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Foci of *Schistosomiasis mekongi*, Northern Cambodia: II. Distribution of infection and morbidity

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Summary In the province of Kracheh, in Northern Cambodia, a baseline epidemiological survey on *Schistosoma mekongi* was conducted along the Mekong River between December 1994 and April 1995. The results of household surveys of highly affected villages of the East and the West bank of the river and of school surveys in 20 primary schools are presented. In household surveys 1396 people were examined. An overall prevalence of infection of 49.3% was detected by a single stool examination with the Kato-Katz technique. The overall intensity of infection was 118.2 eggs per gram of stool (epg). There was no difference between the population of the east and west shore of the Mekong for prevalence ($P = 0.3$) or intensity ($P = 0.9$) of infection. Severe morbidity was very frequent. Hepatomegaly of the left lobe was detected in 48.7% of the population. Splenomegaly was seen in 26.8% of the study participants. Visible diverted circulation was found in 7.2% of the population, and ascites in 0.1%. Significantly more hepatomegaly ($P = 0.001$), splenomegaly ($P = 0.001$) and patients with diverted circulation ($P = 0.001$) were present on the west bank of the Mekong. The age group of 10–14 years was most affected. The prevalence of infection in this group was 71.8% and 71.9% in the population of the West and East of the Mekong, respectively. The intensity of infection was 172.4 and 194.2 epg on the West and the East bank, respectively. In the peak age group hepatomegaly reached a prevalence of 88.1% on the west and 82.8% on the east bank. In the 20 schools 2391 children aged 6–16 years were examined. The overall prevalence of infection was 40.0%, ranging from 7.7% to 72.9% per school. The overalls mean intensity of infection was 110.1 epg (range by school: 26.7–187.5 epg). Both prevalence ($P = 0.001$) and intensity of infection ($P = 0.001$) were significantly higher in schools on the east side of the Mekong. Hepatomegaly (55.2%), splenomegaly (23.6%), diverted circulation (4.1%), ascites (0.5%), reported blood (26.7%) and mucus (24.3%) were very frequent. Hepatomegaly ($P = 0.001$), splenomegaly ($P = 0.001$), diverted circulation ($P = 0.001$) and blood in stool ($P = 0.001$) were significantly more frequent in schools of the east side of the Mekong. Boys suffered more frequently from splenomegaly ($P = 0.05$), ascites ($P = 0.05$) and bloody stools ($P = 0.004$) than girls. No difference in sex was found for the prevalence and intensity of infection and prevalence of hepatomegaly. On the school level prevalence and intensity of infection were highly associated ($r = 0.93$, $P = 0.0001$). The intensity of infection was significantly associated only with the prevalence of hepatomegaly ($r = 0.44$, $P = 0.05$) and blood in stool ($r = 0.40$, $P = 0.02$). This comprehensive epidemiological study documents for the first time the public health importance of schistosomiasis mekongi in the Province of Kracheh, Northern Cambodia and points at key epidemiological features of this schistosome species, in particular the high level of morbidity associated with infection.

keywords *Schistosoma mekongi*, schistosomiasis, Cambodia, epidemiology, morbidity, Mekong River

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Introduction

In 1992 a focus of *Schistosoma mekongi* was rediscovered in Northern Cambodia. A supervisory visit for the control of malaria took place in the provincial hospital of Kracheh by the Cambodian Ministry of Health in collaboration with a representative of Action Internationale Contre La Faim. Patients with severe infections with *S. mekongi* were detected in the

