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Comparison between schistosomiasis transmission modelings considering acquired immunity and age-structured contact pattern with infested water

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Abstract

In order to analyze the effects of acquired immunity and the contact pattern with infested water on the overall transmission of schistosomiasis, a semi-stochastic model is proposed. The model's assumptions are the simplest possible to enhance the differences between two hypotheses. With respect to the human host, it is assumed the mounting of an immune response after elapsing a fixed period of time L from the first infection, which is partially effective and never lost. With respect to the contact pattern with infested water, it is assumed a decreasing age-related function. Both models are compared to a purely random model, which is taken as the basic model.

Keywords: Schistosomiasis; Acquired immunity; Age-dependent contact pattern; Epidemiology; Mathematical model

1. Introduction

Schistosomiasis is the human infection, probably, with the most complex biological cycle, which involves at least two host species (human and snail), two free-living transmission stages of the parasite (cercariae and miracidia) and distinct environments. Humans are the principal definitive host for the five schistosome species. Adult worms live in the venous system of intestine (*S. mansoni*, *S. japonicum*, *S. mekongi* and *S. intercalatum*) or the urinary bladder (*S. haematobium*) [1].

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As a result of the parasite sexual reproduction in different human organs, the characteristically shaped eggs pass through the vesical or intestinal wall in order to find their way to outside via the host excreta. In fresh water the eggs hatch and release ciliated motile miracidia that soon penetrate into the snail (the intermediate host). Inside the snail the miracidia multiply asexually, and in 4–6 weeks hundreds of thousands of motile forked-tail cercariaes emerge. These are the infective forms to the human host. For each species of schistosome and for each geographic region there is a specific snail as the intermediate host. Therefore, it is believed that the geographic distribution of schistosomiasis depends on the distribution of the specific snails. On encountering human skin, the cercariae actively penetrate it, causing a local reaction. In the process of invasion, the cercariaes lose their tails and change into schistosomulaes that migrate to the lungs and liver; in about 6 weeks they mature to adult worms, mate and descend, via the venous system, to their final habitat. The life-span of adult worms is still a controversy, ranging from 5 to 10 years to more than 30 years [2,3].

The most used epidemiological data to describe the schistosomiasis is the so-called *prevalence curve*, that is, the proportion of individuals shedding viable eggs in faeces (or urine) plotted against age. The essential relationship between prevalence and age, which is repeatedly observed in the studies of age-specific prevalence data of schistosomiasis, is a build up in the early years, peaking around 10–20 years of age, dropping thereafter, and stabilizing at some endemic level [4,5]. It is remarkable that this behaviour of the prevalence curve is observed even when the prevalence is very low, reaching a peak of only 5% [6].

Mathematical models have great potential for advancing the understanding of schistosome transmission and as a tool for the design of control programmes [7]. As the life-cycle of schistosome is extremely complex, it is very difficult to understand the quantitative contribution of different components of transmission to the level of infection in a human population. For the same reason, it is difficult to predict the quantitative effects of intervention on human infection and disease. As prediction is central to the question of decision about competing intervention options, models with predictive capacity can be a powerful tool to help the disease control problems.

To be of any use, however, models must be sufficiently realistic and grounded in what is understood of the schistosome biology [7]. This implies the inclusion of some biological details such as the role of acquired immunity on the disease dynamics, the pattern of contacts (related to age and spatial) of individuals with cercariae infested water or the effects related to the environment. Models which incorporate neither the acquired resistance to infection nor the age-dependent parameters cannot reproduce typical age–intensity or age–prevalence patterns. For a review of schistosome infection modelling see [7,8].

Acquired immunity among the humans has important consequences for the epidemiology of schistosome infection [7,9–11]. The question of whether humans mount an immune response to schistosomiasis is of basic biological interest and important in the context of disease control [12]. There is accumulating evidence that the human host develops a protective immune response to schistosome infection [13,14]. However, the immune response to this and other large parasites differs from that of viruses and bacteria, and appears to be acquired gradually, concomitant, and may afford only partial protection against further infections. In addition, acquired host responses can act to reduce rates of parasite establishment, fecundity and survival [15].

Another aspects to be considered in the dynamics of schistosomiasis transmission is the observed frequency of contacts among humans with presumably contaminated water [16–18]. The lowering in the prevalence among elder individuals can be thought of decreasing in the contacts with infested water. The introduction of this kind of information is the basis of the Holford and Hardy's stochastic model [5].

The second most used data is the age-dependent *egg output curve*. This curve is also characterized by an early build up, peaking slightly earlier than the prevalence curve [19]. Following this peak, there is a decline in the egg output but the decline does not reach zero, rather it approaches some other asymptote [20,21]. The mean population worm burden can be obtained from this set of data.

The third kind of data is the age-dependent variance in the egg output among the human population. This kind of data is difficult to obtain but is very important to what follows. This variance divided by mean egg output is the well known *dispersion curve* and typically assumes high values at lower ages, dropping quickly to a minimum value around 10–15 years, raising thereafter to stabilize at a certain level [21]. The mean population worm dispersion can be obtained from this set of data.

The fourth type of data described in the literature is the proportion of shedding snails (those releasing cercariaes), or the combined proportion of latent (those already infected but not releasing cercariaes yet) and shedding snails [22].

From the first set of data the age–prevalence curve $P(a)$ can be derived, and from the second and third sets of data, assuming that each worm produces a certain number of eggs, the age-mean number of worms harboured by the human population $m(a)$ and the parasite age–dispersion curve $d(a)$ can be derived [21]. Instead of these latter two variables, in this paper we consider the population mean worm burden m and mean worm dispersion d.

In this paper we present the comparison between simple models considering acquired immunity against schistosomiasis [23] and age-structured contact pattern with cercariae infested water taking into account the above four kinds of data related to the schistosomiasis transmission. The acquired immunity is partially protective, that is, after the first infection there is a fixed length of time L after which the rate of infection is dramatically reduced [24–26]. The contact pattern with infested water is constrained to the infective parameter, setting an age-related function. The results obtained from both models are compared between them and with the basal results yielded from a purely random process (Poisson) model.

This paper is organized as follows. Section 2 presents the general model, from which we derive three special cases given in Sections 2.1, 2.2 and 2.3; and in Section 2.4 we derive the basic reproduction ratio. Section 3 deals with the epidemiological values: the prevalence curve (Section 3.1), the mean worm burden and the mean dispersion (Section 3.2) and the basic reproduction ratio (Section 3.3) obtained from the models taking into account field data. The epidemiological findings are discussed in Section 4 and some conclusions are summarized in Section 5.

2. The model

We develop a general model including acquired immunity and contact pattern with infested water. Since the role of immunity in controlling re-infection is not entirely known [12], we have to

construct a model for the acquired immunity assuming its existence. With respect to the contact pattern, we assume that the frequency of contacts with infested water is described by an age-dependent function. The classical models related to schistosomiasis can be divided into two distinct groups: fitting-prevalence [5,7] and transmission dynamics analyses [8].

The general semi-stochastic model [27] is presented in Appendix A, where the acquisition of worms by humans is treated stochastically (migration–death type) and the age-distribution of the individuals is treated deterministically. Briefly, the probability of a non-immune person with age between a and $a + \mathrm{d}a$ being infected in the steady state is $\lambda(a)\,\mathrm{d}a$, where $\lambda(a)$ is the transmission rate (or force of infection) among non-immune individuals. It also reflects the fact that all invading cercariaes maturate to adult form; the human host build an immune response up after elapsing a fixed period of time L from the first infection, which is partially effective, that is, protection against further infections is not fully avoided but controlled to some extent, and everlasting, that is, in the absence of the adult worm the immunity processes do not fade away. So the probability of a partially immune person with age between a and $a + \mathrm{d}a$ (with $a > L$) being infected in the steady state is $\lambda'(a)\,\mathrm{d}a$, where $\lambda'(a)$ is the transmission rate among immune individuals; adult worms inside the host die with a constant rate μ_{w} and the human population is treated deterministically under a constant death rate μ_{h}. With respect to the snail population, it is treated deterministically, which is exactly equal to May's model [28], considering that the snail population is constant. As pointed out by May, this is a very strong assumption. He also considered that the snails begun to release cercariaes after a period of time τ from the first infection.

With respect to the transmission rate $\lambda(a)$, we recall the general age-dependent function proposed by Holford and Hardy [5], which is

$$\lambda(a) = (b_1 + b_2 a)\,\mathrm{e}^{-b_3 a} + b_4, \tag{1}$$

where the parameters b_i, for $i = 1, 2, 3$ and 4, are related to the environment. These parameters also take into account the water contact pattern and the degree of infestation of water with cercariaes eliminated by infected snails. In some manner, the frequency of contacts of humans with the infested water is allowed to vary with age [18]; however the acquired immunity can be described by the parameter L (a time delay to build up the immune response) and different age-dependent transmission rates according to the immune status.

