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Control of *Schistosoma mekongi* in Cambodia. Results of eight years of control activities in the two endemic provinces

M. Sinuon^a, R. Tsuyuoka^b, D. Socheat^a, P. Odermatt^c, H. Ohmae^d, H. Matsuda^e, A. Montresor^f, and K. Palmer^g

^aNational Center for Parasitology, Entomology and Malaria Control, Ministry of Health of Cambodia Phnom Penh, Cambodia ^bWHO Office, Phnom Penh, Cambodia ^cSwiss Tropical Institute, Basel, Switzerland ^dNational Institute of Infectious Diseases, MoHLW, Japan ^eDokkyo University, School of Medicine, Japan ^fWHO Office, Hanoi, Vietnam ^gWHO Western Pacific Regional Office, Manila, Philippines

Abstract

In Cambodia, schistosomiasis is transmitted in the provinces of Kratie and Stung Treng where approximately 80 000 individuals are estimated to be at risk of infection.

The baseline prevalence of infection was estimated between 73% and 88% and cases of severe morbidity (hepato-spleno-megaly, puberty retardation ...) and mortality were very common in the area. The Ministry of Health of Cambodia started in 1994 schistosomiasis control applying universal chemotherapy with praziquantel (40 mg/Kg). The coverage of the programme was between 62% and 86% for 8 years. This simple control measure resulted in the control of the disease: no cases have been reported in 2004 and only 3 cases were reported in 2005. In addition, cases of schistosomiasis severe morbidity are not reported any more. Since the beginning of the control programme, single dose of mebendazole (500 mg) has been combined with praziquantel during the mass chemotherapy, as a result the prevalence of *Ascaris lumbricoides* and hookworms dropped respectively from 74.5% to 10% and from 86% to 40%. The experience in Cambodia demonstrates that with political commitment, parasitic diseases control is achievable even in situation of minimal resources. The programme represents a successful model for other developing countries.

Introduction

Schistosomiasis is one of the most prevalent parasitic infections in the world. It is endemic in 76 countries and continues to be a public health concern in the developing world (Engels et al. 2002). In Cambodia the disease is caused by *Schistosoma mekongi* (Voge et al. 1978), the intermediate host is *Neotricula aperta* a river-snail that lives in the fissures of partially

Conflict of interests

Corresponding Author: Dr Antonio MONTRESOR, Public Health Specialist, Vectorborne and other Parasitic Diseases; World Health Organization, 63 Tran Hung Dao Street, Mail P.O. Box 52, Ha Noi - VIET NAM, Tel +(84 4) 943 3734 /5 /6 ext 29, Fax +(84 4) 943 3740, montresora@vtn.wpro.who.int.

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submerged rocks (Mouchet, 1995). Pigs and dogs have been found to be animal reservoir of the parasite (Strandgaard et al., 2001). Symptoms and signs associated with *S. mekongi* infection include cachexia, hepatosplenomegaly, stunting and retardation of puberty, portal hypertension, ascites and rupture of esophageal varices (Biays et al., 1999). Pathology associated with the infection consists in periportal thickening and portal vein enlargement (Hatz et al., 2001).

In 1994, 20 villages in Kratie Provinces were identified as origin of severe cases of schistosomiasis (Stich et al 1999). The same year, the Ministry of Health start control activities with the initial support of Médicins Sans Frontières (MSF) and successively of the World Health Organization (WHO). The control measure consisted mainly on periodical administration of praziquantel 40 mg/Kg to the entire population (children under 2 years of age and pregnant women were not treated).

At the same time surveys were progressively conducted to accurately establish the extension of the endemic area. From 2000 the campaigns covered districts in Stung Treng province, which were inaccessible in the past due to lack of security. Since 2001 the campaign has covered 80,000 people in Kratie and Stung Treng (figure 1). No new endemic areas were identified since then

The parasitological stool surveys carried out for schistosomiasis monitoring revealed also high infection rates for soil-transmitted helminths (STH). This finding lead to the simultaneous administration of mebendazole (single dose 500 mg) to all the individual treated with praziquantel.

The data presented in this paper were collected for monitoring purposes. Despite some gaps and lacks of continuity in the intervention and in the data collection and recording processes (due to temporary lack of funds, armed conflicts and other unpredictable events), we consider the present data interesting for managers of similar programmes.

The paper aim to document that a mayor reduction of schistosomiasis prevalence can be obtained with mass distribution of anthelminthic and that this can be obtained also in situation of minimal resources. The paper also presents the feasibility of integrating different anthelminthics in the same distribution system.

