Tropical Medicine and International Health

VOLUME 1 NO. 6 PP 753–764 DECEMBER 1996

Control strategies for sleeping sickness in Central Africa: a model-based approach

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Summary Vector control and the detection (followed by treatment) of infected individuals are the two methods currently available for the control of sleeping sickness. The basic reproduction rate of a compartmental model is used to analyse and compare the two strategies. The efficiency of each strategy will depend on two epidemiologic parameters; the intrinsic contamination rate Q (closely related to the index of new contaminations) that captures the potential spread of the disease, and the intrinsic removal rate from the first stage (intrinsic to the particular trypanosome strain and to the population's susceptibility). The model shows that when the intrinsic removal rate is low (that is, when there is a long first stage characteristic of an endemic situation) the detection of sick individuals is more efficient than vector control. The situation is reversed when the removal rate is high (in an epidemic situation). The conclusions of the analysis are shown to be in general agreement with results obtained in two different sleeping sickness foci of Central Africa.

keywords sleeping sickness, models, epidemiology, control strategy, Central Africa

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Introduction

The main problem faced by public health officials is that of an optimal allocation of resources. This problem is particularly acute in developing countries faced with major tropical epidemics.

In the case of Gambian trypanosomiasis, the issue is one of allocation of limited resources between the two main control strategies: detection and treatment of patients and vector control. Both strategies are useful in controlling the epidemic but there are disagreements as to whether vector control should be used. These are controversial issues and contradictions abound in the literature. Indeed, in one forum (Habbema & De Muynck 1991) specialists were divided. Some feel that finding and treating infected people is sufficient to control the disease (Van Nieuwenhove 1991; Mentens 1991) while others feel that vector control is necessary (Laveissière & Meda 1991; Lancien 1991).

Historically, the detection and treatment of infected people has been an efficient means of control. For example, the widespread sleeping sickness epidemic that devastated Central Africa in the 1920s was controlled almost exclusively through the detection of sick people which removed the human reservoir of *Trypanosoma brucei gambiense* (Jamot 1932; Janssens 1971). Control of the epidemic was achieved in large part thanks to the mobile detection teams made famous by Dr Jamot (Lapeyssonnie 1987).

Vector control has long been hindered by technical problems but modern trapping methods are now efficient and simple to implement (WHO 1986). Trapping drastically decreases vector densities in savanna foci (Gouteux & Sinda 1990) and in forest

foci when conducted on a large scale (Laveissière *et al.* 1980). However, the epidemiologic impact of vector control is difficult to measure because for ethical reasons vector control cannot be used without detection and treatment. In this case ascertaining the relative contribution of each control strategy is difficult.

In this paper we use a mathematical model developed elsewhere (Artzrouni & Gouteux 1996) to address these questions which cannot be answered solely on the basis of empirical methods or observations (De Muynck & Rogers 1989).

The model

Description

The model we have developed involves two populations: human hosts and tsetse flies. Animal reservoirs are ignored because they have a negligible effect on the spread of sleeping sickness in Central Africa (Kageruka 1989; Noireau *et al.* 1986).

For humans the model consists of four compartments: susceptibles, incubating individuals, asymptomatic carriers (i.e. infected individuals in the first stage of the disease during which they can transmit the parasite) and a compartment of removed individuals. This compartment includes (a) untreated patients in the second, meningo-encephalitic stage of the disease who cannot transmit the disease because they are less exposed to flies and less infective; and (b) persons identified as patients who have been taken to hospital (regardless of the stage). This removed compartment may also include persons who have developed immunity after recovery. The model assumes that removed individuals cannot transmit the disease because they cannot be bitten.

There are three compartments for the tsetse population: susceptibles, incubating flies, and 'actively infected' flies which can transmit the disease. The compartments are depicted in Figure 1.