In the steady state, the semi-stochastic function relating the probability generating function for the number of worms distributed among non-immune individuals with age between a and $a + \mathrm{d}a$ (Appendix A) is given by

$$F(a,x) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}} a} \int_{a-L}^{a} \lambda(s)\,\mathrm{e}^{-\Lambda(s)}\left[1 + (x-1)\,\mathrm{e}^{-\mu_{\mathrm{w}}(a-s)}\right] \mathrm{e}^{(x-1)\mathrm{e}^{-\mu_{\mathrm{w}}(a-s)}\Psi(a,s)}\,\mathrm{d}s, \tag{2}$$

where μ_{h} and μ_{w} are the mortality rates associated to humans and worms, respectively, and the function relating the probability generating function for the number of worms distributed among the immune individuals with age between a and $a + \mathrm{d}a$ (with $a > L$) is given by

$$\begin{aligned} F'(a,x) = {} & S_0\,\mathrm{e}^{-\mu_{\mathrm{h}} a} \int_{0}^{a-L} \lambda(s)\,\mathrm{e}^{-\Lambda(s)}\left[1 + (x-1)\mathrm{e}^{-\mu_{\mathrm{w}}(a-s)}\right] \\ & \times \mathrm{e}^{(x-1)\,\mathrm{e}^{-\mu_{\mathrm{w}}(a-s)}\Psi(a_0+L,s)}\,\mathrm{e}^{(x-1)\,\mathrm{e}^{-\mu_{\mathrm{w}}(a-s-L)}\Psi'(a,s)}\,\mathrm{d}s. \end{aligned} \tag{3}$$

The parameter S_0 is the new-born rate and the functions $\Lambda(s)$, $\Psi(a,s)$ and $\Psi'(a,s)$ are given by

$$\begin{cases} \Lambda(s) = \int_0^s \lambda(\tau)\,\mathrm{d}\tau, \\ \Psi(a,s) = \int_{a_0}^a \lambda(\tau)\,\mathrm{e}^{\mu_w(\tau-s)}\,\mathrm{d}\tau, \\ \Psi'(a,s) = \int_{a_0+L}^a \lambda'(\tau)\,\mathrm{e}^{\mu_w(\tau-s-L)}\,\mathrm{d}\tau. \end{cases} \tag{4}$$

These probability generating functions describe the model that considers the susceptible individual having the first infection at age A, becoming immune after elapsed a period of time L and mounting up an age-related resistance to infection (see [29,30] for multiple cercariae infections per event).

From the probability generating functions $F(a,x)$ and $F'(a,x)$ we can derive the age–prevalence curve, the mean worm burden per person and the dispersion of worms per person. The age–prevalence curve can be obtained directly from the probability generating functions, which can be interpreted as the risk (probability) of an individual being infected at the age a. The last two variables are derived from the first and the second moments of the probability generating functions. Both results can be thought of corresponding to the deterministic approach.

Our aim is to compare the epidemiological findings obtained from models considering the acquired immunity or the water contact pattern. In order to do this, we split the general semi-stochastic model into two sub-models, which are fitted to the prevalence curve to estimate the model's parameters. Then we examine the effects of both features in the schistosomiasis transmission calculating epidemiological parameters like the basic reproduction ratio. Initially, however, we present the purely random (Poisson) model to set a referential framework.

2.1. Model 1: Poisson model

The pure Poisson model is presented to fix the basic model. In this model, the transmission rate does not depend on any variable, assuming a constant value. By the fact that the transition probability assumes a constant value, we have a purely random model (the Poisson distribution). The pure Poisson process is obtained from Eq. (2) by letting $\lambda(a) = \lambda$. This model has the probability generating functions given by

$$F(a,x) = S_0\,\mathrm{e}^{-\mu_h a}\exp\left((x-1)\lambda\frac{1-\mathrm{e}^{-\mu_w a}}{\mu_w}\right) \tag{5}$$

and $F'(a,x) = 0$, since the immunity is not being taken into account ($L \to \infty$).

Considering the probability generating function given by Eq. (5), we use Eqs. (A.26) and (A.29), from Appendix A, to derive the age–prevalence curve $P(a)$, the mean number of parasites m and the mean dispersion d. They are

$$P_1(a) = 1 - \exp\left(-\lambda\frac{1-\mathrm{e}^{-\mu_w a}}{\mu_w}\right), \tag{6}$$

$$m_1 = \frac{\lambda}{\mu_h + \mu_w} \tag{7}$$

and

$$d_1 = 1 + \frac{\lambda\mu_h}{(\mu_h + \mu_w)(\mu_h + 2\mu_w)}. \tag{8}$$

Observe that, if $\mu_h = 0$ (there is not renewal of individuals), then $d_1 = 1$, resulting in the pure random (Poisson) process.

2.2. Model 2: simple water contact pattern model

The simple age-structured contact pattern with infested water is obtained from Eq. (2) by letting $\lambda(a) = \lambda e^{-ba}$, which comes from Eq. (1) by setting $b_2 = b_4 = 0$. Note that we are considering the simplest dependency of the water contact pattern with age. This model has the probability generating functions given by

$$F(a,x) = \begin{cases} S_0 e^{-\mu_h a} \exp\left((x-1)\lambda \frac{e^{-ba} - e^{-\mu_w a}}{\mu_w - b}\right) & \text{for } \mu_w \neq b, \\ S_0 e^{-\mu_h a} \exp((x-1)\lambda a e^{-\mu_w a}) & \text{for } \mu_w = b \end{cases} \tag{9}$$

and $F'(a,x) = 0$, since the immunity is not being taken into account ($L \to \infty$). The parameter b is the avoidance rate, which increases with the age and avoids contacts with infested water. This is a parameter depending on the changes of habits induced by sanitary education and of economic activities.

Considering the probability generating function given by Eq. (9), we use Eqs. (A.26) and (A.29), from Appendix A, to derive the age–prevalence curve $P(a)$, the mean number of parasites m and the mean dispersion d. They are

$$P_2(a) = \begin{cases} 1 - \exp\left(-\lambda \frac{e^{-ba} - e^{-\mu_w a}}{\mu_w - b}\right) & \text{for } \mu_w \neq b, \\ 1 - \exp(-\lambda a e^{-\mu_w a}) & \text{for } \mu_w = b, \end{cases} \tag{10}$$

$$m_2 = \frac{\lambda\mu_h}{(\mu_h + \mu_w)(\mu_h + b)} \tag{11}$$

and

$$d_2 = 1 - \frac{\lambda\mu_h}{(\mu_h + \mu_w)(\mu_h + b)} + \frac{2\lambda(\mu_h + \mu_w)(\mu_h + b)}{(\mu_h + 2\mu_w)(\mu_h + \mu_w + b)(\mu_h + 2b)}. \tag{12}$$

This dispersion shows a deviation from the Poisson process.

The mean worm burden m_2 is limited and monotonically decreasing function with respect to b, which has the limiting values given by

$$m_2 = \begin{cases} \dfrac{\lambda}{\mu_h + \mu_w} & \text{for } b = 0, \\ 0 & \text{for } b \to \infty. \end{cases}$$

Note that the mean worm burden can reach null value by increasing the avoidance parameter (avoiding the contact with infested water by sanitary education).

2.3. Model 3: simple acquired immunity model

The acquired immunity model is obtained from Eqs. (2) and (3) by letting $\lambda'(a) = \lambda'$ and $\lambda(a) = \lambda$. Note that we are considering the simplest form for the acquired immunity consideration. This model has the probability generating functions given by

$$F(a,x) = \begin{cases} S_0 \mathrm{e}^{-\mu_h a}\left[\exp\left((x-1)\lambda\frac{1-\mathrm{e}^{-\mu_w a}}{\mu_w}\right) - \mathrm{e}^{-\lambda a}\right] & \text{for } a \leqslant L, \\ S_0 \mathrm{e}^{-\mu_h a}\left\{\exp\left(-\lambda\left[(a-L) - (x-1)\frac{1-\mathrm{e}^{-\mu_w L}}{\mu_w}\right]\right) - \mathrm{e}^{-\lambda a}\right\} & \text{for } a > L \end{cases} \tag{13}$$

for non-immune individuals, and

$$F'(a,x) = \begin{cases} 0 \quad \text{for } a \leqslant L, \\ S_0 \mathrm{e}^{-\mu_h a}\int_0^{a-L} \lambda[1+(x-1)\mathrm{e}^{-\mu_w(a-s)}]\mathrm{e}^{-\lambda s}\exp\left((x-1)\lambda\left[\frac{\mathrm{e}^{-\mu_w(a-s-L)} - \mathrm{e}^{-\mu_w(a-s)}}{\mu_w} + \frac{\lambda'}{\lambda}\frac{1-\mathrm{e}^{-\mu_w(a-s-L)}}{\mu_w}\right]\right)\mathrm{d}s \\ \quad \text{for } a > L \end{cases} \tag{14}$$

for immune individuals.

