Mosquito Host Choice and the Epidemiology of Malaria

Joel G. Kingsolver

American Naturalist, Volume 130, Issue 6 (Dec., 1987), 811-827.

Vol. 130, No. 6 The American Naturalist December 1987

MOSQUITO HOST CHOICE AND THE EPIDEMIOLOGY OF MALARIA

JOEL G. KINGSOLVER*

Graduate Program in Ecology and Evolutionary Biology, Division of Biology and Medicine, Brown University, Providence, Rhode Island 02912

Submitted May 20, 1986; Revised November 3, 1986, and February 9, 1987; Accepted April 17, 1987

Various mathematical models have been developed to describe the interactions of mosquito vectors, vertebrate hosts, and malarial parasites. Of particular interest is the identification of factors that enable the stable persistence of the parasite in the host population and that determine the trajectories and equilibrium levels of infection in the hosts and vectors. These models generally assume that mosquitoes choose and feed on hosts irrespective of the absence or presence of infection in the hosts (for a review, see Aron and May 1982).

In fact, several recent lines of evidence suggest that mosquitoes do not feed randomly with respect to host infection. Nonrandom feeding may be expressed at three different stages: attraction and penetration, probing and the location of blood, and blood intake (Edman et al. 1985). In paired-choice laboratory experiments, mosquitoes preferentially fed on malaria-infected rather than control (uninfected) mice; this preference was strongest when the gametocytic form of the parasite (the infective stage for the mosquito vector) was most prevalent (Day and Edman 1983; Day et al. 1983). A related study (Mahon and Gibbs 1982) with hens infected with arbovirus shows that mosquitoes preferentially bit infected rather than control hens and were preferentially attracted to infected hens even in situations where they were prevented from actual biting (see also Turell et al. 1984). Similarly, lambs infected with Rift Valley fever virus were fed on more frequently by mosquitoes than were uninfected lambs; and the frequency of mosquito bites was positively correlated with the body temperature of infected lambs (Turell et al. 1985).

Other evidence indicates that parasitic infections in hosts can affect blood location and blood intake. For example, the mean duration of probing (blood location) for *Aedes aegypti* mosquitoes feeding on mice was reduced by at least 1 min when the mosquitoes fed on malaria-infected or arbovirus-infected mice rather than uninfected mice (Rossignol et al. 1985). Similar results have also been reported for trypanosomiasis and tsetse flies (Jenni et al. 1980; but see Moloo and Dar 1985). In addition, a theoretical analysis of optimal feeding behavior and the

* Present address: Department of Zoology, NJ-15, University of Washington, Seattle, Washington 98195.

Am. Nat. 1987. Vol. 130, pp. 811–827.

mechanics of blood sucking indicates that mosquitoes may maximize their rates of protein intake during feeding by choosing human hosts with blood hematocrits of 0.3, a level commonly found in malaria-infected hosts (Daniel and Kingsolver 1983, MS; but see Kesavan and Reddy 1985). All these results suggest that mosquitoes may preferentially choose hosts on the basis of host infection. Such behavior could in turn affect the patterns of malarial transmission. Effects of vector behavior (see, e.g., Ribeiro et al. 1984; Rossignol et al. 1984, 1986; Molyneux and Jeffries 1986) and of host infection on host behavior (reviewed in Dobson 1988) have also been reported but are not considered here.

The purpose of the present study is to develop and analyze a simple model for the dynamics of malarial transmission that incorporates nonrandom feeding behavior by the mosquito vector. The results show that such behaviors can quantitatively and qualitatively alter the conditions for the existence, stability, and levels of infection at equilibrium; the results also suggest that such feeding behavior must be studied in greater detail if we are to understand the dynamics of malarial infection.

THE MODEL

General Formulation

The model is a straightforward extension of the Ross-Macdonald (here called R-M) model for the dynamics of malarial infection (Ross 1911; Macdonald 1952, 1957, 1973). The principal variables of interest are the infected proportions of the human host populations (x) and of the mosquito vector population (y). The basic model may be written as a coupled pair of ordinary differential equations describing the time course of x and y:

$$dx/dt = ky\beta_u(x)M/N - rx , \tag{1}$$

$$dy/dt = \beta_i(x)(1 - y) - \mu y , \tag{2}$$

where N is the size of the human population; M is the size of the female mosquito population; $m = M/N$ is the number of female mosquitoes per human host; k is the proportion of infected bites on human hosts that produce an infection; $\beta_i(x)$ and $\beta_u(x)$ are functions describing the rates of biting per female mosquito on infected and uninfected hosts, respectively; r is the per capita rate of recovery for human hosts; and μ is the per capita mortality rate for mosquitoes.

Aron and May (1982) have discussed the many limitations of this simple model, including constant human and mosquito population size and mortality rate; the lack of a distinction between different developmental stages of the parasite; and the lack of induced immunity or host mortality. Nevertheless, the model has proved useful in describing the important aspects of the transmission process.

In the R-M model, the biting-rate functions take a simple form:

$$\beta_i(x) = Bx , \tag{3}$$

$$\beta_u(x) = B(1 - x) , \tag{4}$$

where B is the total rate of biting per unit of time [$B = \beta_i(x) + \beta_u(x)$]. In this formulation, bites are distributed between infected and uninfected hosts according to their relative abundances; that is, mosquitoes are assumed to choose hosts at random.

One principal result from analysis of the R-M model is the identification of a parameter (R) that governs the model's behavior. Thus, when

$$R \equiv kmB^2/\mu r > 1 , \tag{5}$$

an infection will persist and lead to a stable equilibrium at which an infection is maintained in both the host and vector populations. Conversely, if $R < 1$, any infection will die out, and the uninfected equilibrium point ($\hat{x} = 0, \hat{y} = 0$) is stable. R, often called the net reproductive (or net replacement) rate of the parasite, occurs in many epidemiological models (Bailey 1982; Levin et al. 1982).