Material and methods

Identification of the endemic area

Epidemiological assessments were conducted in the zones previously reported as endemic: Kratie (Audebaud et al. 1968, Jolly et al. 1970) Strung Treng (Urbani et al 1997) Rattanakiri and Kampong Cham (Ijima 1970).

Three methods were used in order to delimitate the area of intervention:

- Questionnaires
- Stool surveys in households and schools

Serological surveys

Normally the first investigation was done with questionnaire and then the positive data confirmed with parasitological or serological method.

Over 30 000 questionnaire were distributed in the provinces of Kratie, Stung Treng, Rattanakiri and Kompong Cham (Urbani et al. 2002), over 1300 individuals were investigated using Kato-Katz method (WHO 1980) with household survey and over 1200 during school survey (Stich et al.1999), 12 villages were screened using ELISA method with soluble egg antigen of *S. japonicum* (Homae 2004).

The data collected with the different assessments were analyzed, checked for consistency, assembled and then utilized to prepare maps presenting the areas to cover with mass distribution of anthelminthics.

<u>Control intervention</u>: Every year, between February and April the campaign was conducted by a team composed by personnel form the National Center for Parasitology, Entomology and Malaria Control (NMC) and local health staff. Drugs were administered under direct observation of health staff. Treatments were combined with health education, in order to increase health awareness and to reduce the water contacts in rocky banks of the river.

From 1994 to 2005 the area of intervention increased from the 20 villages where schistosomiasis was originally reported to include all new areas that were progressively identified. Since 2001 the campaign has covered 80,000 people. Details on the type of mass treatment applied at different year and the target population for each campaign is presented in table 1.

The <u>programme coverage</u> has been evaluated through the drug distribution reports: in occasion of each drug distribution campaign, forms recording age, sex, weight and number of tablets of praziquantel given to each individual, were compiled by health staff. The coverage was calculated as the number of people treated divided by population estimations (census data periodically updated by the health centers).

The <u>programme impact on schistosomiasis</u> prevalence has been periodically estimated with three methods:

- Parasitological surveys conducted in randomly selected villages: between 2 000 and 3 000 individuals in an average of 20 villages were selected every year. The sample size in each village was between 70 and 150. The laboratory method used was Kato-Katz. While conducting stool examination with Kato-Katz method for schistosomiasis data on Soil Transmitted Helminthiasis were also collected.
- Annual parasitological surveys conducted in primary school of four sentinel villages in Kratie province (Achen, Chatnaol, Srekheurn and Sambok) (from 1995) and in Sdau village in Stung Treng province (from 1997): After the year 2000 in each site, 3 consecutive stool samples have been examined with Kato Katz method.

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Active search and follow up of cases of severe schistosomiasis during the masstreatment and the parasitological survey.

The monitoring surveys have been conducted in school-aged children because this age group is easily accessible and can provide indications on the situation in other age groups (Guyatt et al 1999).

Results

The <u>epidemiological assessment</u> allowed to identify114 villages along the Mekong and its tributaries Sesan and Sekong as endemic for schistosomiasis, administratively the villages were in 2 districts of Kratie Province and in 5 districts of Stung Treng Province (figure 1). About 80,000 individuals leaving along the Mekong were estimated to be a risk of infection (Urbani et al, 2002). The area between Kratie and Sambo, on the left bank of the Mekong River, was identified as the most affected with a percentage of positive answer to the questionnaire over 70%. No evidence of *S. mekongi* transmission came from Kampong Cham and Rattanakiri.

The <u>coverage</u> of mass treatment was maintained between 62% and 74% between 1996 and 2002 with the exception of 1998 where universal drug administration was not conducted because lack of funds. In 2000 and 2001, the campaigns covered new areas, previously inaccessible due to lack of security. Since 2001 the campaign covered 50,000 people in 56 villages in 2 districts of Kratie Province and about 30,000 people in 58 villages in 5 districts, Stung Treng Province.

Programme impact on schistosomiasis

Prevalence: the initial surveys performed by Médicins Sans Frontières (MSF) in Kratie Province between 1994 and 1995 revealed a prevalence of schistosomiasis in primary school children of 72.9% (Stich et al, 1999). Table 2 shows the decline in the number of villages presenting cases of schistosomiasis in Stung Treng and the range of prevalence. For Kratie only the data on declining schistosomiasis prevalence in the 4 sentinel sites are available (figure 2).

