Biology

Microbiology & Immunology fields

Okayama University *Year* 2008

The evaluation of control measures against Schistosoma mekongi in Cambodia by a mathematical model

Naoto Hisakane* Masashi Kirinoki† Yuichi Chigusa‡

Muth Sinuon** Duong Socheat††

Hajime Matsuda‡‡ Hirofumi Ishikawa§

*Department of Human Ecology, Graduate School of Environmental Science, Okayama University

†Center for Tropical Medicine and Parasitology, Dokkyo Medical University School of Medicine

‡Center for Tropical Medicine and Parasitology, Dokkyo Medical University School of Medicine

**National Center for Parasitology, Entomology and Malaria Control, Ministry of Health

††National Center for Parasitology, Entomology and Malaria Control, Ministry of Health

‡‡Institute of International Education and Research, Dokkyo Medical University School of Medicine

§Department of Human Ecology, Graduate School of Environmental Science, Okayama University,, ishikawa@ems.okayama-u.ac.jp

The evaluation of control measures against *Schistosoma mekongi* in Cambodia by a mathematical model

Naoto Hisakane[a], Masashi Kirinoki[b], Yuichi Chigusa[b], Muth Sinuon[c], Duong Socheat[c], Hajime Matsuda[d], Hirofumi Ishikawa[a,*]

[a] Department of Human Ecology, Graduate School of Environmental Science, Okayama University, 700-8530, Japan
[b] Center for Tropical Medicine and Parasitology, Dokkyo Medical University School of Medicine, 321-0293, Japan
[c] National Center for Parasitology, Entomology and Malaria Control, Ministry of Health, Cambodia
[d] Institute of International Education and Research, Dokkyo Medical University School of Medicine, 321-0293, Japan

[*] Address correspondence to: Hirofumi Ishikawa, Prof. Department of Human Ecology, Graduate School of Environmental Science, Okayama University, 700-8530, Okayama, Japan.
Tel. +81-86-251-8826, Fax. +81-86-251-8837, E-mail: ishikawa@ems.okayama-u.ac.jp

Abstract

We constructed a mathematical model for the transmission of *Schistosoma mekongi* in Cambodia. The simulation of the model will be instrumental in planning schistosomiasis control measures. The model includes two definitive hosts, humans and dogs, as animal reservoirs. Dogs are recognized to play an important role in schistosomiasis transmission in Cambodia. For the purpose of dealing with age-specific prevalence and intensity of infection, the human population was classified into eight age categories in the model. To describe the seasonal fluctuation of the intermediate host population of *S. mekongi*, the "Post-Spate Survival" hypothesis was adopted for the population dynamics of *Neotricula aperta* present in the Mekong River. We carried out simulations to evaluate the effect of universal treatment (UT) and targeted mass treatment (TT) with praziquantel on the reduction in prevalence of *S. mekongi*. The simulations indicated that biyearly UT for 8 years or yearly TT for 5 years after three courses of yearly UT could reduce the prevalence to below 5% when a UT or TT coverage of 85% of inhabitants was achieved. The simulation suggested that the suppression of *S. mekongi* in Cambodia would be possible by UT or TT with a high coverage rate.

Key words: *Schistosoma mekongi*; Cambodia; mathematical model; *Neotricula aperta*; Mekong River

1. Introduction

Schistosomiasis mekongi is prevalent in the Mekong River basin from the Khong district in southern Laos to Kratie province in northern Cambodia. The total population at risk for schistosomiasis mekongi is estimated as 60,000 in Laos and 80,000 in Cambodia [1].

Schistosoma mekongi can be parasitic in various mammalian hosts such as humans, dogs, and pigs [2]. *Neotricula aperta*, an aquatic snail, is known to be the intermediate host of *S. mekongi* [3]. It was observed that the water level of the Mekong River fluctuates seasonally; the period of low water lasts from February to May, while that of high water lasts from June to January. The transmission of *S. mekongi* from snails to humans occurs during the low water period because water contact of humans is practicable [1].

In Cambodia, a control program of annual mass drug administration was initiated by the Ministry of Health, Cambodia and Médicins Sans Frontières in 1995 (present program conductor: National Center for Parasitology, Entomology and Malaria Control) [4]. Sasakawa Memorial Health Foundation (SMHF) joined the cooperative program in 1997, and mainly took charge of examination of animal reservoirs, serodiagnostic surveys, and evaluation of morbidity using ultrasound. The control programs in Cambodia are considered to be successful because of the low level of detection of egg positive cases in recent years, although there remains a high positive rate by ELISA in several villages where *S. mekongi* is endemic [5]. In Laos, the average prevalence of schistosomiasis mekongi among the villages decreased to less than 1% after six courses of mass treatment with praziquantel during a 10-year control program, which resulted in

a cessation of the control program in 1999 [6]. Thereafter, the resurgence of schistosomiasis in the Khong district of Laos was confirmed by epidemiological surveys by WHO in 2003 [7], and it was revealed that the prevalence was restored to 20-50% in the same area [8]. The situation of re-emergence of *S. mekongi* in Laos indicates the necessity for the continuation of both surveillance and control programs, which are required in order to adopt more cost-effective measures, in Cambodia despite the low rate infection of *S. mekongi* [4].