My purpose is to introduce biting-rate functions, $\beta_i(x)$ and $\beta_u(x)$, that describe nonrandom host choice by the mosquito with respect to host infections and to examine the consequences of such behaviors for the dynamics of infection. By "nonrandom" I mean any aspect of the vector's behavioral interaction with the host or environment that produces a biting-rate function not described by equations (3) and (4). I consider three types of nonrandom host choice: (1) a consistent preference for infected hosts at all levels of host infection; (2) a switching behavior in which the preference depends on the relative abundance of infected and uninfected hosts; and (3) an increasing preference for the host as the level of host infection increases. To allow direct comparison with the R-M model, I assume in each case that the total biting rate on hosts is a constant B. This assumption implies that the host density is sufficiently large for both infected and uninfected host types to be readily available to a searching mosquito. In the analysis that follows, it is assumed that $0 \le x \le 1$, $0 \le y \le 1$, and all model parameters are positive.

Consistent Host-Preference Model

A simple function that describes a consistent preference for infected hosts is

$$\beta_i(x) = B(1 - e^{-cx}) , \tag{6}$$

$$\beta_u(x) = B - \beta_i(x) = Be^{-cx} , \tag{7}$$

where c is a positive constant that reflects the intensity of the preference: increasing c increases the biting rate on infected hosts at all values of x (fig. 1). The parameter c must be chosen such that $\beta_i(x)$ approaches B as x approaches 1. Equations (6) and (7) have the drawback that $\beta_i(x)$ approaches B only asymptotically, such that $\beta_i(1) = B$ only when $c = \infty$ (but see eqs. 13, 14). However, this does not affect the qualitative behavior of the resulting model except when an equilibrium point lies very near $x = 1$.

The system of equations (1) and (2) can then be written

$$dx/dt = Bkmye^{-cx} - rx , \tag{8}$$

$$dy/dt = B(1 - e^{-cx})(1 - y) - \mu y . \tag{9}$$

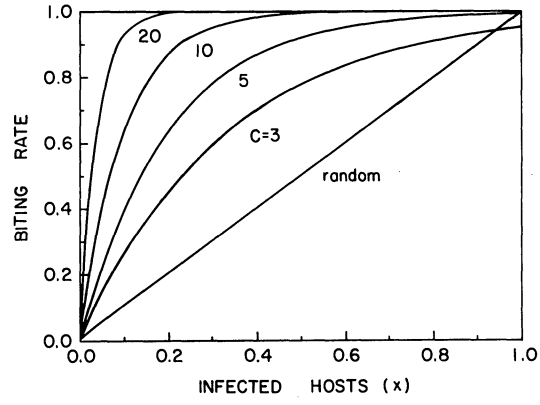

FIG. 1.—The biting-rate function on infected hosts [$\beta_i(x)$, standardized to a total biting rate $B = 1$] as a function of the infected proportion of the host population (x), for the consistent-preference model for several different values of preference, c. The biting function for random host choice is also given.

Consider the y null-cline, along which $dy/dt = 0$, and the x null-cline, along which $dx/dt = 0$. The x null-cline is given by

$$f_x(x) = \frac{rx}{kmBe^{-cx}} = y , \tag{10}$$

and the y null-cline is given by

$$f_y(x) = \frac{B(1 - e^{-cx})}{\mu + B(1 - e^{-cx})} = y . \tag{11}$$

The following results apply.

1. Both $f_x(x)$ and $f_y(x)$ are nonnegative, increasing functions of x.
2. $f_x(x)$ is convex ($d^2[f_x]/dx^2 > 0$), whereas $f_y(x)$ is concave ($d^2[f_y]/dx^2 < 0$).
3. The point ($\hat{x} = 0$, $\hat{y} = 0$) is always an equilibrium point (here termed the zero, or uninfected, equilibrium).
4. Given results 1–3 above, the condition for a second, nonzero equilibrium is given by

$$R_1 \equiv ckmB^2/\mu r > 1 . \tag{12}$$

This is easily obtained by considering the initial slopes of the two null-clines (see Aron and May 1982).

5. Local-stability analysis (see the Appendix) shows that the uninfected equilibrium (0,0) is locally stable if and only if $R_1 < 1$. Thus, the uninfected equilibrium is stable when it is the only equilibrium point and unstable when a second, nonzero equilibrium exists.

6. Phase-plane analysis shows that the nonzero equilibrium is globally stable when it exists (fig. 2).

These qualitative features of equilibrium and stability for the preference model

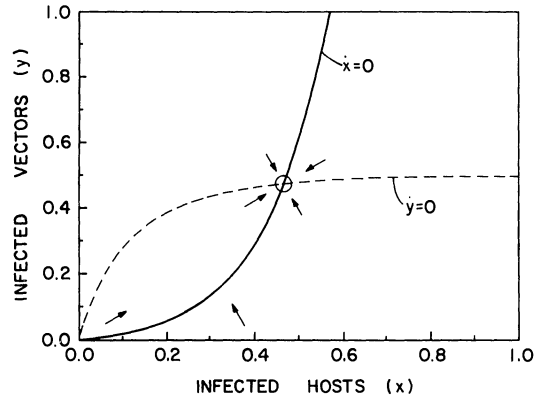

FIG. 2.—Phase-plane plot of the infected proportion of the vector population (y, vertical axis) and the host population (x, horizontal axis) for the consistent-preference model. *Solid line*, x null-cline ($\dot{x} = 0$); *dashed line*, y null-cline ($\dot{y} = 0$). The nonzero equilibrium point is circled. *Arrows*, Vectors indicating the direction of change in the phase plane; all trajectories lead to the nonzero equilibrium. Parameter values: $B = 10$, $km/r = 1$, $\mu = 10$, $c = 5$.