Clinical Morbidity: before the start of the intervention several new cases of severe schistosomiasis morbidity (hepatosplenomegaly, cachexia, anaemia, ascites, haematoemesis) and mortality were reported every at the Provincial Hospital of Kratie and the District Hospital of Sambour as well as in the surrounding communities (Biays et al, 1999). In a survey in 1999, the number of cases identified with signs and symptoms of severe schistosomiasis reached 124 in Kratie Province. After treatment with praziquantel, 101 of them improved and are where then able to perform light labor, 4 patients died and in 8 cases the disease remained severe. Of the 11 patients that received surgical treatment between 2000 and 2002 at the National Calmette Hospital, 10 patients recovered and 1 patient died few days after operation. In Stung Treng Province, the registration and follow-up could not be done because people are more mobile from villages to field huts in farms.

Clinical examination during the stool survey has been conducted to assess signs and symptoms including liver and spleen enlargement every year. Since 2003 no new symptomatic case was observed in the provinces' health facilities.

Soil Transmitted Helminth

The prevalence soil transmitted helminths were examined in a sample of villages in Kratie and Stung Treng in 1997.

In Kratie, the prevalence of *A. lumbricoides* was between 9.5% and 74.5%, *T. trichiura* between 0% and 15.9%, and hookworms between 18.2% and 86%. Since 1997, mebendazole 500 mg has been combined with praziquantel during the mass drug administration. The prevalence of *A. lumbricoides* and *T. trichiura* decreased dramatically while the prevalence of hookworms has been halved but remains relatively high. Table 3 presents the STH prevalence in villages for which both data in 1997 and 2005 are available.

Discussion

According to the UNDP Human Development Report (2003), Cambodia ranks 130th out of 175 countries on the human development index. Despite this low ranking and because decision makers are strongly committed, Cambodia was able to organize universal drug administration with praziquantel and mebendazole for 8 years that resulted in a reduction of schistosomiasis and STH infection to levels that:

- No new cases of severe morbidity due to schistosomiasis are reported in the last 4 years in the health facilities in the area
- Relevant nutritional benefits are expected after the reduction of STH ((WHO 2002).

We interpret the presence of new cases in three villages in 2005 probably due to contamination by animal reservoirs (Strandgaard et al., 2001), immigrants from Laos or infected people that were not covered by the control programme. The new cases demonstrate also that all the conditions are in place for the re-insurgence of the disease once the control measures are interrupted. Experiences from Lao PDR demonstrated that, after the drastic reduction of the prevalence, if the drug pressure is not maintained the parasite could easily return to original levels (Urbani et al. 2002). We assume that the drug distribution should be maintained until sanitation standard will improve significantly. A possible option to maintain the disease under control and to reduce the cost of the yearly mass distribution could be to increase the intervals between mass administrations (i.e. every two years) and associate this with a very sensitive (ELISA) monitoring of the prevalence of the infection (Homae et al 2004).

The experience in Cambodia demonstrates that with political commitment, parasitic diseases control is achievable even in situation of minimal resources and that different anthelminthic drug can be provided by the same delivery system. The programme represents a successful model for other developing countries.

Acknowledgement

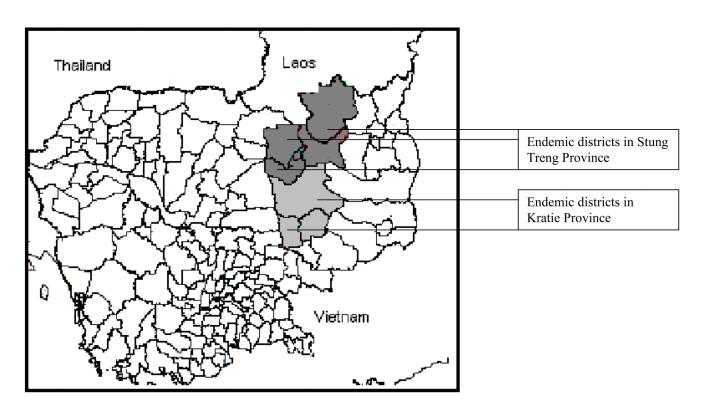
This article is dedicated to Dr. Carlo Urbani. An indispensable contribution was made by MSF. We would like to appreciate all the staff from the National Center for Parasitology, Entomology and Malaria Control, Provincial Health Department in Kratie and Stung Treng, Ministry of Health, Calmette Hospital, Ministry of Education Youth and Sports. The programme has been funded by Médecins Sans Frontières (1994-1999) and Sasakawa Memorial Health Foundation and Japanese Government through World Health Organisation (1999 to present).

