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# A MATHEMATICAL MODEL OF THE DYNAMICS OF SCHISTOSOMIASIS

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# نموذج رياضي لديناميكية البلهارسيا

يحيى بدران - قسم الإحصاء - كلية العلوم - جامعة الكويت - الكويت
هاني شريف - قسم الرياضيات - كلية العلوم - جامعة قطر - قطر

في هذا العمل يقوم المؤلفان بتكوين نموذج رياضي لديناميكية طفيل هلمنتي رئيسي من طفيليات الإنسان. النموذج هو نظام من المعادلات الغير خطية المتداخله . تجارب عددية على النموذج كشفت الإتزان الفائق لديناميكية البلهارسيا. حالة الثبات تحدث دائماً خلال ١٠ - ١٥ عاماً من بدء العدوى. حل عددي للنموذج يؤيد المشاهدة كثيرة الذكر وكثيرة النقاش التي تقول "الشكل المعتاد لمنحنى شدة العدوى مع العمر هو نتيجة التغير في طرق التعامل مع المياه بين مجموعات الأعمار ومناعة للعدوى مكتسبة ببطئ" . كذلك يبين أن تقعر علاقة العمر - الشدة يمكن أن يكون نتيجة التغير في طرق التعامل مع المياه بين مجموعات الأعمار فقط . النموذج يمكن أن يستعمل للإجابة على أسئلة من نوع «ماذا لو» عن ديناميكية البلهارسيا وخاصة مايتعلق ببرامج مكافحة المرض .

## ABSTRACT

In this work the authors develop a mathematical model for the dynamics of a major helminth parasite of man, schistosomiasis. The model is a system of coupled non-linear equations. Numerical experimentations with the model reveal the remarkable stability of the dynamics of schistosomiasis. The steady state is invariably reached within 10-15 years of the start of the infection. A numerical solution of the model supports the often-stated and often-debated observation that "the usual shape of the curve of the intensity of infection by age is produced through variability of water-contact behaviour among age groups and a slowly-acquired immunity to re-infection." It also indicates that convexity of the age-intensity profile can be due to variability of water-contact activities among age groups alone. The model can be used to answer questions of the "what if" variety about the dynamics of schistosomiasis especially as they relate to proposed schemes for the control of the disease.

## INTRODUCTION

Parasitism in man and animals saps the energy and endeavour of millions in the world and directly affects agricultural production by lowering productivity of food animals and the energy input to draft animals (Soulsby [30]). The major helminth infections of man are among the most prevalent of all human infectious diseases. Most parasitized people are miniature ecosystems of multiple infections which may interact (Larouze [22]; Stephenson [31]).

Schistosomiasis is a widespread parasitic infection of man in tropical and subtropical areas. Over 200 million persons may be infected worldwide and more than 500 million people are at risk. It is endemic in more than 73

countries and the infection of entire communities is common (Iarotski & Davis [17]).

Schistosome worms were discovered in 1852 by the German pathologist Theodore Bilharz while performing an autopsy in Cairo, Egypt (Jordan [18]). Schistosomiasis is caused by species of the genus schistosoma of flatworms (Brown & Neva [8]). The adult worms inhabit the blood vessels; hence the worms are also known as blood flukes. Three major species of schistosoma infect humans and at least nine other species infect domestic animals. The major human schistosomes are Schistosoma mansoni (S.m.), Schistosoma haematobium (S.h.), and Schistosoma japonicum (S.j.). S.h. inhabit the veins around the urinary bladder whereas S.m. and S.j. inhabit the intestinal veins. S.m. is the most common schistosome species infecting humans. It is widespread in Africa, the Middle East, South America, and the Caribbean Islands. Infection with S.h. occurs in extensive areas of Africa and in the Middle East. In Egypt, urinary schistosomiasis is considered the most common cause of malignancy of the bladder in the male agricultural workers. S.j. is prevalent in China, Taiwan, the Philippine Islands, and Indonesia. S.j. infects not only man but a wide range of animals as well. (Braunwald [7]).

The distribution of schistosomiasis is greatly affected by the creation of irrigation systems, man-made lakes, and other types of water development projects required for food production and generation of hydroelectric power. Such projects and the resultant population movements have exacerbated the transmission of schistosomiasis in some endemic areas. This is particularly true of schistosomiasis in Africa and South America where developments for the production of hydro-electricity and irrigation are proceeding too rapidly for the public health authorities to be able to cope. The Aswan High Dam in Egypt and the Volta Dam in Ghana are examples of major economic developments resulting in the spread of schistosomiasis. The difficulties in preventing the spread of the disease in irrigated areas is well illustrated by the Gezira scheme in the Sudan. Here, in what was formerly part of an arid Sahara, more than 2,000,000 acres are now under irrigation from a single water source (Amin [2]). With schistosomiasis, the dilemma is that in the endemic areas any increase in the economic development of the community is likely to lead to an increase in the prevalence of the disease.

The control of schistosomiasis depends essentially on breaking the cycle of transmission between the definite and intermediate hosts. While this can be achieved by destruction of snails or modification of the environment to reduce human water-contact (Chandiwana, Taylor & Clarke [11]; Jordan [18]); (Kvasvig & Schutte [21]), these schemes are often too expensive to be implemented by developing countries where schistosomiasis is endemic. With the introduction of safe and effective drugs for the treatment of schistosomiasis, the treatment of heavily infected populations in endemic areas has been suggested as a possible approach to the control of schistosomiasis. The aim of such treatment is to substantially reduce the number of eggs excreted into the environment thereby reducing the probability of snail infection.

The ideal method of preventing this disease is to keep people away from snail-bearing water. But who can prevent children from swimming and washing in the only available water in countries where the midday temperature is usually over 90
There is very little hope of eliminating schistosomiasis from the world without drastic changes in human water-contact behaviour.

