



Models for heartwater epidemiology: Practical implications and suggestions for future research

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ABSTRACT

YONOW, T., BREWSTER, C.C., ALLEN, J.C. & MELTZER, M.I. 1998. Models for heartwater epidemiology: Practical implications and suggestions for future research. *Onderstepoort Journal of Veterinary Research*, 65:263–273

We present a simple model of the dynamics of heartwater that we use to explore and better understand various aspects of this disease. We adapted the Ross-Macdonald model for malaria epidemiology so that we could consider both host and vector populations, and evaluate the interactions between the two. We then use two more biologically detailed models to examine heartwater epidemiology. The first includes a carrier state and host mortality, and the second includes density dependence. The results from all three models indicate that a stable equilibrium with high disease levels is probably the standard situation for heartwater (R_0 between 5.7 and 22.4). More than 80% of cattle become infected with heartwater if only 12% of infected tick bites produce an infection in cattle, if tick burdens are as low as only five ticks per host per day, or if tick lifespans are as short as 7 d. A host recovery rate of 30 d results in over 50% of the cattle becoming infected with heartwater. Our analyses indicate that it is quite difficult to prevent the establishment and maintenance of high levels of heartwater in a herd, thereby supporting previous suggestions that any attempts at controlling this disease through stringent tick control regimens are not warranted.

Keywords: *Amblyomma hebraeum*, *Cowdria ruminantium*, epidemiology, heartwater, modelling, ticks

INTRODUCTION

Heartwater, caused by the rickettsia *Cowdria ruminantium*, is a major disease of livestock in Africa, and also occurs in the Caribbean. It can result in approximately 40% mortality in a susceptible herd of cattle,

and up to 95% mortality in a susceptible herd of Merino sheep (Norval, Meltzer & BurrIDGE 1992). The disease is transmitted to livestock by tick vectors of the genus *Amblyomma* (Bezuidenhout 1987; Petney, Horak & Rechav 1987). *A. variegatum* is the most important vector, occurring throughout tropical Africa as well as in the Caribbean, followed by *A. hebraeum*, which occurs in southern Africa (Uilenberg 1983; Bezuidenhout 1987). *Amblyomma* ticks are all three-host ticks, which means that engorged larvae and nymphs must drop from their respective hosts in order to moult into the next stage, and adult females must drop from their host to lay their eggs.

Current control of heartwater relies primarily on tick control, either by intensive dipping regimens or spraying with acaricides. However, the justification of dipping to control tick-borne diseases has been questioned (e.g. Norval 1983; Norval, Barrett, Perry, & Mukhebi 1991a; Meltzer 1992; Meltzer, Norval & Donachie 1995), and the possibility of promoting a state

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of enzootic stability has been raised (e.g. Bezuidenhout 1985; Meltzer *et al.* 1995). As defined by Callow (1977), enzootic stability is a situation in which there is frequent transmission of the parasites, and infection of all young animals occurs during the period when they are protected by age-related resistance and/or maternal antibodies. Thereafter, immunity is maintained by the perpetuation of the carrier state through continuous re-infection, and few, if any, cases of disease outbreak occur as almost all animals are immune.

The terms 'enzootic stability' and 'endemic stability' seem to have been used interchangeably in the heartwater literature, and, as defined above by Callow (1977), enzootic stability would result in a high proportion of cattle being infected with heartwater, with continuous re-infection ensuring their immunity. Strictly speaking, though, endemic and enzootic stability both refer to the stable persistence of a disease, without specifying the level of infection. It would therefore be possible to have endemic (or enzootic) stability with low levels of infection, although such a situation could reduce the level of immunity in a population of cattle and so increase the risk of cattle experiencing acute symptoms. In this paper, we use the term 'endemic stability' to reflect the persistence of heartwater. However, we also indicate the levels of infection in the herd obtained by our analyses to provide an indication of the level of immunity that will exist.

Despite its importance, the epidemiology of heartwater is poorly understood. There are now some data on the transmission efficiency of *C. ruminantium* from infected cattle to ticks (Peter, Deem, Barbet, Norval, Simbi, Kelly & Mahan 1994), and on the establishment and maintenance of endemic stability (Deem, Norval, Yonow, Peter, Mahan & Burrige 1996). However, it is still not clear how long it takes cattle to recover from *C. ruminantium* infection. Some believe that infection only persists for relatively short periods (less than 3 months) (Neitz 1939; Ilemobade 1978), while others believe that cattle maintain *C. ruminantium* infection for at least 240 d (Andrew & Norval 1989). The issue of endemic stability is also unresolved, with some researchers claiming that it does not occur (e.g. Uilenberg 1983, 1990; Camus & Barré 1992), and others claiming it may (e.g. Norval & Lawrence 1979; Deem *et al.* 1996). Furthermore, there are no data on other important aspects of heartwater epidemiology, such as the proportion of infected tick bites that transmit *C. ruminantium* to cattle.

Because heartwater is such an important livestock disease, and because some recent advances have been made in understanding its epidemiology, we decided to construct a simple model of the disease dynamics. We used the model to examine the conditions under which endemic stability occurs within a herd, since the establishment of endemic stability with high levels of infection in a herd might offer a

cheap alternative to chemical control of the disease. We used the model to investigate the resilience, or robustness, of endemic stability once it is established in a herd, and to explore values for those parameters on which we have either conflicting or no data, and thereby provide other researchers with various hypotheses to test. By examining a range of potential parameter values, we also hoped to identify key areas for further research on heartwater epidemiology. We were interested to see how easy or difficult it would be, by manipulating different parameter values, to prevent a high level of the disease from occurring in a herd. The more difficult it is to prevent the establishment and maintenance of heartwater, the more reason for now allowing the controlled spread of heartwater, and eliminating the need for expensive tick control measures to control the disease.

