Modelling the dynamics and control of Schistosoma japonicum transmission on Bohol island, the Philippines

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Abstract

We have investigated a mathematical model for the transmission of *Schistosoma japonicum* in the infested region of northeastern Bohol island in the Philippines. The development of transmission models is important for planning control strategies. Since *S. japonicum* has a complicated mode of transmission, the rates of transmission among its hosts cannot be measured directly by field observation. Instead, they have been estimated through model analysis. The model takes into account the seasonal variations and includes a function of control measures. In 1981, a project to eliminate schistosomiasis started on Bohol island. The prevalence decreased dramatically and has kept low level less than 1%. The simulations based on the model predicted that there is little probability of resurgence of an epidemic in the northeastern endemic villages of Bohol island due to the fact that the project has attained a high coverage of selective mass treatment based on stool examination accompanied by a successful snail control operation.

Keywords: schistosomiasis japonica; control; mathematical model; *Philippines; Bohol*

1. Introduction

Schistosomiasis is an important disease problem in the Philippines, as well as one of the most prevalent parasitic diseases in the world [1]. A mathematical model for the schistosome transmission would be useful for understanding changes of the prevalence of disease and for designing control programs. Since 1965, there have been many studies involving mathematical modeling of schistosome transmission, mainly from the theoretical point of view [2-5]. Anderson and May [6] studied the prevalence of snail infection based on empirical evidence. A stochastic model for schistosomiasis developed from a model for onchocerciasis aimed to evaluate control strategies [7]. A series of works treated of modelling of *Schistosoma japonicum* transmission and control in China [8-10].

The work reported here focused on modeling the dynamics of *S. japonicum* transmission in a particular infected region, Bohol island in the Philippines to describe the prevalence quantitatively. *S. japonicum* has a complicated mode of transmission. As part of the life cycle occurs in the environment outside of the host, it is difficult to measure the transmission rate on the basis of field observations. Therefore, it is necessary to estimate the transmission rate using model analysis. We have developed a model that takes into account seasonal variations adjusted to the target region. Moreover, a function of control measures is incorporated into the model.

A collaborative project of the Schistosomiasis Control Service of the Philippine

Department of Health and Sasakawa Memorial Health Foundation of Japan has been continuing since 1981 in Bohol island [11]. The rate of prevalence in Sto. Thomas village (see 2.1) in which the infection was endemic in the pre-control period was reduced from 15% to less than 1% after implementation of the project for a decade. We made an estimate of the change in the prevalence of *S. japonicum* for each village in Bohol island where the infection was prevalent. A 10-year study demonstrated that the model agreed with the surveillance data. The simulation based on the model suggested that, among various possible control measures, a selective mass treatment program coordinated with snail control would be effective for the elimination of *S. japonicum*. The simulation predicted that there is little probability of the resurgence of an epidemic for several years in the northeastern villages of Bohol island.

2. Materials and Methods

2.1 Study Area

Bohol island is located centrally in the Philippine archipelago and has the islands of Cebu and Leyte as its nearest neighbors. The average life expectancy at birth was estimated to be 68.19 and 72.93 years for males and females, respectively, for the period 2000-2005 (the Provincial Government of Bohol, 2004). Blas and Dazo [12] reported the prevalence of *S. japonicum* and localities of snail colonies in Bohol island. Limited foci of *S. japonicum* in Bohol were recognized in 3 and 4 villages in the Trinidad and

Talibon municipalities, respectively, in the northeastern part of the island [11]. In the present article, we choose two villages, Sto. Thomas and San Vicente in the Trinidad municipality, and one village, San Roque in the Talibon municipality as study areas, which had a population of 608 (1986), 542 (1984) and 1314 (1981), respectively. There is little difference in the conditions of *S. japonicum* transmission among three villages. Table 1 shows the changes of the prevalence of *S. japonicum* infection based on stool examination since the beginning of the control project in 3 villages in which a high rate of prevalence was detected in the villagers in the pre-control period.