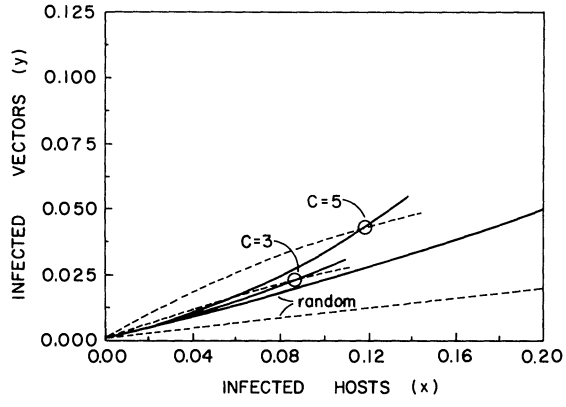

FIG. 3.—Phase-plane plot as in figure 2. The x null-clines ($\dot{x} = 0$, *solid lines*) and y null-clines ($\dot{y} = 0$, *dashed lines*) are given for several different values of preference, c, and for the random-choice model. For the random-choice model, there is no nonzero equilibrium; as preference increases, a stable nonzero (infected) equilibrium point appears (circled). Parameter values: $B = 10$, $km/r = 0.5$, $\mu = 100$.

are similar to those of the original R-M model. One important difference is in the conditions for the existence of the stable infection in the host and vector populations (eqs. 5, 12). The condition R_1 for stable infection for the host-preference model is simply $R_1 = cR$, where R is the equivalent condition for stable infection for the random-biting (R-M) model. Thus, increasing preference for infected hosts increases the ability to allow a stable equilibrium infection. This is illustrated in figure 3. Here, under random biting there is no nonzero equilibrium; as host

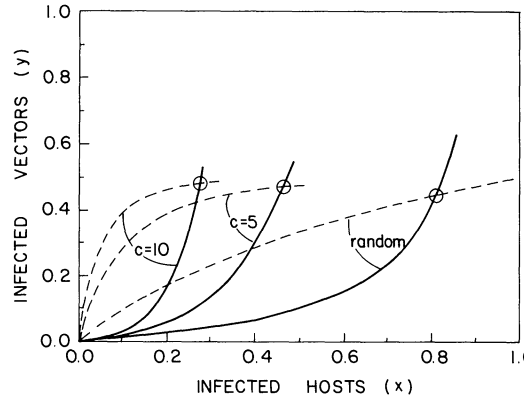

FIG. 4.—Phase-plane plot as in figure 2. The x null-clines ($\dot{x} = 0$, *solid lines*) and y null-clines ($\dot{y} = 0$, *dashed lines*) are given for several different values of preference, c, and for the random-choice model. The nonzero equilibrium in each case is circled. As preference increases, the equilibrium level of infection in the host population decreases. Parameter values: $B = 10$, $km/r = 1$, $\mu = 10$.

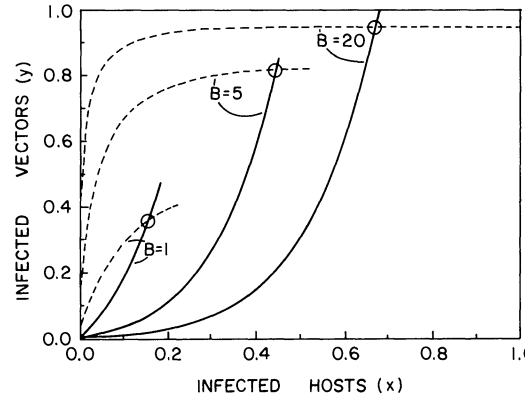

FIG. 5.—Phase-plane plot as in figure 2. The x null-clines ($\dot{x} = 0$, *solid lines*) and y null-clines ($\dot{y} = 0$, *dashed lines*) are given for several different values of total biting rate, B. The nonzero equilibrium point for each case is circled. As biting rate increases, the equilibrium levels of infection in the host and vector populations increase. Parameter values: $km/r = 1$, $\mu = 1$, $c = 5$.

preference (c) increases, a stable nonzero equilibrium point appears, and the equilibrium values of infection in the host and vector populations increase.

The equilibrium level of infection in the vector population always increases as preference increases (figs. 3, 4). However, the equilibrium infection level in the host population can either increase (fig. 3) or decrease (fig. 4) with increasing preference. By contrast, increasing the total biting rate B always increases the equilibrium infection level in the host in both the R-M and the preference models (fig. 5). Thus, biting rate and host preference may have different effects on the level of host infection.

I have also considered a quadratic form for the consistent-preference biting-rate function:

$$\beta_i(x) = B\left[\frac{Px}{1 + (P - 1)x}\right], \tag{13}$$

$$\beta_u(x) = B\left[1 - \frac{Px}{1 + (P - 1)x}\right]. \tag{14}$$

Here P denotes the preference for infected hosts: for $P = 1$, the model is identical to the R-M model (random host choice); and there is increasing preference as P increases above one. Note that $\beta_i(x) = B$ when $x = 1$ for any value of P. By an analysis analogous to the above, it can be shown that the above results 1–6 apply for this quadratic biting function, where P replaces c in equation (12).

In fact, these results appear to be quite general. Consider a generalized biting function with the following properties:

$$0 \leq \beta_i(x) \leq B\,, \qquad \beta_i(0) = 0\,, \qquad \beta_i(1) = B\,,$$
$$d[\beta_i(x)]/dx \geq 0\,, \qquad d^2[\beta_i(x)]/dx^2 \leq 0\,.$$

For many classes of functions with these properties, the qualitative results 1–3, 5, and 6 hold (see the Appendix).

Switching-Behavior Model

I now consider host-choice behavior in which preference depends on the relative abundance of infected and uninfected hosts: uninfected hosts are preferred at relatively low levels of infected hosts, whereas infected hosts are preferred at relatively high levels. The host-infection level at which the preference switches is called the switch point. A simple biting function that exhibits this behavior is

$$\beta_i(x) = \frac{B(1 - e^{-cx})}{1 + ae^{-cx}}\,, \tag{15}$$

$$\beta_u(x) = B - \beta_i(x) = \frac{(a + 1)Be^{-cx}}{1 + ae^{-cx}}\,, \tag{16}$$

where a, c, and B are positive constants. The parameters a and c must be chosen so that $\beta_i(x)$ approaches one as x approaches one. The parameter a affects the position of the switch point (fig. 6*A*), and c affects both the switch point and the rate at which the switch occurs (fig. 6*B*). Equations (15) and (16) have the same drawback as equations (6) and (7): $\beta_i(1) = B$ only when $c = \infty$ (but see eq. 24 for an alternative). Again, this does not affect the qualitative behavior of the resulting model except when an equilibrium point lies very near $x = 1$.

