Prediction of Schistosome Cercarial Shedding with a Physiological-Time Model*

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While making longitudinal observations on schistosome cercarial shedding, Pitchford and Visser found that there is an annual fluctuation in the minimum time for cercarial development, which is apparently related to temperature (1). Schistosome control strategy could be designed to take advantage of this fluctuation if it were predictable. Inspired by the successes of physiological time models ('heat-unit models') in predicting life-stage durations of various agricultural pests (2,3), we have developed a model of this type for the schistosomes. This model fits the data of Pitchford and Visser quite well. Coupled with recent temperature history and short term temperature forecast, it could be a useful tool for predicting the onset of cercarial shedding.

I. BASIC PHYSIOLOGICAL-TIME MODEL

Entomologists have for some time recognized the effects of ambient temperature on rates of development of insects in various life stages: several mathematical models to describe the relationship between temperature and development rate have been proposed (3). Perhaps the simplest of these models is based on the assumption that below a certain (threshold) temperature, development does not proceed at all and at higher temperatures the rate of development is directly proportional to the difference between actual ambient temperature and threshold temperature. Integrating this difference over time, therefore, we would obtain the model's prediction of the total progress of development. There are two ways to envisage this integral: (1) as an accumulation of heat, over time, or (2) as an accumulation of development time, with each time increment weighted appropriately with respect to temperature. The first interpretation led to the older label 'heat unit model' and the second to the more recent label 'physiological time model'.

Regardless of its label, the model has been quite successful in predicting development of various insect stages both under controlled laboratory conditions (2) and more recently in the field (4). In the light of this success, we decided to attempt to apply this concept to the development of schistosome cercariae.

Consider a cohort of miracidia that have invaded snails: before the members of this cohort ultimately emerge as cercariae, they must undergo a development process. If all parameters of the larval schistosomes' environment were constant, then one might also expect the maturation time to be relatively constant. Because of the homeostatic mechanisms of the snail host, most of the parameters of the internal milieu are buffered from the external environment and vary little, but the major exception is temperature as the snail is poikilothermic. We make the following assumptions:

1. that the observed variations in maturation time of schistosome larvae in snail hosts are the direct result of variations in ambient temperature patterns;
2. that maturation proceeds only when the ambient temperature exceeds a certain threshold, and when the temperature falls below this threshold the maturation process stops but does not reverse;
3. that when the temperature exceeds threshold, the maturation rate is directly proportional to the difference between the actual ambient temperature and the threshold;
that maturation must reach a threshold level for cercarial shedding to begin.

Thus we assume that the progress made towards initiation of shedding is directly proportional to a 'physiological time' variable measured in units of degree days. We denote the temperature threshold as \( \beta_1 \), the maturation threshold as \( \beta_0 \), the time of miracidia invasion of snail hosts as time 0. Let

\[
T(t) = \text{the temperature at time } t, \tag{1}
\]

\[
X(t) = \begin{cases} 1 & \text{if } T(t) \geq \beta_1, \\ 0 & \text{otherwise} \end{cases} \tag{2}
\]

\[
z(t) = \text{total maturation accumulated from time 0 to time } t, \tag{3}
\]

\[
x(t) = \text{amount of time between 0 and } t \text{ during which } T \geq \beta_1, \tag{4}
\]

\[t_* = \text{time of initiation of cercarial shedding.} \tag{5}\]

Then we have

\[
x(t) = \int_0^t X(\tau) \, d\tau, \tag{6}
\]

and

\[
z(t) = \int_0^t X(\tau) [T(\tau) - \beta_1] \, d\tau
= \int_0^t X(\tau) \, d\tau - \beta_1 \int_0^t X(\tau) \, d\tau
= \int_0^t X(\tau) \, d\tau - \beta_1 x(t). \tag{7}
\]

According to our assumptions, when \( z(t) \) reaches \( \beta_0 \), the shedding starts. Therefore,

\[
\beta_0 = z(t_*)
= \int_0^{t_*} X(\tau) \, d\tau - \beta_1 x(t_*). \tag{8}
\]

Let

\[
x(t) = \int_0^t X(\tau) T(\tau) \, d\tau, \tag{9}
\]

then

\[
\beta_0 = y(t_*) - \beta_1 x(t_*), \tag{10}
\]

or

\[
y(t_*) = \beta_0 + \beta_1 x(t_*). \tag{11}
\]

This, then, is our physiological-time model for schistosome larval stages in snail hosts. It has two parameters, \( \beta_0 \) and \( \beta_1 \). The first step in testing the potential use of this model is to determine how well it can be made to fit existing data by proper choice of the values of these two parameters. If, from available experimental data such as that of Pitchford and Visser, we have the time from snail penetration to initiation of shedding, the temperature history over that time, and an educated guess of the value of \( \beta_0 \), we can obtain \( y(t_*) \) and \( x(t_*) \).