Snail density varies according to time and circumstances, and sometimes new colonies of snails are discovered. Therefore, it is difficult to make an accurate estimate of snail density for a village, and similarly it is difficult to estimate the rate of infection. The snail surveys were reported as the number of snails per man per hour that were collected by well-trained men. As the initial infection rates and the initial snail densities of each three villages using in simulations, we adopt the average infection rate and the average snail density on 3 (Sto. Thomas), 4 (San Vicente) and 3 snails colonies (San Roque) based on snail surveys in 1986 (Table 2). In order to use the seasonal variation of water area in the model, the relative water area (r_w) in the drier season compared to the wet season (June-December, 136-186 mm) was introduced as 0.95 (January, 104 mm of rainfall), 0.9 (February, 75 mm), 0.8 (March, 57 mm), 0.7 (April, 45 mm) and 0.9 (May, 77 mm), respectively, according to the average monthly rainfall of during 30 years

(1973-2002) at the Cebu Pagasa complex reported by the Philippine Atmospheric, Geophysical & Astronomical Services Administration.

[Table 1]

[Table 2]

2.2 Intermediate hosts: Snails

Oncomelania quadrasi was identified as an intermediate snail host in the Philippines [11, 13]. Experimental infections of snails showed that the shortest and the average latent period from infection to release of cercariae, and the average period of cercarial output were 42, 62 and 32 days, respectively, for single infection, and 45, 64, and 66 days for multiple infections, and that abundant cercarial output was released from infected snails during about the initial 3 weeks, and thereafter the amount of output fell off [13]. Thus, we adopted 8 weeks as the latent period (τ_c), 3 weeks as the high cercaria releasing period (τ_h), and 4 weeks as the low cercaria releasing period (τ_l) in the model without making a distinction between single and multiple infections. The ratio (r_c) of output in the low releasing period to that in the high releasing period was estimated to be 0.2 on the basis of experimental data about the amount of cercariae output per snail day and the percentage of snails releasing [13]. In regard to longevity, the mortality rate among infected snails is higher than that among uninfected snails [6, 13]. Longevity studies in the laboratory showed that daily mortality rates for uninfected, preshedding (latent) and shedding snails were estimated as 0.3-0.4%, 1.2% and 1.3-1.6%, while the daily mortality rate for snails (δ_s) was estimated as 0.90% in the field [13].

2.3 Definitive hosts: Human population & Animal reservoirs

Humans are the major definitive host of *S. japonicum* in Bohol. Field surveys on animal infection observed that only rats were infected, with a low prevalence rate of 0.8% [11], while many domestic animals such as dogs, pigs, and cows were found to be reservoirs in Leyte [14]. Cercariae, which penetrate into individuals via the skin, develop into mature adults. In the experimental infections of mice, a female adult worm begins to produce eggs 30days [15], 25-68 days [16] after infection ; and faecal eggs were first observed 6-7 weeks after infection [15]. The reproductive life span lasts for 3.4 years [17], 5 years [18],. Thus, we adopted the average pre-depositing fecal eggs period (τ_m) as 45 days, and the duration of egg production (τ_e) as 4 years. Since an infected small mammals such as rats make a far smaller contribution to the infection of snails than infected human individuals because of both low egg output and low hatching rate [14], the ratio of the transmission index to snails of rats (r_{rat}) compared to humans was assumed to be 0.01 in the model. We also assumed that the frequency of water contact by definitive hosts would be proportional to the water area.