For the switching biting functions (eqs. 15, 16), the model becomes

$$\frac{dx}{dt} = \frac{(a + 1)kmBye^{-cx}}{1 + ae^{-cx}} - rx\,, \tag{17}$$

$$\frac{dy}{dt} = \frac{B(1 - e^{-cx})(1 - y)}{1 + ae^{-cx}} - \mu y\,. \tag{18}$$

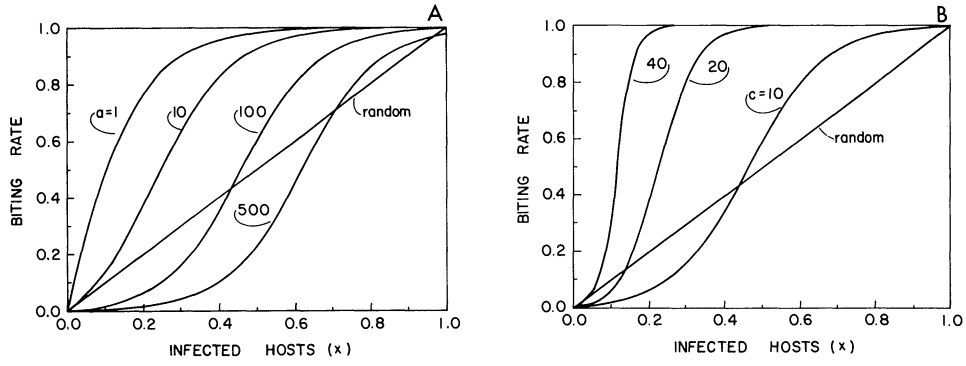

FIG. 6.—The biting-rate function on infected hosts [$\beta_i(x)$, standardized to a total biting rate $B = 1$] as a function of the infected proportion of the host population (x) for the switching-behavior model. The biting function for random host choice is also given. *A*, Biting functions for several different values of a, where $c = 10$. Increasing a increases the switch point of preference. *B*, Biting functions for several different values of c, where $a = 100$. Increasing c decreases the switch point and increases the rate at which switching occurs.

As before, we can find the x null-cline [$f_x(x)$] and y null-cline [$f_y(x)$]:

$$f_x(x) = y = \frac{rx(1 + ae^{-cx})}{Bkm(a + 1)e^{-cx}} \tag{19}$$

$$f_y(x) = y = \frac{B(1 - e^{-cx})}{\mu(1 + ae^{-cx}) + B(1 - e^{-cx})} . \tag{20}$$

The following results then apply.

1. The null-clines are both nonnegative, increasing functions of x.
2. The x null-cline is convex ($d^2(f_x)/dx^2 > 0$).
3. The y null-cline is sigmoid when

$$\beta_i(x) \to 1 \quad \text{as} \quad x \to 1 \tag{21}$$

and

$$c + 2B < 2a\mu . \tag{22}$$

Note that condition (21) is required for any biologically meaningful biting function.

4. The point ($\hat{x} = 0$, $\hat{y} = 0$) is always an equilibrium point, called the zero or uninfected equilibrium.

5. Given results 1–4 above, analysis of the initial slopes of the null-clines gives a condition for the existence of nonzero (infected) equilibrium point(s). If

$$R_2 \equiv cB^2km/\mu r(a + 1) > 1 , \tag{23}$$

then there is one (and only one) nonzero equilibrium point (fig. 7*A*). If $R_2 < 1$, there are either zero or two nonzero equilibrium points (figs. 7*B*,*C*).