Our model comprises incubating stages as separate compartments for both humans and vectors. We feel that incubation periods (in the absence of the risk of mortality) of about 12 days for humans and 25 days for vectors (Rogers 1988a,b; 1989) are significant,

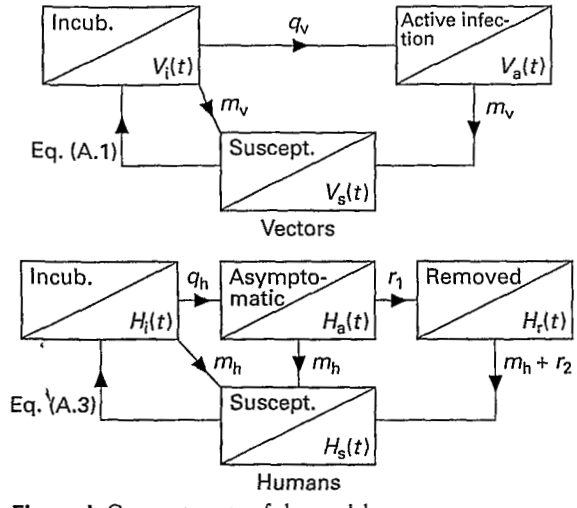

Figure 1 Compartments of the model.

particularly given the vector's relatively short life expectancy of 1–2 months and the long maturation time of *T. brucei gambiense* in the fly.

Human and vector death rates (m_h and m_v) are assumed equal to the corresponding birth rates. The vector and human populations (V and H) are thus assumed constant; therefore, a death is either compensated by the birth of a new susceptible or by the arrival of an uninfected immigrant (the two are mathematically indistinguishable).

Time will be considered continuous and the unit of time has been taken as 3 days, the average time between blood meals. The parameter τ_1 is then defined as the probability that a fly will have a blood meal on a human during one unit of time (one 3-day period); τ_2, the intrinsic vectorial capacity, is the probability that a blood meal on an infected human will result in a mature infection in the fly (Le Ray 1989); and τ_3, the human susceptibility, is the probability that an infected fly bite on a susceptible human will lead to an infection.

The parameters q_v and q_h are the rates at which vectors and humans leave the incubating stage. For humans, r_1 is the rate at which individuals leave the asymptomatic stage to enter the removed compartment and r_2 is the recovery rate. (Thus in the absence of the risk of mortality $1/r_1$ is the average duration of the first stage and $1/r_2$ the average removal time, in units of 3 days; thus, for example $r_1 = 1/40$ means that the average time in the first

stage is 40 3-day time units, i.e. 120 days or 4 months).

We chose to model the system with a set of five differential equations (given in Appendix 1). Differential equations are useful when the modelled phenomena occur in continuous time, which is the case here. Also, such equations imply that transitions occur deterministically and that the variables are continuous. Those are approximations here. For example, a fraction τ_1 of flies has a blood meal and therefore every 3 days there are $\tau_1 V$ blood meals on humans, which is in fact an average value. Deterministic models of this kind therefore assume average values in all transitions.

The basic reproduction rate R_0 is the average number of humans from a susceptible population that will be infected (via the flies) by one asymptomatic carrier (i.e. an infected individual in the first stage); R_0 is a threshold for disease transmission at the beginning of an epidemic, when infection prevalences are low and the effect of density dependence is negligible. The parameter R_0 is derived in Appendix 2 and is equal to:

$$R_0=\frac{\tau_1^2\tau_2\tau_3 q_h V q_v}{(m_v+q_v)(r_1+m_h)(m_h+q_h)H} \qquad (1)$$

In accordance with classic epidemiologic theory, we have shown that when the system is close to the origin (low infection prevalence among humans and flies), the epidemic goes to extinction if $R_0<1$ and flares up when $R_0>1$.

The average time spent by a newly infected person in the asymptomatic stage is the product $[q_h/(m_h+q_h)]\times[1/(r_1+m_h)]$: the first term is the probability that a newly infected person reaches the asymptomatic stage (before dying) and the second term is the time spent in that stage. The rate R_0 can then be written as

$$R_0=[q_h/(m_h+q_h)]\times[1/(r_1+m_h)]\times M \qquad (2)$$

where $M=\tau_1^2\tau_2\tau_3 V q_v/[H(q_v+m_v)]$ is the rate of new contaminations per unit of time: it is the average number of new human infections eventually produced by an infected individual, per unit of time.

