Theoretical Ecology

PRINCIPLES AND APPLICATIONS

EDITED BY

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Schistosomiasis:
A Human Host-Parasite System

JOEL E. COHEN*

13.1 Introduction

Human schistosomiasis (pronounced SHIS-to-so-MY-uh-sis, or sometimes, synonymously, bilharzia) is a family of diseases caused primarily by three species of the genus *Schistosoma* of flatworms. The adult worms inhabit the blood vessels lining either the bladder or intestine, depending on the species of worm. Hence the worms are also known as blood flukes.

Jordan and Webbe (1969) provide a monographic review of human schistosomiasis. Malek's (1961) shorter review emphasizes the ecological point of view. The insatiable reader is invited to consult the 10,286 references cited by Warren and Newill (1967), which do not include most of those on which this chapter is based.

Aside from its human impact, schistosomiasis is a marvellous source of puzzles for the biologist. How does this metazoan parasite escape annihilation by human immune responses? How do genetic factors in snails condition susceptibility to infection by the asexual stages? How do worms of opposite sex find each other in the dark?

How does the schistosome cope with successive environments of human faeces, water, snail tissue, water again, and human serum and other tissues? Why is the fraction of snails observed to be infected in natural populations so remarkably low (Warren, 1973)? Are there immunological cross reactions between human schistosomes, as has been suggested for malaria (Cohen, 1973a)?

How do human behaviour and agricultural practices combine to propagate an insidious pest, and how can people balance conflicting demands of economics and health in controlling it?

The worldwide prevalence of schistosomal infections has not been

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measured credibly. A figure conventionally cited is 200 million people, or approximately one out of every twenty people on the planet. The disease is virtually unknown in the rich countries of the world. Thus it is concentrated among those people least able financially to defend themselves against it.

According to a foundation which devotes a substantial fraction of its money to research on schistosomiasis, 'preliminary calculations indicate that global control would cost at least $2 billion per year at today's prices with the best current methods!' (Hoffman, 1975, p. 26). The exclamation point is intended, in context, to emphasize how expensive global control would be. But the resulting estimate of $10 per case for worldwide control of schistosomiasis should be compared with the $30 per case spent in the United States for research alone on muscular dystrophy, and with the alternate uses $2 billion have been put to recently.

'There is little doubt that all three schistosomes can cause considerable pathological change, sometimes in a comparatively large proportion of the population, but the evidence suggests that only a proportion of those so affected die of the disease' (Jordan and Webbe, 1969, p. 168). The absence of quantitative information from this assessment of the impact of the infection on health fairly reflects the information available.

After a schematic description of the life cycle and ecology of *Schistosoma mansoni*, this chapter will review several mathematical models of aspects of schistosomiasis. To date no mathematical model of the disease has come close to representing faithfully most of what is known about the natural history of the disease; none, in fact, has even tried. So the field is still open. The juxtaposition of these models will make clear the selective emphasis, and some of the omissions, of each.

13.2   A life cycle of schistosomiasis

The common features of all three schistosome species which are the major parasites of man are summarized in Fig. 13.1 (from Jordan and Webbe, 1969, p. 7, from whom the following brief description is also drawn). The life cycle consists of an obligatory alternation of sexual and asexual generations. The sexual generation occurs in man (or sometimes other mammals). The asexual generation must pass through specific snails.

Paired mature Worms

Veins of bladder—*S. haematobium*

Mesenteric vessels—*S. mansoni*
of bowel—*S. japonicum*

DEFINITIVE HOST
MAN

RETAINED IN TISSUES

Hepatic portal vessels ♂

Arteries

Heart

6-12 weeks   Lungs

Heart

Veins

Schistosomules

EXCRETION

COMMON EXTERNAL ENVIRONMENT
IN WATER

Cercariae
penetrate skin

Free swimming
Cercariae

♂

♀

48 hours

EGGS
S. mansoni
S. haematobium   *S. japonicum*

INTERMEDIATE HOSTS
Bulinus sp.   Eggs evacuated in Urine or Faeces in water

Mother sporocyst

Daughter sporocysts

Cercariae
produced within
Snail

4-7 weeks   *Biomphalaria* sp.