6. Local stability analysis (Appendix) shows that the uninfected equilibrium

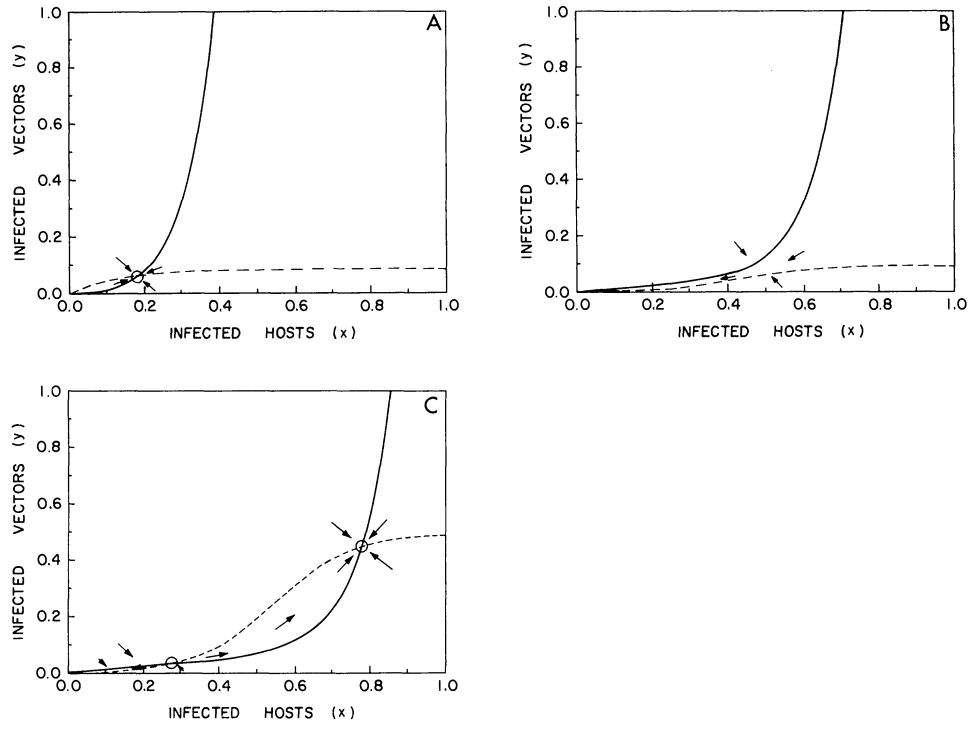

FIG. 7.—Phase-plane plot of the infected proportions of the vector population (y, vertical axis) and the host population (x, horizontal axis) for the switching-behavior model. The x null-cline ($\dot{x} = 0$, *solid lines*) and y null-cline ($\dot{y} = 0$, *dashed lines*) are given; nonzero equilibrium points are circled. *Arrows*, Vectors indicating the direction of change in the phase plane. *A*, A single, stable, nonzero equilibrium point, to which all trajectories lead. Parameter values: $B = 10$, $km/r = 1$, $c = 10$, $\mu = 100$, $a = 1$. *B*, No nonzero equilibrium exists, and all trajectories lead to the stable , uninfected (zero) equilibrium. Parameter values: $B = 10$, $km/r = 1$, $c = 10$, $\mu = 100$, $a = 100$. *C*, The upper nonzero equilibrium is locally stable. The lower nonzero equilibrium is unstable; trajectories below and to the left of this equilibrium lead to the zero (uninfected) equilibrium, which is locally stable. Parameter values: $B = 10$, $km/r = 1$, $c = 10$, $\mu = 10$, $a = 500$.

is stable if and only if $R_2 < 1$. Thus, the uninfected equilibrium is stable either when it is the only equilibrium point (fig. 7*B*) or when there are two nonzero equilibria.

7. Phase-plane analysis shows that when there is one nonzero equilibrium point, it is globally stable (fig. 7*A*). When there are two nonzero equilibria, the upper equilibrium is locally stable and the lower equilibrium is unstable (fig. 7*C*).

Thus, there are several important differences between the switching-behavior and the consistent-preference models. The conditions for instability of the uninfected equilibrium for the switching model (R^2, eq. 23) are different from those for the preference model (R_1, eq. 12); under equivalent situations, $R_2 = R_1/(a + 1)$. Thus, as the location of the switch point increases (fig. 6), it is increasingly easier

for the zero equilibrium to remain stable. Unlike the stability of the uninfected equilibrium for the preference model, that for the switching model need not imply that a stable infection cannot be maintained: multiple stable equilibria are now possible.

The phase-plane analyses for the three-equilibria situation (1 zero equilibrium + 2 nonzero equilibria) show that, in a region of state space that is below the lower, unstable nonzero equilibria, trajectories lead to the uninfected (stable) equilibrium; above this region, trajectories lead to the higher, nonzero (stable) equilibrium (fig. 7*C*). Thus, the qualitative outcome of the dynamics depends on the initial levels of infection in the host and vector populations.

An alternative biting function that exhibits switching behavior is

$$\beta_i(x) = B\left[\frac{P_1 x}{1 + (P_1 - 1)x}(1 - x) + x\frac{P_2 x}{1 + (P_2 - 1)x}\right]. \tag{24}$$

In contrast to equation (15), equation (24) has the desirable property that $\beta_i(1) = B$ for any realistic values of P_1 and P_2. Simulations suggest that equation (24) leads to qualitative model behavior similar to that for equation (15), but the model incorporating equation (24) is more difficult to examine analytically.

Increasing-Host-Preference Model

Here I briefly consider a biting-rate function in which the degree of preference increases with an increasing level of host infection:

$$\beta_i(x) = B\left[x(1 - x) + \frac{Px^2}{1 + (P - 1)x}\right] \tag{25}$$

$$\beta_u(x) = B\left[1 - x(1 - x) - \frac{Px^2}{1 + (P - 1)x}\right]. \tag{26}$$

As with the consistent-preference model described by equations (13) and (14), here for $P = 1$, the model is identical to the R-M model, and increasing P indicates an increasing preference for infected hosts. For equations (25) and (26), however, biting is essentially random (i.e., $\beta_i(x) \simeq Bx$) for low levels of host infection, but there is an increasing preference for infected hosts as host infection increases (fig. 8*A*).

When this biting-rate function is incorporated into equations (1) and (2), the following results are obtained. (1) The null-clines are both nonnegative, increasing functions of x. (2) The uninfected equilibrium ($\hat{x} = 0, \hat{y} = 0$) always exists, and it is locally stable if and only if

$$R \equiv kmB^2/\mu r < 1 . \tag{27}$$

Other aspects of the model's behavior are difficult to examine analytically. Simulation results show, however, that this model exhibits the same three qualitative behaviors as the switching-behavior model, which are described by results 6 and 7 above and by figure 7. In particular, under some conditions for the increasing-host-preference model, a locally stable, uninfected equilibrium occurs simul-

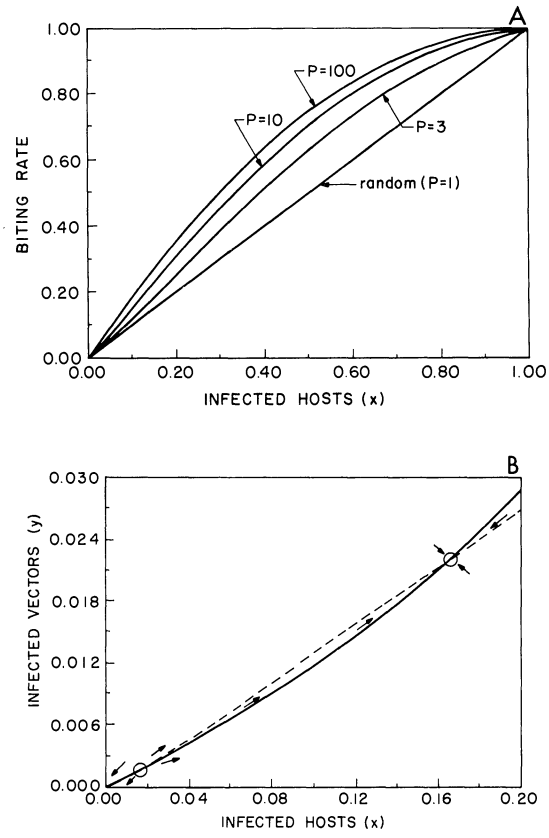

FIG. 8.—The increasing-preference model. *A*, The biting-rate function on infected hosts [$\beta_i(x)$, standardized to a total biting rate $B = 1$] as a function of the infected proportion of the host population (x) for several different values of preference, P. *B*, Phase-plane plot of the infected proportions of the vector population (y, vertical axis) and host population (x, horizontal axis). The x null-cline ($\dot{x} = 0$, *solid line*) and y null-cline ($\dot{y} = 0$, *dashed line*) are given; the nonzero (infected) equilibrium points are circled. *Arrows*, Vectors indicating the direction of change in the phase plane. In this case, the upper nonzero equilibrium point is locally stable. The lower nonzero equilibrium point is unstable; trajectories below and to the left of this point lead to the zero (uninfected) equilibrium point, which is locally stable. Parameter values: $P = 10$, $B = 10$, $km/r = 1$, $\mu = 110$; hence, $R < 1$.