As the initial model we built was relatively simple, we then used two other models to examine the resilience of endemic stability in heartwater. The first of these models was an extension of our basic model, but allowed for different host categories (susceptible, acutely infected, carrier), and for additional mortality on acutely infected cattle. The second model used was the De Leo & Dobson (1996) model, which has very different assumptions, and relies on the relationship between the carrying capacity and the mass of individual host animals to determine parasite transmission probabilities and basic reproductive rates (R_0).

METHODS

Basic model

There have been various attempts at modelling aspects of tick-borne diseases of livestock (e.g. Mahoney 1969; Ross & Mahoney 1974; Smith 1983; Byrom & Gettinby 1992; Medley, Perry & Young 1993). To model the epidemiology of heartwater, we adapted the Ross-Macdonald model for malaria epidemiology, summarized by Aron & May (1982). This model allows us to consider both host and vector populations, and to evaluate the interactions between the two populations. The model consists of the following two equations:

$$dx/dt = (abM/N)y(1-x) - rx \quad \text{Eqn. 1}$$

$$dy/dt = acx(1-y) - \mu y \quad \text{Eqn. 2}$$

where—in considering a tick-cattle interaction—

- x = proportion of cattle population infected
- y = proportion of tick population infected
- M = size of tick population
- N = size of cattle population
- a = number of bites per day (bite rate for a single tick)
- b = proportion of infected tick bites producing an infection in cattle
- c = proportion of ticks becoming infected by feeding on an infected cow
- μ = per capita mortality rate per day for ticks ($1/\mu$ = average lifetime of a tick)

r = per capita recovery rate per day of cattle ($1/r$ = average duration of infection in cattle). This indicates how long cattle maintain the infection and therefore how long they remain part of the 'infected' pool, before reverting to the 'susceptible' pool

We constructed and ran the model using the simulation package MATLAB™ with SIMULINK™ (MathWorks Inc. 1994). Feeding by ticks on cattle provides a link between cattle and ticks, and allows for the transmission of *C. ruminantium* infection from infected cattle to uninfected ticks and from infected ticks to uninfected cattle. This two-equation system makes both the cattle and tick components of the disease dynamics and their interaction transparent.

Parameter values

Table 1 contains the parameter values used for the initial run of the model, and for subsequent runs to test the sensitivity of the results. Values for N (size of cattle population) can come from various sources, depending on the area under consideration. However, real values for M (size of tick population) are more difficult to obtain, since the tick population comprises both ticks on hosts and ticks on pasture. To avoid this data problem, we set N at 1,0 and consider M to be the number of ticks per head of cattle. M does not distinguish between various tick instars, but refers to a total average number of ticks per head of cattle. We assigned this parameter an initial value of 10, which is low, considering the range of numbers of *A. hebraeum* collected from cattle by various authors (Norval 1977a; Du Plessis & Malan 1987; Meltzer & Norval 1993; Norval, Donovan, Meltzer, Deem & Mahan 1994a).

We based the number of bites per tick per day (a) on the number of days that a tick instar feeds on a cow. For *A. hebraeum*, Petney *et al.* (1987) give feeding periods for larvae as 6–8 d; for nymphs, 6–9 d; and for females, 6–12 d from mating. Males can remain on a host feeding intermittently for up to 6 months (Norval, Andrew & Meltzer 1991b), and can remain attached for as long as 8 months (Jordaan & Baker 1981). We set the initial value of this parameter at 0,1, defining the mean feeding period of a tick instar as 10 d. Whilst this may be a slight overestimate for the immature stages, it is well within the published range for females, and is an underestimate of the values published for males.

As there are no published data on the proportion of infected tick bites that transmit *C. ruminantium* to cattle (b), we set the initial value at 25%. The actual value could depend on various factors, such as whether the tick is a nymph or an adult, the sex of the adult, the *C. ruminantium* strain, and the breed of cattle. We explored the impact of this parameter by reducing its value to 12% and 6%.

The proportion of ticks that become infected when feeding on an infected cow (c) was set using pub-

lished estimates. Using a polymerase chain reaction (PCR), Peter *et al.* (1994) showed that an average of 28% (range: 6,67–66,67%) of adult *A. hebraeum* ticks were infected with *C. ruminantium* after feeding as nymphs on infected cattle. Du Plessis & Malan (1987) reported lower infection rates of ticks (mean = 7%; range = 1,6–30%), but they detected *C. ruminantium* infection in ticks by an immunofluorescent antibody (IFA) test, which is less sensitive than a PCR. When fed on clinically infected hosts, 86% (Peter *et al.* 1994) to 93% (Mahan, Tebele, Mukwedeya, Semu, Nyathi, Wassink, Kelly, Peter & Barbet 1993) of ticks became infected. In an endemic region, however, a greater proportion of cattle will be carriers rather than clinically ill. Thus, these large estimates were not used. The Peter *et al.* (1994) estimate was adjusted to account for the fact that they only tested adult male and female ticks that fed as nymphs on infected cattle. We assume that since nymphs take more blood than larvae, adult ticks are more likely to be infected than nymphal ticks. Transovarial transmission of *C. ruminantium* (transmission of the infective agent from adult female tick to the eggs and thence to the emerging larvae) is generally considered not to occur, or to occur only as a rare exception (Uilenberg 1981; Bezuidenhout & Jacobsz 1986), so all larval ticks can be considered "clean". To account for the presence of a larger number of less infective immature stages, the Peter *et al.* (1994) average value of 28% was therefore halved to 14%.