Free swimming
Miracidium

24 hours
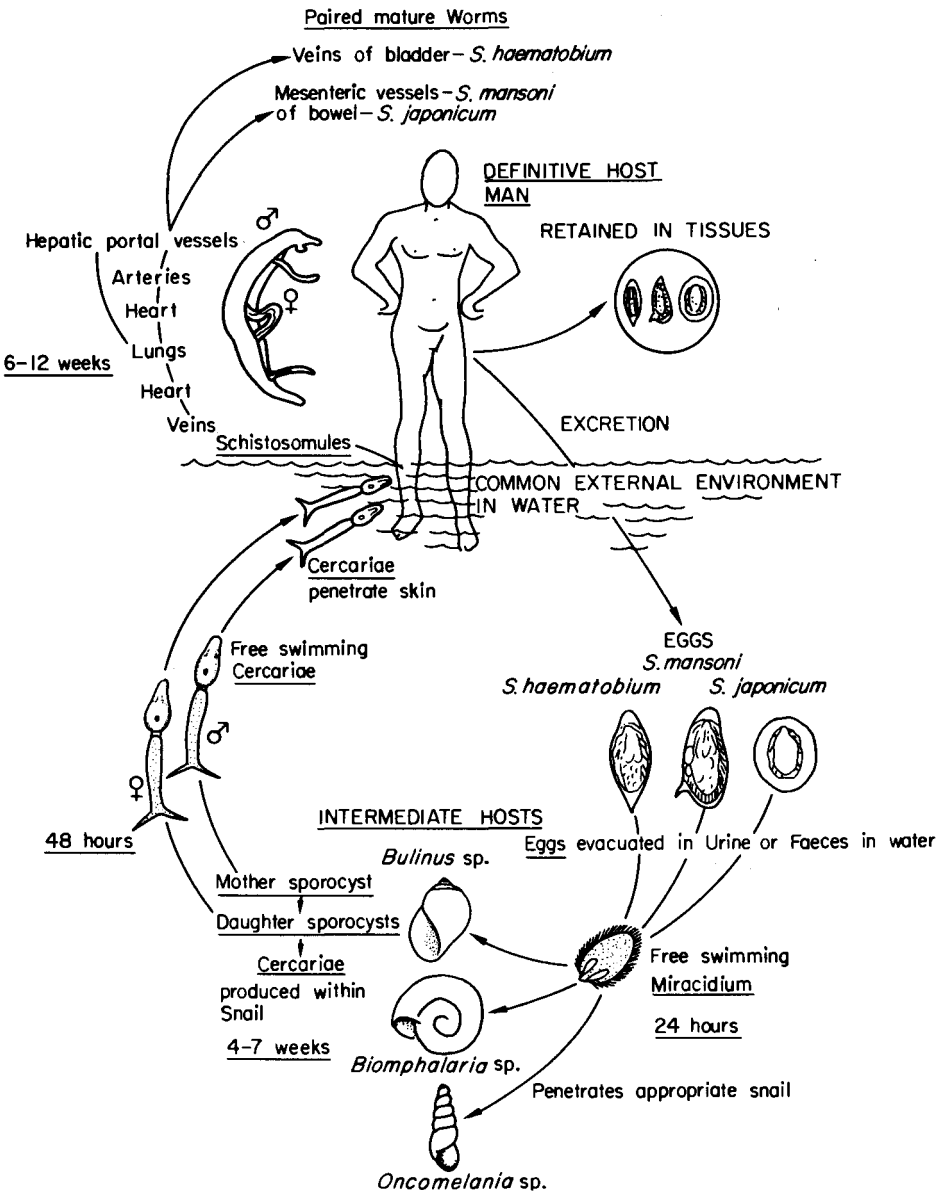
Penetrates appropriate snail

Oncomelania sp.

Fig. 13.1. The life cycle. (From Jordan and Webbe, 1969, p. 7.)

Eggs produced by the sexual stage leave people in urine (in the case of *S. haematobium*) or faeces (*S. mansoni* and *S. japonicum*). Eggs that reach water (a stream, an irrigation canal, a pond, puddle, or ritual

ablution bath near a mosque) shed their shells and hatch a ciliated free-swimming stage called a miracidium.

The quantitative estimates in the following refer chiefly to *S. mansoni*.

A miracidium that locates a snail within approximately one day penetrates it. If the snail has the right genotype, the miracidium develops through two larval stages into thousands of cercariae. Each cercaria that escapes from the snail, starting 4 to 5 weeks after the initial infection, can swim up to two days. When cercariae penetrate the skin of host species in which they cannot develop, they die, producing a skin irritation. When one of the human schistosomal cercariae enters human skin, it becomes a wormlike 'schistosomule'.

Here we follow the course, as far as it is known, of a schistosomule of *S. mansoni*. The schistosomule migrates to the lung, sometimes producing a cough, then appears in the portal system of the liver, where it reaches sexual maturity and mates. Worm pairs then migrate to the blood vessels lining the lower small intestine and the large intestine.

At this point the happy couple of worms resemble (roughly) a hot dog in a roll. The female, 7 to 17 mm long, lies in the gynecophoric canal of the male, who is 6 to 13 mm long and cylindrically shaped to correspond to the walls of their home, a blood vessel. The female is estimated to lay from 100 to 300 eggs a day.

Some of these eggs work through the wall of the blood vessel, into the lumen of the intestine. Carried by faeces, these eggs again begin the life cycle. The interval from the entry of cercariae into human skin to the first detectable passage of eggs in the faeces varies from 5 to 6 weeks.

Most of the disease caused by the infection results from the eggs that do not escape with faeces. Some eggs get stuck in the tissue near where they are laid, causing fibrosis and granuloma as the host tries to protect itself. Other eggs get washed to the liver and spleen where they cause similar damage.

The medicines available to kill the schistosomes in people have so many dangerous side effects that they must be administered under medical supervision; and they are costly. So they may help rich tourists returned home; but by themselves they do nothing to protect a person in an endemic area against reinfection once he or she leaves the clinic. Even if enough medical personnel were available to treat all the infected population in a single month, the snail (and sometimes

other mammalian) reservoirs of infection would persist. The control or eradication of schistosomiasis is a truly ecological problem.

13.3 Proportion ever infected

If present conditions influencing infection with a parasite existed since well before the oldest people alive were born, then every age group should have the same proportion infected as did the community's oldest members when they were at each corresponding age. Assuming constant conditions, a snapshot of the distribution of infection according to age in a community today provides a picture of the life experience of a cohort (a group of people all born at the same time).

The mathematical models described in this section and the next take advantage of that possibility by using data about the prevalence of previous or present infection in a population at one point in time to make inferences about the dynamics of infection over time in a cohort.