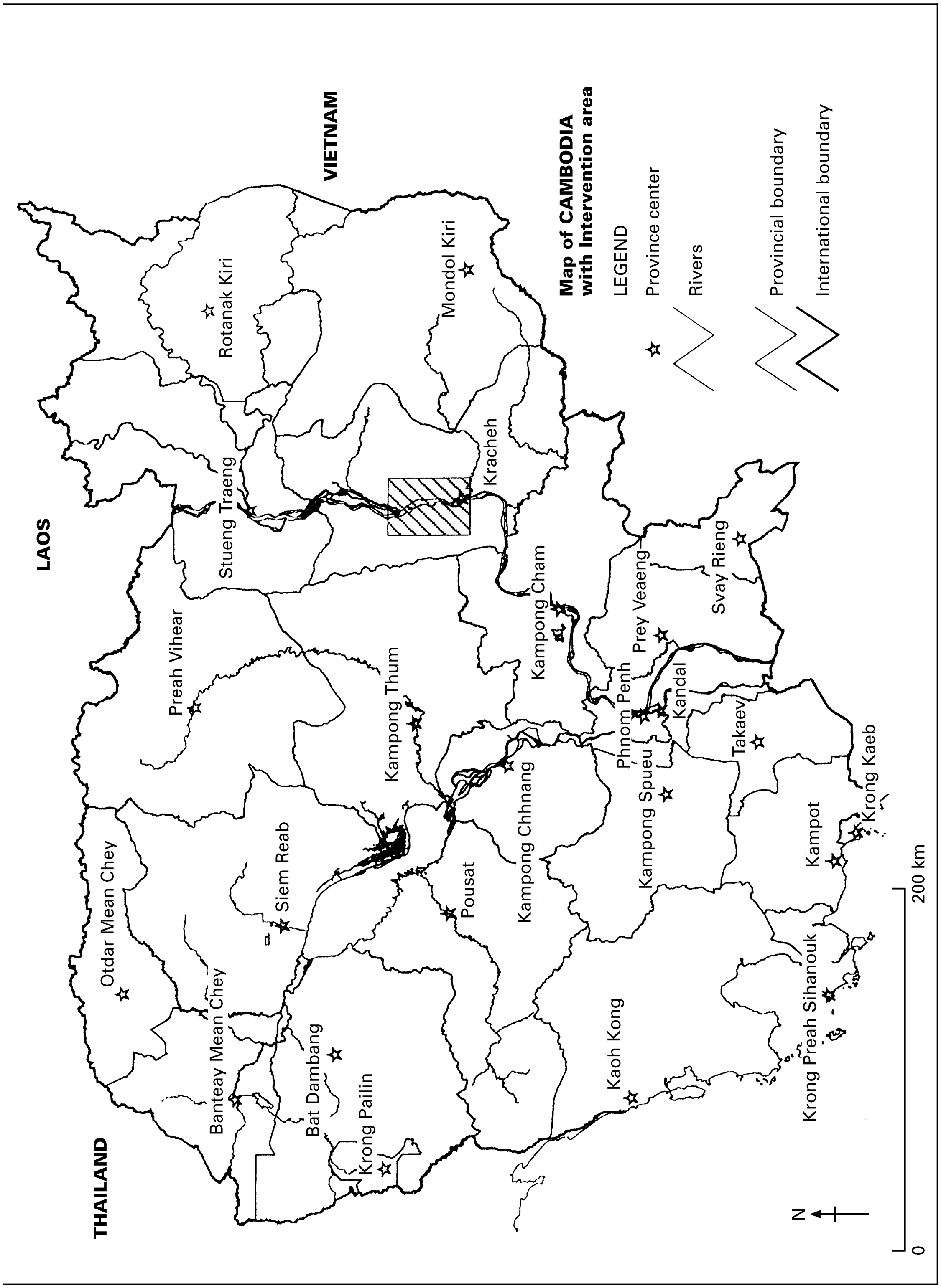

Figure 1 Map of Cambodia with Province of Kracheh

area of Kracheh, presenting hepatomegaly of the left lobe, signs of severe portal hypertension (splenomegaly, haematemesis, ascites) and severely impaired general condition (poor nutritional status, stunting). Fatal outcome of the infection was frequent. A preliminary study performed by Médecins Sans Frontières (MSF) revealed a prevalence of schistosomiasis of up to 84% in primary school children (Goubert *et al*. 1994)

S. mekongi was first described in 1957 in Paris, when Vic-Dupont *et al*. (1957) found it in a patient originating from the Khong Island in Southern Laos. Barbier (1966) detected another five cases of this new form of schistosomiasis in patients from Asia, also in Paris. In the following years, transmission was demonstrated on Khong Island in the Mekong River, Southern Laos, located only some 30 km north of the border with Cambodia (Sornmani *et al*. 1976). The first cases of *Schistosomiasis mekongi* were diagnosed in Cambodia in 1968. Audebaud *et al*. (1968) reported a 12-year-old Vietnamese girl who was infected with *S. mekongi* in a hospital in Phnom Penh, Cambodia. The girl originated from Kracheh town, the capital of the Province of Kracheh, Northern Cambodia, which is located on the shore of the Mekong river some 250 km north of Phnom Penh (Figure 1). A subsequent survey conducted in Kracheh town by Jolly *et al*. (1970) in 1968 detected *S. mekongi* infection and related morbidity in the community of Vietnamese fishermen living in houseboats on the Mekong River close to Kracheh. The schistosomiasis survey conducted in 1968/9 (Ijima 1970) using an *S. japonicum* antigen test along the Mekong River from Stung Treng to the Vietnamese border concluded that the disease was present in several provinces, Stung Treng, Kracheh, Kampong Cham and close to the Vietnamese border. The highest prevalences were found in the Province of Kracheh.

In the following years of civil war and unrest, the schistosomiasis focus of Kracheh was 'forgotten'. Hundreds of thousands of Cambodian refugees settled in camps along the border of Thailand. But reports of laboratory examination of stools samples of refugees in these camps concluded that schistosomiasis due to *S. mekongi* was transmitted in several provinces in Cambodia, namely in the provinces of Kracheh, Stung Treng and Battambang (Keittivuti *et al*. 1982). Even after 1992 work could only be conducted in the communities with substantial security precautions.

In the province of Kracheh the period of transmission of *Schistosoma mekongi* is the dry and hot season between February and April. The Mekong river reaches low water and current slows, which allows the development of large snail populations. In Kracheh, *Neotricula aperta* was shown to be the intermediate host snail of *S. mekongi* in 1994 (Mouchet 1995). It is associated with rocks and stones on the river bed.

In 1993 a project to rehabilitate the provincial hospital of Kracheh and the district hospital of Sambour was launched by Médecins Sans Frontières (Figure 2). Observations at the two hospitals and in the surrounding communities revealed severe schistosomiasis morbidity and mortality (Biays *et al*.