2.4 General description of transmission model

We designed a mathematical model for the transmission for *S. japonicum* in which we assumed that there are three host populations: two definitive hosts, that is, humans and rats as animal reservoirs, and only one intermediate host, snails. Each definitive host population is divided into three epidemiological classes: negative, infected but not depositing parasite eggs, and depositing parasite eggs, which are symbolized by x_1, x_2, x_3 for humans, z_1, z_2, z_3 for rats, respectively. On the other hand, the snail population is divided into four epidemiological classes: negative, infected but not shedding cercariae, high cercaria shedding, and low cercaria shedding, which are symbolized by y_1, y_2, y_3, y_4, respectively. The prevalence in human population and in snail population are expressed by the formulae $x_3/(x_1+x_2+x_3)$ and $(y_2+y_3+y_4)/(y_1+y_2+y_3+y_4)$, respectively. For simplification of the model, we set members of the above epidemiological classes on the basis of contribution to the transmission cycle. Thus, x_2 or z_2 class in the definitive hosts is limited to individuals or rats having a female worm that will develop to maturity and produce eggs, while the y_2 class of snails is limited to infected snails developing to shed cercariae. The repercussion of the above limitation will be rectified by being transferred to the transmission rates, which will be considered in the next section. The number of the population in each epidemiological class is measured by density in the initial water area (a=100 m^2 as a unit). It is assumed that the total rat population would be ten times the number of the total human population [14]. The actual number could not be measured due to the lack of census data in Bohol. The model properly takes into account the dynamics of host populations.

The transfers in the definitive hosts from (x_1, z_1) to (x_2, z_2) are traceable to cercariae released from (y_3, y_4) and the water contact, while the transfer in the intermediate hosts from (y_1) to (y_2) are traceable to miracidia hatching out of parasite eggs that are discharged from (x_3, z_3). The symbols β_h, β_r and β_s signify the transmission rate from snails to humans, from snails to rats and from humans to snails, respectively. The transfer rates (λ) are expressed by the following formulae:

$$\lambda_a(t) = \beta_a\, r_w(t)\, (y_3(t)+r_c\, y_4(t)), \qquad a = h, r$$

$$\lambda_s(t) = \beta_s\, (x_3(t)+r_{rat}\, z_3(t))$$

The other classes transfer to the subsequent classes (Fig.1) according to the durations which are introduced in the previous sections. The basic scheme of our model is shown diagrammatically in Fig.1. The parameters used in the model are tabulated with the assumed and adjusted values in Table 3.

[Fig. 1]

[Table 3]

3. Results

3.1 Transmission rates

The transmission rates are influenced by human behavior, and the water area and meteorological conditions, so they vary geographically. Moreover, there are no methods of measuring the transmission rates directly on the basis of field surveys, because the transmission routes among hosts of *S. japonicum* pass through water in the forms of egg/miracidium and cercaria. A couple of the optimum values of the transmission rates from snails to humans and from humans to snails should realize the initial infection rates of hosts (Table 2). To get the optimum values of transmission rates for each village, we evaluate the differences of the infection rates between the initial value and the equilibrium value in humans and snails, respectively, which are obtained by a long-term simulation of the model stretching over 10years. Fig. 2 shows how to narrow the suitable range of (β_h, β_s) for Sto. Thomas village as an example. The adjusted values of (β_h, β_s) for each village are summarized in Table 2.

[Fig. 2]

3.2 Simulations for the *S. japonicum* control measures

The major approach to the control of *S. japonicum* consists of two methods: the detection of infected individuals and chemotherapeutic treatment, and snail control by environmental change such as land reclamation and cement lining of ditches, and using molluscicides. Firstly, we planned a comparative study on the change of prevalence to investigate the design of control methods in a village of Bohol island in which infection was endemic. The simulations have been carried out for three cases: human control with selective mass treatment, snail control with use of molluscicides, and both human and snail control under the conditions that for human control, about 50% of villagers would be examined by stool examination once a year for 4 years and almost all egg-positive cases would be treated with praziquantel, and that for snail control, molluscicides application would be done at half-year intervals for 4 years and the removal rate of snails would be assumed to 50%. The result shows that the rate of prevalence in inhabitants and the density of infected snails will be restored swiftly after the expiration of human control measures without snail control, while the rate of prevalence in inhabitants will be reduced gradually by snail control measures alone (Fig. 3), and that snail control alone will maintain the infection rate in snails in contrast with the density of infected snails (not shown in figure). The prevalence curve by the simulation for San Vicente and San Roque show the same trend as Sto. Thomas.