taneously with a locally stable, infected equilibrium, separated by an unstable, infected equilibrium point (fig. 8*B*).

Note that the condition for stability of the uninfected equilibrium in this model (eq. 27) is identical to that in the R-M model (eq. 5); this reflects the random host choice in both models as x approaches zero. The most important result, however, is that multiple stable equilibria can occur for both the increasing-preference and the switching-behavior models. It appears that such behavior is the result of an inflection point in the biting-rate function.

DISCUSSION

Current empirical evidence for biting preference by mosquitoes with respect to infection in their hosts is limited to a few laboratory experiments (see the introduction). How such preferences might translate into differential biting rates on infected and uninfected hosts under natural conditions is currently unknown. Until such information is available, it seems unwise to consider models that are more realistic (and less analytically tractable) than the simple extensions of the Ross-Macdonald model developed here. Instead, I have focused on how aspects of nonrandom host choice might affect qualitative aspects of the interaction of human hosts and mosquito vectors in determining levels of malarial infection.

Because no relevant field data are currently available, the plausibility of the different biting-rate functions remains unknown. The laboratory results cited in the introduction suggest that preferential biting on infected hosts can occur at least when the relative densities of infected and uninfected hosts are similar; this is the basis for the consistent-preference model. Data relevant to the increasing-preference and switching models are not available for biting preferences at low relative densities of infected hosts. Note that Mahon and Gibbs (1982) showed that mosquitoes are preferentially attracted to infected hosts even when biting does not occur. Thus, mosquitoes need not directly assess the prevalence of infection in the host population in order for preference to increase with prevalence, as required by the increasing-preference and switching models. For example, an increasing-preference biting function could result from a preferential attraction to infected hosts coupled with a "giving-up time," whereby the mosquito would bite the next host encountered if it did not encounter an infected host within a certain search period. In many insects, such a giving-up time requires only that feeding behavior be influenced by hunger level, as detected, for example, by stretch receptors in the gut (Dethier 1976). Such changes in preference associated with giving-up times have been well documented for insects among parasitoids (reviewed in Van Alphen and Vet 1986), herbivores (reviewed in Rausher 1983), and generalist predators (see Murdoch 1969). No current data suggest a preference for uninfected hosts when their numbers are few, as required for the switching model. The switching model is included here for completeness because such switching behavior is commonly observed in insects (Murdoch 1969; Cornell and Pimentel 1978; Rausher 1978; Heinrich 1979; Prokopy et al. 1982). The important point is that the increasing-preference and switching models lead to qualitatively identical results.

I emphasize that the biting-rate functions explored in this paper are a phenomenological description of the outcome of a complex feeding process involving habitat choice, attraction, defensive behavior of the host, probing and blood location, blood intake, and parasite transmission (Edman et al. 1985). I have discussed these biting-rate functions in the context of behavioral choice by individual mosquitoes, but other processes could generate such biting functions. For example, functions like those of the increasing-preference or the switching model might also occur as a result of nonrandom host distribution and vector aggregation (Hassell 1978). A more complete model should include a mechanistic description

of each stage of the feeding process (Ribeiro et al. 1985) incorporated into the vector-host-parasite interactions.

A consistent preference for infected hosts does not alter the basic properties of the system, relative to random host choice: there is only one stable equilibrium at any time, and a single condition (eq. 5 or eq. 12) governs whether the stable equilibrium is the zero (uninfected) or nonzero (infected) equilibrium. Increasing the strength of the consistent preference does make it easier to maintain a stable infection in the host population and increases the equilibrium level of infection in the vector population. However, increasing the strength of the consistent preference increases the equilibrium level of infection of the host population when the equilibrium value is small but decreases the equilibrium level when the equilibrium value is larger. It appears that when levels of host infection are low, preference for infected hosts results in a sufficient number of bites on infected hosts to increase the infection level of vectors and allow a stable infected equilibrium. When levels of host infection are higher, however, preference results in most of the bites occurring on infected hosts, and host infection spreads only when infected vectors bite uninfected hosts.

Both the increasing-preference and the switching-behavior models, in which preference for infected hosts increases as the levels of host infection increase, can lead to qualitatively different system behaviors. If $R_2 > 1$ ($R > 1$ for the increasing-preference model), the results obtained are similar to those for the consistent-preference models (where $R_1 > 1$). For $R_2 < 1$ ($R < 1$ for the increasing-preference model), however, stable equilibria might occur simultaneously at both zero (uninfected) and nonzero (infected) levels. In this case, the state space is divided (by a separatrix) into a lower region, in which trajectories lead to the uninfected state, and an upper region, in which trajectories lead to a high and stable infection level. This sort of dynamic behavior commonly occurs in models of predator-prey systems in which the predator exhibits changes in preference or aggregation behavior (e.g., Hassell 1978); this behavior also occurs in some other epidemiological models (see Bailey 1982; Nåsell 1985). In the present context, such behavior would mean that random perturbations could lead to erratic changes between high, persistent levels of host infection and the elimination of the infection.