If we define the quantity $Q=\tau_1^2\tau_2\tau_3 V/H$ then $Q=M(q_v+m_v)/q_v$. For fixed q_v and m_v, Q is proportional to M and is therefore a measure of the potential spread of the epidemic. The parameter Q will play an important role in the sequel and we call it the intrinsic contamination rate (ICR). In terms of Q, the basic reproduction rate is then:

$$R_0=Q\cdot\frac{q_v}{q_v+m_v}[q_h/(m_h+q_h)]\times[1/(r_1+m_h)] \qquad (3)$$

We note that the basic reproduction rate R_0 in equation (3) is now expressed in terms of six independent quantities: Q, r_1, q_v, m_v, m_h and q_h.

Modelling of control strategies

We will consider two approaches to the control of sleeping sickness: the detection of infected individuals in the asymptomatic stage; and vector control.

Detection of infected individuals

There are two methods for the active detection of infected individuals: periodic large-scale screenings ('vertical detection') and continuous detection by primary health care centres ('horizontal detection'). Immunologic tests such as IFIT or TESTRYP CATT, which are useful for the detection of asymptomatic carriers, can be used in addition to traditional glandular palpation (Frezil *et al.* 1977; Mentens 1991). The model will translate the horizontal detection method through an increase in the removal rate r_1.

In order to quantify this increase we decompose r_1 into a sum $r_1=r_{1,int}+r_{1,ext}$ of two terms; first, an intrinsic removal rate $r_{1,int}$ which depends on the pathogenicity for the population of the particular strain of *Trypanosoma brucei gambiense*; and second, an extrinsic removal rate $r_{1,ext}$ which results from the detection of infected individuals. Given that the model is continuous the proportion detected during a time interval $(0, t)$ is then $1-\exp(-r_{1,ext}t)$ and because the unit of time is 3 days the proportion detected in one month (expressed as a percentage) will be $100[1-\exp(-10r_{1,ext})]$. We will re-parameterize the instantaneous rate $r_{1,ext}$ by considering this monthly percentage and calling it $\delta_h=100[1-\exp(-10r_{1,ext})]$. Then $r_1=r_{1,int}-0.1\times\ln[1-\delta_h/100]$.

Vector control

Vector control is achieved primarily through the sustained use of trapping, insecticide-impregnated target

screens or the spraying of insecticide, all of which increase the fly mortality m_v. During a transient period the vector population V may decrease and reach a new equilibrium value that depends on the potential for population replacement (e.g. possible increased immigration) and on density-dependence phenomena. If the fly population is very isolated, immigration cannot compensate the increased mortality and the fly population V may then drastically decrease, for example in savanna areas, where trapping can be very effective and result in a lowered vector density (Gouteux & Sinda 1990). If the fly population is not too isolated (e.g. in forest areas), immigration can compensate for an increased mortality m_v and therefore V may not decrease much (Rogers *et al.* 1984).

In order to model an increased mortality of vectors we decompose m_v into a sum $m_v=m_{v,int}+m_{v,ext}$ of two terms: an intrinsic mortality rate $m_{v,int}$ and an added (or 'extrinsic') death rate $m_{v,ext}$ due to vector control. We will re-parameterize $m_{v,ext}$ by considering a daily percentage of flies δ_v killed which is a parameter that has been used by others (Weidhaas & Haile 1978). As the unit of time is 3 days we have $\delta_v=100[1-\exp(-\frac{1}{3}m_{v,ext})]$ and therefore $m_v=m_{v,int}-3\times\ln(1-\delta_v/100)$.