A mathematical model is useful to predict of the effect of various control measures on suppression of infectious diseases. Macdonald [9] first proposed a mathematical model for the transmission of schistosomiasis, and thereafter a number of mathematical models for schistosomiasis transmission have been published [10-14]. Chan and Bundy [15] constructed an age-structured model for *Schistosoma mansoni* transmission to predict the prevalence and morbidity for the long-term consequences of drug treatment. Ishikawa *et al*. [16] developed a model of *Schistosoma japonicum* transmission that took account of a seasonal variation of snail density to predict the effect of control measures against *S. japonicum* in the Philippines. We previously proposed a mathematical model for the transmission of *S. mekongi* in Cambodia that was described by a system of partial differential equations of time and age, which was aimed at estimating the coverage rate and range of ages in targeted mass treatment to interrupt schistosomiasis transmission [17].

In this study, we constructed a mathematical model for *S. mekongi* transmission to evaluate the effect of control measures in Chatnaol village in Cambodia. We incorporated the fluctuation of water level in the Mekong River, dynamics of the intermediate snail host population, and the contribution of an animal reservoir, dogs, to

the prevalence of *S. mekongi* into the model. We applied the dynamics of the intermediate snail host based on the Post Spate Survival hypothesis [18]. In the model, snails that survive during the high water period of the Mekong River start to lay eggs from January, and afterwards an abundance of new-born snails appear in the low water period in April-May, when the transmission of *S. mekongi* occurs mainly. In Cambodia, dogs are known to play an important role as an animal reservoir in *S. mekongi* transmission [19]. Therefore, there were two kinds of definitive hosts in the model, humans and dogs. The parameter values in the model were estimated by field data or experimental data. The human population in the model was divided into 8 age categories because the prevalence and the intensity of infection are strongly dependent on age.

We focused on simulations of the transition in the prevalence of *S. mekongi* in a village together with the execution of control measures for humans. An application of molluscicide against *S. mekongi* appeared to be ineffective in the Mekong River basin [6]. The simulation results showed that a biyearly universal treatment or a yearly targeted mass treatment for children 5-19 years old with a 85% coverage rate, which was more effective than a yearly universal treatment with a 70% coverage rate, could sustain a low prevalence in humans after three courses of yearly universal treatment. Health intervention for 8 years, which is presumed to reduce both a probability of water contact and an amount of fecal output of humans to 50%, would make the prevalence of *S. mekongi* in both humans and dogs reduce to half. The simulations predicted that the suppression of schistosomiasis would be possible in Cambodia by maintaining control strategies for humans such as biyearly universal treatment or yearly targeted mass treatment with a 85% coverage rate.

2. Materials and Methods

2.1. Study area

Kratie province is located on northern Cambodia where the Mekong River runs from north to south. The population at risk of schistosomiasis mekongi was estimated to be about 50,000 in the province [20].

In Cambodia, universal treatment with praziquantel has been conducted annually since 1995 (except for 1998 because of a luck of funds and 2003 when targeted mass treatment for ages of 6-22 years-olds was applied) [4,20]. Annual parasitological surveys were conducted in Achen, Chatnaol, Srekoeun, and Sambok, which served as sentinel villages, reported that the prevalence of *S. mekongi* in these villages decreased from 50-70% in 1994 to less than 5% in 2002 [4].

In this study, we chose Chatnaol as the study area where the population was about 500 in 1999. The average prevalence and intensity of infection were estimated as approximately 52% and 115 eggs per gram of stool, respectively, in 1994-1995 before the launching of control programs in Cambodia [21]. The age-dependent prevalence and intensity of infection showed a peak in the age group of 10-14 years-old [21].

2.2. Water level of the Mekong River

The rainy season begins in March in Cambodia, and heavy rainfall lasts from June to October (Fig.1). The rainfall dramatically drops in November, and thereafter the dry season lasts from December to February.

The heavy rainfall in June results in rising water levels in the Mekong River, so the

high water period begins in June. The water level reaches a peak during September-October. After the arrival of the dry season, the water level drops gradually, and the low water period begins in February (Fig.1).

It is recognized that the available transmission period for *S. mekongi* begins in February when water contact of humans is practicable [1]. We determined that the low water period lasts from February to mid-May on the basis of water level data in Kratie province from 1989-2002 measured by the Mekong River Commission (Fig.1), when water contact and water contamination of the definitive hosts can occur.