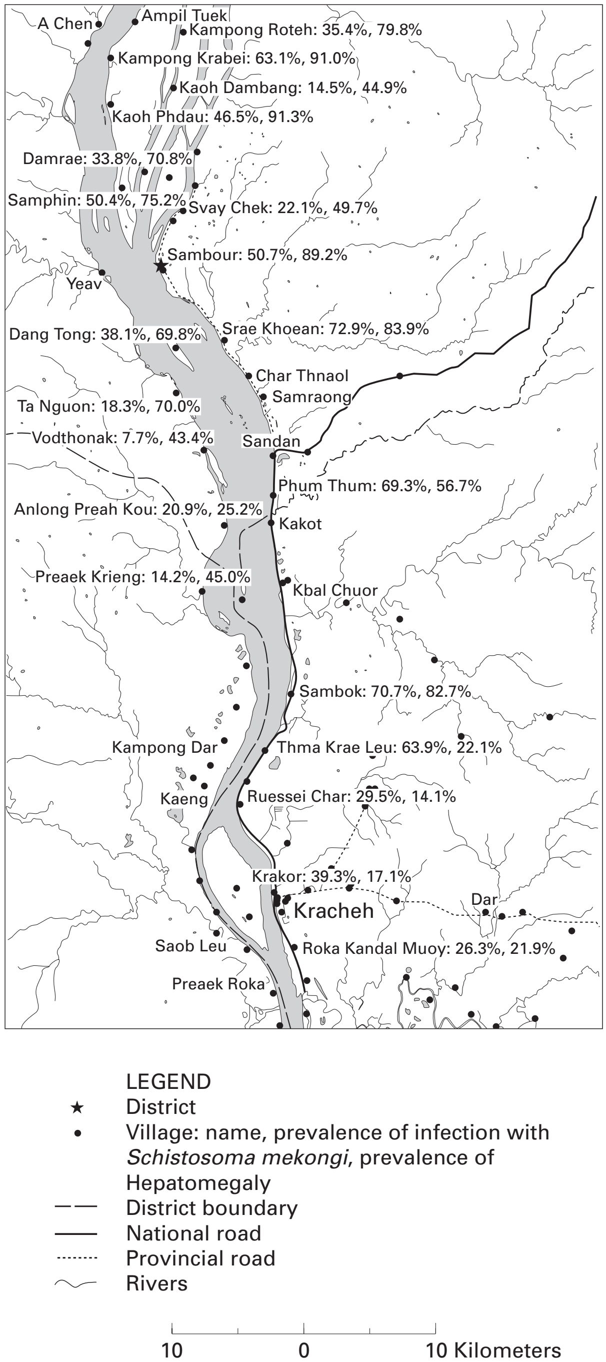

Figure 2 Study area in the Province of Kracheh with results of primary school surveys 1994/5. Prevalence of infection with *Schistosoma mekongi* and prevalence of hepatomegaly.

1999). In the first months of 1994 more than 40% of the outpatients at the hospital were schistosomiasis cases. Five to 10 patients with severe symptoms associated with portal hypertension (ascites) were permanently to be found in the inpatient ward. Death due to rupture of oesophageal varicoses was frequent.

The first community treatments were undertaken between December 1994 and April 1995. Visits to the communities for the treatment campaigns were also used to collect baseline data. The objective of the investigation was to describe the distribution of infection and morbidity by age, sex and location in order to establish baseline epidemiological data for the targeted control. We report the results of these baseline surveys with respect to infection with *S. mekongi* and related morbidity. Extensive descriptions on severe cases of schistosomiasis in Kracheh province are published in Biays *et al*. (1999).

Study area and population

The investigation was performed in the two northern districts, Sambour and Kracheh districts, of the province of Kracheh, Northern Cambodia (Figures 1 and 2). The study area corresponded with the intervention area of the schistosomiasis control programme conducted by Médecins Sans Frontières. It was based on the origin of the schistosomiasis cases seen at the provincial and district hospitals. The study area was populated by some 32 000 people in 29 villages (1992 census of the United Nations Transitory Authority for Cambodia), of which 20 villages had a primary school. Most people live along the Mekong river, which is intensively used for personal hygiene, household use, fishing, horticulture and recreation. Although in 1992 a development project had begun providing hand-pump wells to villages, only very few households had access to safe water at the time of our investigation in 1994/5. In the villages of the study area latrines were virtually nonexistent. The eastern bank of the Mekong is the most populated part. In the dry and hot season (between February and April) the steep shoreline (up to 20 m) is visible as well as the riverbed rocks and sandy spots towards the south. During the rainy season (June to September) the water rises up to the level of the houses and flooding in parts of villages is common. The western bank of the Mekong river is sparsely populated. The slight curve of the Mekong in the southern half of the study area favours the sedimentation of sand on that side of the river. During the dry season large sandy beaches emerge, constituting the main ecological feature.

The district capital of Sambour is located in the North of the study area (Figure 2). The southern limit of the study area was the village of Roka Kandal, south of the provincial capital Kracheh. Here the ecology of the river undergoes very obvious changes: whereas north of it water currents along rocky beaches predominate, towards the south the Mekong develops into a vast stream along sandy shores. The northern limit of the study area was approximately 50 km upstream from Kracheh town in Achen. North of it there are only scattered houses.

Approach

Two approaches were used. Firstly, household surveys were conducted in comparable villages on the two sides of the river in order to study the age distribution of infection and morbidity in the population of the east and west shore of the Mekong. For this the entire population of these villages was examined. Secondly, a sample of pupils was examined in all the 20 primary schools of the study area, which provided data on the geographical distribution of infection and morbidity within the study area. Before all investigations, consent was obtained from the provincial, district and village authorities, primary school teachers and the study participants. All study participants except pregnant women and children under 2 years of age received a curative dose with Praziquantel (40 mg/kg body weight) combined with Mebendazol (500 mg) after the survey.

Household survey

Villages with a severe schistosomiasis burden were chosen. The hospital records of Sambour district hospital were used to identify villages from which severe schistosomiasis patients were seen frequently. Achen village was chosen on the west bank and Char Thnaol and Samraong on the east shore of the Mekong. The latter two neighbouring villages have comparable populations and habitats on the shore as Achen village. Furthermore, the appearance of the river and its shore are very similar in the Char Thnaol and Samraong.

On the first survey day all members of all households were registered (household, name, age and sex) and given a stool container. On the next day, households were revisited, the stool samples collected and all participants clinically examined. 1739 persons were enrolled in the household survey. Of these 1735 (= 99.8%) were correctly registered, 1464 (= 81.2%) study participants provided stool samples for parasitological examinations and 1488 (= 85.6%) underwent a clinical examination. 1396 (= 80.3%) individuals possessed a complete record with clinical and parasitological examinations. Only these data were further processed.

School survey

We surveyed all 20 primary schools of the study area. In larger schools, a random sample of children ($n = 150$) was selected, while in smaller schools all children were enrolled. On the first day children were selected and given stool containers. On the following day the stool samples were collected and the children clinically examined.

We registered 2786 children *in toto*, aged 6–16 years, of whom 2391 (= 85.8%) completed all examinations. Non-compliant pupils were significantly older (*t*-test, $P = 0.01$) than compliant ones, albeit by only 0.2 years (11.1 *vs.* 10.9 years of mean age). As the sample size is large the difference is significant; however, for exposure to schistosomiasis transmission this difference in age is irrelevant. Compliance varied widely between the villages from 100% in Kaoh Dambang to 64.6% in Krakor. But the association between sex ratio and compliance is not influenced by location (χ^2-test, controlled for village: $P = 0.9$).

Parasitological examination

After collection the stool samples were transported in cooled containers to the laboratory of the Provincial Hospital in Kracheh where they were processed within 36 h after collection. One Kato-Katz examination (using approximately 0.042 g of stool) was performed per stool and per person (Katz *et al.* 1972). An experienced laboratory technician counted the number of eggs of *S. mekongi* per slide. Another examiner checked 10% of the slides for quality control.