The expression for R_o, considered now a function of δ_h and δ_v becomes:

$$R_0(\delta_h,\delta_v)=\frac{Qq_v[q_h/(m_h+q_h)][1/(r_{1,int}-0.1\times\ln(1-\delta_h/100)+m_h)]}{q_v+m_{v,int}-3\times\ln(1-\delta_v/100)} \quad (4)$$

Our goal will be to study the combinations of detection (through δ_h) and vector control strategies (through δ_v and possibly Q (since Q is proportional to V)) that will bring the basic reproduction rate R_o below 1. We do this by setting $R_o(\delta_h, \delta_v)=1$ in equation (4) and expressing δ_v as a function δ_v (δ_h) of δ_h. We thus obtain:

$$\delta_v(\delta_h)=100\left\{1-\exp\left[-\frac{1}{3}\left(\frac{Qq_vq_h}{(m_h+q_h)(r_{1,int}-0.1\times\ln(1-\delta_h/100)+m_h)}-m_{v,int}-q_v\right)\right]\right\} \quad (5)$$

In the sequel we will also need the expression for Q as a function of $r_{1,int}$, δ_v and δ_h (Q is obtained from equation (5)):

$$Q(r_{1,int},\delta_v,\delta_h)=\{[m_{v,int}+q_v-3\times\ln(1-\delta_v/100](m_h+q_h)(r_{1,int}-0.1\times\ln(1-\delta_h/100)+m_h]/q_vq_h \quad (6)$$

Equation (5) yields in the (δ_h, δ_v) plane the locus of points for which $R_o=1$ and for fixed δ_v, δ_h the linear function $Q(r_{1,int}, \delta_v, \delta_h)$ of $r_{1,int}$ (equation (6)) represents the same locus in the ($r_{1,int}$, Q) plane. This last function will be used to study the feasible control strategies (δ_h, δ_v) as functions of ($r_{1,int}$, Q). We begin by specifying parameter values.

Model parameter values

In equations (5) and (6) we will take the parameters m_h, $m_{v,int}$, q_v, q_h as fixed and study control strategies (δ_h, δ_v) as functions of ($r_{1,int}$, Q).

Unchanging parameters m_h, $m_{v,int}$, q_v, q_h

We assume that the mortality rate m_h corresponds to a life expectancy of 50 years, i.e. $m_h=1.644\times10^{-4}$. In the absence of vector control the life expectancy of a fly is taken to equal 1.5 months, which means $m_{v,int}=1/15$. Following Rogers (1988a,b) we assume that in the absence of the risk of mortality the average incubation periods are 25 days for vectors and 12 days for humans, which translate into rates $q_v=1/(25/3)=0.12$ and $q_h=1/(12/3)=0.25$. The average time spent by flies in the incubating compartment is then $0.1/(0.12+1/15)$ months or 16 days. We note that m_h is negligible compared to $r_{1,int}$ so that with very little error m_h could be set equal to 0, which also makes q_h cancel out in equations (5) and (6). Thus only q_v and $m_{v,int}$ are of significance and the values of m_h and q_h have little impact on the results.

Parameters Q *and* $r_{1,int}$

Given the uncertainties concerning the values of the five parameters τ_1, τ_2, τ_3, V and H that make up the intrinsic contamination rate $Q=\tau_1^2\tau_2\tau_3 V/H$, the analysis must be thought of in global terms through the effect of these parameters together on Q. We will derive a realistic range of values for Q on the basis of plausible values for these five parameters.

Table 1 Illustrative values of the intrinsic contamination rate Q, with corresponding values of τ_1 (other parameters are fixed—see text)

Scenario	A	B	C	D	E	F
Q	0.002	0.010	0.018	0.040	0.050	0.060
τ_1	0.044	0.098	0.132	0.197	0.220	0.241

We assume with Rogers (1988a) that τ_3=0.62. For τ_2 we choose 0.1, which is an average value found for various species among the *palpalis* group of tsetse flies (Aert *et al.* 1985; Kazadi *et al.* 1992; Le Ray 1989; Moloo *et al.* 1986; Taylor 1932). We consider that the parameter τ_1 can vary depending on the type of epidemic in a range roughly between 0.05 and 0.25 (Gouteux *et al.* 1982b; Moloo 1993).

Our model applies to an 'epidemiologic unit' typically consisting of a village of about H=300 inhabitants. Infection occurs only close to the village. This mode of transmission was termed 'peridomestic' by Frezil *et al.* (1980).

