Supporting Text

Model

Our study of schistosomiasis japonica in the Xichang area surrounding Qionghai Lake has shown that village of residence and occupation are major risk factors determining human infection intensity, whereas individual characteristics including age, gender, and kinship have minor roles explaining variations in infections within and between villages (1). The findings are in good agreement with those from the same region by our colleagues at Sichuan Institute of Parasitic Disease, China (2, 3). Moreover, buffaloes, cows, and horses were found to play a marginal role in the local transmission in the study area surrounding Qionghai Lake (1-3). For example, in the 2000 cross-sectional survey carried out in the Xichang Study Area, no buffaloes were found in Shian 5 and Xinlong 7, but two were found in Xinming 3; all cows and horses from the three villages were surveyed, and none of them was found to be infected. Therefore, age, gender, and buffalo were not factored into the model, which was developed to understand the impact of site-specific factors on the local transmission of disease and its control. Detailed descriptions of the model formulation are provided elsewhere (4, 5) and will be only briefly introduced here. The model consists of a set of three submodels, which describe the changes in infection intensity in the risk groups (as defined by occupation), and infected and susceptible snail densities in the environment over time.

The mean worm burden in occupational group i is given by the solution of the state equation:

$$\frac{dw_i}{dt} = \alpha e^{-\mu_w \tau_w} s_i(t-\tau_w)\gamma_i C(t-\tau_w) f(w_i) - \mu_w w_i(t)$$

Constant parameters like α are defined in Table 1. Similar information is given for time-variable parameters like $s_i(t)$, the water contact index in Table 2. Parameter estimates and their sources are given elsewhere (5). Biologically meaningful quantities, including those derived from other underlying parameters, are:

- $f(w_i)$ follows Anderson and May and is the density dependent worm establishment function, which describes a process in which the likelihood of developing into an adult worm is assumed to be reduced when the worm burden is high due to a "crowding effect", to the concomitant immunity, or both. In the present study, we assume this to be a constant;

- $C(t-\tau_w)$ is the mean spatial density of cercariae, the free-swimming form of the parasite infective to mammals, in the irrigation system at time $t-\tau_w$. The time delay is due to the fact that the rate of change in the number of adult worms at time *t* is due to exposure to cercariae at time $t-\tau_w$ where τ_w is the worm development period in human hosts. *C(t)* depends on the infected snail population, as modified by environmental factors;

$$C(t) = I_c(T_1)\frac{r_c(t)}{A_s}\sigma A_h z(t)$$

where z(t), the infected snail density, is given by the solution of:

$$\frac{dz}{dt} = \rho e^{-\mu_z \tau_z}\xi(T_1)M(t-\tau_z)x(t-\tau_z) - \mu_z z$$

and

- *x(t)* is the density of susceptible snails. Because the infection rate in snails rarely exceeds 1%, *x(t)* is treated as a time-variable parameter rather than an additional state variable ;

• *M(t)* is the mean density of miracidia, the free-swimming form of the parasite infective to snails, in the village irrigation system. The net effective density of miracidia, *M(t)*, is related to the eggs excreted into environment by infected humans, *E(t),* by the expression:

$$M(t) = I_m(T_1)\frac{r_e(t)}{A_s}\beta E(t)$$

and

$$E(t) = \tfrac{1}{2}h\sum_i g_i n_i w_i \Phi(w_i, \kappa_{w_i})$$

where $\Phi(w_i, \kappa_{w_i})$ is worm mating probability following May (6).

Field data

Table 3 shows schedule for field data collection and interventions from 2000 to 2004. The interventions instituted based on model-based analyses of the villages' specific transmission circumstances, together with additional interventions carried out locally (unplanned by the project), are summarized in Table 4. The actually implemented interventions were input in the models, and the model-based forecasts of infection intensity in the three human groups in each village were compared with field data collected at the end of the 2004 infection season, as summarized in Table 5.