One of the first works to deal with quantitative aspects of schistosome populations was done by Hairston [15]). He tried to predict the number of snails expected to become infected as well as the number of mammalian infections on the basis of simple, but hard to estimate, probabilities. Mcdonald [23] explored the significance of heterosexual mating in the dynamics of infection using some simple probabilistic models in a computer simulation and pointed the way to the development of a model. Motivated by the work of Macdonald [23], Nasel & Hirsch [26] constructed the first dynamic model to take into consideration the interaction between the snail and the human populations. Unfortunately, their model is based upon unrealistically simplifying assumptions. They were mainly interested in proving the existence and uniqueness of a tractable set of equations. Anderson & May [4] tried to describe the temporal dynamics of human helminth populations in terms of one variable, the mean adult worm abundance per host.

The majority of the models that appeared in the literature describe either the human or snail half of the schistosome cycle, never both. To date no mathematical model of the disease has come close to representing faithfully most of what is known about its natural history (Nasel [24]-[25]; Rosenfield, Smith, and Wolman [28]; Barbour [6]). For example, the level of infection in snails required by these models to sustain transmission usually exceeds snail infection rates from field data and these models predict a uniform increase in prevalence and intensity of infection with age, but survey results consistently display a peak in the teenage years - which may be accounted for by either an immune effect or reduced exposure in older ages (Jordan & Webbe [19]). The present work aims to develop a comprehensive model which can be used as a "what if machine." Our interest in modeling is not in mere mathematical refinements but in the potentialities for improved practical policy (Bailey [5]); Dietz, Molineaux & Thomas [13]).

In this introduction we outlined the problem and stated the aim of our work. The second section presents background information. The model is constructed in the third section. Section four presents a numerical example where the output of the model is found to support the often-stated observation that the "usual shape of the curve of the intensity of infection by age is produced through variability of water-contact behaviour among age groups and a slowly-acquired resistance to re-infection." Finally, section five presents a summary and conclusions.

## BACKGROUND

There is extensive literature on almost every aspect of schistosomiasis. We found Jordan [18], Jordan & Webbe [19], and Soulsby [30], to be particularly helpful general sources about the epidemiology, treatment, control, and immunology and schistosomiasis. In this section we present an overview of the necessary information to be captured by our model.

The schistosome species all share the same basic life cycle, but differ from each other in a number of important ways presenting different problems from the point of view of control. The life cycle consists of an obligatory alternation of sexually produced eggs and asexually produced cercariae. Humans become infected with schistosomiasis after contact with fresh water containing the infective stage of the parasite, the "cercaria." Cercaria attach to and penetrate the unbroken skin with the help of secreted enzymes as the surface film of water drains off. In the skin they transform into "schistosomules" or developing schistosomes. If ingested with water, the cercariae penetrate the mucous membranes of the mouth and throat (Brown & Neva [8]). The very young schistosomules (2-3 days after skin penetration) are transported through the blood to the right heart and lungs, taking 4 to 7 days. They then travel in the systemic circulation to the portal vein. Here the blood flukes feed and grow rapidly, and at about 3 weeks after skin exposure the maturing male and female schistosomes pair and migrate to the venules of the intestines, bladder, or ureters, depending on the species of schistosomes, and begin to deposit eggs. The adult worms reside in pairs, the female lying in the gynaecophoric canal of the male, and migrate in the blood vessels without eliciting a local inflammatory reaction (Braunwald [7]). Adult worms do not multiply in humans and, depending upon the species of the worm, from 300-3500 eggs are passed daily into the venules. A larval form, the miracidium, develops within the egg and its lytic enzymes along with the contraction of the venule rupture the wall of the venule, liberating the egg into the tissues of the intestine or urinary bladder. Once released, eggs are either retained in the tissues at the site of deposition, swept back (mostly to the liver in the case of intestinal schistosomes), or extruded into the lumen of the intestines, bladder, or ureters and are evacuated in the feces or the urine On contact with fresh water the miracidia hatch from the eggs. This free-swimming ciliated stage "seeks" the proper intermediate snail host and burrows into the soft tissues of the snail within 24 hours or dies. After 1-2 months, depending on the species of parasite, the miracidium develops into a primary sporocyst and then, by a process of repeated asexual multiplication within the snail, thousands of a second larval form, cercariae, are produced. All cercariae resulting from a single miracidium are of the same sex. When mature, the cercariae are shed periodically by the snail throughout the lifetime of its infection which coincides, more or less, with the lifetime of the snail. Thousands of cercariae can be released daily from each infected snail. They then enter a free-swimming stage designed for the invasion of the definitive host. Cercariae are most infectious immediately after shedding and are not viable 48 hours after being shed (Braunwald [7]). On coming into contact with a human, a cercaria attaches itself to the skin and quite rapidly penetrates it to become a schistosomule and begins the cycle all over again. Figs. 1 and 2 summarize the above information.

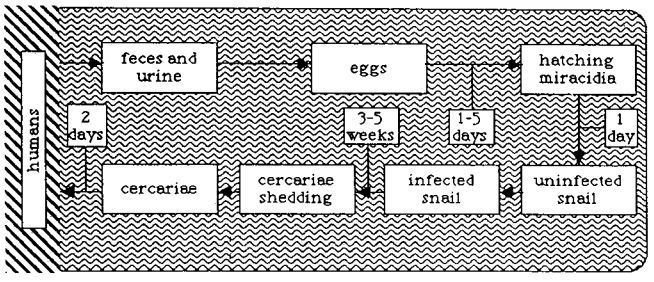


Fig. 1: Life cycle of *schistosomiasis* in the intermediate host

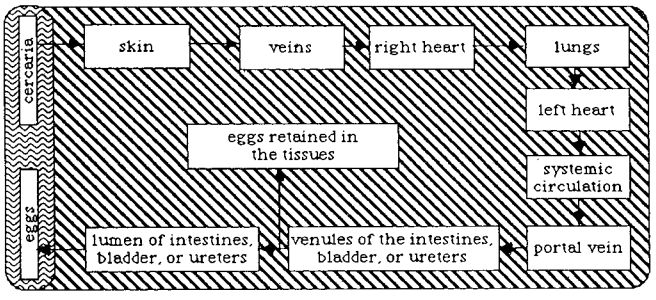


Fig. 2: Life cycle of *schistosomiasis* in the definitive host

Our environment contains a large variety of infectious agents (viruses, bacteria, fungi and parasites) many of which can cause pathological damage and, if they multiply unchecked eventually kill their host. It is evident that the great majority of infections in normal individuals are of limited duration and leave very little permanent damage. This is due to the individual's immune system which combats infectious agents (Roitt, Brostoff, and Male [27]). Parasitic infections are generally chronic. Among the consequences of chronic infection are the presence of circulating antigens, persistent antigenic stimulation, immunosuppression, and immunopathological effects (e.g. granulomata formation around schistosome eggs in the liver leading to its fibrosis). The severity of disease depends on the number of eggs deposited in the tissues and this depends on the duration of infection and on the number of adult worms. It is the inflammatory and fibrotic response to these eggs which is responsible for most of the morbidity and mortality associated with schistosomiasis (Hiatt 1976; Khalil [20]; Smith, Warren, and Mahmoud [29]).