Suppose a cohort is entirely susceptible to infection at some initial time, usually taken to be birth. Suppose that this cohort is exposed to a constant force of infection per unit time. 'This force is to be measured in effective contacts per unit time, no matter how complex may be the events leading up to these contacts' (Muench, 1959, p. 16). Here the force of infection a summarizes everything that has to do with the contact between cercariae and people and with the subsequent establishment of a detectable infection. Suppose also that it is possible to classify each individual as ever having been infected or not.

Let N be the total number of individuals initially in the cohort. Let $x(t)$ be the fraction of the cohort that has not been infected, and $y(t)$ the fraction that has ever been infected, by time t. By definition $x(t) + y(t) = 1$. Assume $x(0) = 1$ and $y(0) = 0$. Then $Nx(t)$ is the number of individuals never infected at time t. These individuals are constantly exposed to a force a of infection. So the change per unit time in the number $Nx(t)$ of people never infected is

$$d[Nx(t)]/dt = -aNx(t),$$

or, cancelling N, assumed constant,

$$dx/dt = -ax, \qquad x(0) = 1. \qquad (13.1)$$

Similarly, for the number ever infected,

$$dy/dt = ax = a(1-y), \qquad y(0) = 0. \qquad (13.2)$$

The solution of eq. (13.2) is simply

$$y(t) = 1 - e^{-at}. \tag{13.3}$$

This model assumes no change in the size of the cohort due to death or emigration. Death or emigration will have no effect on the fraction $y(t)$, so long as the death or emigration rates have identical values, $\mu(t)$, for both previously infected and never infected individuals (Cohen, 1972). To see this, we write the appropriate equations, where now the total population $N(t)$ is no longer constant:

$$d[N(t)\,x(t)]/dt = -aN(t)\,x(t) - \mu(t)\,N(t)\,x(t); \tag{13.4}$$

$$d[N(t)\,y(t)]/dt = aN(t)\,x(t) - \mu(t)\,N(t)\,y(t). \tag{13.5}$$

By writing $N(t) = N(0) \cdot \exp\left[-\int_0^t \mu(s)\,ds\right]$ here, we recover precisely eqs. (13.1) and (13.2) for the *fractional* population functions $x(t)$ and $y(t)$.
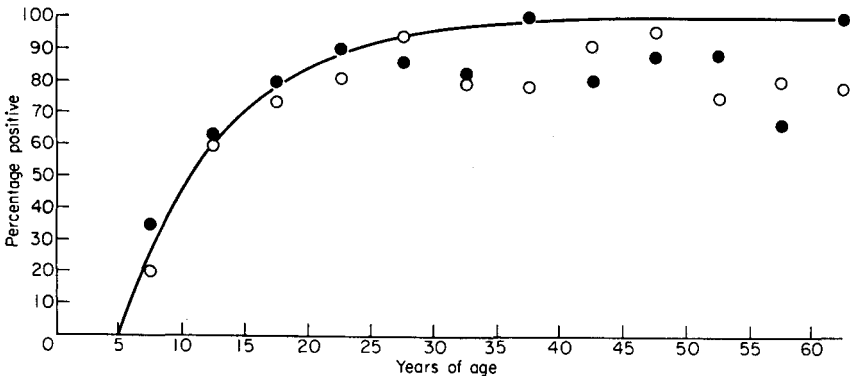

Fig. 13.2. The proportions observed positive in response to *S. japonicum* antigen skin tests as a function of age in the coastal division, Palo, Philippines. Open circles, 1954; solid circles, 1962. Solid line, prediction from eq. (13.3). (Adapted from Hairston, 1965b, p. 172.)

If conditions were constant over the past, and the means of detecting previous infection include individuals infected long ago, then (Hairston, 1965b) a survey of all age groups in a population at a given time should give a graph of the fraction of people ever infected as a function of age that looks like eq. (13.3).

Figure 13.2 takes $t = 0$ as 5 years of age. Infections before that age are neglected. The data are the fractions of people in each age group judged ever to have been infected with schistosomes on the basis

of skin tests in 1954 and 1962. Simple in theory, in practice these tests suffer from many difficulties (Kagan, 1968).

Particularly for the younger age groups, the fit of eq. (13.3) to the data is reasonable. The systematic discrepancy between data and observation at the upper ages is plausibly explained by Hairston (1965b), on the basis of other calculations, as due to an insensitivity of the skin test to previous infection if the person has not recently been exposed to female cercariae or has no living female worms.

The numerical value of the parameter $a = 0 \cdot 12$ used in Fig. 13.2 was not obtained by fitting that curve to those data. The parameter was estimated by fitting another eq. (13.9) below to different data, from stool examinations, on the same population. This finding, which I consider one of the most remarkable in the epidemiology of schistosomiasis, suggests that an incredibly simple, and simple-minded, mathematical model can usefully interpret the age distribution of previous infection and yield information about the dynamics of infection which would otherwise be unavailable.

13.4 Proportion currently infected

Female *S. mansoni* worms in human beings live an average 3 to 4 years; other species of human schistosomes are comparable (Hairston, 1965a, p. 52; Jordan and Webbe, 1969, p. 152).

A person in whom all female worms have died no longer excretes eggs. (A person may also no longer excrete eggs because tissue traps the eggs or because living females are unmated. We ignore these complications.) Hence some individuals previously infected may pass from currently excreting eggs to no longer excreting.

13.4.1 *A model allowing loss of infection*

Let $y(t)$ (not the same as in section 13.3) be the proportion of a cohort which is currently giving evidence of infection by excreting eggs and $z(t)$ be the proportion which has been previously infected but is no longer passing eggs. As before, let $x(t)$ be the proportion of the cohort at time t which has never been infected. Assume no death or emigration, so $x(t) + y(t) + z(t) = 1$.