[Fig. 3a, b]

Secondly, we investigated the influence of the coverage of examination and treatment for inhabitants on the prevalence of *S. japonicum*. Maintaining a high coverage rate of stool examinations and administration of praziquantel requires a good deal of effort. The simulation has been carried out for an executive plan of annual examination for 8 years with covering rates in inhabitants of 30%, 50%, or 70%. The results indicate that naturally, the parasite rate depends on the covering rate, and that an executive plan of low coverage (30%, 50%) can reduce but cannot eliminate the prevalence of *S. japonicum*, while an epidemic will surely be stamped out in the case of high coverage

(70%). Fig .4 shows variations in the prevalence in the Sto. Thomas situation, and other two villages' situations are almost same.

[Fig. 4]

Finally, we compared the change of prevalence which was derived from the model with the observed value based on a mass examination of villagers (Table 1). Following the executed plan in Sto. Thomas, the simulation used the actual value as coverage. In this area, a snail control program using molluscicides was operated from 1986. The effective rate of molluscicides was assumed to be 30%. Because we could not determine the exact change of the density of infected snails (Section 2.2), we showed the change of infection rate in snails instead of the density in Sto. Thomas (Fig. 5). It should be noted that the change of the density of infected snails is more useful than that of the infection rate in snails for making the assessment of transmission from snail hosts to definitive hosts due to abundance of cercariae in water. The χ^2-value for 5 points of time when the number of positive cases will be expected to be beyond 1 (1986-90) is estimated at 9.0 ($P>0.05$, $d.f.=5$), and the differences of positive rates for the other points of time (1991-95) stay within 0.7%, while the correlation coefficient between simulated and observed positive cases of all 10 points is 0.99. On the other hand, though we could not make a precise comparison between the simulated and observed infection rates in snails because of the instability of observed data, their correlation coefficient was 0.92. From the above point of view, the transition curve of prevalence derived from the model is in the accordance with the observed data. The transition curves of prevalence derived from the model for the remaining two villages were less accordant with the observed data than that for Sto. Thomas (figures not shown). The correlation coefficients are 0.90 and 0.93 for San Vicente (1986-94) and San Roque (1985-93), respectively, while the χ^2-values for the points of time except when positive cases are above 1 could not be confirmed for $P>0.05$.

[Fig. 5a, b]

4. Discussion

It is important to consider the relationship between the model and the reality. It is unavoidable for the model of transmission for *S. japonicum* to have a somewhat complicated structure, because *S. japonicum* has a complicated life cycle which involves human and animal reservoirs, and snail hosts, and is exposed to the environment. To avoid too much complexity, we have aimed at a simple model structure so that all the epidemiological parameters involved in the model except transmission rates are determined in field surveys and studies of experimental infections. Thus, we did not introduce mating mechanism, immune mechanism in the model, or the intensity of *S. japonicum* in humans or snail.

A distinct feature of the model is the division of the shedding stage in snails into two classes according to cercaria output. This is adequate to prevent overestimating or underestimating the abundance of cercariae because of a long shedding duration.

The range of theoretical reproduction potential of an adult worm pair may increase from 1 to 10^{11} [19]. The transmission rates cannot be measured directly by the field observation and are also influenced by various human and environmental factors. Therefore, we have used a set of equilibrium values which can describe an epidemic situation among hosts for a pre-control period in the model as transmission rates. Those values chosen for an endemic village are reflected on by regional differences (Table 2, Fig. 5). Social behavioral changes have an influence on the transmission rates, and therefore regarding the prevalence of *S. japonicum*, further research from the viewpoint of a model incorporating behavioral changes is desirable.