Clinical examination

Each individual was examined clinically for splenomegaly, hepatomegaly and presence of diverted circulation and ascites. Spleen enlargement was registered using the Hackett score (Hackett 1944). Hepatomegaly was scored by palpating the left liver lobe along the xiphoid-umbelicus line. Hepatomegaly was defined as absent when the left liver lobe was not palpable and as present when the left liver lobe was palpable under the xiphoid. The presence of ascites was assessed by palpation. Two experienced clinicians performed the examinations, and cross-examinations were done for quality control. In addition school children were asked whether they had observed blood and/or mucus in their stools over the past three days.

Data analysis

The data were entered into EpiInfo (Version 6.0). All entries were cross-checked against data sheets. Analysis of the data was performed using the SAS statistic package. Geometric means were calculated on egg counts of infected individuals. *T*-tests were used to compare means of age and egg-counts (log(egg-count)), and the Mantel Haenszel χ^2-test (controlling for age and/or sex) to compare prevalence of infection and morbidity. Pearson correlation was used to examine the association of two prevalences.

Results

Household surveys

Table 1 gives the age and sex indicators of the population and the results of the clinical and parasitological examinations of the study participants. On the east bank 737 and on the west bank 659 individuals were examined. The overall mean age of the study participants was 22.1 years, with a range from 0 to 81 years and a standard deviation of 17.6 years. Significance testing of mean age between the two riverbanks (*t*-test: $P = 0.1$) and between the villages of the east bank (*t*-test: $P = 0.1$) did not show any significant difference (Table 1). Furthermore, the age range and the standard deviation were comparable in all the villages. The study population of the two river banks therefore possessed a comparable age-sex structure.

Almost half (49.3%) of the study population was infected with *S. mekongi*. The prevalences of both Mekong banks were very close to the overall prevalence and not significantly different (χ^2-test, controlled for age and sex: $P = 0.3$). The infection rates of Char Thnaol and Samraong (χ^2-test, controlled for age and sex: $P = 0.6$) were similar. The overall mean intensity of infection was 118.2 epg, with a mean intensity of 114.6 epg in Char Thnaol, 131.8 epg in Samraong and 116.5 epg in Achen. There was no significant difference between river banks (*t*-test: $P = 0.9$), nor between Char Thnaol and Samraong (*t*-test: $P = 0.6$).

Figure 3(a,b) shows the age-specific prevalence curve for infection indicators. The observed curves are typical age-prevalence/intensity of infection for foci of schistosomiasis, which have been established for several decades. Figure 3(a) displays the age-specific prevalence and 3b the age-specific intensity of infection with *S. mekongi* of the studied population on the east (Char Thnaol and Samraong pooled) and west side of the Mekong. Both prevalence and intensity of infection curves possess peaks in the group of 10–14 year-olds. The peak prevalence of infection reached 71.8% on the west shore and 71.9% on the east bank. 10% of the children are already infected by the age of 4 and more than 20% of adults of 50 years and older still shed *Schistosoma* eggs. The peak intensity of infection was 172.4 epg on the west side and 194.2 epg on the east side of the river (Figure 3b). There was no significant difference in prevalence of infection between the riverbanks in any of the age groups (χ^2-test, controlled for sex: $P > 0.3$), whereas the intensity of infection did differ. Adults from the east bank shed significantly more eggs in the 30–39 (*t*-test: $P = 0.01$) and 40–49 age groups (*t*-test: $P = 0.03$). In the remaining groups there were no differences in intensity of infection.

Table 1 Household study: study participants and prevalence and intensity of infection with *Schistosoma mekongi* ($n = 1396$)

	East shore			Difference between villages	West shore	All total	Difference: East–west
	Chatnaol	Samraong	Total		Achen		
Examined:							
n	496	241	737		659	1396	
Sex ratio:m/f	0.97	0.87	0.93	0.5*	0.97	0.95	0.7*
Age (years)							
Male: mean	21.5	22.0	21.6	0.1**	21.7	21.7	0.2
Female: mean	22.2	22.7	22.4	0.5	22.7	22.5	0.5
Total: mean	22.9	22.3	22.0	0.1	22.2	22.1	0.1
Range	1–81	0–77	0–81		0–75	0–81	
SD	17.6	19.2	18.1		17.1	17.6	
Infection:							
Prevalence							
Male	52.9	50.0	51.2		48.2	50.2	
Female	50.4	45.7	48.8		48.1	48.5	
Total	51.6	47.7	50.3	0.6**	48.1	49.3	0.3**
Intensity***all infected: (eggs/gram)							
Male:	116.9	126.9	119.9	0.8	120.4	120.1	0.9
Female:	112.3	136.9	119.6	0.6	112.8	116.4	0.7
Total:	114.6	131.8	119.7	0.6	116.5	118.2	0.9
Symptoms:							
Hepatomegaly							
Male	52.9	42.9	49.7		50.0	49.9	
Female	42.5	36.4	40.4		55.9	47.6	
Total	47.6	39.4	44.9	0.01	53.0	48.7	0.001
Splenomegaly							
Male	17.2	2.7	12.6		45.4	28.2	
Female	8.3	3.9	6.8		46.6	25.4	
Total	12.7	3.3	9.9	0.001	46.0	26.8	0.001
Diverted circulation							
Male	4.9	2.7	4.2		11.7	7.8	
Female	2.8	3.1	2.9		10.8	6.6	
Total	3.8	2.9	3.5	0.5	10.2	7.2	0.001
Ascites							
Male	0	0	0		0.3	0.2	
Female	0.4	0	0.3		0	0.1	
Total	0.2	0	0.1	0.5	0.2	0.1	0.9

* Maentel-Haenzel χ^2-test, controlled for age; ** *t*-test; *** intensity of infection in eggs/gram stool; † Maentel-Haenzel c∂2-test, controlled for age and sex.