2.3. Life cycle of S. mekongi

Definitive hosts

Schistosomes can infect various mammalian hosts including humans. Due to the involvement of animal reservoirs with schistosomiasis transmission, human chemotherapy alone is insufficient to reduce the prevalence of infection [22]. Dogs and pigs have been known to act as animal reservoirs for *S. mekongi* [23,24]. In Laos, the prevalence in dogs was estimated at 11% [23] and 29.2% [25]. SMHF has conducted several surveys to detect animal reservoirs in Cambodia by stool examinations, which revealed that dogs were the definitive host of *S. mekongi* [5,19]. Despite the low prevalence in dogs, one infected dog showed high egg density in its feces [19]. We consider dogs to be definitive hosts besides humans in the model.

Cercarial penetration of an individual through the skin can occur when in contact with the water of the Mekong River. A pair of adult worms commences egg production 4-6 weeks after invasion [26]. The life span of a worm is estimated at 3-5 years [10]. In

this study, we supposed that the duration of infection in definitive hosts is 5 years.

Intermediate hosts

Neotricula aperta, which is composed of three strains (α, β, and γ) is recognized as the intermediate host of *S. mekongi* [2,27]. *N. aperta*, which is penetrated by a miracidia releases cercariae after a latent period of 45-53 days [28]. Thus, we adopted 6 weeks as the latent period in the model. Experimental studies with *N. aperta* showed that the mortality per week was approximately 1.8% [29] to 2.1% [30]. It was confirmed that for the other schistosome species there is a significant difference in mortality among negative and infected snails. [31]. However, such a difference was not observed for *S. mekongi* [32]. In this study, we assume that the mortality of infected snails is equivalent to that of negative snails, and that the value of the mortality rate (d) was estimated at about 2% per week. Due to the fact that infection rate of *N. aperta* in the field is very low, 0.22% [29] to 0.14% [30], we held the infection rate below 1% at all times in the model.

The biology of *N. aperta* is still largely unknown because of the impracticality of field observations during the high water period of the Mekong River, although the population dynamics of the snails will affect schistosomiasis transmission. To represent the population dynamics of *N. aperta*, we adopted a "Post-Spate Survival (PSS)" hypothesis that *N. aperta* survive and copulate during high water period of the Mekong River, but that laying eggs would be delayed until next January, and that thereafter the eggs would hatch from February [18]. Fig. 2 shows briefly the life cycle of *N. aperta* based on this PSS hypothesis. The snail population is divided into two age-groups, old and new−born snails. New-born snails survive during the high water period, June to

October, by sticking to rocks [33]. It is accepted that the severe water conditions cause considerable mortality in snails during this period [34]. The proportion of females to males (ξ) is estimated to be about 0.67. New-born snails that pass the year-end join the old snails group. The number of eggs produced per female per month (b_v) is approximately 10 [35]. Old snails may die out in late March, because of exhaustion following a period of prolonged egg-laying. Eggs begin to hatch in February after a 4-5 week incubation period [36]. There are no data available about the time necessary to grow to participate in *S. mekongi* transmission. Because an abundance of snails is observed in April-May in the field, we assume a maturity time (τ_m) of 1 month.

2.4. Mathematical model

We built a transmission model for *S. mekongi* based on Van Druten's and Barbour's works [37,38]. Our model contains three host populations: humans (H) and dogs (D) as the definitive hosts, and snails (V) as the intermediate hosts. The two definitive hosts are separated into two epidemiological classes: negative (H_1, D_1) and infected (H_2, D_2). The snail population consists of two subpopulations: old snails (V_O) and new-born snails (V_N). Each subpopulation was divided into three epidemiological classes: negative, latent, and infected (which are represented by V_1, V_2, V_3 for old snails and by V_4, V_5, V_6 for new-born snails, respectively). Because both the prevalence and the intensity of infection vary by age, the human population was subdivided into 8 age categories (which are indexed by k). The human population was assumed to be 500 with 50% initial overall prevalence of *S. mekongi*. Each age category is assigned to the initial prevalence and the intensity of infection as shown in Table 1. Although several surveys of animal reservoirs revealed the prevalence in dogs was from 0.3% [19] to 29.2% [25],

the dog population was assumed to be 200 with 10% initial prevalence in the model.

In this study, it was assumed that each transfer rate of the definitive hosts (humans and dogs) from negative to infected ($\alpha_{H,}$ α_D) was in proportion to the total number of infected snails. The proportional coefficients for humans and dogs are expressed by β_H and β_D, respectively. The estimated values of proportional coefficient for age-categories of humans and also dogs are shown in Table 2. Hence, we obtained the following formulae for the transfer rate of the definitive hosts:

$$\alpha_H^{(k)}(t) = \beta_H^{(k)} c_t(t)(V_3(t) + V_6(t)),$$

$$\alpha_D(t) = \beta_D c_t(t)(V_3(t) + V_6(t)).$$

Herein, $c_t(t)$ stands for the probability of water contact of definitive hosts at time t.