In a 10-year study, we found less accordance of the transition curves of prevalence derived from the model for San Vicente and San Roque with the observed data than for Sto. Thomas. This would be attributable to a small epidemic that was observed in 1991-92 in San Vicente and San Roque (see Table 1). The model works well provided that there is no immigration or emigration in the target region, but it was reported that there was actually some immigration and emigration.

In the model, we have to give careful consideration to animal reservoirs. When they play a part in the reproduction of *S. japonicum*, it is difficult to eliminate *S. japonicum* by means of chemotherapy for people only. Generally, it is difficult to manage control of animal reservoirs. Field surveys showed that rats might contribute to *S. japonicum* prevalence. The simulation suggested that rats had a small influence on the prevalence of *S. japonicum*. It is possible that *S. japonicum* would prevail in other animals if the prevalence rate rose by a large margin.

Using the model for *S. japonicum,* Williams et al. [8] evaluated the anti-fecundity bovine vaccine in Jiangxi Providence of China, where bovines are the major reservoirs and play an important part of *S. japonicum* transmission. This vaccine was not used in the endemic villages of Bohol island. Their result of simulation was similar to the variation in the prevalence of *S. japonicum* under human control only with selected mass treatment in Sto. Thomas (Fig. 3). The comparison predicted that the prevalence in the human population would recover swiftly after annual mass treatment of humans for 5 years, and that, after a program of 5 years mass treatment for both humans and bovines, the prevalence would decrease for up to 5 years but that the equilibrium prevalence would remain at the initial level [8]. In the World Bank Schistosomiasis control project in China, snail control was limited [20], while in the Schistosomiasis Control Project on Bohol island, control procedures were carried out twice a year. If the density of snails in a target region cannot be reduced, the prevalence in inhabitants will resurge swiftly after 4-year selective mass chemotherapy. On the other hand, selective mass treatment together with snail control has a conspicuous and continuous effect on decline (Fig. 3). Therefore, an effective plan for snail control is necessary to maintain the elimination of schistosomiasis for a long time. The simulation showed that there is little probability of resurgence of an epidemic in the northeastern villages of Bohol island for several years because the program in Bohol has attained a high coverage of selected mass treatment based on stool examination and has been accompanied by snail control operation since its commencement.

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Table 1 Epidemiological survey of *S. japonicum* in Bohol.

Sto. Thomas (TRINIDAD)				San Vicente (TRINIDAD)				San Roque (TALIBON		
No. Examined	No. of egg Positive [a]	Prevalence (%)	Coverage (%) of Stool Examination	No. Examined	No. of egg Positive [a]	Prevalence (%)	Coverage (%) of Stool Examination	No. Examined	No. of egg Positive [a]	Prevalence (%)
-	-	-	-	-	-	-	-	1124	57	5.1%
-	-	-	-	465	72	15.5%	85.8%	-	-	-
-	-	-	-	-	-	-	-	1178	52	4.4%
413	62	15.0%	64.9%	400	60	15.0%	62.9%	-	-	-
381	35	9.2%	59.3%	-	-	-	-	-	-	-
545	16	2.9%	97.5%	537	9	1.7%	96.1%	869	4	0.5%
345	6	1.7%	68.6%	450	7	1.6%	84.4%	1235	1	0.1%
516	5	1.0%	81.1%	578	4	0.7%	90.9%	1316	2	0.2%
716	6	0.8%	94.2%	621	10	1.6%	96.4%	1688	6	0.4%
668	5	0.7%	85.2%	630	12	1.9%	94.9%	1303	5	0.4%
656	0	0.0%	87.2%	584	2	0.3%	84.6%	1078	4	0.4%
660	1	0.2%	83.7%	595	5	0.8%	82.3%	1554	2	0.1%
439	1	0.2%	54.3%	273	5	1.8%	36.8%	1417	0	0.0%

590	1	0.2%	85.4%	623	0	0.0%	86.6%	895	4	0.4%
617	1	0.2%	93.3%	593	2	0.3%	68.4%	1400	7	0.5%
559	1	0.2%	93.5%	964	5	0.5%	93.3%	1372	0	0.0%
667	0	0.0%	100.0%	707	2	0.3%	78.4%	1358	3	0.2%
622	0	0.0%	97.0%	718	2	0.3%	77.3%	1227	5	0.4%
633	1	0.2%	93.9%	679	2	0.3%	75.5%	1169	0	0.0%

[a] All egg positive cases were treated with praziquantel.