Aron & May (1982) defined μ as the per capita mortality rate of mosquitoes ($1/\mu$ = average lifetime of a mosquito). We chose an average tick lifespan of 20 d, thus making 1/20 (or 0,05) the initial daily value for μ . A tick therefore has 5 d to find a host after moulting, an average of 10 d to feed, and 5 d after detaching from the host to moult into the next instar, or, in the case of females, to lay eggs. This is a very short average tick lifespan, as the non-parasitic, off-host stages can survive for considerable periods of time (Norval 1977b).

It is not clear how long it takes cattle to recover from *C. ruminantium* infection. Some believe that infection only persists for relatively short periods (less than 3 months) (Neitz 1939; Ilemobade 1978). Others believe that cattle can maintain *C. ruminantium* infection for at least 240 d (Andrew & Norval 1989). We used the latter value, and set the initial daily recovery rate (r) at 1/240 d.

Assumptions

We make some fundamental assumptions in adapting the Ross-Macdonald model to the tick-cattle-heartwater system:

- First, we assume that when an infected tick bites an uninfected cow, the cow becomes both infected and infectious. Thus, the model does not allow for

a latent period of *C. ruminantium* infection in the cow. Allowing for such a time lag would add another equation to the model, and would effectively reduce the rate of transmission of the infection. We avoid the increased complexity that another equation would incur, and account for the latent period of infection by altering parameter values. For example, we reduce the proportion of infected tick bites that produce an infection in cattle (*b*).

- Secondly, as there is no evidence to the contrary at present, we assume there is no differential mortality between uninfected ticks and ticks infected with *C. ruminantium*.
- Thirdly, we assume that superinfection, or constant re-infection of an already infected cow, does not occur. Superinfection would only prolong the carrier status of an infected cow, thereby increasing the proportion of infected cattle (*x*) and possibly also their levels of parasitaemia. This, in turn, would increase cattle infectivity to ticks, leading to a more rapid spread and establishment of heartwater. By ignoring superinfection, however, the model underestimates the cattle-to-tick transmission dynamics, and thus represents a conservative underestimate of the rate of spread of heartwater.
- Fourthly, we assume that after the recovery period, a cow is immediately susceptible to re-infection. This is because the recovery period in our model does not represent recovery from clinical illness, but represents instead the entire duration of the infection, including the duration of the carrier status. The recovery period thus accounts for the full period during which a cow is infected and therefore immune from re-infection (since, as stated above, we are also assuming that superinfection does not occur). Once a cow is no longer infected, it then becomes immediately susceptible to re-infection.

Model equilibrium and stability criteria

We wanted to determine the robustness of our model, and to assess the impact of different parameter values on the extent of endemic stability. At least two methods are available for determining whether or not an infectious disease can maintain itself. The first, a geometrical method, involves deriving the equilibrium and stability conditions for the system. By assigning $A = abM/N$ and $C = ac$ in equations (1) and (2) respectively, the equilibrium conditions (after setting $dx/dt = dy/dt = 0$) for our system are:

$$\hat{x} = \frac{AC - r\mu}{C(A + r)} \tag{Eqn. 3}$$

$$\hat{y} = \frac{AC - r\mu}{A(C + \mu)} \tag{Eqn. 4}$$

For positive equilibrium states to exist (i.e., for the disease to persist), $AC - r\mu > 0$, or $AC > r\mu$. In terms of the original parameters, a stable system with positive equilibrium exists if $(abM/N)^*(ac) > r\mu$, or by rearrangement, if $(ac/\mu) > (r/abM/N)$. In phase-plane, (ac/μ) and $(r/abM/N)$ represent the initial slopes of the isoclines ($dy/dt = 0$, $dx/dt = 0$) of *y* and *x*, respectively (see Fig. 5.2 in Aron & May 1982). As outlined by Macdonald (1957), these slopes determine the extent of stability of the system.

The second measure of the likely persistence of a disease is given by the basic reproductive rate, R_0 , of the parasite (Macdonald 1952; Aron & May 1982; Dye 1994). The definition of R_0 depends on whether one is referring to a micro- or macro-parasite (Anderson 1982). In our case, for a microparasite, R_0 is the number of secondary infected hosts produced by one primary infection (Anderson 1982; Aron & May 1982). Since *C. ruminantium* will only establish and maintain itself in the population if $(abM/N)^*(ac) > r\mu$ or $(abM/N)^*(ac) / r\mu > 1$, then

$$R_0 = \frac{M}{N} \frac{a^2bc}{\mu r} \tag{Eqn. 5}$$

If R_0 becomes less than unity, the equilibrium in equations 3 and 4 is unstable and the disease cannot maintain itself.