In schistosomiasis, each worm can mature into an adult worm, and adult worms of early infection may continue to survive for many years and, despite the focal nature of transmission in many areas, the usual observation is that, in an endemic area, there is a slow rise in the mean intensity of egg output during the first 10 to 20 years of life, and this is then followed by a slow decline (Abdel-Wahab [1]; Taylor & Makura [32]). Survey results consistently display

a peak in the teenage years. Figures 3, 4 and 5 show, respectively, the patterns of intensity by age found in an Egyptian village in the Nile delta, in a Kenyan community and in settlements in St. Lucia (Abdel-Wahab [1]; Jordan [18]; Smith, Warren, and Mahmoud [29]).

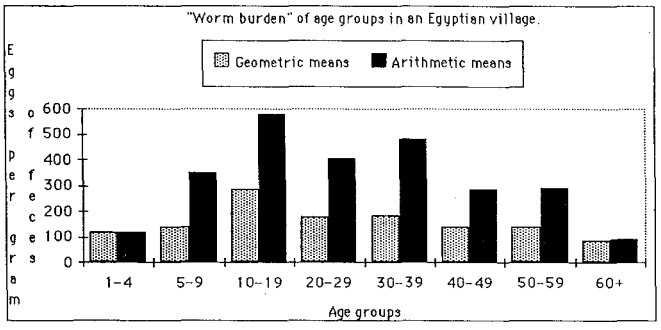


Fig. 3: Geometric and arithmetic means of eggs per gram of feces of age groups in the population of an Egyptian village in the Nile Delta.

It usually is assumed that the latter decline is attributable to a spontaneous death of the adult worms of early infections, together with a slowly-acquired immunity to re-infection. This has been partially confirmed by epidemiological observations (Butterworth [9]). In support of the idea of "a slowly-acquired immunity to re-infection" and suggesting that

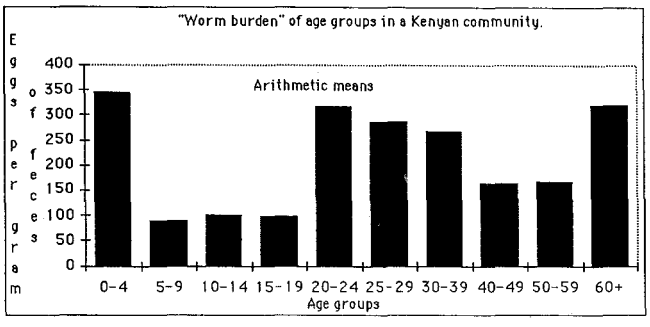


Fig. 4: Arithmetic means of eggs per gram of feces of age groups in a population of a community in Kisumu, Kenya.

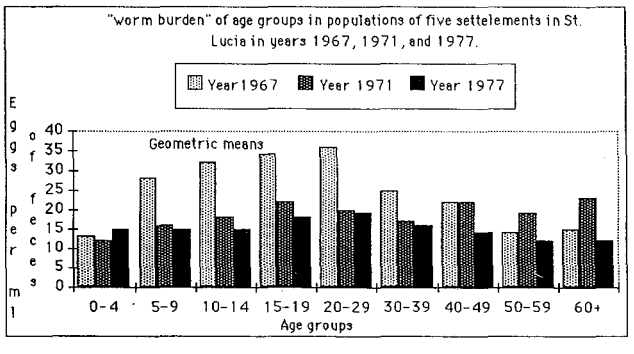


Fig. 5: Geometric means of eggs per ml of feces of age groups in the populations of five settlements in St. Lucia in the years 1967, 1971, and 1977.

immunity takes 15 or more years to develop, is the finding that amongst a population of uninfected adults who immigrated into an S. mansoni endemic area, irrespective of age, a peak intensity was found after 15-19 years of residence; those who had been there longer showed declining rates. The peak thus appeared to be associated with the duration of exposure to infection and not with reduced contact (Jordan & Webbe [19]). Further evidence in support of the existence of immunity in man comes from observations of patients who by virtue of their occupation are known to be exposed to high risk of infection. If environmental exposure is high, and if worm burdens are relatively low in persons at high risk, then it is reasonable to assume that immunological mechanisms operate to prevent accumulation of high worm numbers. However, some re-infection undoubtedly occurs.

Much experimental evidence, supported by epidemiological observations in humans, has pointed to the invasive stage of parasite, i.e. schistosomulum, as the main target of the various killing mechanisms of protective immunity. The parasite appears to lose its susceptibility to immune attack within a period of 2 to 3 days (Khalil [20]). Likewise, the adult population seems relatively unaffected by immune effector mechanisms. Recent studies suggest that the progressive loss of susceptibility to damage by immune systems is an active process on the part of schistosomulum. Studies concerning parasite survival in the immune host have revealed their remarkable ingenuity in escaping the full effects of the host immune response (Capron & Deessaint [10]; Garcia & Mitchell [14]) – resistance to re-infection is never complete nor does vaccination induce complete protection: a "slip through" parasite may be antigenetically different from the existing worms or worms used as vaccine (Garcia & Mitchell [14]). Apparently, millions of years of evolution have selected the parasites that are well adapted to their host and a balanced relationship has been set up.