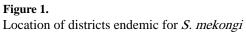
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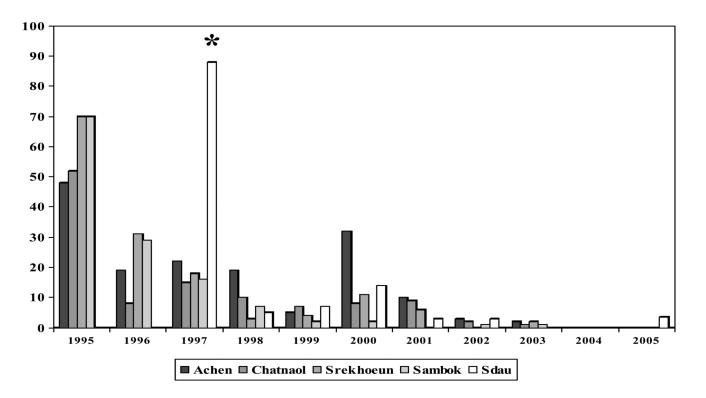


Figure 2.

Change in schistosomiasis prevalence in sentinel sites during the programme implementation.

Table 1

Details on the mass drug administration campaigns for the control of schistosomiasis in Cambodia from 1994-2005.

Year	Province covered	Type of mass treatment conducted	Organizing institution	Approximate target population	
1994 -95	Kratie	Universal	MoH - MSF	45 000	
1996	Kratie	Universal	MoH - MSF	45 000	
1997	Kratie and Strung Treng	Universal	NMC-MSF	60 000	
1998	Kratie and Strung Treng	No MDA 1	NMC-MSF	NA	
1999	Kratie and Strung Treng	Universal	NMC-MSF	60 000	
2000	Kratie and Strung Treng	Universal	NMC-MSF- WHO	70 000	
2001	Kratie and Strung Treng	Universal	NMC-WHO	80 000	
2002	Kratie and Strung Treng	Universal	NMC-WHO	80 000	
2003	Kratie and Strung Treng	Targeted ²	NMC-WHO	78 500	
	Kratie and Strung Treng	Universal ³	NMC-WHO	1 500	
2004	Kratie and Strung Treng	Universal	NMC-WHO	80 000	
2005	Kratie and Strung Treng	Universal	NMC-WHO	80 000	

¹Mass Drug Administration was not conducted because of lack of fund

 $\frac{2}{\text{in }112}$ villages

 $\frac{3}{1}$ in 3 villages

MoH Ministry of Health MSF Médicins Sans Frontières NMC National Center for Parasitology, Entomology and Malaria Control WHO World Health Organization

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Table 2

Prevalence of S. mekongi in Stung Treng (estimated in villages randomly selected every year)

Year	Coverage		alence survey (by village)		
		Number of villages surveyed	Number of exams	Number of villages with active transmission (%)	Range of prevalence in positive villages
1997	64%	13	1033	11 (85%)	6% - 88%
1998	NA	6	401	9 (83%)	5.1% - 43.1%
1999	63%	8	676	5 (62%)	1.8% - 7.7%
2000	64%	13	849	10 (76%)	2% - 19.6%
2001	67%	13	1029	5 (39%)	1.4% - 7.2%
2002	62%	13	999	5 (39%)	1.3% - 4.5%
2003	**	14	1573	0 (-)	-
		5	502	0 (-)	-
2004	83.6%	8	905	0 (-)	-
2005	81.5%	10	1298	3 (30%)	0.7% - 3.5%

*Mass Drug Administration was not conducted because of lack of fund was not conducted for lack of fund

** Coverage survey was not conducted

Table 3

Changes in prevalence of Soil Transmitted Helminth in selected villages of Kratie and Stung Treng between 1997 and 2005

	1997			2005		
	A. lumbricoides	T. trichura	Hookworms	A. lumbricoides	T. trichura	Hookworms
Achen	25	1.6	54.7	0	0	14.3
Chartnol	9.5	2.4	46.4	0.9	0	6.1
Sambok	16.2	2.1	45.1	0	0	9
Srekhoeun	13.8	3.4	50	0	0	5.7
Sdau	51.3	9.5	86	0	0.7	18.4
Koh Sneng	34	2.1	55.3	5.4	2.0	15.6
K. Chanh Tuk	69.6	2.2	67.4	0	0	26