If the cohort is subject to a constant force of infection a, and those individuals currently giving evidence of infection are now further

subject to a constant risk of loss of infection b, then under constant conditions the proportions x, y and z behave (Muench, 1959) according to

$$dx/dt = -ax, \qquad x(0) = 1, \qquad (13.6)$$

$$dy/dt = +ax - by, \qquad y(0) = 0, \qquad (13.7)$$

$$dz/dt = +by, \qquad z(0) = 0. \qquad (13.8)$$

All individuals are uninfected initially. The sum of the derivatives is zero, as it must be since the cohort does not change size. Then if $a \neq b$,

$$y(t) = a(e^{-bt} - e^{-at})/(a - b). \qquad (13.9)$$

Repeating the argument in section 13.3 shows that if death and emigration occur at equal rates in all three fractions of the cohort, the same equations (13.6) to (13.8) still hold.

In the limit as t gets large, $y(t)$ approaches 0, because eqs. (13.6) to (13.8) really assume that once having lost infection, an individual does not regain it. There is no re-entry from the category measured by $z(t)$ to the category measured by $y(t)$. Hence $z(t)$ must be interpreted as the proportion having lost infection and not exposed to risk of further infection.
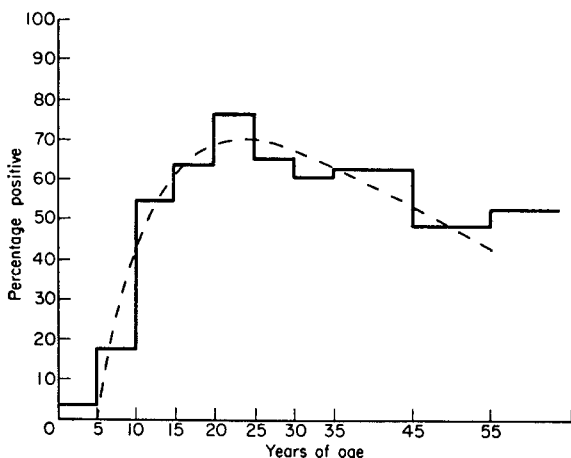

Fig. 13.3. Observed age prevalence (solid line) and theoretical age prevalence (dashed line) from eq. (13.9) of human infection with *S. japonicum* in the coastal division, Palo, Philippines, neglecting transmission before 5 years of age. (From Hairston, 1965b, p. 171.)

As Warren (1973) emphasizes, it is not more plausible to assume that such individuals are immune to further reinfection than it is to suppose that, for cultural and behavioural reasons, they simply have less contact with cercaria-laden water.

Figure 13.3 plots $y(t)$ and the observed proportions with *S. japonicum* eggs in their faeces by age in the same Philippine population pictured in Fig. 13.2 (Hairston, 1965b). The annual rate $b = 0 \cdot 02$ of becoming negative is not the annual death rate of individual female worms because (assuming the eggs are not blocked in the person's tissues) all the females in the person have to die, without replacement, for the person to stop excreting eggs.

Snails too pass through the stages of being never infected, infected and shedding (cercariae, instead of eggs), and (possibly) no longer infected (Fig. 13.4). Sturrock and Webbe (1971) plot proportions of snails shedding as a function of age, which they estimate by size.
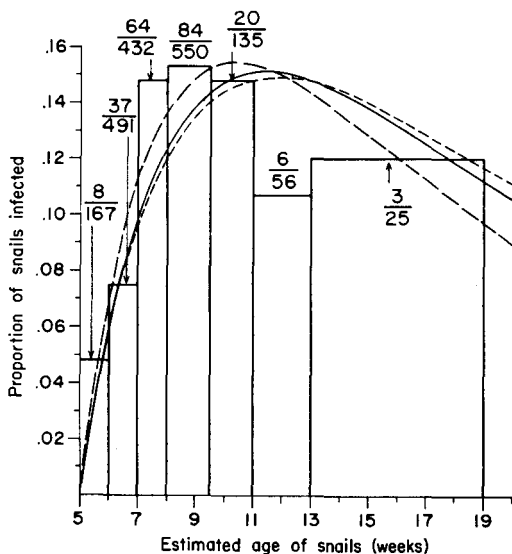

Fig. 13.4. Observed age prevalence (histogram) of infection in *Biomphalaria glabrata* snails in St Lucia, starting from the first week when snails shed cercariae; and three predicted age prevalence curves: solid curve, eq. (13.9); long dashes, force of infection a adjusted for differential mortality of infected individuals; short dashes, loss of infection b adjusted for differential mortality. (From Cohen, 1973b, p. 210.)

13.4.2 *Differential mortality due to infection*

Infection with schistosomes is unhealthy for both people and snails. For people, the increment in the probability of death at any age due to infecting schistosomes has never been measured credibly.