The transfer rate of snails from negative to latent (α_V) was assumed to be in proportion to the number of eggs per snail where the proportional coefficient for snails is represented by β_V. The total number of eggs that are excreted by infected humans and dogs is expressed by the product of the amount of fecal output (f_H, f_D), the number of schistosome eggs per gram of stool (e_H, e_D), and the number of infected definitive hosts (H_2, D_2). The transfer rate of snails is expressed as:

$$\alpha_V(t) = \beta_V c_n(t) \frac{(\sum_k f_H e_H^{(k)} H_2^{(k)}(t) + f_D e_D D_2(t))}{V_O(t) + V_N(t)}.$$

Herein, the probability of water contamination of definitive host stands for $c_n(t)$ at time t.

After the latent period (τ_C), snails are transferred from the latent class to the infected class. The other relevant parameter values in the model are estimated by experimental and field data (Table 3). The flowchart of the model is shown in Fig. 3.

3. Results

3.1. Seasonal variation of N. aperta in the transmission model

It is infeasible to observe *N. aperta* throughout the year due to the seasonal spate of the Mekong River. We postulate that there are 20,000 old snails in January every year and that the population dynamics of *N. aperta* follow the PSS hypothesis. Then, we estimated the seasonal variation of the snail population (Fig. 4). The snail population had a peak between April-May, and afterwards it reduced dramatically during the high water period due to severe mortality. Female snails that survive start to lay eggs next January. The transmission of *S. mekongi* occurs actively during the low water period, especially late March to early May.

3.2. Prevalence in definitive hosts

The initial prevalence in humans and dogs were set to be 50% and 10%, respectively. Fig. 5 shows the variation in the prevalence of schistosomiasis mekongi in both humans and dogs without control measures. The prevalence gradually declines in January. For the low water period, prevalence rises swiftly in February-March, and rises steeply in April-May together with an increase in the snail population. Thereafter, the rate decreases in the high water period due to the absence of water contact.

3.3. Simulation of control measures for S. mekongi

Mass drug treatment combined with health education has been applied in Cambodia. We carried out simulations on the situation resulting from the execution of several control measures for humans: universal treatment (UT), targeted mass treatment (TT), a

combination of UT and TT, and health intervention.

Firstly, we conducted a series of simulations of yearly UT with three coverage rates: 30%, 50%, and 70% (Fig. 6). Yearly UT with 50% and 70% coverage rates decreased the prevalence in humans from 50% to less than 5% after 8 years, while yearly UT with a 30% coverage rate only decreased the prevalence to almost 20%.

Secondly, we compared the effects of the suppression of *S. mekongi* between yearly UT and biyearly UT (Fig. 7). Yearly and biyearly UT for 8 years with a 70% coverage rate reduced the prevalence in humans to 1% and 10%, respectively. Biyearly UT for 8 years with a 85% coverage rate reduced the prevalence to 5%, which was similar to yearly UT with a 50% coverage rate (Fig. 6).

Thirdly, we observed the effect of TT after three courses of yearly UT on the prevalence in both humans and dogs (Fig. 8). We assumed that children of 5-19 years-old, who show higher prevalence and intensity of infection, were treated by TT. Three courses of yearly UT with a 70% coverage rate reduced the prevalence in humans to 10% and in dogs to 6%. Yearly TT with a 85% coverage rate after three courses of yearly UT kept the prevalence in humans low and also reduces the prevalence in dogs throughout the 8-year simulation. For the situation of an interruption of mass treatment after three courses of yearly UT, the prevalence in humans increased swiftly and the prevalence in dogs was restored gradually after the interruption.

Finally, we checked the effect of health intervention on the prevalence in both humans and dogs (Fig. 9). We assumed that health intervention reduced to half both the probability of water contact and amount of fecal output by humans. Health intervention for 8 years without UT or TT slightly reduced the prevalence in both humans and dogs, while health intervention for 8 years with yearly UT for initial 3 years drastically

reduced the prevalence in humans.

4. Discussion

General mathematical models are helpful to understand the dynamics of schistosomiasis transmission [10-12], although, these models should be expanded to fit the local condition of endemic areas with a view to aiding to design schistosomiasis control programs. In this paper, a mathematical model incorporating with some key transmission factors was developed to evaluate the effect of control measures against schistosomiasis mekongi in Cambodia, quantitatively.