The snail intermediate hosts of the schistosome parasite reside in fresh water and belong to the genera Biomphalaria, Bulinus, or Oncomelania. The snail intermediate hosts are found in many different habitat types, including small ponds (permanent or semipermanent), marshes and swamps, perennial and seasonal rivers and streams, very large permanent bodies of water such as man-made lakes and habitats such as irrigation channels, drains, dams and rice fields. They are found in fresh-water with pH varying between 5.3 and 9, in tropical forest regions, as well as in arid situations, at low or at high altitudes, and at water temperatures ranging between 18°C and 30°C. The general topography of an area may influence the distribution of snails. Rainfall and temperature are among the most important climatic factors that affect the life history of snails and determine seasonal fluctuations in their densities - rainfall may result in sharp reductions in population density where streams and rivers are flushed out; low temperature in winter reduce breeding or stop it completely in temperate and sub-tropical zones, it is then resumed when temperatures increase. Aquatic snail intermediate hosts have the capacity to survive out of water

for weeks or even months. The capacity of snails to survive in dried mud may thus be an important factor in their dissemination and colonialisation of new habitats through the agency of animals, birds and even vegetation. Apart from the extrinsic factors, which are generally seasonal, the density and age structure of a snail population is controlled by intrinsically operating factors, such as birth rate, natural morality and environmental resistance, which are not constant for a population and will vary with the size and composition of different populations and environmental conditions (Jordan and Webbe [19]).

## A MATHEMATICAL MODEL

We shall assume that we have a community of H(t) individuals at time t. The population is divided into several classes according to age. We did not consider sex as a categorizing factor under the assumption that the values of the parameters considered for each class are the average values for this age class for both sexes. Let $H_j(t)$ be the number of individuals in age class j at time t. Clearly

$$\sum_{j=0}^{C_h} H_j(t) = H(t) \qquad (3.1)$$

where $C_h$ is the number of classes and $H_0(t)$ is the number of the newly born at time t. Let rX(t) denotes $X(t+\eta) - X(t)$ where $\eta$ is the time step. The size of the time step $\eta$ is less than or equal to the minimum of the life spans of humans, worms, snails, cercaria, and miracidia. If the "length" of any age class in $\eta L$, that is, L time steps, and $\mu_j$ and $\nu_j$ are respectively the per capita deaths and births for age class j, we have the accounting relations

$$H_{j+1}(t+\eta L) = (1 - \mu_j) H_j(t) \qquad (3.2)$$

$$H(t+\eta L) - H(t) = \sum_{j=0}^{C_h} (\nu_j - \mu_j) H_j(t) \qquad (3.3)$$

and

$$H_0(t+\eta L) = \sum_{j=0}^{C_h} \nu_j H_j(t)$$

$$= H(t+\eta L) - H(t) + \sum_{j=0}^{C_h} \mu_j H_j(t) \qquad (3.4)$$

Each individual in class j, as far as schistosomiasis is concerned, is characterized by several attributes. The first such attributes is $W_j(t)$, j = 0, 1, 2, ... Ch; t ≥ 0, which denotes the number of paired worms that are established at time t in an individual age class j. Actually this attribute is not directly observable but Cheever [12] has shown that the number of eggs excreted in the faeces is a multiple of the worm burden. We did not classify the worms as male or female, due to the fact that unpaired worms are few in number and contribute very little to the dynamics of disease transmission (Cheever [12]). The other attributes relate to the individual's water-contact behaviour. An individual can have different water contact activities during the time step $\eta$. For example, he may be in contact with water while working, washing, bathing, playing, fording, or collecting water (Jordan [18]).

Let

$\alpha_{kj}(t)$ k = 1, 2, ..., $C_w$, j = 0, 1, ..., $C_h$; t ≥0,

$\tau_{kj}(t)$ k = 1, 2, ..., $C_w$, j = 0, 1, ..., $C_h$; t ≥0,

$\phi_{kj}(t)$ k = 1, 2, ..., $C_w$, j = 0, 1, ..., $C_h$; t ≥0,

denote respectively, the area of skin in contact with water, the duration of that water contact, and the frequency of that contact for an individual in age class engaged in water activity k during time step $\eta$. Also, let

$\pi_{kj}(t)$ k = 1, 2, ..., $C_w$, j = 0, 1, ..., $C_h$; t ≥0,

denotes the fraction of schistosome eggs passed into water during the time step h by an individual of age class j engaged in water activity k. Naturally,

$$\sum_{k=1}^{C_w} \pi_{kj}(t) \le 1, \; j = 0, 1, ..., C_h \qquad (3.5)$$

We also assume that we have a total of S(t) snails at time t residing in the water bodies frequented by the community. Let

$$rS(t) = (\nu_s - \mu_s(t))\, S(t) \qquad (3.6)$$

where $\nu_s$ and $\mu_s(t)$ are the birth and death rates of snails at time t. The birth rate $\nu_s$ is a biological constant whereas the death rate $\mu_s(t)$ is dependent upon the environment as typified, among their things, by $K_s(t)$, the water bodies carrying capacity for snails at time t. The Simplest such dependence is

$$\mu_s(t) = \nu_s \frac{S(t)}{K_s(t)} \qquad (3.7)$$

Thus equation (3.6) takes the form of the logistic law of population growth with time dependent carrying capacity

$$\Delta S(t) = \nu_s \left(1 - \frac{S(t)}{K_s(t)}\right) S(t) \qquad (3.8)$$

Let IS(t) denote the number of infected snails at time t. IS(t) is governed by the formula

$$rIS(t) = \ni(S(t) - IS(t)) - \mu_s(t)\, IS(t) \qquad (3.9)$$

where $\Gamma$ is the probability that during the time step $\eta$ a randomly selected uninfected snail will get infected. The first term in the above equation represents the expected number of newly infected snails and the second term represents the decrease in the number of infected snails due

to death. Clearly ə depends on the number of viable miracidia in the snail-bearing waters at time t, M(t), on the physical/biological characteristics of miracidia, and on the nature of a randomly selected standard cell of these waters – extent, flow, temperature, salinity, turbidity (Jordan [18]).