Laboratory experiments of Pan (1965) with the snails which transmit *S. mansoni* show unmistakably (Fig. 13.5) an increase in the death rate of snails shedding cercariae compared with uninfected snails.
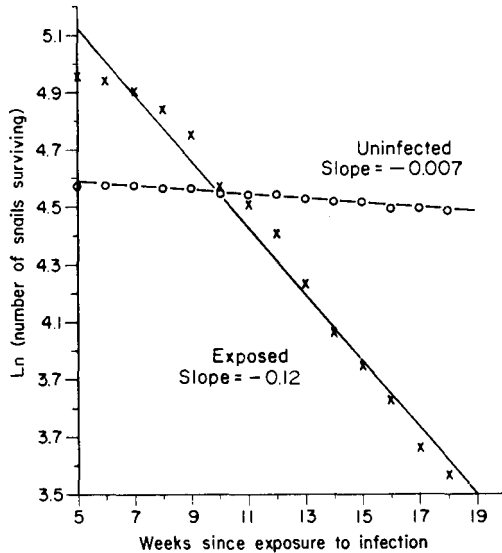

Fig. 13.5. Natural logarithms of the numbers of survivors in a group of snails exposed to *S. mansoni* (x) and in an unexposed group (open circles), based on data of C. T. Pan, and fitted straight lines; starting from first week when snails shed cercariae. The difference between the two slopes estimates ϵ in eq. (13.11). (From Cohen, 1973b, p. 208.)

A slight generalization (Cohen, 1973b) of the models above allows for differential mortality due to current infection. If μ is the constant mortality or emigration rate of individuals not currently shedding eggs (in the case of humans) or cercariae (snails), and $\mu + \epsilon$ is the increased mortality or emigration rate of individuals currently shedding, then suppose

$$(1/N)\, d(Nx)/dt = -ax - \mu x, \qquad\qquad x(0) = 1, \quad (13.10)$$

$$(1/N)\, d(Ny)/dt = +ax - by - (\mu + \epsilon)\, y, \quad y(0) = 0, \quad (13.11)$$

$$(1/N)\, d(Nz)/dt = by - \mu z, \qquad z(0) = 0. \qquad (13.12)$$

The explicit solution for $y(t)$ satisfying eqs. (13.10) to (13.12) appears in Cohen (1973b, p. 200). When $\epsilon = 0$, putting $N(t) = N(0)e^{-\mu t}$ leads back to the eqs. (13.6) to (13.8) and resulting eq. (13.9) of section 13.4.1.

If $y(t)$ obtained from eqs. (13.10) to (13.12) is a better approximation to reality than eq. (13.9), but a curve of the form of eq. (13.9) is fitted to data in ignorance of ϵ, then the resulting estimates of the parameters a and b may be biased. The alternate two theoretical curves in Fig. 13.4 show the result of assuming that all the bias is absorbed either by a or by b. The differences among the predicted age prevalence curves are small, although the possible bias in the parameter estimates is not.

If the differential mortality due to infection is measured in the same population of snails whose age prevalence curve is being studied, even the possible bias in the parameter estimates is small (Sturrock *et al.*, 1975). For estimating rates of gain and loss of infection and describing the age prevalence distribution in the snail populations studied by Sturrock, a little verisimilitude is gained by allowing for differential mortality due to infection, but not much.

This example illustrates a kind of sensitivity analysis which ought, I think, to accompany the study of very simple ecological models. The model is eqs. (13.10) to (13.12) is literally more realistic than the model in eqs. (13.6) to (13.8) because it includes a representation of a real phenomenon known to occur. It is a bit more complicated to study mathematically. It does not cause major alterations in how data studied with eqs. (13.6) to (13.8) are understood. Hence, for rough purposes, one can be more assured of the adequacy of eqs. (13.6) to (13.8); for finer purposes, one has a more refined tool, eqs. (13.10) to (13.12).

13.4.3 *Immunity*

Linhart (1968) analyzes three different stochastic models leading to age-prevalence curves, based on three different formalizations of how an infected (human) individual might develop immunity to infection. Bradley (1974) emphasizes the probable importance of human immunity in the epidemiology of human schistosomiasis, though Warren (1973) favours another view; but so far Linhart's are the only explicit mathematical models incorporating immunity. It is unfortunate that

some of Linhart's predicted age-prevalence curves have never been tested against observations.

An important task in the modeling of schistosomiasis is to see what the burgeoning biological information about the immunology of schistosomiasis (Butterworth, in press) implies for the validity of these and new models, and to translate that information into mathematically explicit, empirically testable, and epidemiologically useful form.

13.5   Snail population dynamics

Biomphalaria glabrata is the snail principally responsible for the transmission of *S. mansoni* in the New World. Jobin and Michelson (1967) raised laboratory populations of these snails with varying amounts F of food (measured in g of watercress), numbers N of snails (each 15 mm in diameter), and volumes V of water (measured in litres), at 25°C. For each such population they measured the fecundity (E) by the numbers of eggs laid per snail per day. Their results (Fig. 13.6) are conveniently summarized by

$$E = kF/(NV). \tag{13.13}$$

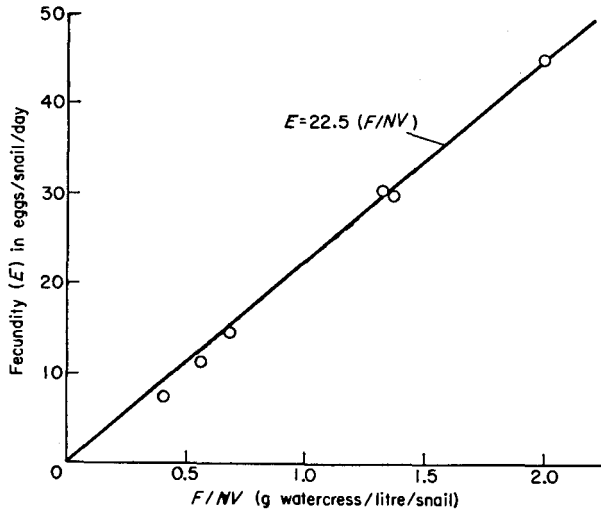It is plausible that, over a certain range at least, fecundity should

Fig. 13.6. Fecundity of *Biomphalaria glabrata* snails as a function of food F, number N of snails, and water volume V. (From Jobin and Michelson, 1967, p. 659.)

increase with food and decrease with the number of snails competing for that food. What is counterintuitive about eq. (13.13) is that a larger volume of water *decreases* fecundity. The reason is that the snails have a harder time finding the food.