Unlike the criteria for the Ross-Macdonald model, the criteria for determining the existence and stability of infected equilibria in these nonrandom feeding models can no longer be easily interpreted as the net reproductive rate of the parasite. For the increasing-preference and the switching-behavior models, a stable infection can be maintained in certain circumstances whether R (or, for switching, R_2) is greater than or less than one. Furthermore, for the consistent-preference model, increasing values of R_1 often decrease the equilibrium levels of host infection.

These results demonstrate that nonrandom host choice by mosquitoes with respect to host infection could have important quantitative and qualitative effects on the dynamics of malarial infection. Further laboratory and field studies of host choice that allow the estimation of the biting-rate functions $\beta_i(x)$ and $\beta_u(x)$ are now needed to evaluate whether such effects are important in natural populations.

SUMMARY

Several recent studies have demonstrated that blood-sucking mosquitoes may preferentially choose hosts infected with malarial parasites. I developed and analyzed a simple model for the dynamics of malarial transmission that incorporates such nonrandom feeding behavior by the mosquito. The dynamic variables of interest are the infected proportions of the human host and mosquito vector populations. I considered three types of nonrandom host choice: consistent preference for the infected host at all levels of host infection; increasing preference for infected hosts as the infection level of the host increases; and a switching behavior in which the mosquito switches preference from uninfected to infected hosts as the level of host infection increases. The results were compared with previous results from models with random host choice.

Both the random-choice and consistent-preference models predict either a stable uninfected state or a stable persistence of the infection. For these models, increasing consistent host preference makes it easier to maintain a stable infection, relative to the random-choice model. However, increasing the strength of consistent host preference can either increase or decrease the equilibrium level of infection in the host population. The increasing-preference and switching-behavior models can produce model behavior in which there are two stable equilibria: one at the uninfected state; the other at a high level of host infection. In this case, the outcome of the malaria dynamics depends on the initial levels of infection in the host and vector populations. These results show that nonrandom host choice can have important quantitative and qualitative effects on the epidemiology of malarial transmission, suggesting that further study of such mosquito feeding behavior is warranted.

ACKNOWLEDGMENTS

A. R. Wait contributed to early modeling efforts on this project. T. Banks, G. Byers, T. Daniel, J. Edman, P. Kareiva, K. Dietz, G. Odell, J. Ribeiro, P. Rossignol, and two anonymous reviewers improved the manuscript and/or provided useful discussion. My special thanks to Professor Dietz for suggesting equations (13), (24), and (25), especially the increasing-preference function (eq. 25). This research was supported in part by National Science Foundation grant BSR8600485.

APPENDIX

GENERAL FORMULATION

For convenience, let $\beta_i(x) \equiv \beta$ and $\beta_u(x) \equiv B - \beta$. Assume that β is a continuous, nonnegative, increasing function of x on $0 \leq x \leq 1$, with $\beta = 0$ at $x = 0$. Let β' and β'' represent the first and second derivatives, respectively, of β with respect to x. Then the model can be written in the form

$$dx/dt = kmy\,(B - \beta) - rx\,, \tag{A1}$$

$$dy/dt = \beta(1 - y) - \mu y\,. \tag{A2}$$

The x null-cline, $f_x(x)$, and the y null-cline, $f_y(x)$, can be written as

$$f_x(x) = y = rx/km(B - \beta) \tag{A3}$$

$$f_y(x) = \beta/(\mu + \beta) . \tag{A4}$$

It can easily be shown that the x null-cline and the y null-cline are nonnegative increasing functions of x if $\beta' > 0$ for $0 \leq x \leq 1$. Note that $f_x(0) = 0$ and $f_y(0) = 0$. Similarly, one can show that $d^2[f_x(x)]/dx^2 \geq 0$, when

$$\beta'' + \frac{2}{x}\beta' + \frac{2}{(B - \beta)}(\beta')^2 \geq 0 , \tag{A5}$$

and that $d^2[f_y(x)]/dx^2 \leq 0$, when

$$(\mu + \beta)\beta'' - 2(\beta')^2 \leq 0 . \tag{A6}$$

These results on the forms of the null-clines are important because they determine the number of possible nonzero (infected) equilibrium points.

As an example, consider a generalized consistent-preference biting-rate function in which $\beta' > 0$, $\beta'' \leq 0$ for $0 \leq x \leq 1$. In this case, equation (A6) clearly holds; and equation (A5) can be shown to hold for many classes of function β. As a result, there is a maximum of one infected equilibrium point, and its existence is determined by the initial slopes of the two null-clines (Aron and May 1982).

LOCAL-STABILITY ANALYSIS

Local-stability analysis was examined by considering the Jacobian matrix for the general model:

$$\begin{pmatrix} -F & G \\ H & I \end{pmatrix}, \tag{A7}$$

where

$$F = kmy\beta' + r , \tag{A8}$$

$$G = km(B - \beta) , \tag{A9}$$

$$H = (1 - y)\beta' , \tag{A10}$$

$$I = \beta + \mu . \tag{A11}$$

Note that $F > 0$, $I > 0$, $G \geq 0$, and $H \geq 0$.

Then, the eigenvalues λ are given by

$$\lambda_{1,2} = \tfrac{1}{2}\{ -(I + F) \pm [(I + F)^2 - 4(IF - HG)]^{1/2}\} . \tag{A12}$$

By inspection and the nonnegative nature of I, F, G, and H, we observe that both eigenvalues are negative if and only if

$$IF - HG > 0 . \tag{A13}$$

One can now evaluate equation (A13) about each equilibrium point $(\hat{x}, \hat{y})$. As an example, consider the uninfected equilibrium $(\hat{x} = 0, \hat{y} = 0)$. Then, equation (A13) holds if and only if

$$kmB\,\beta'(0)/\mu r < 1 , \tag{A14}$$

where $\beta'(0)$ is the slope of the biting-rate function at $x = 0$. Thus, the uninfected equilibrium is locally stable when condition (A14) holds, for each model. For example, for the R-M model, $\beta'(0) = B$, and condition (A14) is equivalent to $R < 1$.

LITERATURE CITED

Aron, J. L., and R. M. May. 1982. The population dynamics of malaria. Pages 139–179 *in* R. M. Anderson, ed. Population dynamics of infectious diseases. Chapman & Hall, New York.