The equation governing M(t) has the form

$$\Delta M(t) = \chi_m \sum_{j=0}^{C_h} \left( \sum_{k=1}^{C_w} \pi_{kj}(t) \right) H_j(t) W_j(t) - \mu_m M(t) \tag{3.10}$$

The first term represents the number of miracidia newly added to the waters to the waters by the infected population (Cheever [12]) and the second term represents the number of miracidia becoming nonviable; $\mu_m$ being the rate at which miracidia become nonviable, and $\chi_m$ is the number of miracidia produced per worm per time step.

Let C(t) be the number of viable cercaria in waters at time t and $\chi_c$ be the number of cercaria shed by an infected snail during the time step. The equation governing C(t) is

$$\Delta C(t) = \chi_c \, CSS(t) - \mu_c C(t) \tag{3.11}$$

where $\mu_c$ is the death rate of cercaria per time step and CSS(t) is the number of snails that are shedding cercaria at time t. CSS(t) is given by the equation

$$CSS(t) = IS(t - \eta p_s) \left( 1 - \frac{\mu_s (1 - \mu_s^{p_s})}{1 - \mu_s} \right) \tag{3.12}$$

where $\eta p_s$ is the prepatent period after which a newly infected snail starts to shed cercaria.

The equation for the number of paired worms $W_j(t)$ is developed as follows. The raw cercarial force of infection an individual in age class j is subjected to during (t, -η, t), $\Psi_j(t)$, is a non-decreasing function of C(t), and $\{\alpha_{kj}(t), \tau_{kj}(t), \phi_{kj}(t), k = 1, 2, ..., C_w\}$, that is

$$\psi_j(t) = \omega(C(t), \{\alpha_{kj}(t), \tau_{kj}(t), \phi_{kj}(t), k = 1, 2, \ldots, C_w\}) \tag{3.13}$$

Let $\eta p_h$ be the time period between a cercarial challenge and the establishment of paired worms due to that challenge. The newly acquired paired worms at time t, $\Psi_j(t)$, is a function of $\{\psi_j(u), W_j(u); u = 0, 1, 2, ..., t\}$, that is,

$$\Psi_t(t) = \Omega(\psi_j(u), W_j(u); u = 0, 1, \ldots, t) \tag{3.14}$$

The equation governing paired worms then takes the form

$$\Delta W_j(t) = \Psi_j(t) - \mu_w W_j(t) \tag{3.15}$$

where $\mu_w$ is the death rate of paired worms. If there was no immunity $\Psi_j$ would depend only on $\psi_j(t - \eta p_h)$.

Equations (3.1)-(3.15) constitute a system of coupled nonlinear equations that represent the dynamic interaction between the definitive host, the intermediate host, and the different stages of the parasite's life cycle. It is clear that the specific behaviour of the system depends on the particular values assigned to its parameters. Some of these parameters are uncontrollable such as the number of eggs produced per worm-pair $\chi_m$, the number of cercaria produced by an infected snail, $\chi_c$, and the natural death rate of paired worms, $\mu_w$. Other parameters that influence the dynamics of the situation are controllable, for example, the attributes of the age classes, $W_j(t)$, $\pi_{kj}(t)$, $\alpha_{kj}(t)$, $\tau_{kj}(t)$, and $\phi_{kj}(t)$. It is the manipulation of the controllable parameters that makes this model a potentially valuable tool for those concerned with the dynamics of schistosomiasis as it relates to proposed programs for the control of the disease. These equations can be used to simulate the actual physical situation in the field. They can also be used to investigate the dynamic behaviour of an endemic state when it is perturbed.

## NUMERICAL EXAMPLE

In this section the numerical solution of the model is obtained under different settings for the parameter controlling resistance to re-infection and for those controlling the water-contact behaviour. The aim is to investigate the shape of the curve of intensity by age as it relates to both the resistance to re-infection and the water-contact behaviour. We investigate intensity by age under four scenarios:

A. Age-dependent constant exposure and no resistance to re-infection.
B. Age-dependent constant exposures and resistance to re-infection.
C. Age-dependent exposures and no resistance to re-infection.
D. Age-dependent exposures and resistance to re-infection.

For the purpose of this section, we propose the following submodels for the quantities Γ, $\{\Psi_j(t), \psi_j(t), \mu_j$, and $\nu_j; j = 0, 1, 2, ..., C_h\}$.

It is clear that Γ, the probability that a randomly selected uninfected snail which is situated within a cell of snail-bearing waters will get infected during the time step η, depends on the number of viable miracidia in that cell at time t, M(t), on the physical/biological characteristics of miracidia, and on the nature of that cell of water (extent, flow, temperature, salinity, turbidity, etc). But during the time step η, the number of viable miracidia that are within a standard cell of water in which an uninfected snail is situated is a random variable whose distribution can be approximately Poisson with mean λ which is a non-decreasing function of M(t). If the events "a randomly selected uninfected snail will be infected during a time step η" and "there are at least ν viable miracidia in a standard

cell of the snail-bearing waters" are equivalent, their probabilities of occurrence are equal and we get

$$\Gamma = 1 - \sum_{x=0}^{x=\nu-1} \frac{\lambda^x e^{-\lambda}}{x!} \qquad (4.1)$$

Since infected snails were observed to constitute a small percentage of the snail population (Warren [33]), a reasonable model for $\lambda$ is

$$\lambda = 6 \log (1 + M(t)) \qquad (4.2)$$

The dependence of $\Gamma$ on the characteristics of miracidia and on the nature of that standard cell of water, is summarized in the values of the parameters < and 6.