Since eq. (13.13) predicts that snails in a vanishingly small volume of water have an infinite fecundity, eq. (13.13) obviously holds over only a limited range of V; in fact the experiments had jars only of 4·5 litres and 7·6 litres.

In very large volumes of water, such as lakes, which are not crowded with snails, the addition of one more snail has no effect on the fecundity of the other snails present. So Jobin and Michelson (1967) assume that the inverse dependence on N in eq. (13.13) disappears whenever the volume of water per snail exceeds a threshold called the 'crowding zone'.

These limitations on eq. (13.13) for small V and for large V show that the direct and inverse proportionalities in eq. (13.13) are deceptively simple. Eq. (13.13) should be regarded as a linearization or tangent approximation to a nonlinear function. This approximation is useful over the range of variables used in one set of experiments.

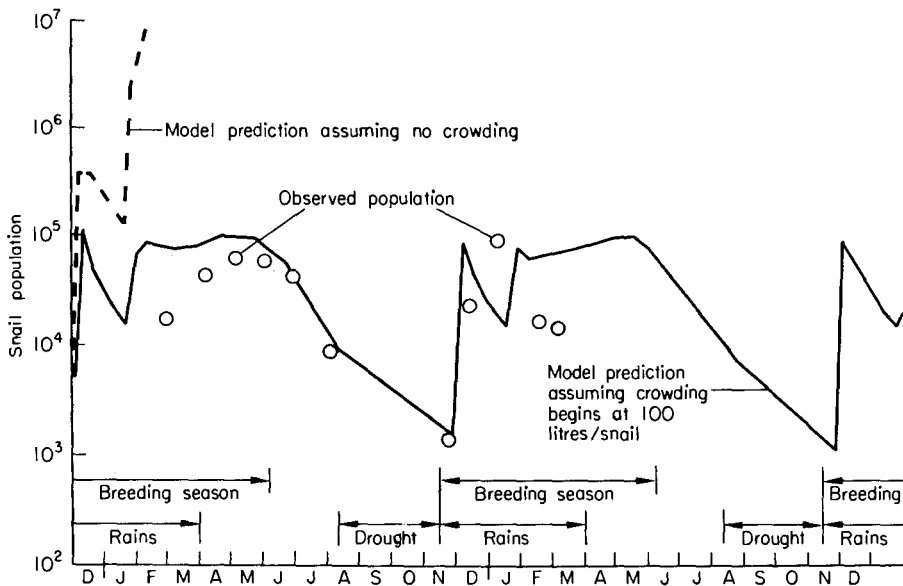In a simulation based on eq. (13.13), Jobin and Michelson (1967)

Fig. 13.7. Predictions (solid and dashed lines) of model for population of *Bulinus globosus* snails compared with field observations (open circles) from Foyle Pond. (From Jobin and Michelson, 1967, p. 661.)

treat the proportionality constant k as a function of the species and age of the snails, the nutritional value of food, and water temperature. Mortality is assumed to depend on demographic and ecological factors. The fecundity and mortality submodels are combined into difference equations whose trajectory is computed. The parameters are estimated from observations by another investigator of *Bulinus globosus*, a Rhodesian snail carrying *S. haematobium*. The model's predictions of snail populations agree roughly with censuses (Fig. 13.7). This study is an encouraging attempt to combine laboratory and field data (albeit from different snail species, since no one species has been studied comprehensively enough).

Sensitivity analysis of the sort discussed in section 13.4.2, with respect to both parameter values and the form of entire components of the model, has not been reported in this case. There is room for much useful work here.

13.6   Sex among the schistosomes

The preceding models describe either the human or the snail half of the schistosome life cycle, never both. A minimally realistic model of the entire life cycle must explicitly recognize that the worms reproduce sexually in people. The effect on egg output, and hence on transmission of infection, of one additional female worm in a person depends on the numbers of males and females already there and upon the mating system and success of worms in people.

Unfortunately, the sexual stage of schistosomes has yet to receive its Masters and Johnson. Mathematical models of mating functions quantify possibilities within the range of present ignorance. Three recent studies which cite earlier work are due to Leyton (1968), Nasell and Hirsch (1973), and Dietz (1975).

13.7   Life cycle models

A few models attempt to comprehend the entire schistosome life cycle.

13.7.1   *A life table model*

In Palo in the Philippines (Hairston, 1962, 1965a), the proportion of people infected with *S. japonicum* at each age changed very little from

1945 to 1959. Hence one suspects that the per capita risk of infection also changed very little over that period. Barring large changes in the human population, it follows that the total worm population must have been stationary (constant in total numbers and age structure). It is therefore appropriate to use a life table, the demographic model of a stationary population, to describe the population of *S. japonicum* there.

In this model, the net rate of reproduction R_o of the worm, previously defined in eq. (2.14), may be written as the product of four factors reflecting four major stages in the worm's life cycle:

Worm's R_o = (Larval R_o in snail) × (Cercariae's probability of infecting a mammal) × (Adult worms' R_o in mammal) × (Eggs' probability of infecting a snail). (13.14)

Hairston (1962) further decomposes each of these factors. For example, he represents the probability of an egg's infecting a snail (1962, p. 39) as the product of the probability that an egg is able to hatch times the probability that the egg is deposited near snails times the probability of penetrating a snail times the probability of establishing an infection in the snail after penetration.