Considering the probability generating functions given by Eqs. (13) and (14), we use Eqs. (A.26) and (A.29), from Appendix A, to derive the age–prevalence curve $P(a)$, the mean number of parasites m and the mean dispersion d. They are

$$P_3(a) = \begin{cases} 1 - \exp\left(-\lambda\frac{1-\mathrm{e}^{-\mu_w a}}{\mu_w}\right) \quad \text{for } a \leqslant L, \\ 1 - \exp\left(-\lambda\left[(a-L) + \frac{1-\mathrm{e}^{-\mu_w L}}{\mu_w}\right]\right) - \int_0^{a-L}\lambda[1-\mathrm{e}^{-\mu_w(a-s)}]\mathrm{e}^{-\lambda s}\exp\left(-\lambda\left[\frac{\mathrm{e}^{-\mu_w(a-s-L)} - \mathrm{e}^{-\mu_w(a-s)}}{\mu_w} + \frac{\lambda'}{\lambda}\frac{1-\mathrm{e}^{-\mu_w(a-s-L)}}{\mu_w}\right]\right)\mathrm{d}s \\ \quad \text{for } a > L, \end{cases} \tag{15}$$

$$m_3 = \frac{\lambda}{\mu_h + \mu_w}\left[1 - \frac{(\lambda - \lambda')\mathrm{e}^{-\mu_h L}}{\lambda + \mu_h}\right] \tag{16}$$

and

$$d_3 = 1 - \frac{\lambda}{\mu_h + \mu_w}\left[1 - \frac{(\lambda - \lambda')\mathrm{e}^{-\mu_h L}}{\lambda + \mu_h}\right] + \frac{f_1 + \frac{\lambda - \lambda'}{\mu_w}f_2(L) - \frac{(\lambda-\lambda')^2}{\lambda\mu_w}\mathrm{e}^{-\mu_h L}}{\frac{\lambda}{\mu_h+\mu_w}\left[1 - \frac{(\lambda-\lambda')\mathrm{e}^{-\mu_h L}}{\lambda+\mu_h}\right]}, \tag{17}$$

where f_1 and $f_2(L)$ are given by

$$f_1 = \frac{2\lambda^2}{(\mu_h + \mu_w)(\mu_h + 2\mu_w)} \tag{18}$$

and

$$f_2(L) = \frac{\lambda\mu_h \mathrm{e}^{-\mu_h L}}{\mu_w}\left[\frac{\frac{2\lambda'}{\lambda+\mu_h} + \frac{\mu_h+3\mu_w}{\mu_h+2\mu_w}\mathrm{e}^{-\mu_w L}}{\mu_h + \mu_w} + \frac{\frac{\lambda(1-\mathrm{e}^{-\mu_w L})+\lambda'}{\lambda} + \frac{\lambda(1-\mathrm{e}^{-\mu_w L})-\lambda'}{\mu_h+2\mu_w}}{\lambda + \mu_h}\right]. \tag{19}$$

Observe that the worm burden and the dispersion depend on the immunity parameter L.

The mean worm burden m_3 is limited and monotonically increasing function with respect to L, which has the limiting values given by

$$m_3 = \begin{cases} \frac{\lambda}{\mu_h+\mu_w}\frac{\lambda'+\mu_h}{\lambda+\mu_h} & \text{for } L = 0, \\ \frac{\lambda}{\mu_h+\mu_w} & \text{for } L \to \infty. \end{cases}$$

The delay (immunologically weakened individuals) to build up the immunity (high values of L) increases the mean worm burden. Note that the mean worm burden never reaches null value, even that we could have a perfect immune reaction.

Up to this point we developed the model considering only the definitive host. In fact, the transmission rates λ and λ' are unrelated up to this moment to the transmission rate regarded to the snail population. To close the life-cycle of the schistosome infection we need the proportion of snails that are infected and shedding cercariaes. In order to do this we consider May's model [28] for the snail population.

2.4. The overall schistosomiasis transmission

In this section, taking into account the average values calculated from the first and the second moments of the probability generating functions, we deal with the overall schistosomiasis transmission, which corresponds to the deterministic approach. Hence, the complete description of the schistosomiasis transmission is done considering the mean worm burden in the community, given by one of Eqs. (7), (11) or (16) depending on the model under study, with the mean proportion of the shedding snails. The main goal of the model considering the interaction between human host and snail population is to obtain the basic reproduction ratio R_0, which provides the average number of female worms produced by one coupled female worm during its entire life-span.

With respect to the snail population, they are subdivided as susceptible, latent (infected but not eliminating cercariaes) and infected (those that had survived the incubation period τ and are eliminating cercariaes). According to May's model [28] related to the snail population, the proportion of shedding snails z in the equilibrium is given by

$$z = \left(\frac{\mu_s''}{\lambda_s e^{-\mu_s'\tau}} + \frac{1}{z^*} \right)^{-1}, \tag{20}$$

where λ_s is the snail transmission rate, μ_s' is the mortality rate of the latent snails, μ_s'' is the mortality rate of the infected snails, i.e., the shedding snails, and z^* is the maximum attainable value for the proportion of shedding snails, which is given by

$$z^* = \frac{e^{-\mu_s'\tau}}{\frac{\mu_s''}{\mu_s'} - \left(\frac{\mu_s''}{\mu_s'} - 1\right) e^{-\mu_s'\tau}}. \tag{21}$$

May's model is a modification of Macdonald's [31] model encompassing the differential mortality rates among infected snails and the incubation period τ. The limiting values for z are $z(\lambda_s = 0) = 0$ and $z(\lambda_s \to \infty) = z^*$.

Macdonald's model predicts the proportion of infected snails at equilibrium with unrealistically large values when compared with current epidemiological data [22,32,33] when the value of R_0 is

great. On the other hand, low values of R_0 are incompatible with the endemic stability (in the sense of opposing to controlling efforts) of schistosomiasis. A similar qualitative criticism was previously made by Jordan [34] to Macdonald's model [31]. A stochastic version of Macdonald's model was proposed by Nåsell and Hirsch [35]. Although this version obviously improves the simple deterministic Macdonald's model, it results essentially in the same endemic instability.

May's [28] developments represent a major improvement on Macdonald's model, although it still fails to explain some aspects of the epidemiology of schistosomiasis. It is true, however, that it explains the observed low value of z, but it does not explain the stability of the endemic level of the disease [36]. It should be mentioned that one of the main purpose of May's paper was to investigate the influences of the mating function and the breaking point [37] in the schistosomiasis transmission, which have not been considered in this paper.

The overall schistosomiasis transmission is analyzed in terms of the dimensionless transmission parameters T_1 and T_2, which were used by Nåsell and Hirsch [35] and May [28], instead of the previous transmission rates λ, λ' and λ_s.

The parameter T_1 is the overall transmission coefficient from human to snail encompassing all the probabilistic events occurring in the environment. It is given by

$$T_1 = \frac{\frac{1}{2}\eta_E P_1 N_h}{\mu_s''}, \tag{22}$$

where η_E is the number of eggs shed by each couple of schistosomes per unit of time; P_1 is the probability of a released egg to develop to miracidia and to infect a snail; N_h is the total population of human host; and μ_s'' is the mortality rate of the shedding snails. As mentioned above, we are not concerning about the mating between male and female worms, given by mating function $\phi(m)$ [28]; for this reason we set half for the probability of mating when there is m mean worm burden. This constant mating function, $\phi(m) = 1/2$, also describes hermaphroditic helminthiasis modeling [38].

The parameter T_2 is the overall transmission coefficient from snail to human encompassing all the probabilistic events occurring in the environment. It is given by

$$T_2 = \frac{\eta_C P_2 N_s}{\mu_w}, \tag{23}$$

where η_C is the number of cercariae released by an infected snail per unit of time; P_2 is the probability of a cercariae to infect a human host; N_s is the total population of snails; and μ_w is the death rate of adult worms.

Therefore, we can relate the transmission rates λ, λ' and λ_s to the dimensionless transmission coefficients T_1 and T_2, according to Nåsell and Hirsch [35]. The snail transmission rate can be set as

$$\lambda_s = \mu_s'' m_i T_1, \tag{24}$$

where the index i stands for the model on consideration, with $i = 1$, 2 or 3.

The worm transmission rate among non-immune individuals can be set as

$$\lambda = (\mu_h + \mu_w) z T_2, \tag{25}$$

which depends on the environment due to the parameters z and T_2. With respect to the worm transmission rate among immune individuals, since the role of acquired immunity in controlling

re-infection is not entirely known, we suppose that the infection among immune individuals is also influenced by the environment, in which case we have

$$\lambda' \equiv \beta\lambda = (\mu_h + \mu_w)\beta z T_2, \tag{26}$$

where β, with $0 \leqslant \beta < 1$, is the partial protection conferred by the immunity. Note that the risk of the infection among immune individuals depends on the fluctuation in the environment's parameters but situates always at a lower level in comparison with the risk among non-immune individuals ($\lambda' < \lambda$).