Morbidity

Schistosomiasis morbidity was very frequent (Table 1). Almost half (48.7%) of the individuals examined were suffering from left lobe hepatomegaly, and more than a quarter (26.8%) suffered from splenomegaly. Diverted circulation, a sign of portal hypertension, was observed in 7.2% of the persons examined and two villagers (0.1%) were found to suffer from clinically detectable ascites. Most morbidity was detected in Achen, where the prevalences of hepatomegaly ($P = 0.001$), splenomegaly ($P = 0.001$) and diverted circulation ($P = 0.001$) were significantly higher than in the villages of the opposite bank. Furthermore, in Char Thnaol on the east bank significantly more hepatomegalies ($P = 0.01$) and splenomegalies ($P = 0.001$) were diagnosed than in Samraong.

While the prevalence of left liver lobe enlargements was high on both river banks, splenomegaly and diverted circulation prevalences are much lower on the east bank. The overall prevalence of hepatomegaly was not associated with sex ($P = 0.7$, controlled for age). However, on the east side significantly more males ($P = 0.004$) and on the west side of the

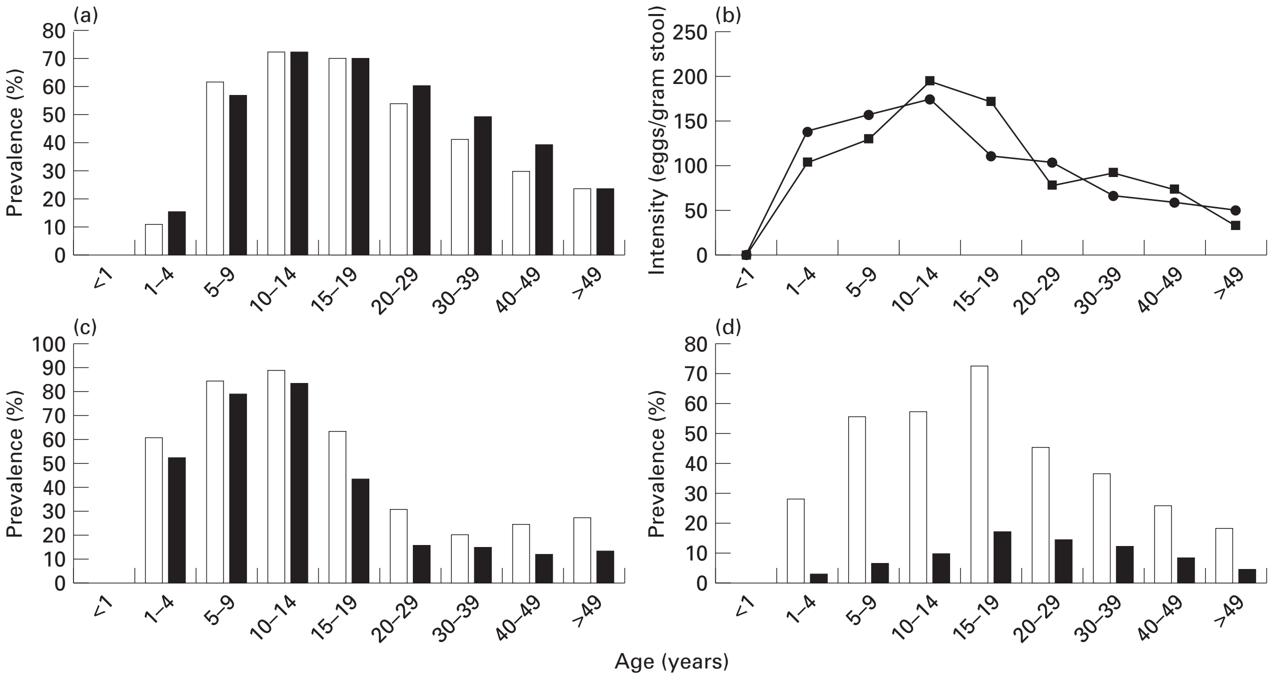

Figure 3 a, Age distribution of prevalence of infection with *Schistosoma mekongi* in a household survey on the west (Achen: □) and east (Char Thnaol and Samraong: ■) bank of the Mekong River. b, Age distribution of intensity of infection (geometric means) with *S. mekongi* in the household survey on the west (Achen: ●) and east (Char Thnaol and Samraong: ■) bank of the Mekong River. c, Age distribution of hepatomegaly in the household survey on the west (Achen: □) and east (Char Thnaol and Samraong: ■) bank of the Mekong River. d, Age distribution of splenomegaly in the household survey on the west (Achen: □) and east (Char Thnaol and Samraong: ■) bank of the Mekong River.

river more females ($P = 0.01$, controlled for age) were suffering from left liver lobe enlargement. The overall prevalence of splenomegaly was equal for both sexes ($P = 0.3$). In Achen splenomegaly was found in both sexes with the same frequency ($P = 0.4$, controlled for age). But on the east bank of the river more males suffered from splenomegaly ($P = 0.006$, controlled for age). Only in Char Thnaol we found a significant difference between sexes ($P = 0.003$, controlled for age).

The age-specific prevalence of hepatomegaly (Figure 3c) revealed that children between 10 and 14 suffered most morbidity resulting from *S. mekongi* infections. The peak was 88.1% in the west and 82.8% east of the Mekong. Severe morbidity was detected also in very young children. More than half of the children on both riverbanks suffer from hepatomegaly before they reach 5 years of age.

In all the age groups the observed prevalence of hepatomegaly was higher on the west bank. These differences, however, were only significant for 15–19 year-olds (χ^2-test, controlled for sex: $P = 0.03$), 20–29 year-olds (χ^2-test, controlled for sex: $P = 0.01$) and the oldest age group (χ^2-test, controlled for sex: $P = 0.05$).

The age distribution of the prevalence of splenomegaly (Figure 3d) was shaped similarly on both riverbanks, but reached much higher levels on the west side. Prevalence differences in all age classes were highly significant (χ^2-test, controlled for sex: $p \leq 0.01$). The peak prevalence reached 72.6% on the west and 17.4% on the east side of the river, and on both banks affected young adults aged 15–19 rather than 10–14 year-olds, as was the case for hepatomegaly and infection and intensity of infection.