Internal Potential

(1) Water contact index

As described in the main text, our epidemiological investigations suggest that the endemic level is determined by a set of local factors relating to agricultural practices, the

snail population, and water contact. Together, these factors comprise internal potential. Water contact, appearing in the model as s_i, water contact index, is derived for each risk group from a questionnaire survey. s_i is defined as average water contact area.time/unit time (e.g., m^2.minute/day) for *i*th risk group and can be estimated from the time-activity data. In estimating $s_i(t)$, a contact m^2.minute for host *j* at time t, denoted as $\eta_j(t)$, is first estimated from

$$\eta_j(t) = \sum_{\ell} \sum_{b} A_b I_{\ell b}(t) D_{\ell b}(t) \quad \ell_j = 1,2,...,L_j,\ b_j = 1,2,...,B_j;$$

where A is exposure area for activity *b*, $I_{\ell b}(t)$ is corresponding frequency of contact, D duration of contact. $I_{\ell b}(t)$ is directly calculated from

$$I_{\ell b}(t) = day(s)/month * times/day$$

To explore temporal dynamics of endemic level of infection, as a result of internal potential modulated by weather and other factors, the full model was simplified by reducing the three human risk groups to one comprised of all villagers. To account for the fact that farmers, students, and others have different water contact patterns and different population sizes (n_i), a population weighted average water contact profile is used, i.e.

$$s(t) = \frac{n_1 s_1(t) + n_2 s_2(t) + n_3 s_3(t)}{\sum n_i}$$

(2) Constant and time variable parameters

In Eq. **1.1**, the new parameter groups are further represented as:

$$a_{11} = \alpha\sigma\gamma S \frac{A_h}{A_s} e^{-\mu_w \tau_w} \quad a_{21} = \frac{1}{2A_s} \rho\xi\beta h g_0 n X$$

and

$$\alpha_{11}(t-\tau_w) = s_n(t-\tau_w)I_c(t-\tau_w)r_c(t-\tau_w)$$

$$\alpha_{21}(t-\tau_z) = x(t-\tau_z)r_e(t-\tau_z)I_m(t-\tau_z)e^{-\mu_z\tau_z}$$

Fig. 2 shows the gating functions from a Shian 5 simulation in which α_{21} decreases abruptly in the fall as a result of the lengthening of the developmental delay, τ_z, as the environmental temperature undergoes its seasonal decline.

The rainfall/irrigation parameters $r_c(t)$ and $r_e(t)$ are also defined to vary between 0 and 1. These parameters represent the fraction of the irrigation system with sufficient water flow to transport the free-swimming forms of the parasite (7). Note, in the above equations, that the developmental delay of worms *in vivo*, τ_w, is constant, but the delay between snail infection and parasite maturation in snails, τ_z, is a degree-day function of environmental temperature that results in a ≈3-fold variation in τ_z over the year. Hence, the exponential loss function of τ_w is in a_{11}, but the corresponding τ_z term in α_{21}.

(3) Analysis of simulation

We conducted a qualitative analysis of the trajectories from simulations of the full non-linear model with delays in each of three villages discussed in the main text. To capture the trend of the various trajectories, a single exponential function, $ke^{\lambda t}$, was fit to the worm burden trajectory of the farmer group from 2004 to 2009 for each Monte Carlo realization of Scenario I, sustained environmental control without chemotherapy after 2003, for Shian 5 and Xinming 3. The median trajectory of this set of realizations is shown by the cyan lines of Fig. 1. Recall that each of the Monte Carlo realizations reflects the residual parametric variability or uncertainty remaining after calibration. For

each realization in each village, the corresponding value of P_sP_b was calculated and the exponent, λ, estimated. Fig. 3 shows a plot of the results for Shian 5. The four quadrants surrounding (1,0) are labeled clockwise from A to D with A being the lower left. If Eq.**1.4** were a necessary and sufficient condition for λ to be negative, i.e. for the worm burden to decline over time, all points in the figure would lie in quadrants A and correspondingly in quadrant C if this condition was not satisfied. Presumably those points in quadrant B reflect parameter combinations for which the destabilizing effect of the delays exceeds the stabilizing effects of the gating functions and vice versa in quadrant D. Hence, the condition that $P_sP_b < 1$ is conservative in those parameter combinations lying in quadrant D but an insufficient condition for combinations in only quadrant B.

The results for Xinmin 3 and Xinlong 7 are similar in the distribution of the realizations by quadrant. In all three cases, the majority of the points lie in the band of $-3 < \lambda < 2$ i.e., a range of roughly ±10% to 15% per year change in infection intensity, the semistable behavior that motivated this line of enquiry. For the case in which no further intervention is exercised after the 2004 chemotherapy in Shian 5, all of the realizations but one showed increasing infection intensity over time and only two had values of $P_sP_b < 1$.

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