We can, now, write the mean worm burden m and the mean proportion of shedding snails z as functions of the dimensionless parameters T_1 and T_2 and the basic reproduction ratio R_0.

2.4.1. Model 1: Poisson model

The proportion of infected snails and the mean worm burden, given by Eqs. (20) and (7), respectively, can be rewritten in terms of the dimensionless transmission coefficients T_1 and T_2 using Eqs. (24) and (25). They are

$$\begin{cases} z_1 = z^*\left(1 - \frac{1}{R_0^1}\right), \\ m_1 = \frac{z^*(R_0^1 - 1)}{e^{-\mu_s'\tau} T_1}, \end{cases} \tag{27}$$

where

$$R_0^1 = e^{-\mu_s'\tau} T_1 T_2 \tag{28}$$

is the basic reproduction ratio related to the Poisson model.

Note that for $R_0^1 < 1$, the only biologically viable solution is $z = 0$ and $m_1 = 0$, in which situation we have the eradication of the disease; while the unique biologically viable endemic situation is attained if we have $R_0^1 > 1$. Therefore, at $R_0^1 = 1$ we have the change from trivial to non-trivial solution.

The results related to Macdonald's model [31] can be retrieved from Eqs. (27) and (28) letting $\tau = 0$. The maximum attainable fraction of shedding snails is $z^* = 1$ and the basic reproduction ratio is $R_0 = T_1 T_2$. Therefore, May's model diminished drastically the value of z^*, but at the expenses of decreasing in the same proportion the value of the basic reproduction ratio.

This pure random model states that schistosomiasis can be eradicated by improving the sanitary conditions and chemotherapy (diminishing the transmission coefficients T_1 and T_2) and/or by applying the molluscicides (increasing the mortality rate μ_s'). The parameters μ_s' and τ vary greatly with temperature, hence abiotic conditions act strongly upon the schistosomiasis transmission.

2.4.2. Model 2: simple water contact pattern model

The proportion of infected snails and the mean worm burden, given by Eqs. (20) and (11), respectively, can be rewritten in terms of the dimensionless transmission coefficients T_1 and T_2 using Eqs. (24) and (25). They are

$$\begin{cases} z_2 = z^*\left(1 - \frac{1}{R_0^2}\right), \\ m_2 = \frac{z^*(R_0^2 - 1)}{e^{-\mu_s'\tau} T_1}, \end{cases} \tag{29}$$

where

$$R_0^2 = \frac{\mu_h}{\mu_h + b} e^{-\mu'_s \tau} T_1 T_2 \tag{30}$$

is the basic reproduction ratio related to the water contact pattern model.

The basic reproduction ratio R_0^2 is limited and monotonically decreasing function with respect to b, which has the limiting values given by

$$R_0^2 = \begin{cases} R_0^1 & \text{for } b = 0, \\ 0 & \text{for } b \to \infty. \end{cases}$$

Besides the environment parameters T_1 and T_2, the basic reproduction ratio depends on the parameter b related to the interaction human-environment.

Note that the eradication condition can be achieved acting only on the avoidance parameter, since we can obtain a value for b such that $R_0^2 = 1$. The appearance of this new parameter to reach the eradication condition shows that we do not need so much efforts to eradicate schistosomiasis.

2.4.3. Model 3: simple acquired immunity model

The proportion of infected snails and the mean worm burden, given by Eqs. (20) and (16), respectively, can be rewritten in terms of the dimensionless transmission coefficients T_1 and T_2. In the acquired immunity model the transmission rates are related to the dimensionless transmission coefficients T_1 and T_2 according to Eqs. (24)–(26).

In this model, we have

$$\begin{cases} z_3 = \left(2\frac{M_1}{M_2} T_2\right)^{-1} \left\{ T_2 z^* \left(\frac{M_1}{M_2} - \frac{1}{M_2 R_0^3}\right) - 1 + \sqrt{\left[T_2 z^* \left(\frac{M_1}{M_2} - \frac{1}{M_2 R_0^3}\right) - 1\right]^2 + 4\frac{M_1 T_2 z^*}{M_2}\left(1 - \frac{1}{R_0^3}\right)} \right\}, \\ m_3 = \frac{M_2 T_2 z^*}{2(M_2 + T_2 z^*)} \left\{ T_2 z^* \left(\frac{M_1}{M_2} - \frac{1}{M_2 R_0^3}\right) - \left(\frac{2}{R_0^3} - 1\right) + \sqrt{\left[T_2 z^* \left(\frac{M_1}{M_2} - \frac{1}{M_2 R_0^3}\right) - \left(\frac{2}{R_0^3} - 1\right)\right]^2 + 4\frac{M_2 + T_2 z^*}{M_2 R_0^3}\left(1 - \frac{1}{R_0^3}\right)} \right\}, \end{cases} \tag{31}$$

where

$$\begin{cases} M_1 = 1 - (1 - \beta) e^{-\mu_h L}, \\ M_2 = \frac{\mu_h}{\mu_h + \mu_w}, \end{cases}$$

and

$$R_0^3 \equiv R_0^1 = e^{-\mu'_s \tau} T_1 T_2 \tag{32}$$

is the basic reproduction ratio related to the acquired immunity model.

When both λ and λ' are dependent on the environment, the classical result related to the directly transmitted infections is retrieved, that is, the immunity does not matter on the basic reproduction ratio. The reason behind it is the polluted water, which plays the main role in the transmission of schistosomiasis, once the human immune reactions avoid only partially new infection and do not eliminate the previously harboured worms. However, we can analyze, by introducing the vaccination effort in this model, the existence of the schistosomiasis eradication condition by vaccine (when available) [39].

3. Epidemiological findings

In this section we are concerned with the fitting of the age–prevalence curve of schistosomiasis with the aim of estimating the model's parameters. The first attempt we are aware of is due to Hairston [4] who used a modified catalytic model [40] to determine the force of infection to schistosomiasis by fitting the age-related prevalence curves from many distinct endemic regions. In some areas he obtained reasonable model fittings while in others the model fittings were not appropriately obtained, hence it was necessary to use different curves to fit the data from different age groups in the same region. Another attempt is due to Holford and Hardy [5] who fitted a stochastic model to the same set of data [20,21] used by Hairston [4]. Although a best fitting was obtained with the model that used four parameters, the descendent phase of the prevalence curve is explained as a reduction of the water contact pattern that increases with age. This is not entirely supported by experimental evidence [17,41]. The latter work compared the egg outputs by males and females and found essentially no difference, although the two groups have different water contact patterns.

3.1. Fitting the model

We present the maximum likelihood fitting [42] of the data, using the equations related to the prevalence curve, from two distinct highly endemic areas, namely, Touros district, Brazil [43], and the region of Misungwi, Tanzania [21]. In the first region, schistosomiasis is due only to *S. mansoni*, while in the second, it is due only to *S. haematobium.* The logarithm of likelihood, disregarding the constant term, is

$$l = \sum_{i=1}^{n} \{np_i \ln[P_j(a_i)] + nn_i \ln[1 - P_j(a_i)]\} \quad \text{for } j = 1, 2 \text{ or } 3, \tag{33}$$

where n is the number of age intervals, np_i and nn_i are the numbers of individuals with presence and absence of parasite eggs, respectively, in each age interval a_i, and the subscript j stands for one of the three models. The prevalence curve $P_j(a_i)$ is one of the functions given by Eqs. (6), (10) and (15), according to the model. This expression is maximized using the non-linear Levenberg–Marquardt method [44] (Appendix B).

The prevalence curves obtained from the models are fitted against field data. Tables 1 and 2 show the estimated model's parameters: the rates λ, μ_w, b and λ'; the elapsing time L and the logarithm of likelihood of the fitting l for the data from Touros and Misungwi, respectively.

The human mortality rate μ_h was obtained from actuarial data, and its value was found to be 0.015 years^{-1}. The sensitivity analysis of the model's parameters can be done using the values presented in these tables [45], which is left to a further work.

Figs. 1 and 2 show the age–prevalence curves fitted to epidemiological data from Touros and Misungwi areas.

The fitted parameters are those given in Tables 1 and 2. We observe that the models 2 and 3 improved substantially the fittings in comparison with the model 1, nevertheless the model 3 presented the best fitting. Note that in this paper we are comparing the simplest forms for the acquired immunity and age-structured contact pattern hypotheses.

