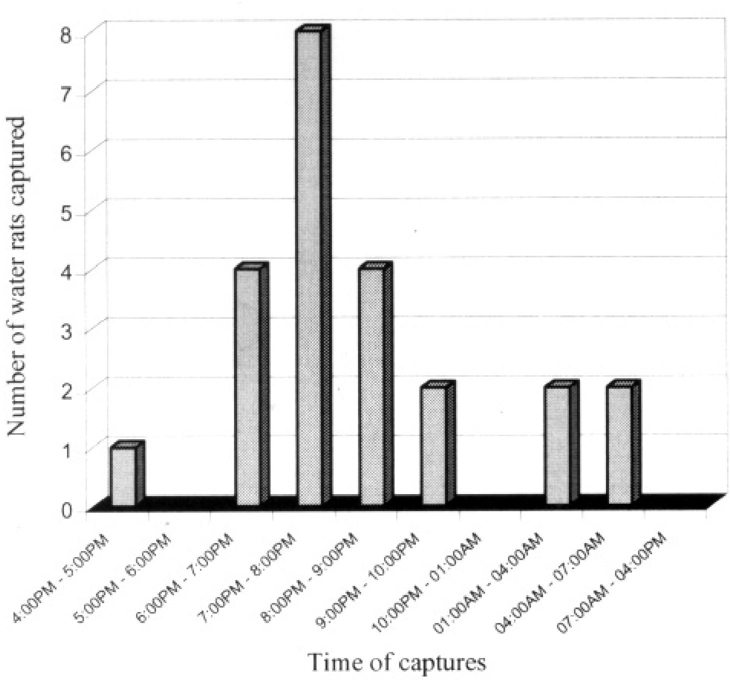

Fig. 9. Daily activity pattern of the water-rat *Nectomys squamipes*. Source: D'Andrea et al., 2002.

(Souza et al. 1992) and iso-enzyme patterns (Oliveira, 1996). These biological differences, coupled with the existence of two different patterns of cercariae emission (diurnal and crepuscular / nocturnal), led to the hypothesis that there could be differences at the molecular level between the human and rodent strains and between different geographical regions (Gentile & Oliveira, 2008). Several studies had previously shown intra-specific *S. mansoni* differences in enzymes (Fletcher et al., 1981; Navarro et al., 1992), molecular mitochondrial DNA (Blair et al., 1999; Després et al., 1991; Després et al., 1993; Le et al . 2000; Pena et al., 1995) and total DNA (Barral et al., 1993; Barral et al., 1996; Neto et al., 1993; Simpson et al., 1995; Sire et al., 1999).

6. Conclusions

The information obtained in these studies provides a more realistic and innovative support to the schistosomiasis control program in Sumidouro by contributing to the knowledge of the epidemiological complexity in the study area and, in particular, by elucidating the role of wild rodents in the local transmission of this disease. It is important to note that despite not having ideal conditions, as achieved in the work of Théron & Pointier (1995), the information obtained by this empirical long-term study carried out in Sumidouro, as well as the results of the laboratory experiments, allows for the establishment of a set of criteria for characterizing *N. squamipes* as a host-reservoir of *S. mansoni*:

1. High susceptibility to infection: The species proved to be extremely susceptible to contracting the infection, even in areas of low endemicity.
2. Ability to complete the parasite cycle: The water-rat eliminates viable eggs of *S. mansoni* in its stool, and because of its semi-aquatic habit, these eggs are very likely to hatch, allowing the infection of intermediate hosts and the completion of the cycle of the parasite.
3. The rodent is not affected by the infection, allowing transmission of the parasite throughout its life - the data show that natural infection with *S. mansoni* does not affect survival, reproduction or mobility, and, in general, the infection causes no reduction in the fitness of infected individuals or interference with population dynamics.
4. The infection is chronic and persistent over the life time of the animal - data from experimental infections show mild disease with no change in the survival of the animal and, under natural conditions, show that the disease is cumulative, that there is no immunization or self-healing, and that the elimination of viable eggs of the parasite is persistent throughout the life of the animal.
5. Overlap of areas of *S. mansoni* distribution and reservoir distribution - there is overlap between the geographic and ecological distribution of *N. squamipes* and schistosomiasis in Brazil.
6. The reservoir must make the link between the wild and domestic environment - the water-rat is an abundant rodent and totally adapted to degraded natural areas and rural areas, which occur frequently in the surroundings of domicile areas and small crops, thereby increasing transmission to human populations.
7. The reservoir must maintain the infection in the absence of man - experiments in controlled conditions (semi-natural) and evidence from this study suggest that possibility.
8. The possibility of adaptation of *S. mansoni* to *N. squamipes* with an independent parasitic cycle - chronobiological differences between rodents and humans