Then we can treat equation (11) as a linear regression model and obtain a least-square estimator, \( \beta_0 \), for \( \beta_0 \). However, in this process a least-square estimator, \( \beta_1 \), for \( \beta_1 \) accompanies \( \beta_0 \) and this \( \beta_1 \) may not be the same as our initial guess of \( \beta_1 \). Then an iterative method can be used to obtain estimates of these threshold values for our model. Let

\[
b_0(0) \text{ be the initial guess of } \beta_0,
\]

\[
b_1(0) \text{ and } b_1(i) \text{ be the least square estimators for } \beta_0 \text{ and } \beta_1, \text{ respectively in the } i\text{th iteration},
\]

\[i = 1, 2, ..., n \]

\[n \text{ be the number of observations},
\]

\[
x_j \text{ be the value of } x \text{ of the } j\text{th observation},
\]

\[j = 1, 2, ..., n \]

\[
y_j \text{ be the value of } y \text{ of the } j\text{th observation},
\]

\[j = 1, 2, ..., n \]

\[x \text{ be the vector } [x_1, x_2, ..., x_n]^T,
\]

\[
y \text{ be the vector } [y_1, y_2, ..., y_n]^T.
\]

Note that \( x \) and \( y \) have to be calculated with a \( \beta_1 \) value given. Also let

\[
x_j(i) \text{ be the value of } x_j \text{ used in the } i\text{th iteration},
\]

\[i = 1, 2, ..., n \]

\[
y_j(i) \text{ be the value of } y_j \text{ used in the } i\text{th iteration},
\]

\[i = 1, 2, ..., n \]

\[
x(i) \text{ be } [x_1(i), x_2(i), ..., x_n(i)]^T, \text{ } i = 1, 2, ..., n
\]

\[
y(i) \text{ be } [y_1(i), y_2(i), ..., y_n(i)]^T, \text{ } i = 1, 2, ..., n
\]

Therefore, we start with an initial guess of \( \beta_0(0) \) and obtain \( x(1) \), \( y(1) \) to be used in the first iteration for obtaining \( \beta_0(1) \) and \( \beta_1(1) \). \( \beta_0(1) \) is then used to obtain \( x(2) \), \( y(2) \) which are later to be used in the second iteration to get \( \beta_0(2) \) and \( \beta_1(2) \), and so on. If this process converges for the data we use, it is stopped when certain preset conditions are met. Different rules can be applied. In the following two examples we stop the iteration when

\[
\beta_0(i) - \beta_0(i-1) \leq (1/100) \beta_0(i-1), \tag{12}
\]

\[
\beta_1(i) - \beta_1(i-1) \leq (1/100) \beta_1(i-1) \text{ } i > 1
\]

Notice that if the initial guess of \( \beta_1 \) (i.e., \( \beta_1(0) \)) and
PREDICTION OF SCHISTOSOME CERCARIAL SHEDDING

the first least square estimator of \( \beta_1 \) (i.e., \( \hat{\beta}_1(1) \)) both are no greater than the minimum observed temperature, then no further iteration is needed.

II. APPLICATION OF THE MODEL TO SCHISTOSOMA MANSONI

In this section, our model is applied to a set of data on the minimum cercarial incubation period of *Schistosoma mansoni* in snails of the species *Biomphalaria pfeifferi* (1). Batches of 30 new snails were exposed every two weeks to *S. mansoni* miracidia and the first cercarial sheddings recorded. We adopt the data for 24 snail cohorts for which corresponding weekly water temperature records are available. The temperature data reproduced in Figure 1 are taken from Figure 2 of reference (1).

We have \( n = 24 \). Assume that \( \beta_1 \) is any value below 14.00°C, which is the lowest temperature during the entire observation period. Then for each cohort, the \( X(t) = 1 \) throughout the period from time 0 to time \( t_s \). The calculated \( x(1) \) and \( y(1) \) are listed in Table I. Based on \( x(1) \) and \( y(1) \), the least square estimators \( \hat{\beta}_0(1) \) and \( \hat{\beta}_1(1) \) in equation (11) are

\[
\hat{\beta}_0(1) = 460.27,
\]

\[
\hat{\beta}_1(1) = 14.09. \tag{13}
\]

Since

\[
\begin{align*}
\beta_1(1) - \beta_1(0) &= 14.09 - 14.00 \\
&= 0.09 \\
&< (1/100) \beta_1(0),
\end{align*}
\]

we do not need to do any further iteration.