Table 1
Parameters fitted against data ($n = 15$) from the region of Touros, Brazil, where 'df' stands for the degree of freedom

	Model 1	Model 2	Model 3
λ	0.160 ± 0.021	0.13 ± 0.40	0.120 ± 0.010
μ_w	0.217 ± 0.033	0.110 ± 0.024	0.090 ± 0.024
λ' or $b^{(*)}$	–	$0.017 \pm 0.004^{(*)}$	0.047 ± 0.012
L	–	–	8.07 ± 0.10
l	−1515.24	−1498.82	−1493.69
df	12	11	10

Table 2
Parameters fitted against data ($n = 39$) from the region of Misungwi, Tanzania, where 'df' stands for the degree of freedom

	Model 1	Model 2	Model 3
λ	0.355 ± 0.040	0.28 ± 0.46	0.221 ± 0.010
μ_w	0.333 ± 0.041	0.126 ± 0.015	0.079 ± 0.010
λ' or $b^{(*)}$	–	$0.027 \pm 0.003^{(*)}$	0.042 ± 0.005
L	–	–	8.96 ± 0.03
l	−2705.98	−2587.12	−2534.34
df	36	35	34

The improvement in the fittings can be seen applying the model selection criteria, specially the Schwarz criterion [46]. The criterion proposed by Schwarz is

$$\mathrm{BIC} = l - \frac{k}{2}\ln(n),$$

where l is the logarithm of the likelihood of the fitting, k is the number of model's parameters and n is the number of observations. The penalty associated with the number of estimated parameters in this criterion is stronger than in the Akaike criterion.

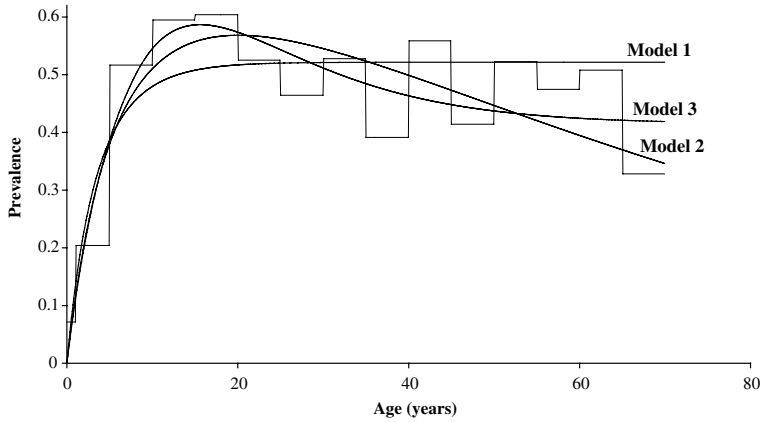

Fig. 1. Age–prevalence curves fitted to data from Touros, Brazil. The curves show the fittings of the models 1, 2 and 3.

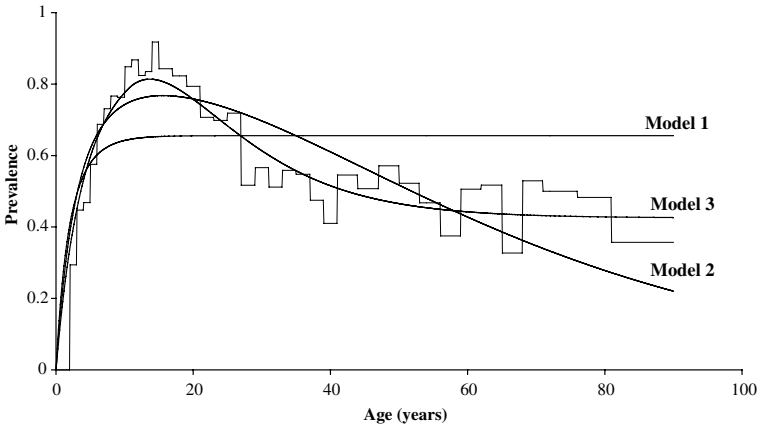

Fig. 2. Age–prevalence curves fitted to data from Misungwi, Tanzania. The curves show the fittings of the models 1, 2 and 3.

Table 3 shows the Schwarz criterion (Bayesian Information Criterion) values based on the logarithm of the likelihood of the fittings given in Tables 1 and 2.

We note the fittings getting better in the models 1, 2 and 3, in this order. The BIC difference (designed by 'bic') is high when comparing models 2 and 3 with model 1, but between models 2 and 3, the difference is low.

The hypotheses related to the acquired immunity and age-structured contact pattern can describe, in some extent, the ascending and descending phases of the characteristic age-dependent prevalence curve related to schistosomiasis. However, the prevalence alone is not a good epidemiological measure, for this reason the better understanding of the schistosomiasis transmission requires the knowledge about the intensity of the infection [47].

Table 3
The value of BIC using Schwarz criterion based on the penalization of the logarithms of likelihood of the fitting l of the three models for Touros, Brazil, and Misungwi, Tanzania

	Touros, Brazil			Misungwi, Tanzania		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
−BIC	1517.95	1502.88	1499.11	2709.64	2592.62	2541.67
k	2	3	4	2	3	4
n	15	15	15	39	39	39
bic_{21}	–	15.07 (0.99%)	–	–	117.0 (4.32%)	–
bic_{31}	–	–	18.84 (1.24%)	–	–	168.0 (6.20%)
bic_{32}	–	–	3.776 (0.25%)	–	–	50.95 (1.97%)

We calculated the difference between BICs, defined by $\text{bic}_{ij} = \text{BIC}_i - \text{BIC}_j$, and the corresponding relative value, given by $100 \times \text{bic}_{ij}/|\text{BIC}_i|$ (which is given between parenthesis), where the subscript i stands for the type of the model. k and n stand, respectively, for the number of model's parameters and the number of observations.

3.2. The mean worm burden and the dispersion

To give a more reliable analysis of the schistosomiasis transmission, we can now use the fitted parameters shown in Tables 1 and 2 to calculate the mean worm burden per person and the mean dispersion per person for the two regions.

The mean worm burden per person shows the intensity of the infection in the community. This value measures the degree of morbidity and the level of the parasite transmission in the community. The dispersion per person in a community shows how the parasite is distributed in the community: randomly distributed ($d = 1$, distributed like Poisson), distributed in an aggregate ($d > 1$, negative binomial distribution) or statistically over-dispersed ($d < 1$, binomial distribution) fashion. For instance, as the dispersion d becomes larger and larger the mean worm burden m is increasingly realized by having most people with zero worms and a few people with many worms [48]. This feature indicates that the individuals with heavy worm burden (in general, symptomatic) are easily found in the community, which is not true in relation to individuals with light worm burden. Conversely, as the dispersion d becomes smaller and smaller, we have the most people harbouring the same amount of worms, which makes easy the task of finding the infected individuals.

We use Eqs. (7) and (8); (11) and (12); and (16) and (17), respectively, for models 1, 2 and 3, to calculate the mean worm burden and the dispersion for Touros district, Brazil, and the region of Misungwi, Tanzania. These values are shown in Table 4.

Remember that in the region of Touros we have the transmission of *S. mansoni*, while in the region of Misungwi, we have *S. haematobium*.

Observe that the competing models (labelled 2 and 3) present quite same amounts of the mean worm burden, which are lower than the basic model (labelled 1). This implies that the hypotheses considering the acquired immunity and the age-structured contact pattern can avoid the hyper-infection. However, the dispersion is much more increased in the acquired immunity model than the age-structured contact pattern model (especially for the *S. haematobium* transmission in Tanzania). Therefore, the acquired immunity appears to act in such a manner that the distribution of the parasite among the individuals in the community [47] tends to the aggregated fashion. One of the effects of this aggregation is to difficult the controlling mechanisms, specially those based on the parasitological examination. This epidemiological procedure finds individuals harbouring moderate to heavy worms; for this reason the transmission can be maintained by the asymptomatic (presenting low worm parasite charge, hence evading the parasitological examination) individuals, which represent a large group of individuals.

Therefore, the acquired immunity modeling can explain the great difficult to control the schistosomiasis transmission. It is worth to mention that the paper by Barbour and Kafetzaki [49]

Table 4
The mean worm burden and the mean dispersion for Touros, Brazil, and Misungwi, Tanzania

	Touros, Brazil			Misungwi, Tanzania		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
m	0.689	0.506	0.593	1.020	0.712	0.795
d	1.023	1.151	1.603	1.023	1.368	6.713

have attempted to explain the dispersion of worms by invoking concomitant immunity and multiple entrances.

3.3. The basic reproduction ratio

The last epidemiological parameter to be considered to compare the competing models is the basic reproduction ratio. To calculate the basic reproduction ratio R_0, we need the estimated values of the following parameters.