In most endemic countries, the highest prevalence and intensity of *Schistosoma* infection are found in young children [39]. A similar trend was confirmed at Chatnaol, which was chosen as our study area and was one of the sentinel villages selected in Cambodia in 1994-1995 [21]. This trend probably resulted from frequent water contact by children and the acquired immunity of adults caused by past repeated infections, which reduces susceptibility [40]. We assigned proportional coefficients to each age category in humans instead of the effect of acquired immunity (Table 2).

One of features of our model is the allowance for the dynamics of the *N. aperta* population. We adopted the PSS hypothesis [18] for *N. aperta* dynamics to predict the seasonal variation of the snail population. Although the life cycle of *N. aperta* is still largely unknown [5], the seasonal variation of the snail population is of great influence in transmitting *S. mekongi* to the definitive hosts. The simulation showed that the snail population reached a peak in April-May due to a delay of egg-laying during the high water period (Fig. 4). Since there is some difficulty in estimating the acute mortality in snails during the high water period, we chose its value to maintain a constant snail

population size every year. In the field, the living sites of *N. aperta* and their population vary from year to year because of changes in water flow, water level, and the form of the riverbed, *etc* [5]. It is desirable to conduct further surveys of *N. aperta* to make the transmission model more realistic.

We carried out simulations of conditions where the initial overall prevalence in humans was 50% based on the epidemiological data of Chatnaol in 1994 [21]. The transmission of *S. mekongi* to humans is considered to occur mainly in April when humans comes into contact with the water in the Mekong River frequently and an abundance of snails is observable [18]. The model simulation showed the high prevalence of schistosomiasis mekongi in humans in May when the *N. aperta* population reaches a peak (Fig. 5). We assumed simply that the transmission from snails to the definitive hosts, humans and dogs, can occur during the low water period, (c_t=1) and that it cannot occur during the high water period (c_t=0). Future observations of the frequency of water contact and exposure time of humans in the low water period will be reflected in improvement in the simulations of the transmission model.

Following on from stool examinations for animal reservoirs in Cambodia, we involved dogs as a definitive host in the model. Dogs were observed swimming in the Mekong River, and one infected dog was revealed to have a high density of schistosome eggs per gram of stool [19]. Therefore, dogs are considered to play an important role in schistosomiasis transmission in Cambodia. The simulation under the assumption that the number of dogs was 200 with 10% initial prevalence shows that only UT for humans had a good effect on the reduction in prevalence in dogs (Fig. 8 (B)).

Some of model simulations indicated that snail control such as applying chemical molluscicide had an impact on the reduction of disease infection [16,41]. In the Mekong

River, an application of chemical molluscicide was ineffective due to long reaches of the river and a large of volume of water flow [6]. Therefore, this study aimed at evaluating effects of control measures for humans only.

We estimated the effect of control measures for humans including UT, TT, and health intervention on the prevalence of schistosomiasis mekongi in the definitive hosts. In Cambodia, mass drug administration with coverage rates between 62% and 86% has been conducted annually since 1995, which reduced the prevalence in 4 sentinel villages to below 5% on average in 2002 [4]. The simulation results showed that yearly UT for 8 years with a 70% coverage rate reduced the prevalence in humans from 50% to 2% (Fig. 6), which suggested an effective coverage rate for MDA in Cambodia to suppress endemic of the disease. It was suggested to prolong the interval between UT with a view to cost saving [4]. The simulation indicated that biyearly UT with a 85% coverage rate also sufficiently reduced the prevalence in humans (Fig. 7). TT aimed at schoolchildren is another cost-effective alternative method [39]. Yearly TT with a 85% coverage rate aimed at 5-19 years-old following three courses of yearly UT with a 70% coverage rate achieved low prevalence below 5% in humans and below 2% in dogs (Fig. 8). Health intervention such as health education and provision of latrines has an important role in the control of helminth infection [42]. In this study, we assumed that the probability of water contact (c_t) and an amount of fecal output of humans (e_H) were reduced to half as the result of health intervention. The performance of health intervention for 8 years without mass drug administration reduced the prevalence in both humans and dogs to half the initiate level in the simulation (Fig. 9). The combination of yearly UT with health intervention had a strong effect on reduction of the prevalence in both definitive hosts in the simulation (Fig. 9).

With regard to the re-emergence of schistosomiasis in Laos, it is necessary to continue performing control programs and surveillance using ELISA in Cambodia [2]. In addition, there is a need to convert control measures with good cost-effectiveness because few positive cases were detected in recent years [4]. The simulation results show that biyearly UT or yearly TT is efficacious in restricting *S. mekongi* infections if the coverage rate is kept at more than 85%. The reduction in the probability of water contact or the amount of fecal output by infected humans also impacts on the suppression of transmission of *S. mekongi*. The simulation results suggested that the suppression of *S. mekongi* in Cambodia would be possible by sustaining the control program and surveillance.