The figure of 300 is an average value based on 22 villages observed in the Central African focus of Nola-Bilolo (Gouteux *et al.* 1993b). A rough estimate of the number of vectors in and around such a village is V=5000. This figure, which is used by Rogers (1988a), is consistent with the range of 1000–9000 obtained through capture–recapture methods used in an Ivory Coast village (Gouteux *et al.* 1981, 1982a; Gouteux & Buckland 1984). The number of vectors can however vary considerably, and 5000 is just an order of magnitude.

We will consider six possible values of Q, consistent with these estimates (Table 1). For each value of Q (scenarios A to F) the parameters τ_2, τ_3, H and V are fixed at their values given above (0.1, 0.62, 300 and 5000) and τ_1 will be the value needed in order for Q to have each one of the prescribed values in the 0.002–0.060 range. The corresponding values for τ_1 are in the range 0.044–0.241. These are plausible minimum and maximum values depending on the number of pigs in and around the village: pigs are a fly's favorite host, so a large population of pigs reduces τ_1 and vice versa.

When there is no medical intervention infected people stay for a long time in the first (asymptomatic) stage and enter the removed compartment only when they reach the meningo-encephalitic stage of the disease (second stage). In such an endemic situation the average time $1/r_{1,int}$ spent in the first stage can be several years (Frezil *et al.* 1977; Ginoux & Frezil 1981). We chose a value of $r_{1,int}$=3/3650 (corresponding to 10 years) to illustrate this situation.

When the parasite is virulent, the average time $1/r_{1,int}$ in the asymptomatic stage can be just a few months (Burke 1964). In such an epidemic situation infected individuals rapidly move into the removed compartment which contains a high proportion of the sick population. A value of $r_{1,int}$=1/40 (corresponding to 4 months) will be chosen to illustrate this scenario.

We will consider that each of the six values for Q (scenarios A–F) can be combined with $r_{1,int}$=3/3650 (scenarios A′–F′) or with $r_{1,int}$=1/40 (scenarios A″–F″).

Results

To assess the feasibility of different control strategies we will assume that δ_v and δ_h can both have a maximum realistic value of 10%. Thus we assume that the maximum added daily mortality of flies is 10% and the maximum monthly detection rate is 10%. These are plausible maximums today although in the past much higher detection rates were obtained using drastic methods that could not be employed today (Dozon 1985).

In the 'feasibility diagram' depicted in Figure 2 we have plotted in the ($r_{1,int}$, Q) plane the four straight lines $Q(r_{1int}, 0, 0)$, $Q(r_{1,int}, 10, 0)$, $Q(r_{1,int}, 0, 10)$, $Q(r_{1,int}, 10, 10)$, labelled L1, L2, L3, and L4, respectively. For example the L2 line is interpreted in the following manner: if a point ($r_{1,int}$, Q) is below that line then with no detection (δ_h=0) there is a value of δ_v<10 for which R_0<1, i.e. for which extinction will occur. Above that line, with no detection, there is no value δ_v<10 for which there is extinction. Thus for example the small triangle A_3 (between the L2 and L3 lines) is the region of the ($r_{1,int}$, Q) plane for which detection alone (at some level δ_v<10) will bring about extinction, but vector control alone cannot lead to extinction. The other regions have similar interpretations detailed in the figure's legend.