The parameters related to the intermediate host are obtained from the literature. From data described by Sturrock, for *Biomphalaria glabrata* [50] and for *Bulinus (Physopsis) nasutus productus* [51] snails, we can estimate the snail transmission rate fitting these data using Eq. (20). Considering the values $\mu_s' = 10.8$ years^{-1}, $\mu_s'' = 21.6$ years^{-1} and $\tau = 0.083$ years, the estimated value is $a_s = 0.921$ years^{-1} [23]. Taking into account these values, the maximum attainable value for the proportion of shedding snails can be calculated using Eq. (21), resulting in $z^* = 0.25$. The steady-state value for z was arbitrarily set at 0.01.

The values for the dimensionless transmission coefficients T_1 and T_2, defined by Eqs. (22) and (23), are calculated using Eqs. (24) and (25) for the models 1 and 2. The parameters related to the snails are those given above, and the values for λ, μ_w and m are given in Tables 1, 2 and 4. With respect to the parameter T_2, observe that we must consider carefully Eq. (26), which relates T_2 with λ', for the model 3. The factor β in Eq. (26) provides a higher value for T_2 than that provided by Eq. (25). In this case, we neglect the second calculation and use the lower value for T_2, which corresponds to consider only Eq. (25).

The basic reproduction ratio R_0 is obtained for the models 1, 2 and 3 using, respectively, Eqs. (28), (30) and (32). Table 5 shows the calculated transmission coefficients T_1 and T_2, and the resulting basic reproduction ratio.

Observe that the age-structured contact pattern modeling practically unchanged the value of the basic reproduction ratio, while the acquired immunity modeling increased substantially this value, in comparison with the basic model.

The consideration of the acquired immunity in the schistosomiasis modeling shows that the eradicating efforts of schistosomiasis is highly increased (if we consider the value of R_0 as the measure of controlling effort), besides the aggregation of the parasites in the community. Both features facilitate the perpetuation of the worm by two manners: the small core of individuals harbouring high number of worms produces a great number of eggs (R_0 great), and the large group of individuals harbouring low number of parasites (characteristic of d great) presents high probability of evading controlling mechanisms (specially chemotherapy), which maintains the

Table 5
The basic reproduction ratio R_0 for Touros, Brazil, and Misungwi, Tanzania

	Touros, Brazil			Misungwi, Tanzania		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
T_1	0.0619	0.0842	0.0719	0.0418	0.0599	0.0537
T_2	68.907	106.84	114.12	102.03	200.95	235.09
R_0	1.7397	1.7395	3.3486	1.73986	1.73988	5.1475

prevalence at low level. Therefore, it seems that the immunity is a strong factor to stabilize the interaction parasite–human.

4. Discussion

We developed a semi-stochastic model to understand the transmission dynamics of schistosomiasis in highly endemic regions. The main point of this paper is to compare a model dealing with the role of human acquired immunity with a model taking into account the age-structured contact pattern with infested water. The introduction of the parasite mating probability [28] and/or the conservation of snail biomass density [52] in both models did not improve the results [23].

In the absence of immunity in the human host or the age-structured contact pattern, we must have hyper-infection to maintain the disease (model 1) due to low prevalence of shedding snails. In relation to the model 2, the hyper-infection can be avoided in some extent, while the worms are practically homogeneously distributed. In relation to the model 3, the hyper-infection is avoided because the acquired immunity protects the human host from further cercariaes invasions, and the worms harboured by individuals from this community are distributed in a aggregated fashion (Table 4), which explains the existence of a core of individuals who have a heavy worm charge while the population as a whole has a low worm burden. The latter consideration makes reasonable our approximation of assigning half to the mating function introduced by May [28].

With respect to the basic reproduction ratio, the age-structured contact pattern modeling and the basic model predict quite similar values, which is not true in relation to the acquired immunity modeling. Since the age-structured contact pattern cannot aggregate the parasite among the individuals in the community, the viable female descendants produced by the fertile female are not increased. On the other hand, the worm aggregation facilitates the production of female parasites due to the high worm burden among small proportion of infected individuals, which increases the probability of female parasite be mated. For this reason, when immunity consideration is included in the model to explain the robust transmission of schistosomiasis, we observe that very low worm burden per person is capable to maintain the disease in the community.

We discussed succinctly the controlling mechanisms corresponding to the epidemiological parameters T_1, T_2, b, μ_s', β and L. Now we discuss the massive drug treatment applied in a community, which diminishes the worm burden by increasing the worm mortality rate μ_w. We have two implementation of chemotherapy in the community, according to the model we consider.

The drug treatment based on the stool examination to perform the egg counting of schistosomiasis is a good clinical procedure aiming the controlling of schistosomiasis in highly prevalent regions. In these regions, due to the high intensity of infection, the epidemiological and chemotherapeutic studies based on parasitological examination using the Kato–Katz method are strongly recommended [53]. However, these procedures are not true for regions under massive chemotherapy [6] and regions where the schistosomiasis transmission is very low [54].

In general, when massive drug treatment based on the stool examination is applied, it is observed a drastic diminishing in the prevalence, but it remains in a low value [6]. This is due to the sensitivity of the Kato–Katz method [55], hence the infected individuals presenting low worm

burden are not detected by Kato–Katz method and maintain schistosomiasis transmission. The design of the controlling mechanisms relying upon the models 1 and 2 depend uniquely on the stool examination to detect individuals harbouring parasite.

However, the model 3 gives another approach to control schistosomiasis. Instead of relying upon the chemotherapy of individuals based only on the stool examination, the serological screening can be applied to the entire population to determine the individuals who will receive the drug treatment. This approach is fundamental in regions of low prevalence or regions where the high prevalence was diminished by improving the sanitation conditions and by drug treatment of individuals presenting eggs in their faeces (or urine). If we assume that the levels of IgM and IgG are related to, respectively, acute and chronic infections, then the administration of drugs must be done according to the immune status of the individuals. Based on the level of IgM and IgG concentrations, we can divide the entire population as: susceptible (absence of IgM and IgG), non-immune but infected (presence of IgM), immune with parasite (presence of high concentrations of IgM and IgG) and immune without parasite (presence of low concentration of IgG). A suitable chemotherapy in a low prevalence community must be, then, applied to the individuals classified in the latter three immune status [56], in order to reach all possible infected individuals and to achieve the eradication condition. This chemotherapy is advisable if the drugs do not present collateral effects, since some immune individuals without parasite can be included in the treatment.

5. Conclusion

We summarize our findings in four points:

(1) The introduction of both the acquired immunity via the elapsing time L and the age-structured contact pattern in the schistosomiasis modeling retrieved the field data with good fittings.
(2) Even the model developed by Holford and Hardy [5] comprising the age-structured frequency of contacts with infested water fits very well the prevalence curve, it fails to explain the aggregation of worms and the strong stability of the disease facing external controlling mechanisms. In fact, it predicts quite the same features of the basic model with respect to the epidemiological parameters (mean worm burden, dispersion and basic reproduction ratio) [57].
(3) The model considering the acquired immunity, however, explains in some extent the aggregation of worms (high values for the dispersion) and the facility to maintain the disease (high values for the basic reproduction ratio), which show the difficult in controlling schistosomiasis. Also, very low worm burden per person can maintain the disease in a community.
(4) The chemotherapy controlling of schistosomiasis taking into account the models 1 and 2 must be based on the clinical and parasitological examinations, while the immune reaction taken into account in the model 3 permits the use of seroprevalence screening specially in regions of low prevalence, besides those already cited. Moreover, the vaccine could be considered in the controlling mechanisms in association with the improvement of the sanitation and/or in association with the drug treatment.

Acknowledgements

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Appendix A. Some mathematical results

The basic mathematical details were presented in [58], for this reason we present only some mathematical results in this paper.

Let $w(t,a,A)$ be a random variable that describes the distribution of the number of adult worms k among the fraction of the human host population with age between a and $a+\mathrm{d}a$ that got the first infection at age between A and $A+\mathrm{d}a$, during the instant of time t and $t+\mathrm{d}t$. From the consideration that the human host has deterministic treatment with respect to age, the total number of worms over all age intervals irrespective of the age of the first infection $W(a)$ is given by

$$\begin{cases} W(t,a) = \int_{a-L}^{a} w(t,a,A)\,\mathrm{d}A, \\ W'(t,a) = \int_{0}^{a-L} w(t,a,A)\,\mathrm{d}A, \end{cases} \tag{A.1}$$

where the prime stands for human hosts who have already built up the immune reaction. These integrals represent the count of worms harboured by individuals with age between a and $a+\mathrm{d}a$. The limits of the integrations are related to the attainment of the partial immunity status, that is, if the age a is such that it is lower than $A+L$, then the individual is still developing the immunity (with respect to the infective process, this individual behaves as the susceptible); otherwise, the individual is immune.

Assuming the stochastic process of the above random variables as a Markov chain, we define the transition matrix with its elements given by

$$\Pi(t+\mathrm{d}t, a+\mathrm{d}t, A, k+1; t, a, A, k) \equiv Pr\{w(t+\mathrm{d}t, a+\mathrm{d}t, A) = k+1 | w(t,a,A) = k\}, \tag{A.2}$$

which is the probability of an individual with age between a and $a+\mathrm{d}t$ being infected by one worm, given that the individual has k worms. Note that we have $\mathrm{d}t = \mathrm{d}a$.