Acknowledgements

We would like to thank Dr. H. Ohmae of the National Institute of Infectious Diseases for his helpful comments. We are indebted to Dr. T. Matsumoto of the National Institute for Rural Engineering for providing Mekong River water level data. This work was supported in part by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (Grant no. 16540105), Sasakawa Memorial Health Foundation, and by a Grant-in-Aid from the Ministry of Health, Labour and Welfare, Japan for “Research for Emerging and Re-emerging infections diseases” (Grant no. H17-Sinkou-ippan-019).

References

[1] Urbani C, Sinoun M, Socheat D, Pholsena K, Strandgaard H, Odermatt P, Hatz C. Epidemiology and control of mekongi schistosomiasis. Acta Tropica 2002; 82:

157-168.

[2] Ohmae H, Sinuon M, Kirinoki M, Matsumoto J, Chigusa Y, Socheat D, Matsuda H. Schistosomiasis mekongi: from discovery to control. Parasitol Int 2004; 53: 135-142.

[3] Harinasuta C, Sornmani S, Kitikoon V, Schneider CR, Pathammavong O. Infection of aquatic hydrobiid snails and animals with Schistosoma japonicum-like parasites from Khong Island, southern Laos. Trans Royal Soc Trop Med Hyg 1972; 66: 184-185

[4] Sinuon M, Tsuyuoka R, Socheat D, Odermatt P, Ohmae H, Matsuda H, Montresor A, Palmer K. Control of *Schistosoma mekongi* in Cambodia: results of eight years of control activities in the two endemic provinces. Trans Royal Soc Trop Med Hyg 2007; 101: 34-39.

[5] The Cambodia-Japan Medical Cooperation. Project for the Control of Schistosomiasis in Northern Cambodia. Sasakawa Memorial Health Foundation, Tokyo, 2000-2006.

[6] Khamkeo T, Pholsena K. Control of schistosomiasis due to *Schistosoma mekongi* in Khong District, 1989-1999. In: Crompton DWT, Montresor A, Nesheim MC, Savioli L, editors. Controlling disease due to helminth infections. World Health Organization; 2003: 170-181.

[7] Vongsouvan S. Presentation hand out: Updated status of schistosomiasis mekongi in the Lao PDR. Meeting on Regional Network for Research, Surveillance and Control for Asian Schistosomiasis, Vientiane, Lao PDR, 2003.

[8] Nakamura S, Matsuda H, Kirinoki M, Habe S, Kitikoon V, Watanabe T, Nihei N, Phrommala S, Boupha B, Boutta N. Reconfirmation on high prevalence of *Schistosoma mekongi* infection in southern part of Khong district, Champasack province, Lao PDR. In: Proceedings of the 2nd Vietnam-Laos-Cambodia Symposium. Vietnam National University Publisher, Hanoi, 2004, 236-237.

[9] Macdonald G. The dynamics of helminth infections with special reference to

schistosomes. Trans R Soc Trop Med Hyg 1965; 59: 489-506.

[10] Anderson RM, May RM. Infectious disease of humans, Oxford university press: New York, 1991.

[11] Woolhouse MEJ. On the application of mathematical models of schistosome transmission dynamics. I. Natural transmission. Acta Tropica 1991; 49: 241-270.

[12] Woolhouse MEJ. On the application of mathematical models of schistosome transmission dynamics. II. Control. Acta Tropica 1992; 50: 189-204.

[13] Feng Z, Li C, Milner FA. Schistosomiasis models with density dependence and age of infection in snail dynamics. Math Biosci 2002; 177&178: 271-286.

[14] Allen EJ, Victory Jr HD. Modeling and simulation of a schistosomiasis infection with biological control. Acta Tropica 2003; 87: 251-267.

[15] Chan MS, Bundy DAP. Modelling the dynamic effects of community chemotherapy on patterns of morbidity due to *Schistosoma monsoni.* Trans R Soc Trop Med Hyg 1997; 91: 216-220.

[16] Ishikawa H, Ohmae H, Pangilinan R, Redulla A, Matsuda H. Modeling the dynamics and control of *Schistosoma japonicum* transmission on Bohol island, the Philippines. Parasitol Int 2006; 55: 23-29.

[17] Hisakane N, Ishikawa H, Kirinoki M, Sinuon M, Socheat D, Matsuda H. Mathematical modeling for transmission of *Schistosoma mekongi*: Kratie province in Cambodia. In: Nagao I, Takahashi Y, editors. Parasitic Zoonoses in Asian-Pacific Regions. Japan: Sankeisha, 2006: 81-89.

[18] Attwood SW. Schistosomiasis in the Mekong Region: Epipdemiology and Phylogeography. Adv Parasitol 2001; 50: 88-152.

[19] Matsumoto J, Sinuon M, Socheat D, Matsuda H. The first reported cases of canine schistosomiasis mekongi in Cambodia. Southeast Asian J Trop Med Pub Health 2002; 33: 458-461.