The submodels we propose for $\psi_j(t)$ and $\Psi_j(t)$ are developed next. Let $\psi_{jk}(t)$ denotes the raw cercarial force of infection an individual in age class j engaged in water-contact activity k is subject to during (t-$\eta$, t). Thus

$$\psi_j(t) = \sum_{k=1}^{k=C_w} \psi_{jk}(t)$$

$\psi_{jk}(t)$ is a non-decreasing function of $\{\alpha_{kj}(t)$, $\tau_{kj}(t)$, $\phi_{kj}(t)$ and C(t). In particular, $\psi_{jk}(t)$ should be zero if any of the quantities $\alpha_{kj}(t)$, $\tau_{kj}(t)$, $\phi_{kj}(t)\}$ and C(t) is zero. Let $X_k$ denotes the average number of paired worms that gets established due to exposing unit skin area for unit of time while in water-contact activity k. Thus

$$\psi_{jk}(t) = [\alpha_{kj}(t)\, \tau_{kj}(t)\, \phi_{kj}(t)]\, X_k$$

Naturally $X_k$ should be a no-decreasing function of C(t), the number of viable cercaria present in the waters during (t-$\eta$, t). Since typical values for C(k) are several orders of magnitudes larger than $[\alpha_{kj}(t)\, \tau_{kj}(t)\, \phi_{kj}(t)]$, we assume that

$$X_k = A_k \log [1+C(t)] \qquad (4.3)$$

where $A_k$ is a scaling constant that is interpreted as a weight of the relative importance of water-contact activity k in the transmission of the parasite. Thus

$$\psi_j(t) = \left[\sum_{k=1}^{C_w} [A_k \alpha_{kj}(t) \tau_{kj}(t) \phi_{kj}(t)]\right] \log(1 + C(t)) \qquad (4.4)$$

If there is no resistance to re-infection, the newly acquired paired worms at time t, $\Psi_j(t)$, is simply $\psi_j(t - \eta p_h)$ where $\eta p_h$ is the time period between a cercarial challenge and the establishment of paired worms due to that challenge. However, if there is resistance to re-infection, then $\Psi_j(t)$ would depend on the past history of the infection: duration, intensity, and exposures. For example,

$$\Psi_j(t) = \psi_j(t - \eta p_h) \left(1 + \sum_{\tau=t}^{\tau=t-T} W_j(\tau) \psi_j(\tau)\right)^{-\gamma} \qquad (4.5)$$

where T is the span of immunological memory - immunological memory in mice is estimated at 5 weeks (Anderson and Crombie [3]), and $\gamma$ measures the strength of the resistance to re-infection. In particular, $\gamma = 0$ corresponds to the case when there is no resistance to re-infection.

The number of the newly born during the time period $\eta$L is given by the equation

$$H_0(t + \eta L) = H(t + \eta L) - H(t) + \sum_{j=0}^{C_h} \mu_j H_j(t)$$

We assume an environment that can support a maximum of $K_h$ individuals. We enforce this by assuming that

$$H(t + \eta L) - H(t) = \nu_h \left(1 - \frac{H(t)}{K_h}\right) H(t) \qquad (4.6)$$

where $\nu_h$ and $\nu_h \left(1 - \frac{H(t)}{K_h}\right)$ are, respectively, the per capita number of births for the population and the intrinsic rate of population growth. Thus as the intrinsic rate of growth reaches zero the number of the newly born will equal the number of deaths.

We choose the time step $\eta$ as one calendar day, and interpret the age classes as calendar years. Thus the fifth age class denotes the people in the community that are 5 years old. The annual death rates for age classes, $\mu_j$, j = 0, 1, ..., $C_h$, have been generated, with p = 5, from the formula

$$\mu_j = \left(\frac{j+1}{C_h + 1}\right)^p \left(2^{\frac{j+1}{C_{h+1}}} - 1\right) \quad P \geq 0,\ j = 0, 1, ..., C_h$$

The different age classes are initially set equal in size, that is, $H_j(0) = H(0)/C_h$, j=0, 1, 2, ..., $C_h$. Also, the worm burden for the different age classes is set initially equal to zero, that is, $W_j(0) = 0$, j = 0, 1, 2, ..., $C_h$. The initial value for M(t), M(0), is arbitrarily set to 100,000. The parameters $K_h$, H(0), $\nu_h$, $K_s$, S(0), SI(0) are arbitrarily set, respectively, to 1000, 1000, .02, 50,000, 50,000 and 50. A value for $C_h$ is chosen equal to 75 thus, as far as schistosomiasis is concerned, no human lives beyond 75 years of age. The daily birth rate for the snail intermediate host, $\nu_s$, is taken equal to 0.055 (Hairston [15]). The parameters of the $\Gamma$ submodel, $\nu$ and $\kappa$, were set to 5 and 0.0325 respectively. The parameters $\mu_m$, $\mu_c$, and $\mu_w$, represent daily death rates of miracidia, cercaria, and worms. They are taken, respectively, equal to 0.9, 0.6, and 0.0008 (Braunwald [7]; Jordan [18]). The number of viable miracidia produced by a worm-pair per day, $\chi_m$, and the number of cercaria shed by an infected snail per day, $\chi_c$, are given the respective values of 500 and 2,500 (Brown & Neva [8]). The prepatent periods $P_h$, and $P_s$, are set, respectively, to 21 and 45 days (Brown & Neva [8]).

Values for $\{\alpha_{kj}, \tau_{kj}, \phi_{kj}, k = 1, 2, ..., C_w, j = 0, 1, 2, ..., 75\}$, for the age-dependent duration, frequency, and skin area in contact with water, were taken from Jordan [18]. Table 1 shows the mean values for all water contact activities per individual of age groups 0-4, 5-9, 10-14, 15-19, 20-29, 30-39, 40-49, 50-59, and 60+ years (or simply age groups 1, 2, 3, 4, 5, 6, 7, 8, and 9) of, respectively, the area of skin in $m^2$ exposed to water per contact, mean duration in minutes per contact, and the average number of contacts per day.

**Table 1**

Mean skin area in $m^2$ per contact, mean duration in minutes per contact, and the average number of contacts per day by age groups in years.

| Age group | Mean Area[a] | Mean duration[b] | Mean number of contacts[c] |
|---|---|---|---|
| 0-4 | 0.199 | 6.7 | 0.393 |
| 5-9 | 0.217 | 6.0 | 0.490 |
| 10-14 | 0.323 | 8.6 | 0.594 |
| 15-19 | 0.375 | 11.2 | 0.746 |
| 20-29 | 0.401 | 12.5 | 0.540 |
| 30-39 | 0.366 | 14.7 | 0.747 |
| 40-49 | 0.334 | 14.6 | 0.626 |
| 50-59 | 0.210 | 12.0 | 0.614 |
| 60+ | 0.232 | 12.6 | 0.381 |

a: Col. 2 of Table 13.6; b: Col. 2 of Table 13.4; c: Col. 4 of Table 13.3 ÷ 7 (Jordan 1985)

For the age-independent duration, frequency, and skin area in contact with water we took the respective averages of columns 2, 3 and 4 of table 1, namely 10.3, 0.295, and 0.570.

