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

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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.

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*

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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

2.3.1. 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.

2.3.2. 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

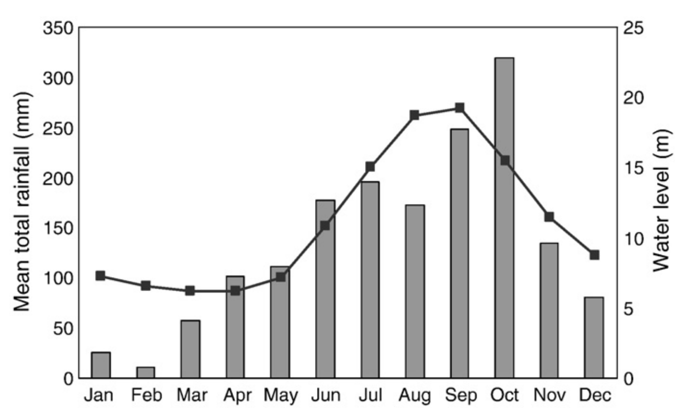

Fig. 1. Monthly average rainfall levels (bars) for 5 years during 1997–2001 in Phnom Penh [World Weather Information Service] and monthly average water levels of the Mekong River (line) for 14 years during 1989–2002 in Kratie province, Cambodia [Mekong River Commission].