[20] National Schistosomiasis and Soil Transmitted Helminth Control Program. Report on Control Activity of Schistosomiasis and Soil Transmitted Helminthiases in Cambodia April 2003 – March 2004, Ministry of Health, Cambodia.

[21] Stich AHR, Biays S, Odermatt P, Men C, Saem C, Sokha K, Ly CS, Legros P, Philips M, Lormand J-D, Tanner M. Foci of Schistosomiasis mekongi, northern Cambodia: II. Distribution of infection and morbidity. Trop Med Int Health 1999; 4: 674-685.

[22] Guo J, Li Y, Gray D, Ning A, Hu G, Chen H, Davis G, Sleigh AC, Feng Z, Mcmanus DP, Williams GM. A drug-based intervention study on the importance of buffaloes for human *Schistosoma japonicum* infection around Poyang lake, People's Republic of China. Am J Trop Med Hyg 2006; 74: 336-341.

[23] Sornmani S, Kitikoon V, Thirachantra S, Harinasuta C. Epidemiology of Mekong schistosomiasis. The Mekong schistosome. Malacol Rev 1980; suppl 2: 9-18.

[24] Strandgaard H, Johansen MV, Pholsena K, Teixayavong K, Christensen NO. The pig as a host for *Schistosoma mekongi* in Laos. J Parasitol 2001; 87: 708-709.

[25] Iijima T, Lo CT, Ito Y. Studies on schistosomiasis in the Mekong Basin I. Morphological observations of the schistosomes and detection of their reservoirs hosts. Jpn J Parasitol 1971; 20: 24-33.

[26] Gryssls B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. Lancet 2006; 368: 1106-1118.

[27] Davis GM, Subba Rao NV, Hoagland KE. In search of *Tricula* (Gastropoda: Pomatiopsidae): *Tricula* defined, and a new genus described. Proc Acad Natl Sci Philadelphia 1986; 138: 426-442.

[28] Sornmani S, Schneider CR, Kitikoon V. Life cycle of *Schistosoma japonicum*-like trematode from Khong Island Southern Laos. Southeast Asian J Trop Med Public Health 1973; 4: 279.

[29] Attwood SW, Upatham ES, Southgate VR. The detection of *Schistosoma mekongi* infections in a natural population of *Neotricula aperta* at Khong Island, Laos and the control of Mekong schistosomiasis. J Moll Stud 2001; 67: 400-405.

[30] Attwood SW, Champbell I, Upatham ES, Rollinson D. Schistosomes in the Xe Kong river of Cambodia: the detection of schistosoma mekongi in a natural population of snails and observations on the intermediate host's distribution. Ann Trop Med Parasitol 2004; 98: 221-230.

[31] Anderson RM, May RM. Prevalence of schistosome infections within molluscan populations: observed patterns and theoretical predictions. Parasitol 1979; 79: 63-94.

[32] Attwood SW, Upatham ES. A new strain of *Neotricula aperta* found in Khammouanne Province, central Laos, and its compatibility with *Schistosoma mekongi*. J Moll Stud 1999; 65: 371-374.

[33] Yasuraoka K, Hata H, Pholsena K, Hongvanthong B, Sayaseng B. Field studies on the bionomics of *Neotricula aperta*, the snail intermediate host of *Schistosoma mekongi*, in Khong District, South Laos. Jpn J Parasitol 1994; 43: 11-17.

[34] Attwood SW. A demographic analysis of *y-Neotricula aperta* (Gastropoda: Pomatiopsidae) populations in Thailand and Southern Laos, in relation to the transmission of Schistosomiasis. J Moll Stud 1995; 61: 29-42.

[35] Bruce JI, Schneider CR. Studies on schistosomiasis in the lower Mekong basin: the aquatic ecology and molluscicide sensitivity of *Lithoglyphopsis aperta*. In: Final Report to the Committee for the Coordination of Investigations in the Lower Mekong Basin, Bangkok, 1976: 9-92.

[36] Liang YS, Kitikoon V. Cultivation of *Lithoglyphopsis aperta* snail vector of *Schistosoma mekongi*. The Mekong schistosome. Malacol Rev 1980; suppl 2: 35-45.

[37] Van Druten JAM. Technical Note. 2 Schistosomiasis: A basic whole-cycle transmission model. Int Inst Land Reclam Improv 1994; 45: 279-294.

[38] Barbour AD. Modeling the transmission of schistosomiasis: An introductory view. Am J Trop Med Hyg 1996; 55: 135-143.

[39] World Health Organization. The control of schistosomiasis. Second report of the WHO Expert Committee, Geneva, 1993.

[40] Bundy DAP. Population ecology of intestinal helminth infections in human communities. Phil Trans R Soc Lond 1988; B321: 405-420.