Analyses

The model was first run using the initial parameter values determined above. Sensitivity analyses were then conducted to assess the robustness of the model. First, apart from parameters *a* and *c* which were considered to be adequately set, each parameter was altered independently of the others, to see by how much its value could be altered before $R_0 < 1$. Second, the initial parameter values were altered in various combinations and the R_0 values were used to assess the effects of these changes on the degree of persistence of heartwater. These results are presented in Table 1. As part of these analyses (Table 1), we conducted extensive simultaneous alterations of M/N and *b*, as control of heartwater is based primarily on control of ticks (i.e., reducing M/N), and as there are no data on likely values for *b*.

More biological detail: A carrier state, host mortality and density dependence

Having explored our basic model, we considered some other models to study the cattle-heartwater system, with the intention that they will serve as starting points for further research into this system. We agree with Nowak & Bangham (1996) that: 'The strategy of successful mathematical modeling is akin to Occam's razor: start with the smallest number of essential assumptions and follow the implications rigorously to their logical conclusions.' We hope that

readers will not be confused by this approach into thinking they must decide which model is 'right' or 'wrong'. These models are simply tools for learning about the system, and any model might be best for a specific objective.

First, we present an extension of the Ross model (Eqn. 1 and 2) that allows for an immune carrier state in cattle. This is a modification of a model suggested to us by G.F. Medley (personal communication). The susceptible host population is w . Following infection, individuals become acutely infected, x , by ticks at rate A [where $A = abM/N$, as in the Ross model (Eqn. 3 and 4)]. They then proceed to recover at rate r to a carrier state z with reduced infectivity to ticks, $A\beta$. We assume that the carrier state is life-long and confers immunity, with overall cattle mortality rate m and a constant cattle population, i.e. $w+x+z = 1$ as if deceased cattle are replaced. These assumptions lead to the following model:

$$\begin{aligned} dw/dt &= m(1-w) - Aw(x+\beta z) \\ dx/dt &= Aw(x+\beta z) - (r+m)x \\ dz/dt &= rx - mz \end{aligned}$$

where the tick vector population has been absorbed into the infection rate parameter A . (Note that one could still allow for an annual cycle in tick abundance by making A into a cyclic parameter.) Since the cattle population is constant, we can get by with only two of these equations for purposes of analysis. Choosing w (susceptible cattle) and x (acute infection) we have:

$$\begin{aligned} dw/dt &= m(1-w) - Aw(x+\beta(1-w-x)) \\ dx/dt &= Aw(x+\beta(1-w-x)) - (r+m)x \end{aligned}$$

The complete system equilibrium points for w , x , and z are given by:

$$w^* = \frac{m(m+r)}{A(m+r\beta)}, \quad x^* = \frac{m(A(m+r\beta) - m(m+r))}{A(m+r)(m+r\beta)}, \quad \text{and } z^* = \frac{r}{m} x^*$$

For a feasible (non-negative) equilibrium for the acute infection (x) or carriers (z), we must have

$$A(m+r\beta) > m(m+r).$$

Following Anderson (1982) and May (1986), we can write the equilibria in the form:

$$w^* = 1/R_0, \quad x^* = \frac{m}{(m+r)} (1 - 1/R_0), \quad \text{and } z^* = \frac{r}{(m+r)} (1 - 1/R_0),$$

where

$$R_0 = \frac{A(m+r\beta)}{m(m+r)}$$

is interpreted as the basic reproductive rate of the pathogen, and we must have $R_0 > 1$ for the patho-

gen to survive in the system. A stability analysis carried out on any two of the three variables reveals that, like the Ross equations, the point (w^*, x^*, z^*) above is asymptotically stable providing that $R_0 > 1$. Otherwise, the system goes to the point $(1, 0, 0)$ with disease extinction—a condition we would obviously prefer.

To compare this R_0 with the value of 16.8 estimated from the Ross equations and best guesses of the parameters (Table 1), we must choose the new parameters m and β in addition to those already chosen in Table 1. We suppose that cattle live for about 10 years giving $m = 1/3600 \text{ d} = 2.78 \times 10^{-4}/\text{d}$, and since β (transmission from carriers) is assumed less than $a(0,1)$, we let $\beta = 0.01$.

Then, if we put additional mortality γ , e.g. $0.1/\text{d}$ [see Shah-Fischer & Say (1989)] on the acute stage y (a very realistic assumption), then R_0 becomes

$$R_0 = \frac{A(m+r\beta)}{m(m+r+\gamma)}$$

a smaller value due to loss of the pathogen in the acute stage.

Second, we consider a rather different mathematical model, with different assumptions (De Leo & Dobson 1996). This model relies on the relationship between the carrying capacity and the mass of individual host animals to determine parasite transmission probabilities (b) and basic reproductive rates (R_0) (De Leo & Dobson 1996). We use their formula for a density-dependent disease process (susceptible, infective, recovered), and assume a carrying capacity of 10 cattle per square kilometre (1 cow per 10 ha), a natural host mortality rate of 0.1 (i.e. a cow lives for 10 years) and a two- to ten-fold reduction in the host life expectancy due to the disease. According to their formulae, this provides a disease-induced mortality rate of 0.1–0.9 (i.e. the life expectancy for cows now falls within the range of 1–10 years). We also assume a recovery rate (which is not a 'rate', but rather the proportion of animals that recover from infection) of 0.4–0.8, and an average body weight of 100–150 kg per animal.

RESULTS

Basic model

A simulation run using the initial parameter values given in Table 1 shows that the spread of heartwater stabilizes with around 92.5% of the cattle and 20.5% of the ticks infected within 250 d (Fig. 1). Under these conditions, R_0 is much greater than unity (Table 1), which together with a phase-plane analysis plot for the tick-host system (Fig. 2), indicates that heartwater is readily maintained within the cattle population.