Table 2 Estimated transmission rates, initial prevalence, infection rates and snail densities

Village	Sto. Thomas	San Vicente	San Roque
Transmission rate from snails to humans	$1.41\%10^{-3}$	$1.71\%10^{-2}$	$1.11\%10^{-3}$
Transmission rate from humans to snails	$2.57\%10^{-3}$	$5.59\%10^{-3}$	$7.20\%10^{-4}$
Initial prevalence in human population	15.0%	15.2%	5.1%
Initial infection rate in snail population	19.0%	9.9%	6.6%
Initial snail density per 1 *a* [a]	3.57	0.57	3.77

[a] Expressed as number per man per hour per 1 *a* ($100m^2$).

Table 3 The model parameters together with their assumed and adjusted values.

Description	Symbol	Estimated value
Pre-depositing fecal eggs period for worm (days)	τ_m	45
Duration of egg production for worm (years)	τ_e	4
No cercaria releasing period (weeks)	τ_c	8
High cercaria releasing period (weeks)	τ_h	3
Low cercaria releasing period (weeks)	τ_l	4
Ratio of output in low to that to high releasing period	r_c	0.2
Ratio of transmission index to snails in rats to humans	r_{rat}	0.01
Life expectancy of inhabitants (years)	$1/\delta_h$	69
Daily mortality rate for uninfected snails (%)	δ_{su}	0.9
Daily mortality rate for preshedding snails (%)	δ_{sp}	2.0
Daily mortality rate for shedding snails (%)	δ_{ss}	1.5
Birth rate for snails per day (%)	δ_{sb}	0.97
Daily mortality rate for rats (%)	δ_r	0.55
Seasonally relative water area	r_w	See text

Legends

Figure 1 The basic scheme of the transmission model for *S. japonicum* showing the transfers among epidemiological classes.

The birth/death rates of the definitive hosts are omitted from this figure.

Figure 2 The illustration of searching for the adjusted values of two transmission rates from snails to humans (human) (β_h), and from humans to snails (snail) (β_s) for the pre-control period in Sto. Thomas where the prevalence was estimated at 15.0% for the human population and the infection rate was estimated at 19.0% for the snail population.

A bar is assigned to a region where the difference between the observed value and equilibrium value for the prevalence in the human population is opposite in sign to the difference between the observed value and equilibrium value for the infection rate in the snail population.

Figure 3 Variations in the infection of *S. japonicum* in Sto. Thomas situation for the human control case with selective mass treatment at a 1 year interval under a covering rate of 50% (solid line), the snail control case with use of molluscicides at half-year intervals under the assumption that its effective rate would be 50% (dotted line), and both the human and snail control case (dashed line), respectively.

a variations in the prevalence (%) in the human population, **b** variations in infected snail densities per 1 *a* (100m^2).

Figure 4 Variations in the prevalence of *S. japonicum* in the Sto. Thomas situation with the human control with selective mass treatment at a 1 year interval.

The cases where the coverage in inhabitants is 30% (dotted line), 50% (dashed line) and 70% (solid line) are shown.

Figure 5 Comparison between the changes of infection of *S. japonicum* derived from the model (line) and the observed data in Sto. Thomas village (square).

In a simulation, we used the actual value as coverage and assumed that the effective rate of molluscicides would be 30%. **a** comparison between the prevalence (%) in villagers derived from the model and the prevalence observed in mass examination, **b** comparison between the infection rate (%) in snails derived from the model and the infection rate obtained by the field surveys.