We define the following stochastic and deterministic transitions between t and $t+\mathrm{d}t$ and a and $a+\mathrm{d}t$. The stochastic transitions are related to the worm migration and death, while the deterministic transition is related to the age-distribution of the individuals in a community.

1. The first infection occurs at age A among completely susceptible individuals. In this case we have

$$\Pi(t+\mathrm{d}t, a+\mathrm{d}t, A, 1; t, a, A, 0) = \lambda(t,a)\mathrm{d}t + \mathrm{o}(\mathrm{d}t), \tag{A.3}$$

   where $\lambda(t,a)$ is the transmission rate of parasites related to the non-immune human hosts and $\mathrm{o}(\mathrm{d}t)$ are terms of superior order.
2. The infections can occur at age $a \leqslant A+L$ (and $a > A$) among non-immune individuals with k parasites. In this case we have

$$\Pi(t+\mathrm{d}t, a+\mathrm{d}t, A, k+1; t, a, A, k) = \lambda(t,a)\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t), \tag{A.4}$$

with $k = 0, 1, 2, \ldots$. This transition is independent of the worm burden because we are treating the infective event as migration.

3. The infections can occur at age $a > A + L$ among partially immune individuals with k parasites. In this case we have

$$\Pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k + 1; t, a, A, k) = \lambda'(t, a)\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t), \tag{A.5}$$

where $\lambda'(t, a)$ is the transmission rate of schistosome for partially immune human hosts.

4. A parasite dies with a transition given by

$$\Pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k - 1; t, a, A, k) = \mu_{\mathrm{w}}(t, a)k\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t), \tag{A.6}$$

where $\mu_{\mathrm{w}}(t, a)$ is the per-capita mortality rate of the worms harboured by the human host (both immune and non-immune individuals).

5. The events related to the non-occurrence of the infection are given by the transitions

$$\Pi^0(t + \mathrm{d}t, a + \mathrm{d}t, A, 0; t, a, A, 0) = 1 - \lambda(t, a)\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t) \tag{A.7}$$

for the individuals at age a that never had contact with parasite, where the superscript 0 stands for the individuals who never got the infection, therefore have zero worms,

$$\Pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k; t, a, A, k) = 1 - [\lambda(t, a) + \mu_{\mathrm{w}}(t, a)k]\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t) \tag{A.8}$$

for the non-immune individuals comprised on the age interval $A < a \leqslant A + L$, and

$$\Pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k; t, a, A, k) = 1 - [\lambda'(t, a) + \mu_{\mathrm{w}}(t, a)k]\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t) \tag{A.9}$$

for the partially immune individuals comprised on the age interval $a > A + L$.

6. The human host is treated deterministically, with the age-distribution being given by

$$\pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k) - \pi(t, a, A, k) = -\mu_{\mathrm{h}}(t, a)\pi(t, a, A, k)\,\mathrm{d}t + \mathrm{o}(\mathrm{d}t), \tag{A.10}$$

where $\mu_{\mathrm{h}}(t, a)$ is the per-capita mortality rate of the human host and $\pi(t, a, A, k)$ is the age-distribution of individuals with age a, who got the first infection at age A and have k worms at time t.

Using the Chapman–Kolmogorov equation,

$$\pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k) = \sum_{j=0}^{\infty} \Pi(t + \mathrm{d}t, a + \mathrm{d}t, A, k; t, a, A, j)\pi(t, a, A, j) \tag{A.11}$$

and the above transitions, we obtain

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\pi(t, a, A, k) &= \lambda(t, a)\pi(t, a, A, k - 1) + (k + 1)\mu_{\mathrm{w}}(t, a)\pi(t, a, A, k + 1) \\ &\quad - [\lambda(t, a) + k\mu_{\mathrm{w}}(t, a) + \mu_{\mathrm{h}}(t, a)]\pi(t, a, A, k),\end{aligned} \tag{A.12}$$

which describes the distribution of worms among non-immune individuals comprised on the age interval $A < a \leqslant A + L$, and

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\pi'(t, a, A, k) &= \lambda'(t, a)\pi'(t, a, A, k - 1) + (k + 1)\mu_{\mathrm{w}}(t, a)\pi'(t, a, A, k + 1) \\ &\quad - [\lambda'(t, a) + k\mu_{\mathrm{w}}(t, a) + \mu_{\mathrm{h}}(t, a)]\pi'(t, a, A, k),\end{aligned} \tag{A.13}$$

which describes the distribution of worms among partially immune individuals comprised on the age interval $a > A + L$.

To determine the age-distribution of individuals who never got the infection, $S(t,a)$, we use the transitions given by Eqs. (A.3), (A.7) and (A.10) obtaining

$$\frac{\mathrm{d}}{\mathrm{d}t}S(t,a) = -[\lambda(t,a) + \mu_{\mathrm{h}}(t,a)]S(t,a), \tag{A.14}$$

where $S(t,a) = \int_0^\infty \pi^0(t,a,A,0)\,\mathrm{d}a$.

The boundary conditions for Eqs. (A.14), (A.12) and (A.13) are, respectively,

$$S(t,0) = S_0(t), \tag{A.15}$$

which is the new-born rate at time t,

$$\begin{cases} \pi(t,A,A,1) = \lambda(t,A)S(t,A), \\ \pi(t,A,A,k) = 0 \quad \text{for } k = 1,2,\ldots \end{cases} \tag{A.16}$$

and

$$\pi'(t,A+L,A,k) = \pi(t,A+L,A,k) \quad \text{for } k = 0,1,2,\ldots, \tag{A.17}$$

which stand for the continuity (hence, the conservation) of the age-distribution of individuals during the transition from non-immune to immune status.

The above equations can be re-written using the probability generating functions given by

$$f(t,a,A,x) = \sum_{k=0}^{\infty} \pi(t,a,A,k)x^k \tag{A.18}$$

and

$$f'(t,a,A,x) = \sum_{k=0}^{\infty} \pi'(t,a,A,k)x^k, \tag{A.19}$$

which are related to the non-immune and immune individuals, respectively. Note that we have the additional probability $\pi^0(t,a,A,0)$ related to the individuals who never had contact with parasite. Eqs. (A.14), (A.12) and (A.13) are, then, written as

$$\begin{cases} \frac{\partial}{\partial t}S(t,a) + \frac{\partial}{\partial a}S(t,a) &= -[\lambda(t,a) + \mu_{\mathrm{h}}(t,a)]S(t,a) \\ \frac{\partial}{\partial t}f(t,a,A,x) + \frac{\partial}{\partial a}f(t,a,A,x) & \\ \quad +\mu_{\mathrm{w}}(t,a)(x-1)\frac{\partial}{\partial x}f(t,a,A,x) &= [\lambda(t,a)(x-1) - \mu_{\mathrm{h}}(t,a)]f(t,a,A,x) \\ & \quad \text{for } A < a \leqslant A+L \\ \frac{\partial}{\partial t}f'(t,a,A,x) + \frac{\partial}{\partial a}f'(t,a,A,x) & \\ \quad +\mu_{\mathrm{w}}(t,a)(x-1)\frac{\partial}{\partial x}f'(t,a,A,x) &= [\lambda'(t,a)(x-1) - \mu_{\mathrm{h}}(t,a)]f'(t,a,A,x) \\ & \quad \text{for } a > A+L \end{cases} \tag{A.20}$$

and the boundary conditions given by Eqs. (A.15), (A.16) and (A.17) become

$$\begin{cases} S(t,0)S_0(t) = S_0(t), \\ f(t,A,A,x_0) = \lambda(t,A)S(t,A)x_0, \\ f'(t,A+L,A,x_0') = f(t,A+L,A,x_0'). \end{cases} \tag{A.21}$$

This system of equations is related to the distribution of the worms among a fraction of age-distributed individuals who got the first infection at age A.

From the solution of the system of Eq. (A.20) we can obtain the distributions of the worms according to the age-distribution of the immune and non-immune individuals, irrespective of the age of the first infection A, through the definition (A.1). They are

$$\begin{cases} F(t,a,x) = \int_{a-L}^{a} f(t,a,A,x)\,\mathrm{d}A & \text{for } a \leqslant A+L, \\ F'(t,a,x) = \int_{0}^{a-L} f'(t,a,A,x)\,\mathrm{d}A & \text{for } a > A+L, \end{cases} \tag{A.22}$$

which are used to derive the prevalence, the mean worm burden and dispersion of the worms in the community.