Even the very extensive field data gathered in Palo are insufficient to estimate all the factors in eq. (13.14) directly. Hairston supplements the data with guesses (of the contribution of swamp rats to transmission, for example), assumptions [of a Poisson distribution of worms per person, for example, though a negative binomial distribution is more likely (Hairston, 1965a, p. 60)], and ingenuity.

For *S. japonicum*, Hairston's (1965a, p. 60) final estimate of the right side of eq. (13.14) is 0·6. Based on less reliable data from Egypt, his estimate for *S. mansoni* is 1·9 and for *S. haematobium* is 2·8. If Hairston's model and observations were correct, these estimates should be 1. That the estimates do not differ from 1 by orders of magnitude is an indication of the coherence of the observations and the approximate correctness of the model, under the given conditions.

Still, some qualifications deserve note.

First, although the age prevalence distribution remained nearly constant from 1945 to 1959, and hence probably also the per capita exposure, if the total human population increased over that period, the worm population may have also. But the rate of increase of the human population is likely to have been low, on the order of a few percent per year. So the deviation of the R_o of the worms from 1 was probably much less than the uncertainty of the data.

Second, the decomposition of the probability of transmission around the life cycle into the product of the probabilities of the elementary events which make up the life cycle implicitly assumes that the simple events may be treated as independent. Independence is so unlikely that Hairston (1962, 1965a) avoids making the assumption in practice by estimating from his data, not the elementary probabilities which appear in some of his formulas, but clusters of these factors representing compound events.

Third, since 'the parasite population is able to come into equilibrium at different rates of transmission' in different ecological settings, 'net reproduction in one or both of the hosts must be curtailed with increasing transmission and enhanced with decreasing transmission', and hence (Hairston, 1965a, pp. 46–47) 'there is a range of transmission rates over which compensatory mechanisms operate to keep the parasite population in equilibrium'. This means that if an intervention programme reduces one of the four factors on the right of eq. (13.14), over at least some range, the other factors on the right will not remain constant but will increase to keep the product near 1.

For example, increasing the number of female worms of *S. japonicum* present in a person of specified age decreases the average daily number of eggs in faeces per female worm (Fig. 13.8; Hairston, 1962). The egg counts are based on direct measurement. The numbers of female worms are estimated from the rates of acquisition of worms and from the death rates of female worms. [See Hairston (1965a, p. 54) for a minor correction of Hairston (1962, p. 54).] These rates are in turn estimated from age prevalence distributions. For each age group in Fig. 13.8, the point with the higher worm load is from data on Palo, while the point with the lower worm load is from a different, urban or coastal area with lower transmission. Since the abscissae are obtained so indirectly from different ecologies, there is much room for discussion of the exact slopes of the lines in Fig. 13.8. But the qualitative point is consistent with a variety of experimental evidence that increasing parasite loads decrease reproductive output per parasite (Kennedy, 1975).

This example illustrates one of several general compensatory mechanisms which parasites have evolved (Bradley, 1974) to regulate population numbers. As a result of such mechanisms, one cannot use Hairston's calculated values of the factors in eq. (13.14) in a simple-minded way when evaluating a control programme which affects the values of some of those factors.
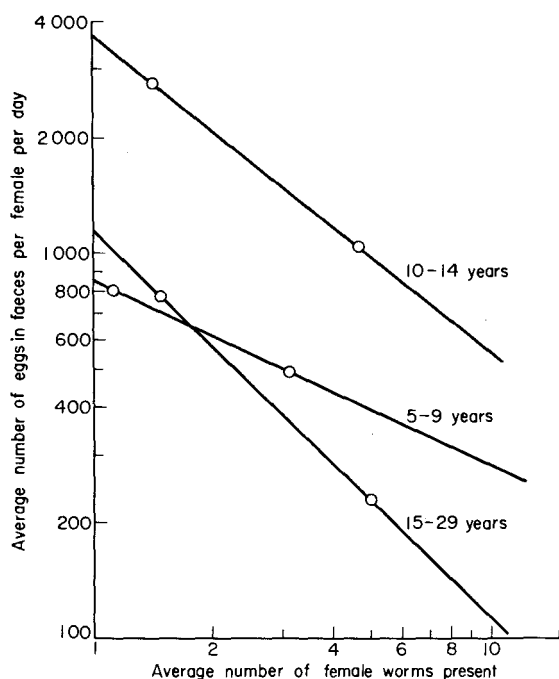
Fig. 13.8. Average daily egg output in faeces per female *S. japonicum* as a function of mean female worm load per person, in three age groups of people. Open circles estimated from data (see text); straight lines are simplest functions through two points. (From Hairston, 1962, p. 52.)

13.7.2   *Dynamic models*

Dynamic models, intended to describe what will happen when the life cycle is perturbed, attempt to represent these regulatory mechanisms and are therefore necessarily nonlinear. One such model (Macdonald, 1965) emphasizes the nonlinearity introduced by supposed monogamous mating in the sexual stage of the worms, and borrows other nonlinear bits from existing models of malaria.

Dynamic models examine the transient and asymptotic behaviour of indicators such as the mean worm load m in people or the fraction of people infected as functions of various parameters, like the probability that an egg reaches and infects a snail, the snail population, and the probability that a cercaria reaches and infects a person. Numerical analysis of one simple model (Macdonald, 1965) suggests the existence of a threshold in m. Once m is below this threshold,

transmission of infection disappears in a few years; once above it, infection remains endemic indefinitely.