Values for the parameters $\pi_{kj}$ are assumed to be directly proportional to the products of the respective values of $\tau_{kj}$ and $\phi_{kj}$, j = 0, 1, 2, ..., 75. More specifically, we assume that

$$\pi_{kj} = \tau_{kj}\, \phi_{kj}/10; \; j = 0, 1, ..., 75 \qquad (4.7)$$

Finally, a value for $\gamma$, the resistance to re-infection parameter, is set equal to 0.25 and each the weights of relative importance $\{A_k, k = 1, ..., C_w\}$ is set to 0.35.

The model was solved iteratively, on an Apple Macintosh Plus personal computer. A computer run is executed for over 200 simulated years for each of the scenarios mentioned above. It took about 15 simulated years for the system to stabilize with no significant change in the overall picture for the next 185 years. There are quantities whose dynamical behaviour is of interest. Foremost among these is the distribution of the "worm-burden" in the population as well as its time development.

The results of these runs are best summarized graphically. Figures 6 and 7 pertain to scenario A, "Age-independent constant exposures and no resistance to re-infection." Although age-independent constant exposures is not expected to human populations, Figs. 6 and 7, however, depict what Anderson & Crombie [3] have called the basic epidemiological profile, namely "worm burdens will attain a stable plateau level in the older age classes of host populations provided that exposures are constant and independent of host age and in the absence of acquired resistance."

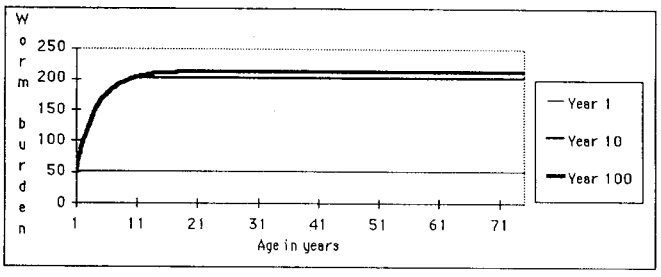


Fig. 6: Worm burden in population after 1, 10, and 100 years of infection. Age-independent constant exposures & no resistance to re-infection.

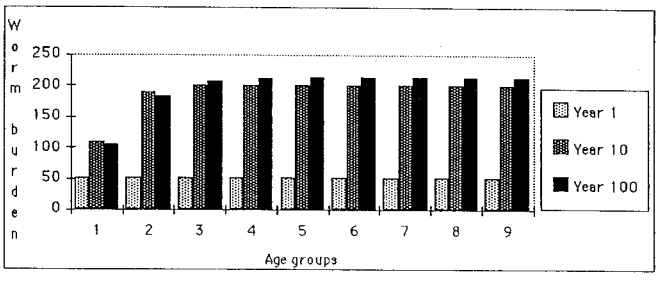


Fig. 7: Worm burden in population's age groups after 1, 10, and 100 years of infection. Age-independent constant exposures & no resistance to re-infection.

Figures 8 and 9 pertain to scenario B, "Age-independent constant exposures and resistance to re-infection." Experimental results with inbred mouse populations exposed to constant numbers of infective stages per unit of time reveal monotonic growth to a stable plateau and convex age-intensity profiles (Anderson and Crombie [3]). While humans are no mice, Figs. 8 and 9, however, confirm these experimental findings. They show that age-independent constant exposures and resistance to re-infection causes the "intensity by age" curve to be convex.

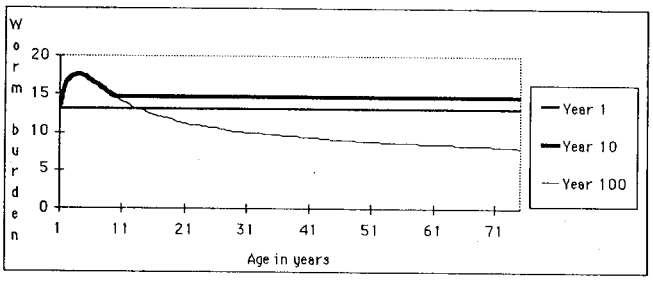


Fig. 8: Worm burden in population after 1, 10, and 100 years of infection. Age-independent constant exposures & resistance to re-infection with gamma = 0.25.

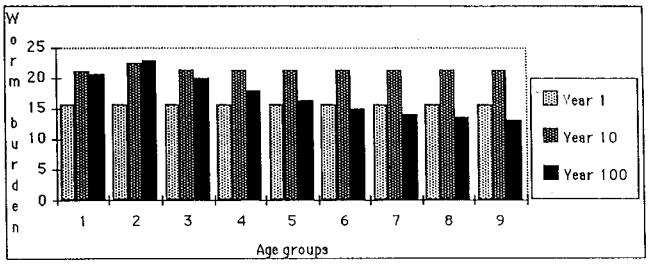


Fig. 9: Worm burden in population's age groups after 1, 10, and 100 years of infection. Age-independent constant exposures & resistance to re-infection with gamma = 0.25

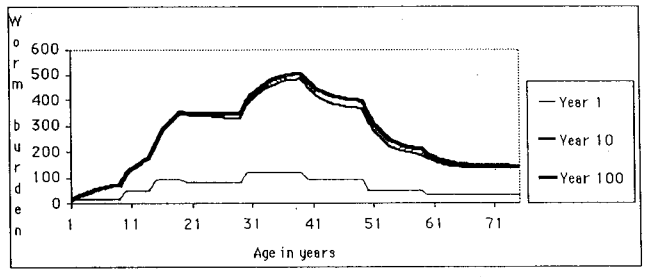


Fig. 10: Worm burden in population after 1, 10, and 100 years of infection. Age-dependent exposures & no resistance to re-infection.