concerning their activity time and exposure to water courses and experimental evidence of two peaks in cercariae emission (one during the day and another at twilight), with the possibility of late infection in rodents, suggest adaptation process of a *S. mansoni* strain to the water-rat.

Observing these criteria in the studied localities, the importance of the water-rats as wild reservoirs of *S. mansoni* in Sumidouro was demonstrated, despite transmission power of different degrees in each area, even on a small regional scale. It was clear that, independent of other reasons for the complexity of the situation, the presence of these rodents must always be taken into account in schistosomiasis control programs, as its participation in transmission increases this complexity. Thus, the main impact of the results was the perception that the solution to the problem of schistosomiasis in Sumidouro must be determined through an approach based both on the needs of the ecosystem and of the human population. This approach must emphasize the presence of the rodent and its participation in the transmission of the parasite to humans, in addition to considering historical, social, economical, anthropological and other peculiarities of the situation. From both social and scientific perspectives, this will represent a favorable conclusion to this long-term study.

This approach must be able to alter schistosomiasis transmission control by dealing with the complexity of the situation, which means considering ethical aspects and other aspects that cannot be mathematically modeled, stimulating the participation of the population of Sumidouro to search for solutions to its problems, and training teachers, doctors, health and environmental agents, and other local professionals for interventions in the local context. To make the establishment of more adequate environmental health public policies possible, this approach must also supply the municipal sectors of health, environment, education and sanitation with qualified and up-to-date technical procedures. In principle, the Ecosystem Approach to Health (OPAS, 2009; Waltner Toews et al., 2008,) fits these objectives.

The Ecosystem Approach to Health, already proposed to deal with schistosomiasis and other parasitic and infectious diseases (Augusto et al., 2005; PAHO, 2009; Waltner-Toews, 2004), is a process of participative management in the health/environment interface that is designed to construct information, foresee changes (as for example, an epidemic), and carry through choices that involve the judgment of values, interests and uncertainties. This approach is adaptive because it is based on methodological pluralism and on a protocol of basic lines fed back by a collective appreciation of the problem. Therefore, it can indicate paths for management strategies and public policies that are adequate to social/ecological systems like those we observed in Sumidouro. The investment in an Ecosystem Approach to Health would certainly answer the desires of our research group in effectively contributing to the improvement of the quality of life of the people in that city.

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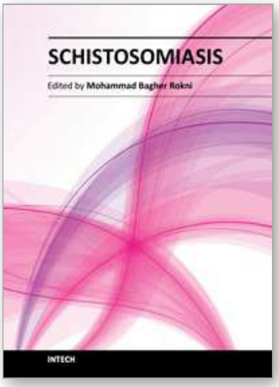

Schistosomiasis

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In the wake of the invitation by InTech, this book was written by a number of prominent researchers in the field. It is set to present a compendium of all necessary and up-to-date data to all who are interested. Schistosomiasis or blood fluke disease, also known as Bilharziasis, is a parasitic disease caused by helminths from a genus of trematodes entitled Schistosoma. It is a snail-borne trematode infection. The disease is among the Neglected Tropical Diseases, catalogued by the Global Plan to combat Neglected Tropical Diseases, 2008-2015 and is considered by the World Health Organization (WHO) to be the second most socioeconomically devastating parasitic disease, next to malaria. WHO demonstrates that schistosomiasis affects at least 200 million people worldwide, more than 700 million people live in endemic areas, and more than 200.000 deaths are reported annually. It leads to the loss of about 4.5 million disability-adjusted life years (DALYs).

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