All but the most sophisticated dynamic models (including Nasell and Hirsch, 1973 and Nasell, unpublished a) posit a single isolated endemic focus, closed against infection from without. When an external source of infection is considered (Nasell, unpublished b) the asymptotic or equilibrium behaviour of the mean worm load m in people changes qualitatively (see Fig. 13.9). Whereas previously the threshold switched m between a positive level of infection and $m = 0$, Fig. 13.9 shows that certain combinations of parameter values make possible a threshold which switches m between two positive levels; moreover, this threshold arises discontinuously as a function of other parameters.
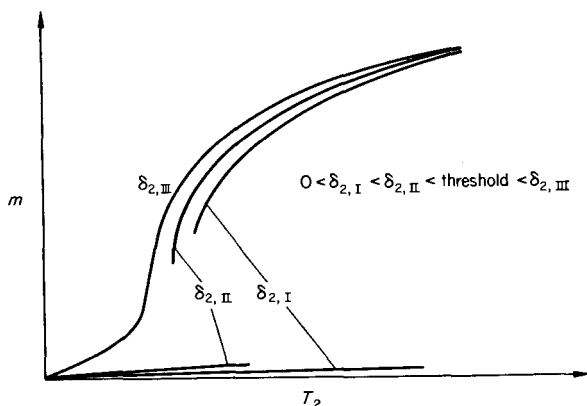

Fig. 13.9. Asymptotic or equilibrium mean worm load m in humans as a function of the amount of transmission T_2 of eggs from people to snails, for various external egg inputs δ_2 and fixed cercarial transmission capacity and fixed external input of cercariae. (Adapted from Nasell, unpublished b, p. 90.)

All the curves in Fig. 13.9 correspond to the same, fixed transmission capacity of cercariae from snails to people and the same, fixed external input of cercariae. The three curves correspond to different levels of external input δ_2 of eggs. The highest level of external egg input $\delta_{2,III}$ leads to a unique worm load as a function of the abscissa T_2, which measures the amount of transmission of eggs from people to snails (T_2 is proportional to the number N_1 of people). In this case the only way to lower m is to lower T_2, and the equilibrium m varies smoothly as T_2 varies. But for smaller values like $\delta_{2,I}$, $\delta_{2,II}$ of

external egg input which are below a certain threshold, m may fall either on the lower or on the upper curve. If m falls on the upper curve, then one strategy of control, as before, is to reduce T_2 and obtain a corresponding smooth reduction in m. A more dramatic possibility is to shift the initial conditions by coordinated programmes of human case finding and treatment so that m shifts to the lower line. Then, if it is still desirable, T_2 can be reduced further. Unfortunately, this possibility leaves the community vulnerable to transfer back to a higher m if an uncontrolled influx of infection effectively reverses the change in initial conditions.

A more detailed review of all these mathematical models of schistosomiasis appears in Cohen (1976). See also Hairston (1973).

13.8   A broader view

"N. A. Croll: Are definitive hosts always idiots?
J. C. Holmes: Definitive hosts are not idiots. Quite the contrary."
(Canning and Wright, 1972, pp. 148–49)

13.8.1   *The ecology of human host-parasite systems*

For concreteness, this chapter focuses on schistosomiasis. Other diseases, described by Crosby (1972), May (1958, 1961), Cockburn (1963), Van Oye (1964), Ford (1971), and, magnificently, Burnet and White (1972), deserve the same ecological approach. When descriptions revel mystically in the incomprehensible subtlety and unmanageable complexity of disease ecology, the success of simple models in schisto-somiasis should not be forgotten.

Some attempts to generalize about human host-parasite systems immediately formalize an image of the transmission of infection, without (at least until recently) overmuch attention to biological mechanisms (Bailey, 1957, whose new edition has recently appeared: 1975; Dietz, 1967; Crofton, 1971a, 1971b). Other attempts to elucidate classes of biological mechanisms (Bradley, 1974) are ripe for, but have yet to receive, adequate mathematical formalization; hence many implications of such attempts remain to be worked out.

In view of the generally primitive level of theoretical ecological understanding of human host-parasite systems, policies for public health which follow from models should probably be presented, not as

unconditional recommendations, but as proposals for experimental tests using the best field controls possible.

13.8.2 *Broader aspects of disease*

The models in this chapter describe the dynamics of infection. Infection is not tantamount to disease. Coping with disease requires, in addition to purely biomedical understanding, a grasp of its significant economic and social aspects.

For example, using quantitative models from economics and demography with extensive observations from St Lucia, a Caribbean island, Weisbrod *et al.* (1973) ask: Does infection cause disease? They find it impossible to evaluate the impact of *S. mansoni* on birth and death rates, the achievement of school children, and the labour productivity of adults without considering four intestinal nematodes of man which are also very widespread there. Throughout the poor countries of the world, most parasitized people are miniature ecosystems of multiple parasites which interact (see also Lehman *et al.*, 1970). Moreover, ecological alterations such as the damming of rivers, the construction of irrigation canals, and the resettlement of human populations into new lands have greatly increased opportunities in some regions for schistosome bearing snails to propagate and to contact people. Other quantitative approaches to evaluating economic and demographic effects of schistosomiasis are presented and cited by Cohen (1974, 1975) and Ansari and Junker (1969).

Because the real world seems painfully negligent of the boundaries between academic departments in universities, models which will be practically useful in coping with that world require an integration of ecology and of the biology of individuals with economics and sociology. The final chapter of this book explores such models.