On the individual level the intensity of infection was significantly but weakly correlated with hepatomegaly ($r = 0.23$, $P < 0.001$), splenomegaly ($r = 0.08$, $P = 0.02$) and the presence of diverted circulation ($r = 0.09$, $P < 0.001$). No significant correlation was found between intensity of infection and the presence of an ascites ($r = -0.01$, $P = 1.0$).

School surveys

The results of the surveys are presented in Tables 2 and 3. 2391 children from all 20 schools (aged: 6–16; mean: 10.8 years) participated, an average of 139 children per village (range: 66–181). The difference between the two river banks was not significant (t-test: $P = 0.2$). For significant testing age

Table 2 School Survey: Population and Prevalence and Intensity of *Schistosoma mekongi* Infection in 20 Primary Schools in the Province of Kracheh, Northern Cambodia ($n = 2391$)

Village	*n* included			Age	Prevalence (%) of infection			Intensity of infection		
(from South to North)	Male	Female	Total	Mean	Male	Female	Total	Male	Female	Total
Eastern bank and island										
Roka Kandal	66	71	137	9.7	25.8	26.8	26.3	113.9	51.4	74.8
Krakor	65	52	117	12.3	43.1	34.6	39.3	97.2	115.3	103.9
Ruessei Char	90	66	156	10.1	37.7	19.7	29.5	54.2	59.4	55.6
Thma Krae Leu	65	57	122	10.8*	67.7	59.6	63.9	136.1	122.4	129.9
Sambok	78	55	133	11.8	69.2	72.7	70.7	152.1	140.1	146.8
Phum Thum	83	67	150	9.2	73.5	64.2	69.3	176.2	155.4	167.3
Srae Khoean	59	59	118	10.6	66.1	79.7	72.9	140.3	207.2	173.6
Sambour	79	69	148	12.8	53.2	47.8	50.7	126.3	100.2	114.1
Svay Check	64	81	145	11.3	21.9	22.2	22.1	78.7	55.2	64.4
Damrae	34	31	65	10.5	29.4	38.7	33.8	67.4	87.1	77.5
Samphin	60	69	129	11.7	45.0	55.1	50.4	135.8	101.5	114.6
Kaoh Dambang	30	39	69	11.0	20.0	10.3	14.5	28.0	25.0	26.7
Kaoh Phdau	59	68	127	11.2	33.9	57.4	46.5 *	106.2	125.5	118.6
Kampong Krabei	60	62	122	11.1	61.7	64.5	63.1	164.5	211.6	187.5
Kampong Roteh	35	44	79	11.1	22.9	47.5	35.4 *	49.1	59.8	56.5
Total	927	890	1817	11.0	47.5	47.0	47.2	120.5	117.7	119.1
Western bank										
Preaek Krieng	89	80	169	10.3	14.6	13.8	14.2	34.5	43.9	38.5
Anlong Preak Kou	77	62	139	10.3	23.4	17.7	20.9	59.2	84.7	67.8
Vodthonak	76	67	143	10.2	9.2	6.0	7.7	59.3	29.6	46.0 *
Tagnuon	34	26	60	10.7	20.6	15.4	18.3	74.9	58.1	68.3
Dang Tong	33	30	63	11.1	39.4	36.7	38.1	60.2	67.5	63.5
Total	309	265	574	10.4	18.8	15.5	17.3	54.2	58.1	55.8
Total	1236	1155	2391	10.8	40.3	39.7	40.0	109.8	110.5	110.1
Difference between Mekong banks (*P*-value)			0.3	0.2			0.001	< 0.001	< 0.001	< 0.001

SD standard deviation all schools tested for difference of sex: for age (mean): *significant difference (t-test: $P < 0.05$) and for intensity of infection (t-test: $P < 0.05$) between sex.

and sex were introduced as confounding factors.

S. mekongi infections were found in 40.0% of all children, with a mean intensity of infection of 110.1 epg. *S. mekongi* infections were found in all schools, but prevalence and intensity of infection varied widely. The prevalence ranged from 7.7% in Vodthonak to 72.9% in Srae Khoean. The intensity of infection varied from 26.7 epg in Kaoh Dambang to 187.5 epg in Kampong Krabei. The difference in sex was not significant for either prevalence (χ^2-test, controlled for age: $P = 0.5$) or intensity of infection (t-test: $P = 0.8$) in the overall data, nor between sexes, for both river banks (prevalence: east: χ^2-test: $P = 0.8$, west: $P = 0.3$; intensity in east: t-test: $P = 0.9$, west: $P = 0.7$). However, the prevalence (χ^2-test, controlled for age and sex: $P = 0.001$) and intensity of infection (t-test: $P = 0.001$) were significantly higher in the eastern than in the western part of the study area.

On the school level, a very strong positive correlation existed between the prevalence and mean intensity of infection (Pearson correlation: $r = 0.93$, $P = 0.0001$, Figure 4).

Morbidity

The prevalence of symptoms associated with *S. mekongi* infection was striking, with 55.2% of the children suffering from hepatomegaly and 23.6% from splenomegaly (Table3). The severity of the disease is substantial, as 4.1% of the children displayed clearly diverted circulation, a sign of portal hypertension. In 12 pupils (0.5%) ascites was diagnosed. One quarter of the children reported blood (26.7%) and mucus (24.3%) in their stools.