The age-intensity profiles under age-dependent exposures and no resistance to re-infection, scenario C, are shown in Figs. 10 and 11. The distinguishing feature of these profiles is their convexity. This means that age-dependent exposures in the absence of resistance to re-infection causes the age-intensity profile to be convex.

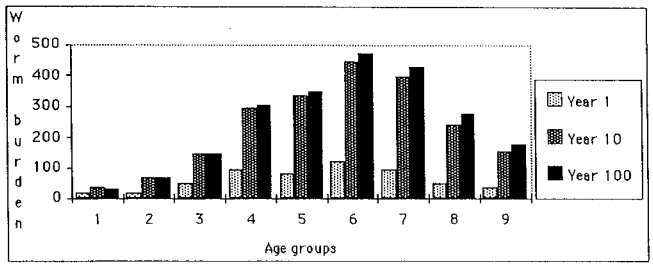


Fig. 11: Worm burden in population's age groups after 1, 10, and 100 years of infection. Age-dependent exposures & no resistance to re-infection.

The exposure data used to generate Figure 11 are those shown in table 1. This is water contact data from St. Lucia (Jordan [18]). Fig. 5, St. Lucian age-intensity profiles, shows the highest intensity to occur in ages 10-29 years, that is, age groups 3, 4, and 5. However, Figure 11 shows the highest intensity to occur in age group 6, those who are 30-39 years old. Furthermore, Fig. 11 indicates a worm burden as large as 500 paired worms for the 30-39 years old. Thus although age-dependent exposures in the absence of resistance to re-infection causes the age-intensity profiles to be convex, the profiles produced are not the types generated from survey data.

Figures 12 and 13 show the age-intensity profiles under age-dependent exposures and resistance to re-infection, scenario D. Fig. 13 shows that the highest intensity occurs in age group 4, that is those who are 15-19 years old. The highest intensity occurs in Fig. 5 in the age groups 3, 4, and 5. It is clear thus that the profile in Fig. 13 is much closer to that of Fig. 5 than that of Fig. 11. Furthermore, Fig. 13 shows a maximum worm burden of about 30 paired worm which is less than that of Fig. 11 by more than an order of magnitude.

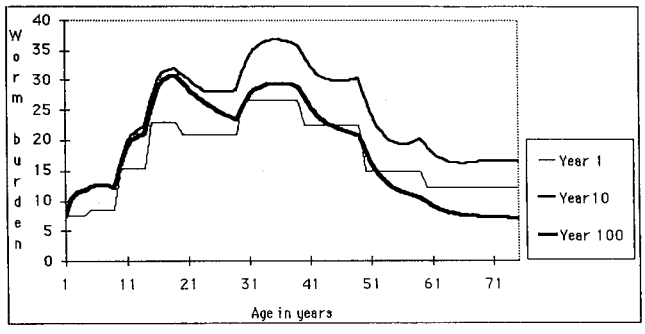


Fig. 12: Worm burden in population 1, 10, and 100 years after infection. Age-dependent exposures & resistance to re-infection with gamma = 0.25.

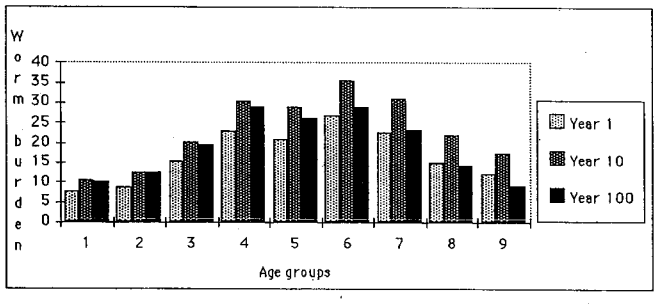


Fig. 13: Worm burden in population's age groups after 1, 10, and 100 years of infection. Age-dependent exposures & resistance to re-infection with gamma = 0.25.

The differences between the profiles in Figs. 13 and 11 are due to one single difference, namely, the value assumed for $\gamma$ in the case of Fig. 11 is zero while that assumed for Fig. 13 is 0.25. Of course the actual value of $\gamma$ has to be estimated from survey data that are specifically collected for that purpose. We conclude therefore that age-intensity profiles observed in epidemiological surveys is produced through variability of water-contact behaviour among age groups and a slowly-acquired resistance to re-infection.

## SUMMARY AND CONCLUSIONS

A mathematical model was constructed for the dynamics of schistosomiasis. It is solved numerically under four scenarios: age-independent constant exposures and no resistance to re-infection, age-independent constant exposures and resistance to re-infection, age-dependent

exposures and no resistance to re-infection, and age-dependent exposures and resistance to re-infection. The model produces the so-called basic epidemiological profile "worm burdens attain a stable plateau level in the older age classes of host populations provided that exposures are constant and independent of host age and in the absence of acquired resistance." It also produces, under "age-independent constant exposures and resistance to re-infection", age-intensity profiles that are consistent with experimental results with inbred mouse populations exposed to constant numbers of infective stages per unit of time-monotonic growth to a plateau followed by a decline in the older host populations (Anderson and Crombie [3]). The model produces the new insight that convexity of the age-intensity profile can be due to variability of water-contact activities among age groups alone. However, the model indicates that age-intensity profiles observed in epidemiological surveys is produced through variability of water-contact behaviour among age groups and a slowly-resistance to re-infection.

The model can be used to investigate the dynamics of schistosomiasis under other submodels for $\Gamma$, $\psi$ and $\Psi$ as well as other scenarios. It is worth mentioning here, however, that the particular submodels used for the functions $\Gamma$, $\psi$ and $\Psi$ simulate to a reasonable extent, respectively, the process of snail infection and the effects of exposure to infected waters and the resistance to re-infection.

The model can be used to investigate a variety of questions of the "what if" type, especially those that relate to possible control program. For example, it can easily answer the question "what will the state of endemicity be and how fast it will be reached if the worm-burden of some age classes are set equal to zero, that is, apply to them chemotherapy treatment?" Finally, when the model is run on a fast computer with graphics display capabilities, it can be a valuable tool in studies of the dynamics of schistosomiasis.

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