![Figure 1](image1.png)

**FIG. 1**
Weekly water temperature at 10 am in the area where shedding data were taken (reproduced from Fig. 2 of reference 1)

![Figure 2](image2.png)

**FIG. 2**
Observed (upper lines) and predicted (lower lines) minimum incubation periods for *S. mansoni*. Numbers on left give dates of infection for each pair of lines.
TABLE I

The values of \( J(1), y(1) \) for calibrating our model in the case of \( S. mansoni \)

<table>
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<th>( j )</th>
<th>( x(1) )</th>
<th>( y(1) )</th>
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</table>

We conclude that we can calculate \( X(t) \) using \( \beta_1 = 14.09 \). If \( T(t) \) is given, the beginning of cercarial shedding \( t_s \) can be calculated by solving

\[
460.27 = \int_0^t X(r) T(r) dr - 14.07 x(t). \tag{16}
\]

The observed minimum incubation periods and the predicted ones based on \( \beta_0, \beta_1 \) as given in equations (13) and (14) are shown in Table II and Figure 2. The average observed minimum incubation period is 62 days and the root mean square error of prediction is 10 days.

III. APPLICATION OF THE MODEL TO SCISTOSOMA HAEMATOBIIUM

The application of our model to the minimum cercarial incubation period data of \( S. haematobium \) (1) is illustrated in this section.

The water temperature data are the same as shown in Figure 1. In the period for which we have temperature data, 22 cohorts of 30 new snails \( B. physopsis \) were exposed every two weeks to \( S. haematobium \) miracidia and their minimum cercarial incubation periods have been recorded (1). Now \( n = 22 \). As in the preceding section, we try a first guess...
According to our stopping rule, we take

\[ \beta_1 = \beta_d(s) = 15 \cdot 30, \]  

and

\[ \beta_0 = \beta_d(s) = 442 \cdot 57. \]  

Thus, if \( T(t) \) is given, \( t_s \) for \( S. \) haematobium can be calculated by solving

\[ 442 \cdot 57 = \int_0^t X(r)T(r)dr - 15 \cdot 30 x(t_s). \]  

The observed minimum incubation periods and the predicted ones with \( \beta_0, \beta_1 \) as given in equations (31) and (30) are shown in Table IV and Figure 3. The average observed minimum incubation period is 90 days and the root mean square error of prediction is 24 days. Eighty-one per cent of the total square error is that of the first cohort.

Comparing equations (32) and (16), we notice that for \( S. \) haematobium the temperature threshold is slightly higher and the maturation threshold slightly lower than for \( S. \) mansoni.

IV. DISCUSSION

At first glance, Figures 2 and 3 indicate a reasonably good overall fit of our adaptation of the physio-

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**Table III**

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**Table IV**

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Fig. 3

Observed (upper lines) and predicted (lower lines) minimum incubation periods for S. haematobium. Numbers on left give dates of infection for each pair of lines.

(rms) error, confirms this subjective conclusion. In the case of S. mansoni, the rms error is 16 per cent of the mean observed value, while in the case of S. haematobium the rms error is 27 per cent of the mean observed value. By its very nature, rms error places disproportionate emphasis on large errors. For example, if the single entry corresponding to 4/7 in Figure 3 is removed, the rms error for S. haematobium is reduced from 27 per cent of the mean to 10 per cent of the mean. Examining the large error entries for both S. haematobium and S. mansoni, one finds that with the exception of that one 4/7 entry, the errors follow an interesting pattern: the model tends to overestimate minimum incubation time when incubation begins in a period of warm ambient temperatures, followed by a period of cold ambient temperatures; and it tends to underestimate minimum incubation time when incubation begins in a period of cold ambient temperatures, followed by a period of warm ambient temperatures. This may indicate that temperature is more important during early phases of development than during later phases. However, if we tried to include such effects in our model, the already large error in the 4/7 entry of Figure 3 would be further increased. It is interesting that the data for the 4/7 entry were taken by Pitchford and Visser for a single shedding snail, whereas the data for most entries were taken for at least ten shedding snails. Therefore, it is possible that the 4/7 entry data is anomalous.

V. CONCLUSION

Bearing the objective of control in mind, instead of modelling the entire transmission dynamics of schistosomiasis (see [5] to [10]) which would require a large-scale effort in field work to determine the parameters, we chose to model a single phase of the life cycle, where good data were already available. The simple model presented here is not intended to interpret the mechanisms underlying sporocyst development, but merely to predict the beginning of cercarial shedding by snails exposed to schistosome miracidia. Coupled with knowledge of the approximate size of a snail population, such predictions could be useful in the timing of control measures (for example one might wish to apply mollusicides just prior to a predicted large emergence of cercariae).

ACKNOWLEDGEMENTS

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REFERENCES


(Revised version received 19 January 1977)