[41] Liang S, Spear RC, Seto E, Hubbard A, Qiu D. A multi-group model of *Schistosoma japonicum* transmission dynamics and control: model calibration and control prediction. Trop Med Int Health 2005;10: 263-278.

[42] Asaolu SO, Ofoezie IE. The role of health education and sanitation in the control of helminth infections. Acta Tropica 2003; 86: 283-294.

Table 1. The population size, initial prevalence, and intensity of infection (the number of eggs per gram of stool) in each age category of humans

Age category	Population*	Initial prevalence (%)$	Intensity (egg/g)$
1-4	75	16	105
5-9	75	58	130
10-14	65	72	195
15-19	60	71	170
20-29	85	62	100
30-39	65	52	95
40-49	40	41	75
49 >	25	28	45
Average		50	115

*According to population census of Kratie province in Cambodia in 1998 [The national Institute of Statistics of Cambodia]

$Estimated based on epidemiological data of Chatnaol in 1994-1995 [21]

Table 2. Estimation of the proportional coefficient values among hosts

Hosts	Age category (years)	Estimated value of proportional coefficient
Human (β_H)	1 – 4	1.13×10^{-4}
	5 – 9	7.52×10^{-4}
	10 – 14	1.18×10^{-3}
	15 – 19	1.03×10^{-3}
	20 – 29	6.39×10^{-4}
	30 – 39	3.97×10^{-4}
	40 – 49	2.47×10^{-4}
	49 >	1.39×10^{-4}
Dog (β_D)		6.32×10^{-5}
Snail (β_V)		5.15×10^{-6}

Table 3. Estimated values of model parameters

Symbol	Interpretation	Estimated value
Human		
B_H	Birth rate (/week)	0.16
δ_H	Death rate (/week)	3.26×10^{-4}
β_H	Proportional coefficient	see table 2
γ_H	Recovery rate (/week)	0.0038
f_H	Amount of fecal output (gram/day)	160
e_H	Number of eggs per gram of stool	see table 1
Dog		
B_D	Birth rate (/week)	0.38
δ_D	Death rate (/week)	0.002
β_D	Proportional coefficient	see table 2
γ_D	Recovery rate (/week)	0.0038
f_D	Amount of fecal output (gram/day)	100
e_D	Number of eggs per gram of stool	100
Snail		
p_h	Probability of egg hatching	0.8
Ξ	Ratio of female to male	0.67
b_v	Average number of eggs produced (/female/month)	10
τ_h	Incubation period (week)	4
τ_m	Maturity period to participate in transmission (week)	4
τ_c	Latent period (week)	6
Θ	Additional mortality for old snails	6-12
Φ	Additional mortality for new-born snails	1-4
D	Mortality (/week)	0.02
β_V	Proportional coefficient	see table 2
Transmission		
c_t	Probability of water contact	0 (high water), 1 (low water)
c_n	Probability of water contamination	0 (high water), 1 (low water)

Legends

Fig. 1 Monthly average rainfall levels (bars) for 5 years during 1997-2001 in Phnom Penh [World Weather Information Service] and monthly average water levels of the Mekong River (line) for 14 years during 1989-2002 in Kratie province, Cambodia [Mekong River Commission].

Fig. 2 Population dynamics of *N. aperta* on the basis of the Post-Spate Survival hypothesis

Fig. 3 The basic scheme of the transmission model for *S. mekongi*. Deaths of hosts are omitted in this scheme. The solid line shows the transfer among epidemiological classes of hosts. The dotted line shows miracidial and cercarial infections.

Fig. 4 The monthly variation of the total snail population.

Fig. 5 Variation of prevalence in both humans (black line) and dogs (gray line) without control measures.

Fig. 6 Variation of the prevalence of *S. mekongi* in humans with yearly universal treatment (UT) for three coverage rates: 30% (solid line), 50% (dashed line), and 70% (dotted line).

Fig. 7 Variation of the prevalence of *S. mekongi* in humans with universal treatment (UT) by changing the interval between treatments with two coverage rates: yearly UT with a 70% coverage rate (solid line), biyearly UT with a 70% coverage rate (dashed line), and biyearly UT with a 85% coverage rate (dotted line).

Fig. 8 Variations of the prevalence in both humans (A) and dogs (B) with 2 control measures. 1: yearly universal treatment (UT) with a 70% coverage rate for the initial 3 years (solid line), 2: after 3 years of annual UT yearly targeted mass treatment (TT) with a 85% coverage rate (dashed line).

Fig. 9 Variations of the prevalence in both humans (A) and dogs (B) with 2 control measures. 1: only health intervention for 8 years (solid line), 2: health intervention for 8 years with yearly universal treatment (UT) with a 70% coverage rate for the initial 3

years (dashed line).