TABLE 1 The basic reproductive rate, R_0 , for different parameter values. If $R_0 > 1$, the disease exists in a stable state. M/N = ticks per host per day; a = tick bites per day; b = proportion of infected tick bites producing an infection in cattle; c = proportion of ticks becoming infected by feeding on an infected cow; $1/\mu$ = average lifetime of a tick; $1/r$ = average duration of infection in cattle, or carrier status; x = proportion of cattle infected; y = proportion of ticks infected

M/N	a	b	c	$1/\mu$	$1/r$	R_0	x	y	Comment
10	0,1	0,25	0,14	20	240	16,80	92,5	20,6	Initial parameters
5	0,1	0,25	0,14	20	240	8,40	85,3	19,3	Reducing M/N
4	0,1	0,25	0,14	20	240	6,72	81,7	18,6	
3	0,1	0,25	0,14	20	240	5,04	75,9	17,5	
2	0,1	0,25	0,14	20	240	3,36	64,8	15,4	
1	0,1	0,25	0,14	20	240	1,68	34,7	8,9	
10	0,1	0,12	0,14	20	240	8,06	84,7	19,2	Reducing b
10	0,1	0,06	0,14	20	240	4,03	70,3	16,4	
10	0,1	0,05	0,14	20	240	3,36	64,8	15,4	
10	0,1	0,02	0,14	20	240	1,34	21,2	5,6	
10	0,1	0,25	0,14	7	240	5,88	81,6	7,4	Reducing $1/\mu$
10	0,1	0,25	0,14	4	240	3,36	69,1	3,7	
10	0,1	0,25	0,14	20	120	8,40	85,3	19,3	Reducing $1/r$
10	0,1	0,25	0,14	20	60	4,20	71,4	16,7	
10	0,1	0,25	0,14	20	30	2,10	46,2	11,5	
10	0,1	0,25	0,14	20	20	1,40	23,8	6,3	
10	0,1	0,25	0,14	20	15	1,05	3,8	1,0	
5	0,1	0,12	0,14	20	240	4,03	70,3	16,4	Reducing M/N and b
5	0,1	0,06	0,14	20	240	2,02	44,3	11,0	
5	0,1	0,04	0,14	20	240	1,34	21,2	5,6	
4	0,1	0,12	0,14	20	240	3,23	63,5	15,1	
4	0,1	0,06	0,14	20	240	1,61	32,4	8,3	
4	0,1	0,04	0,14	20	240	1,08	5,5	1,5	
3	0,1	0,12	0,14	20	240	2,42	52,6	12,8	
3	0,1	0,06	0,14	20	240	1,21	14,1	3,8	
3	0,1	0,04	0,14	20	240	0,81			
2	0,1	0,20	0,14	20	240	2,69	56,9	13,7	
2	0,1	0,12	0,14	20	240	1,61	32,4	8,3	
2	0,1	0,08	0,14	20	240	1,08	5,5	1,5	
2	0,1	0,06	0,14	20	240	0,81			
1	0,1	0,20	0,14	20	240	1,34	21,2	5,6	
1	0,1	0,16	0,14	20	240	1,08	5,5	1,5	
1	0,1	0,12	0,14	20	240	0,81			
5	0,1	0,25	0,14	7	240	2,94	63,9	5,9	and $1/\mu$
5	0,1	0,25	0,14	4	240	1,68	39,2	2,1	
5	0,1	0,25	0,14	20	120	4,20	71,4	16,7	and $1/r$
5	0,1	0,25	0,14	20	60	2,10	46,2	11,5	
5	0,1	0,25	0,14	20	30	1,05	3,8	1,0	
10	0,1	0,12	0,14	7	240	2,82	62,4	5,8	Reducing b and $1/\mu$
10	0,1	0,12	0,14	4	240	1,61	36,7	2,0	
10	0,1	0,06	0,14	7	240	1,41	27,2	2,6	and $1/r$
10	0,1	0,06	0,14	4	240	0,81			
10	0,1	0,12	0,14	20	120	4,03	70,3	16,4	
10	0,1	0,12	0,14	20	60	2,02	44,3	11,0	
10	0,1	0,12	0,14	20	30	1,01	0,6	0,2	
10	0,1	0,06	0,14	20	120	2,02	44,3	11,0	Reducing $1/\mu$ and $1/r$
10	0,1	0,06	0,14	20	60	1,01	0,6	0,2	
10	0,1	0,25	0,14	7	120	2,94	63,9	5,9	
10	0,1	0,25	0,14	7	60	1,47	30,0	2,9	
10	0,1	0,25	0,14	7	30	0,74			
10	0,1	0,25	0,14	4	120	1,68	39,2	2,1	Reducing M/N and b and $1/\mu$
10	0,1	0,25	0,14	4	60	0,84			
5	0,1	0,12	0,14	7	240	1,41	27,2	2,6	b and $1/r$
5	0,1	0,12	0,14	4	240	0,81			
5	0,1	0,06	0,14	7	240	0,71			
5	0,1	0,12	0,14	20	120	2,02	44,3	11,0	$1/\mu$ and $1/r$
5	0,1	0,12	0,14	20	60	1,01	0,6	0,2	
5	0,1	0,06	0,14	20	120	1,01	0,6	0,2	
5	0,1	0,25	0,14	7	120	1,47	30,0	2,9	
5	0,1	0,25	0,14	4	120	0,84			
5	0,1	0,18	0,14	7	120	1,06	5,1	0,5	b , $1/\mu$ and $1/r$
3	0,1	0,15	0,14	14	120	1,06	4,7	0,9	