Bailey, R. 1982. The biomathematics of malaria. Griffin, London.

Cornell, H., and D. Pimentel. 1978. Switching in the parasitoid *Nasonia vitripennis* and its effects on host competition. Ecology 59:297–308.

Daniel, T. L., and J. G. Kingsolver. 1983. Feeding strategy and the mechanics of blood sucking in insects. J. Theor. Biol. 105:661–672.

Day, J. F., and J. D. Edman. 1983. Malaria renders mice susceptible to mosquito feeding when gametocytes are most infective. J. Parasitol. 69:163–170.

Day, J. F., K. M. Ebert, and J. D. Edman. 1983. Feeding patterns of mosquitoes simultaneously exposed to malarious and healthy mice, including a method for separating blood meals from conspecific hosts. J. Med. Entomol. 20:120–127.

Dethier, V. G. 1976. The hungry fly. Harvard University Press, Cambridge, Mass.

Dobson, A. 1988. Parasite-induced changes in host behavior: the population dynamic consequences and evolutionary considerations. Q. Rev. Biol. (in press).

Edman, J., J. Day, and E. Walker. 1985. Vector-host interplay—factors affecting disease transmission. Pages 273–285 *in* L. P. Lounibos, J. R. Rey, and J. H. Frank, eds. Ecology of mosquitoes. Chapman & Hall, New York.

Hassell, M. P. 1978. The dynamics of arthropod predator-prey systems. Princeton University Press, Princeton, N.J.

Heinrich, B. 1979. "Majoring" and "minoring" by foraging bumblebees, *Bombus vagans*: an experimental analysis. Ecology 60:245–255.

Jenni, L., D. H. Molyneux, J. L. Livesey, and R. Galun. 1980. Feeding behaviour of tsetse flies infected with salivarian trypanosomes. Nature (Lond.) 283:383–385.

Kesavan, S. K., and N. P. Reddy. 1985. On the feeding strategy and the mechanics of blood sucking in insects. J. Theor. Biol. 113:781–783.

Levin, B. R., A. C. Allison, H. J. Bremerman, L. L. Cavalli-Sforza, B. C. Clarke, R. Frentzel-Beyme, W. D. Hamilton, S. A. Levin, R. M. May, and H. R. Thieme. 1982. Evolution of parasites and hosts. Pages 213–244 *in* R. M. Anderson and R. M. May, eds. Population biology of infectious diseases. Springer-Verlag, New York.

Macdonald, G. 1952. The analysis of equilibrium in malaria. Trop. Dis. Bull. 49:813–828.

———. 1957. The epidemiology and control of malaria. Oxford University Press, London.

———. 1973. Dynamics of tropical disease: a selection of papers with biographical introduction and bibliography. L. J. Bruce-Chwatt and V. J. Glanville, eds. Oxford University Press, London.

Mahon, R., and A. Gibbs. 1982. Arbovirus-infected hens attract more mosquitoes. Pages 502–504 *in* J. D. Mackenzie, ed. Viral diseases in Southeast Asia and the western Pacific. Academic Press, Sydney.

Moloo, S. K., and F. Dar. 1985. Probing by *Glossina morsitans centralis* infected with pathogenic *Trypanosoma* species. Trans. R. Soc. Trop. Med. Hyg. 79:119–120.

Molyneux, P., and P. Jeffries. 1986. Feeding behavior of pathogen-infected vectors. Parasitology 92:721–736.

Murdoch, W. W. 1969. Switching in general predators: experiments on predator specificity and stability of prey populations. Ecol. Monogr. 39:335–354.

Nåsell, I. 1985. Hybrid models of tropical infections. Lect. Notes Biomath. 59:1–206.

Prokopy, R. J., A. L. Sverill, S. S. Cooley, and C. A. Roitberg. 1982. Associative learning in egglaying site selection by apple maggot flies. Science (Wash., D.C.) 218:76–77.

Rausher, M. D. 1978. Search image for leaf shape in a butterfly. Science (Wash., D.C.) 200:1701–1703.

———. 1983. Ecology of host-selection behavior in phytophagous insects. Pages 223–257 *in* R. F. Denno and M. S. McClure, eds. Variable plants and herbivores in natural and managed systems. Academic Press, New York.

Ribeiro, J. M., P. A. Rossignol, and A. Spielman. 1984. Role of mosquito saliva in blood-vessel location. J. Exp. Biol. 108:1–7.

———. 1985. *Aedes aegypti*: model for blood finding strategy and prediction of parasite manipulation. Exp. Parasitol. 60:118–132.

Ross, R. 1911. The prevention of malaria. 2d ed. Murray, London.

Rossignol, P. A., J. M. Ribeiro, and A. Spielman. 1984. Increased intradermal probing time in sporozoite-infected mosquitoes. Am. J. Trop. Med. Hyg. 33:17–20.

Rossignol, P. A., J. M. C. Ribeiro, M. Jungery, M. J. Turell, A. Spielman, and C. L. Bailey. 1985. Enhanced mosquito blood-finding success on parasitemic hosts: evidence for vector-parasite mutualism. Proc. Natl. Acad. Sci. USA 82:7725–7727.

Rossignol, P. A., J. M. Ribeiro, and A. Spielman. 1986. Increased biting rate and reduced fertility in sporozoite-infected mosquitoes. Am. J. Trop. Med. Hyg. 35:277–279.

Turell, M. J., P. A. Rossignol, A. Spielman, C. A. Rossi, and C. L. Bailey. 1984. Enhanced arboviral transmission by mosquitoes that concurrently ingested microfiloriae. Science (Wash., D.C.) 225:1039–1041.

Turell, M. J., C. L. Bailey, and C. A. Rossi. 1985. Increased mosquito feeding on Rift Valley fever virus–infected lambs. Am. J. Trop. Med. Hyg. 33:1232–1238.

Van Alphen, J. J., and L. E. Vet. 1986. An evolutionary approach to host finding and selection. Pages 23–62 *in* J. Waage and D. Greathead, eds. Insect parasitoids. Academic Press, London.