Let us consider the steady state. For this reason we did not provide initial conditions to the system of Eq. (A.20). Dropping out the time dependence (and setting the time differentiation zero), the second and the third equations of the system (A.20) led to the solutions $f(a,A,x)$ and $f'(a,A,x)$ in equilibrium, given by

$$\begin{cases} f(a,A,x) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}\lambda(A)\,\mathrm{e}^{-\Lambda(A)}[1+(x-1)\,\mathrm{e}^{-\mu_{\mathrm{w}}(a-A)}]\exp\big((x-1)\mathrm{e}^{-\mu_{\mathrm{w}}(a-A)}\Psi(a,A)\big), \\ f'(a,A,x) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}\lambda(A)\,\mathrm{e}^{-\Lambda(A)}[1+(x-1)\,\mathrm{e}^{-\mu_{\mathrm{w}}(a-A)}]\exp\big((x-1)\mathrm{e}^{-\mu_{\mathrm{w}}(a-A)}\Psi(a_0+L,A)\big) \\ \qquad\qquad \times \exp\Big((x-1)\mathrm{e}^{-\mu_{\mathrm{w}}(a-A-L)}\Psi'(a,A)\Big), \end{cases}$$

where S_0 is the new-born rate and the functions $\Lambda(x)$ and $\Psi(x,y)$ are given by Eq. (4). These solutions can be integrated over all age A, according to Eq. (A.22), to yield $F(a,x)$ and $F'(a,x)$ resulting Eqs. (2) and (3) of the main text.

The semi-stochastic feature of the functions (A.22) are better understood when we consider $x=1$ in Eqs. (2) and (3). In this situation we are not concerned with the probabilistic distribution of the worms in the human host, and the human host is distributed according to

$$\begin{cases} F(a,1) = \begin{cases} S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}(1-\mathrm{e}^{-\lambda a}), & a \leqslant L, \\ S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}[\mathrm{e}^{-\lambda(a-L)}-\mathrm{e}^{-\lambda a}], & a > L, \end{cases} \\ F'(a,1) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}[1-\mathrm{e}^{-\lambda(a-L)}], \quad a > L. \end{cases} \tag{A.23}$$

The functions $F(a,1)$ and $F'(a,1)$ describe the age-distribution of non-immune and immune individuals, respectively, that have had the contact with the worms. Finally, the age-distribution of individuals that never have had contact with worms is given by

$$S(a) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}\mathrm{e}^{-\lambda a}. \tag{A.24}$$

Therefore, the age-distribution of the human population can be obtained disregarding the worm contact experience of the community, yielding

$$N(a) = S_0\,\mathrm{e}^{-\mu_{\mathrm{h}}a}, \tag{A.25}$$

which comes summing up the two equations of (A.23) and Eq. (A.24).

From the above functions we can derive the following variables. The age–prevalence curve is given by the relation

$$P(a) = 1 - \frac{F_0(a) + F(a,0) + F'(a,0)}{S(a)}, \tag{A.26}$$

the age-mean worm burden per person is

$$m(a) = \frac{\frac{\partial}{\partial x}F(a,x)\big|_{x=1} + \frac{\partial}{\partial x}F'(a,x)\big|_{x=1}}{S(a)} \tag{A.27}$$

and the age–dispersion (coefficient of variation) of worms per person is given by

$$d(a) = 1 - m(a) + \frac{\frac{\partial^2}{\partial x^2}F(a,x)\Big|_{x=1} + \frac{\partial^2}{\partial x^2}F'(a,x)\Big|_{x=1}}{\frac{S(a)}{m(a)}}, \tag{A.28}$$

where the numerator is the second moment.

From the last two variables $m(a)$ and $d(a)$ we can calculate the corresponding average value per person, which is given by

$$\xi = \frac{\int_0^\infty \xi(a)S(a)\,\mathrm{d}a}{\int_0^\infty S(a)\,\mathrm{d}a}, \tag{A.29}$$

where $\xi(a)$ is one of the variables $m(a)$ and $d(a)$.

Appendix B. Likelihood estimation

The logarithm of likelihood function (33), disregarding the constant term, is estimated by likelihood estimation. To perform this estimation, the initial guess must be provided by the least square method. Let p_i be the observed value. Then the sum of squares approximate the χ^2 value, given by

$$\chi^2(\mathbf{\Omega}_j) = \sum_{i=1}^{n}[P_j(a_i,\mathbf{\Omega}_j) - p_i]^2 \quad \text{for } j = 1,2 \text{ or } 3, \tag{B.1}$$

where $P_j(a_i,\mathbf{\Omega}_j)$ is one of the functions given by Eqs. (6), (10) and (15), with $\mathbf{\Omega}_1 = [\lambda\ \mu_w]^T$, $\mathbf{\Omega}_2 = [\lambda\ \mu_w\ b]^T$ and $\mathbf{\Omega}_3 = [\lambda\ \mu_w\ \lambda'\ L]^T$ being the corresponding spaces of model's parameters to be fitted, and n is the number of age intervals considered. The superscript T stands for the transposition of matrix.

The chi-square (B.1) minimizes, for each j, at

$$\mathbf{y}(\mathbf{\Omega}_j) = \frac{1}{2}\frac{\partial}{\partial\mathbf{\Omega}_j}\chi^2(\mathbf{\Omega}_j) = \sum_{i=1}^{n}[P_j(a_i,\mathbf{\Omega}_j) - p_i]\frac{\partial}{\partial\mathbf{\Omega}_j}P_j(a_i,\mathbf{\Omega}_j) = \mathbf{0}, \tag{B.2}$$

because the second derivative, which is the standard deviation,

$$\boldsymbol{\sigma}^{-2}(\mathbf{\Omega}_j) = \frac{1}{2}\frac{\partial^2}{\partial\mathbf{\Omega}_j^2}\chi^2(\mathbf{\Omega}_j) \sim \sum_{i=1}^{n}\left[\frac{\partial}{\partial\mathbf{\Omega}_j}P_j(a_i,\mathbf{\Omega}_j)\right]^2 \tag{B.3}$$

neglecting the second derivatives with respect to the model's parameters by setting $\sum_{i=1}^{n}[\frac{\partial}{\partial\mathbf{\Omega}_j}P_j(a_i,\mathbf{\Omega}_j)]^2 \gg \sum_{i=1}^{n}[P_j(a_i,\mathbf{\Omega}_j) - p_i]\frac{\partial^2}{\partial\mathbf{\Omega}_j^2}P_j(a_i,\mathbf{\Omega}_j)$, has a positive value.

The estimator that obeys (B.2), $\widehat{\mathbf{\Omega}}_j$, is used as the initial guess in the maximum likelihood estimation method with the logarithm of the likelihood function given by (33). This expression maximizes, for each j, at

$$\mathbf{y}(\mathbf{\Omega}_j) = \frac{\partial}{\partial \mathbf{\Omega}_j} l(\mathbf{\Omega}_j) = \sum_{i=1}^{n} \left[\frac{np_i}{P_j(a_i, \mathbf{\Omega}_j)} - \frac{nn_i}{1 - P_j(a_i, \mathbf{\Omega}_j)} \right] \frac{\partial}{\partial \mathbf{\Omega}_j} P_j(a_i, \mathbf{\Omega}_j) = \mathbf{0}, \tag{B.4}$$

because the second derivative, which is the standard deviation,

$$\boldsymbol{\sigma}^{-2}(\mathbf{\Omega}_j) = -\frac{\partial^2}{\partial \mathbf{\Omega}_j^2} l(\mathbf{\Omega}_j) \sim \sum_{i=1}^{n} \left\{ \frac{np_i}{[P_j(a_i, \mathbf{\Omega}_j)]^2} + \frac{nn_i}{[1 - P_j(a_i, \mathbf{\Omega}_j)]^2} \right\} \left[\frac{\partial}{\partial \mathbf{\Omega}_j} P_j(a_i, \mathbf{\Omega}_j) \right]^2, \tag{B.5}$$

disregarding, again, the second derivatives with respect to the model's parameters, has a negative value. The estimator that obeys (B.4), $\widehat{\mathbf{\Omega}}_j$, is the value searched.

Both the least square and likelihood estimations of the model's parameters are non-linear fitting method. Then we applied the Levenberg–Marquardt method, with the new set of values of the parameters in each iterations are being given by

$$\boldsymbol{\sigma}_{\mathrm{LM}}^{-2}(\mathbf{\Omega}_j) = \begin{cases} \boldsymbol{\sigma}^{-2}(\mathbf{\Omega}_j)(1+\varepsilon) & \text{on the diagonal,} \\ \boldsymbol{\sigma}^{-2}(\mathbf{\Omega}_j) & \text{off the diagonal,} \end{cases} \tag{B.6}$$

where ε is an auxiliary parameter used in the Levenberg–Marquardt method [44]. The parameter L is dependent on θ function (Heaviside), which has the derivative

$$\frac{\partial}{\partial L} \theta(L - t) = \delta(L - t), \tag{B.7}$$

where $\delta(t)$ is the Dirac delta function.

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