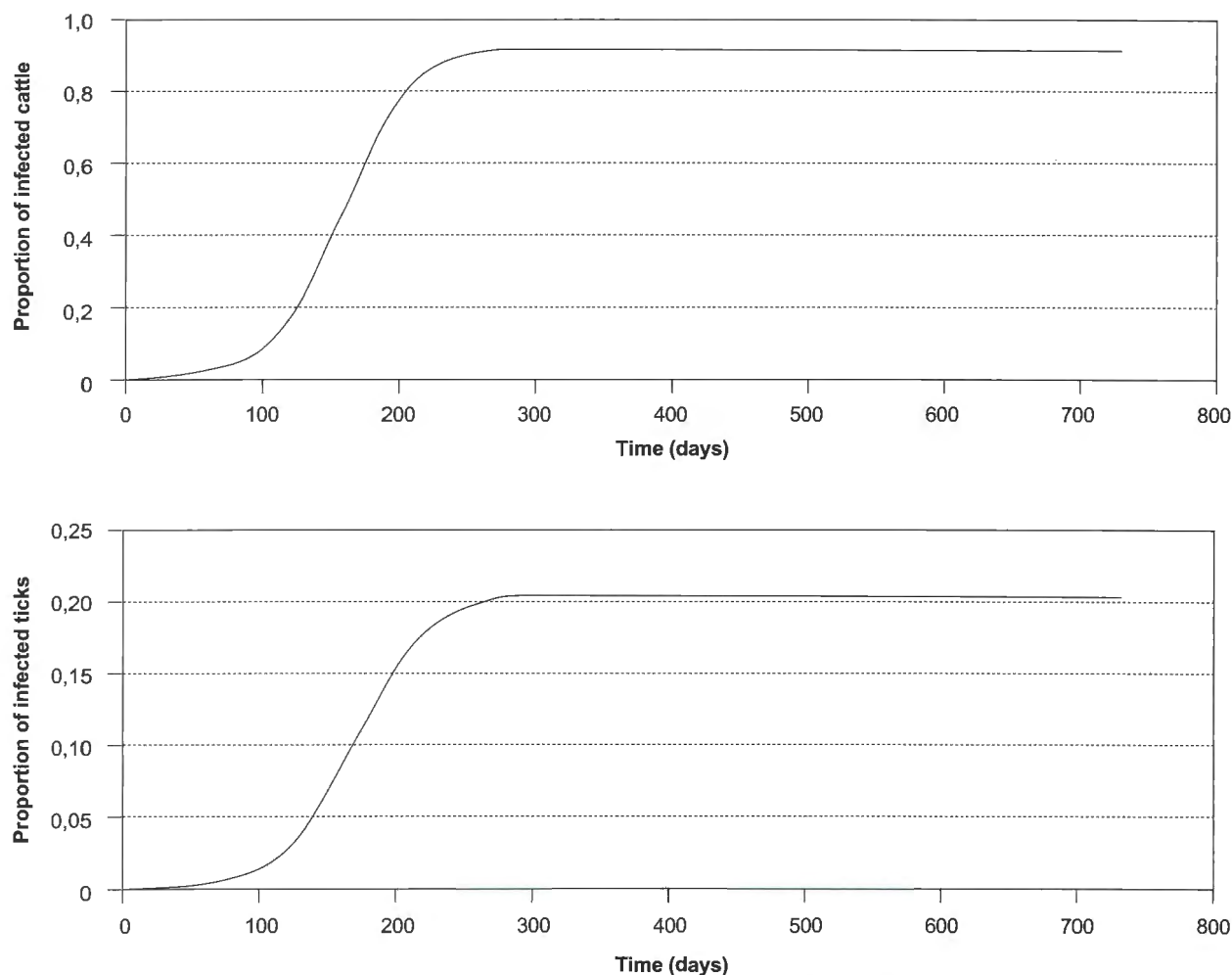


FIG. 1 Graphs showing the modelled spread of heartwater over 2 years, using the initial parameter values of $M = 10$, $N = 1$, $a = 0.1$, $b = 0.25$, $c = 0.14$, $\mu = 0.05$ and $r = 1/240$. Basic reproductive rate (R_0) = 16.80

Although changing the parameter values in Eqn. 3 and 4 individually can reduce the percentage of cattle and ticks infected with heartwater at equilibrium, substantial changes to the default values must be made to obtain fewer than 50% of infected cattle. Major changes from our default values are also necessary to push R_0 below 1 (Table 1).

The various simultaneous alterations of M/N and b (Table 1) indicate that heartwater will spread to a large proportion of cattle unless tick numbers are very low and/or the transmission efficiency from ticks to cattle is very low. Even with a transmission efficiency of only 12% ($b = 0.12$), 5 ticks/animal/day results in more than 70% of the herd infected with heartwater, and 3 ticks/animal/day results in more than 50% of the herd infected with heartwater. With these daily tick loads, transmission efficiency must be reduced below 12% to prevent the spread of heartwater to the majority of the herd. With only 2 ticks/animal/day, the transmission efficiency must be 20%

to infect 50% of the herd, and with 1 tick/animal/day, any decrease in the initial transmission efficiency of 25% results in only a small proportion of the herd being infected.