Hepatomegaly (χ^2-test, controlled for age and sex: $P = 0.001$), splenomegaly (χ^2-test, controlled for age and sex: $P = 0.001$), diverted circulation (χ^2-test, controlled for age and sex: $P = 0.001$) and reported blood in stool (χ^2-test, con-

Table 3 School survey: morbidity related to infection with *Schistosoma mekongi* in 20 primary schools in the province of Kracheh, Northern Cambodia (n = 2391)

Village	Clinical Examination: Prevalence (%) of												Prevalence (%) of reported					
(from South	Hepatomegaly			Splenomegaly			Shunt circulation			Ascites			Blood in stool			Mucus in stool		
to North)	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Eastern bank and island																		
Roka Kandal	18.2	25.4	21.9	7.6	5.6	6.6	0	0	0	0	0	0	12.1	9.9	11.0	18.2	21.1	19.7
Krakor	23.1	9.6	17.1 *	13.8	3.9	9.4	0	0	0	0	0	0	7.7	7.7	7.7	4.3	3.9	4.3
Ruessei Char	13.3	15.2	14.1	10.0	3.0	7.1	0	0	0	0	0	0	21.1	7.6	15.4 *	12.2	4.6	9.0
Thma Krae Leu	27.7	15.8	22.1	12.3	5.3	9.0	0	0	0	0	0	0	27.7	8.7	18.6 *	29.2	14.0	22.1 *
Sambok	91.0	70.9	82.7 *	68.0	47.3	59.4 *	2.6	0	1.5	7.7	0	4.5 *	50.0	47.3	48.9	44.8	49.1	46.6
Phum Thum	60.2	52.2	56.7	18.1	14.9	16.7	1.2	0	0.7	2.4	0	1.3	50.6	62.7	56.0	32.5	44.8	38.0
Srae Khoean	91.5	76.3	83.9 *	20.3	25.4	22.9	1.7	3.4	2.5	0	0	0	33.2	30.5	31.4	28.8	27.1	28.0
Sambour	91.1	87.0	89.2	13.9	10.1	12.2	1.3	0	0.7	0	0	0	31.7	24.6	28.4	26.6	21.7	24.3
Svay Check	53.1	46.9	49.7	12.5	6.2	9.0	0	0	0	0	0	0	9.4	16.1	13.1	9.4	18.5	14.5
Damrae	67.6	71.2	70.8	32.4	29.0	30.8	0	0	0	2.9	0	1.5	32.4	29.0	30.8	17.7	6.5	12.3
Samphin	78.3	72.5	75.2	30.0	39.1	34.9	5.0	0	2.3	0	0	0	30.0	27.5	28.7	25.0	27.5	26.4
Kaoh Dambang	36.7	51.3	44.9	16.7	25.6	21.7	3.3	0	1.5	0	0	0	30.0	25.6	27.5	30.0	25.6	27.5
Kaoh Phdau	94.9	88.2	91.3	55.9	54.4	55.1	25.4	22.1	23.6	0	0	0	52.5	38.2	44.8	50.8	30.9	40.2 *
Kampong Krabei	93.3	88.7	91.0	53.3	59.7	56.6	15.0	24.2	19.7	0	0	0	45.0	27.4	36.1 *	36.7	16.1	26.2 *
Kampong Roteh	77.1	81.8	79.8	80.0	56.8	67.1	37.1	36.4	36.7	0	2.3	1.3	31.4	34.1	32.9	31.4	31.8	31.7
Total	60.2	56.5	58.4	27.7	24.6	26.2	5.0	5.4	5.2	1.0	0.1	0.6 *	31.1	26.2	28.7 *	26.3	23.3	24.8
Western bank																		
Preaek Krieng	46.1	43.8	45.0	6.7	6.3	6.5	0	0	0	0	1.3	0.6	37.1	32.5	34.9	29.2	31.3	30.2
Anlong Preak Kou	26.0	24.2	25.2	11.7	16.1	13.7	0	0	0	0	0	0	5.2	6.5	5.8	33.8	21.0	28.1
Vodthonak	43.4	43.3	43.4	17.1	7.5	12.6	0	0	0	0	0	0	21.1	9.0	15.4 *	14.5	6.0	10.5
Tagnuon	73.5	65.4	70.0	23.5	15.4	20.0	5.9	0	3.3	0	0	0	26.5	7.7	18.3	38.2	3.9	23.3 *
Dang Tong	75.8	63.3	69.8	60.6	26.7	44.4 *	9.1	0	4.8	0	0	0	33.3	23.3	28.6	27.3	10.0	19.1
Total	46.6	43.4	45.1	18.1	12.1	15.3	1.6	0	0.9	0	0.4	0.2	23.6	17.0	20.6 *	27.5	17.4	22.8 *
Total	56.8	53.5	55.2	25.3	21.7	23.6 *	4.1	4.2	4.1 *	0.7	0.2	0.5	29.2	24.1	26.7 *	26.6	21.9	24.3 *
Difference between Mekong banks (*P*-value)**			0.001			0.001			0.001			0.3			0.001			0.2

* Significant difference between sex χ^2-test, controlled for age (all schools tested), ** χ^2-test, controlled for age and sex

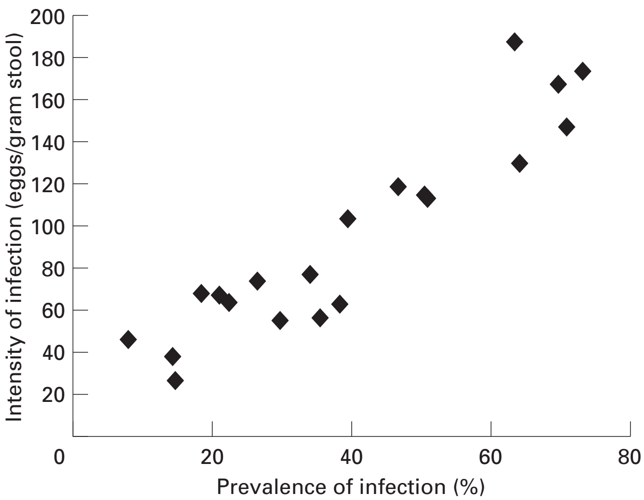

Figure 4 School survey (20 schools): scattergram of intensity of infection (epg) and prevalence of infection (%) with *S. mekongi*.

trolled for age and sex: $P = 0.001$) were significantly more frequent on the eastern bank.

More boys were suffering from morbidity related to *S. mekongi* infection. Significant differences were found for the prevalence of spleen enlargement (χ^2-test, controlled for age: $P = 0.05$), ascites (χ^2-test: $P = 0.05$) and reported blood (χ^2-test, controlled for age: $P = 0.004$) and mucus (χ^2-test, controlled for age: $P = 0.006$) in stool. These differences, however, do not find any correspondence in the infection data, where there was no consistent difference between the sexes (Table 2).