More biological detail: A carrier state, host mortality and density dependence

The first extension of the Ross equations, allowing for an immune carrier state, gives $R_0 = 11.5$, which compares favourably with the 16.8 obtained from the Ross equations. When we put additional mortality on the acutely infected host stage y , then R_0 is somewhat smaller ($R_0 = 5.7$) due to loss of the pathogen in the acute stage. Even so, this implies a tick to cattle ratio (M/N) of about 2, which would be difficult to obtain in practice. This also generally agrees with our results using the Ross equations. These two extended models indicate that in order to control heartwater by controlling ticks, one must reach very low tick to cattle ratios.

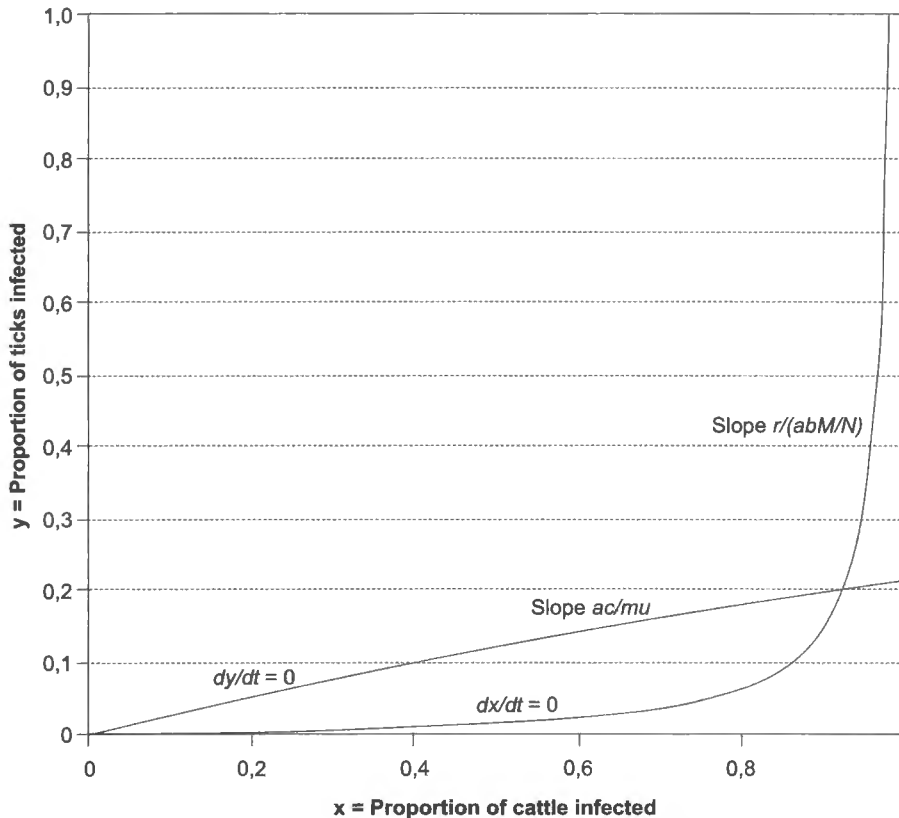


FIG. 2 Phase-plane diagram for the tick-cattle system with the initial parameter values of $M = 10$, $N = 1$, $a = 0,1$, $b = 0,25$, $c = 0,14$, $\mu = 0,05$, and $r = 1/240$. Basic reproductive rate (R_0) = 16,80; ac/μ and $r/(abM/N)$ are the initial slopes of the y and x isoclines

Using the De Leo & Dobson (1996) model, we get $R_0 = 18,7$ for a body mass of 100 kg, and $R_0 = 22,4$ for a body mass of 150 kg. These R_0 values are in the same order of magnitude as that calculated in our basic model ($R_0 = 16,8$) with initial parameter values, although they are somewhat higher than the values when carrier states ($R_0 = 11,5$) and host mortality ($R_0 = 5,7$) are included. Nonetheless, all of these models indicate that heartwater tends towards endemic stability because of high R_0 values. Furthermore, our basic model indicates that with these R_0 values, over 75% of the cattle will be infected (Table 1, when $R_0 = 5,04$, 75,9% of cattle are infected).

DISCUSSION

Regardless of the different assumptions in each of the models we considered, all provided R_0 values substantially greater than unity (R_0 ranges from 5,7 to 22,4). This indicates that endemic stability (as opposed to disease extinction), with a high level of immune carrier infection within a herd (> 75%), is likely to be the norm for heartwater. Analyses with our basic model show that the disease is only prevented

from establishing and persisting when several parameter values are concurrently, and quite significantly, reduced.

An important implication from our simulations is that cattle must be kept essentially tick free to ensure that heartwater does spread to the majority of a herd (Table 1). With two ticks per host per day, $R_0 = 3,36$ and over 60% of the cattle become infected, and with only one tick per host per day, the disease is still maintained with $R_0 = 1,68$ and over 30% of cattle infected (Table 1). Field data from Zimbabwe (Norval 1977a; Norval *et al.* 1991b; Norval *et al.* 1994a) indicate that tick burdens generally exceed these values.

Simulations with our basic model indicate that over 70% of cattle will become infected with a recovery period of only 60 d. Reducing the time to recovery to 20 and 15 d still results in stability, with $R_0 = 1,4$ and $R_0 = 1,05$ respectively, although the proportion of cattle infected is substantially reduced (Table 1). Such short recovery periods are extremely unlikely, as various authors (Uilenberg 1981; Du Plessis 1985; Van de Pypekamp & Prozesky 1987; Mebus & Logan 1988) indicate that prior to clinical illness, incubation alone often lasts more than 2 weeks, and as

animals have been shown to remain carriers for well over a month (Neitz 1939; Ilemobade 1978).

With a recovery period of a month ($1/r = 30$ d), other parameter values must also be concurrently reduced to prevent heartwater from establishing itself with R_0 below unity. Tick burdens (M/N) must be reduced from 10 to below 5 ticks/host, tick to cattle transmission efficiency (b) must be reduced from 25% to below 12%, or the average lifetime of a tick ($1/\mu$) must be reduced from 20 d to less than 10 d (Table 1). If the recovery period is longer than 30 d, then the parameter values of M/N , b and $1/\mu$ must be further reduced to prevent the establishment and maintenance of heartwater.

It would be useful to have more solid information on the carrier status of cattle. We use the latest figure of 240 d (Andrew & Norval 1989) for our initial parameter setting, which is quite different from earlier reported figures of less than 3 months (Neitz 1939; Ilemobade 1978). Although low levels of heartwater can persist with recovery periods as short as 15–20 d (Table 1), a more accurate value, or range of values, for the carrier status of cattle would obviously improve the model.

As indicated in Table 1, transmission efficiencies can be very low, yet still permit disease establishment and maintenance. Simulations with initial parameter values show that if only 5% of bites from infected ticks successfully transmit *C. ruminantium* to cattle, heartwater will be able to establish and persist in a cattle population ($R_0 = 3.36$). In addition, $R_0 > 1$ with only five ticks per host per day and a tick-to-cattle transmission efficiency (b) of only 4%. To our knowledge, there are no data published on the tick-to-cattle transmission efficiency (b). This can provide a testable hypothesis: is tick-to-host transmission efficiency $> 4\%$, which in our model produces disease establishment and maintenance? We urge that this aspect of heartwater epidemiology be studied in greater detail.

Decreasing the average lifetime of a tick, $1/\mu$, does not prevent *C. ruminantium* from establishing itself unless either the length of the carrier state ($1/r$) or the tick burden (M/N) is dramatically reduced at the same time (Table 1). These analyses were conducted to examine the effect of stringent tick control regimes, such as regular acaricide treatments. For example, the four-day tick lifespan could represent a weekly dipping strategy, with a three-day residual effect of the acaricide. The results clearly question the value of weekly dipping regimes to control heartwater, as there are high economic costs associated with imposing such stringent control regimens (Meltzer & Norval 1993).

As a result of the high costs and difficulties in enforcing stringent tick control regimens, many countries are

now reassessing their policies regarding the management of heartwater and other tick-borne diseases (Meltzer 1992). New tools are being developed, such as a heartwater vaccine (Mahan, Burrige & Barbet 1995) and a tick decoy to control *Amblyomma* ticks (Norval, Sonenshine, Meltzer, Burrige & Yunker 1994b). If we now accept that heartwater will readily establish and maintain itself in a cattle population and infect a high percentage of cattle, and that the costs of controlling heartwater are too high, we should be able to use these new technologies to allow heartwater to become endemically stable in large regions of Africa at little loss to productivity (Meltzer *et al.* 1995). Livestock mortality associated with converting herds from being heartwater susceptible to being heartwater carriers could be kept at a minimum by using the new heartwater vaccines. Once heartwater is endemically stable, tick populations would only need to be managed to minimise losses directly attributable to the ticks themselves (e.g. losses in livemass gain of cattle, or damage to hides). This could readily be done using the concept of economic thresholds (Meltzer & Norval 1993).

In summary, we have used some simple models that consider both the vector (tick) and host (cattle) populations to describe heartwater epidemiology. These models are useful because (a), they are solvable, (b), they offer insights into heartwater epidemiology that were not already common knowledge, and (c), they can be validated. The models are solvable because they are relatively simple. They also emphasise the importance of understanding the biology of the two interacting species in more detail.

As a new insight, the models indicate that to prevent the establishment and maintenance of high levels of heartwater, cattle must be kept almost totally tick free, or transmission rates must be very low, or recovery rates of cattle must be very high (short carrier state). Given that current management strategies do not keep cattle entirely free of ticks (even a weekly dipping regime allows some ticks to attach and feed), and that the recovery rate of cattle is unlikely to be shorter than 20 d, then only exceedingly poor transmission efficiencies will prevent heartwater from becoming endemic. By indicating that heartwater is likely to infect a high percentage of cattle, the models also show that if heartwater were allowed to spread throughout the cattle population, immunity will be readily maintained and any risks of the disease will be minimized.

In terms of validity, the model results are sensible and robust over a wide range of plausible values (Table 1). By using the model to examine the effects of altering parameter values, we have provided a range of values that can be tested to assess whether or not our initial values are reasonable. In particular, experiments need to be conducted on the tick to cattle transmission efficiency (b) and on the duration of the

carrier status ($1/r$) to assess the validity of our model as it stands.

ACKNOWLEDGEMENTS

Development of this model was primarily funded by the UF/USAID/SADC Heartwater Research Project, grant number LAG-1328-G-00-3030-06. We dedicate this paper to the memory of Andy Norval, who initiated this work.

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