The Pearson correlation coefficient between the prevalence of infection and the prevalence of hepatomegaly ($r = 0.44$, $P = 0.05$), splenomegaly ($r = 0.38$, $P = 0.1$), diverted circulation ($r = 0.14$, $P = 0.5$) and ascites ($r = 0.36$, $P = 0.1$) and the prevalence of reported blood ($r = 0.58$, $P = 0.007$) and mucus in stool ($r = 0.46$, $P = 0.04$) showed only weak correlations. Similar results were obtained for the correlation between intensity and morbidity indicators. The correlations with prevalence of hepatomegaly ($r = 0.44$, $P = 0.05$) and reported blood in stool ($r = 0.50$, $P = 0.02$) were significant.

Discussion

The results of our surveys reveal the high morbidity level associated with infection with *S. mekongi*. The prevalences of infection and morbidity in under-fives are high. The burden of disease is illustrated by the frequent severe morbidity and mortality encountered in health facilities of the province or reported in the villages (Biays *et al*. 1999). Schistosomiasis is a public health issue of high priority in the Province of Kracheh, Northern Cambodia.

Although our study shows a high burden of infection, it probably underestimates the actual state. It is generally recommended that several (often 3) stool samples per person should be examined with the Kato-Katz technique as it has low sensitivity. Due to time and security constraints only one test could be performed per person. However, in a sample of children ($n = 150$) in Sambok village a Kato-Katz examination was performed on five consecutive days, and the prevalence of infection rose from an initial prevalence of 70.1% to a cumulative prevalence of 91.0% over 5 examinations. Furthermore, school surveys tend to underestimate the infection in school-aged children, as nonschool children may spend more time in the potentially infectious environment and generally belong to parts of communities with lower socio-economic status.

The comparison of infection and morbidity between the east and west banks of the Mekong reveals different patterns. In the school surveys the prevalence of infection and morbidity were both higher on the east bank, but the household survey detected more morbidity on the west bank, while infection was equal on both sides. It is most likely that this observation is due to concomitant infections, in particular due to infection with *Plasmodium* sp. In Cambodia malaria is transmitted in the forest. Achen on the West bank is densely surrounded by the forest, while a belt of rice fields separates the villages on the east bank from the forest. This may explain the higher prevalence of splenomegaly in Achen. It is especially during activities in the forest such as logging, that the population of the eastern side of the Mekong becomes infected. The fact that men, who traditionally work in the forest, present with splenomegaly significantly more often supports this. Therefore it can be concluded that hepatomegaly is the main specific sign of an advanced *S. mekongi* infection in Kracheh Province. This is underlined by the fact that on the school level only hepatomegly was significantly associated with the intensity of infection and not splenomegaly. The contribution of malaria to the spleen morbidity and its interaction with schistosomiasis is currently being studied in detail.

Further concomitant infections such as intestinal parasitosis and hepatitis could also have contributed to liver morbidity and reported intestinal symptoms. *Ascaris*, hookworm and *Trichuris* infections were frequently found in stool examinations. In Laos, the liver fluke infection of *Opisthorchis* sp., acquired through consumption of raw fish, contributes to liver pathology in schistosomiasis patients (Chen Ming Gang 1991). In Khmer communities the consumption of raw fish is not a habit and transmission is therefore unlikely. But in recent examinations in Kracheh province rare infections with *Opisthorchis* sp. could be detected. In recent follow-up surveys in Kracheh province *Strongyloides* sp. was also detected in school children with prevalences of up to 20%. The extent of the contribution of intestinal parasites to symptoms such as diarrhoea and blood and mucus in stools might be substantial and needs further clarification.

Since the baseline surveys were conducted, there have been four mass treatment interventions with praziquantel (40 mg/kg) in the province of Kracheh. Follow-up surveys in 5 sentinel schools showed that the infection rate has dramatically dropped from 60% to 14%. A similar reduction was observed for the reported intestinal symptoms. However, liver morbidity did not resolve in a comparable manner. A detailed evaluation of these observations is in progress.

Village data show an age distribution of symptoms and infection, which can be found in a well-established schistosomiasis focus with a peak burden of infection and morbidity in children between 10 and 15 years. Indeed schistosomiasis is well known by the population in endemic villages. Specific names have been given to the frequent signs and symptoms. The enlargement of the left liver lobe is called *santeas omal* ('nest of hornet' in the abdomen) and splenomegaly *tleak andaek* ('falling tortoise') (Biays *et al.* 1999). Moreover, in several villages the phenomenon of children with ascites is called *teach tuk* ('water in belly') and severe abdominal pain is known as *kdam sir* ('a pipe of crabs'). In certain villages sudden death due to spleen rupture and 'vomiting of blood' were frequently reported.

Our observations show that while schistosomiasis is present in all villages of the study area, the prevalences of infection and morbidity vary considerably. Generally the east bank villages are more affected due to the high population density in these areas. However, environmental factors also play a decisive role. In the high prevalence zone the river is characterized by rocks and rocky substrates which are associated with the intermediate host, *Neotricula aperta* (Mouchet 1995).

There are reasons to suppose that outside the investigated river stretch, schistosomiasis is present. Apart of reports dating from the 50 s and 60 s, evidence of infection was provided by a recent antigen study (against *S. japonicum*) in villages of the province of Kracheh (see map). Antigen-positive school children also live in villages south of the intervention area (personal communication, Matsuda 1998). Furthermore, investigations performed on school children in villages along the Mekong river and its tributaries in Stung Treng province could detect infection with *S. mekongi* in various villages. But only in mid 1998, after the Khmer Rouge army rallied to government, access to all districts of the Stung Treng province became safe. Investigations to clarify the distribution of schistosomiasis in this province are underway.

Our data demonstrate the severe degree of endemicity of *S. mekongi* in the Province of Kracheh in Northern Cambodia not only in terms of infection but, much more importantly, in terms of severe morbidity. As the experience of Kracheh province shows, uncontrolled transmission of schistosomiasis can lead to devastating situations even today.

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