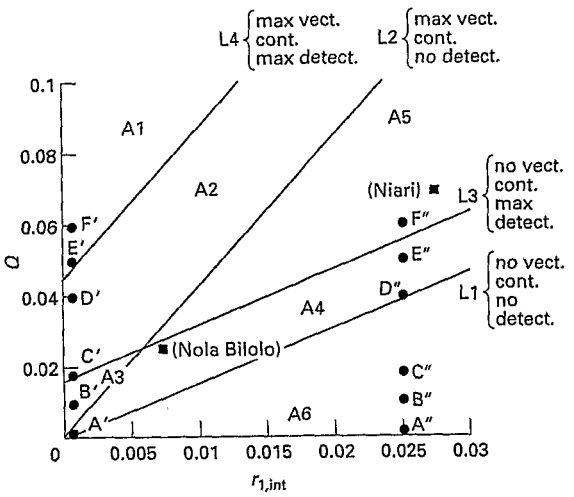

Figure 2 ('Feasibility diagram') Straight lines that divide the ($r_{1,int}$, Q) plane according to the feasibility of the two control strategies. Line L1, R_0=1 with no vector control and no detection: $Q(r_{1,int}, 0, 0)$=0. Line 2,.R_0=1 with maximum vector control and no detection: $Q(r_{1,int}, 10, 0)$=0. Line L3, R_0=1 with maximum detection and no vector control: $Q(r_{1,int}, 0, 10)$=0. Line 4, R_0=1 with maximum detection and vector control: $Q(r_{1,int}, 10, 10)$=0. *Control strategies needed for extinction depending on region in ($r_{1,int}$, Q) plane*: A1, No combination of the control strategies will work. A2, Both are necessary. A3, Detection alone (but not vector control alone) works. A4, One or the other strategy alone works. A5, Vector control alone (but not detection alone) works. A6, Neither strategy is needed for extinction.

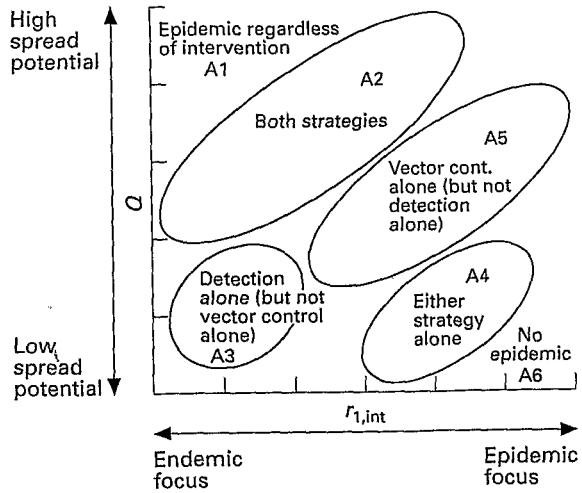

Figure 3 Qualitative feasibility diagram giving the combination of control strategies needed to obtain extinction as a function of ($r_{1,int}$, Q).

In Figure 2 the 12 black dots are marked at points corresponding to scenarios A′–F′ ($r_{1,int}$=3/3650=0.00082) and A″–F″ ($r_{1,int}$=1/40=0.025). Consider first the endemic situation of scenarios A′–F′. In a hypothetical situation with Q=0.06 (F′) no combination of the interventions in the realistic ranges considered will bring about extinction since ($r_{1,int}$, Q) is in A_1. If Q can be lowered to 0.04 (D′) then the point enters A_2 which means that both strategies must be used at some levels δ_h<10 and δ_v<10 to obtain extinction. The decrease in Q can be obtained through a decrease of τ_1 (Table 1) but also through a decrease of τ_2, τ_3 or *V/H*. If Q can be lowered further to 0.010 (B′ in A_3), then detection alone at some level δ_h<10 will being about extinction. The important point here is that Q must decrease to the very low value Q(3/3650, 10, 0)=0.0041 (line L2) before vector control alone is effective (area A_4 where one or the other strategy alone can work). Finally, there is no value of Q for which vector control alone works and detection alone would not (i.e. the point ($r_{1,int}$, Q) cannot be in A_5 for $r_{1,int}$=3/3650).

In an epidemic situation (A″–F″) results concerning the relative efficiencies of the two control strategies are reversed. There is a large area A_5 where vector control alone is sufficient, and Q must be lowered below Q(1/40, 0, 10)=0.055 (line L3) before entering A_4 in which one or the other strategy works alone. There is no value of Q for which detection alone works and vector control alone would not.

In summary, Figure 2 shows that the relative efficiencies of control strategies will depend on the epidemiologic context of a particular focus: if only one strategy is envisaged, in an endemic situation the detection of infected individuals must be attempted first (e.g. for B′ no vector control δ_v<10 will bring about extinction). In an epidemic situation it is vector control that will be more efficient (e.g. for F″). These findings are summarized in qualitative form in Figure 3.

We indicated earlier that m_h and q_h would have little impact on the results, but it is of interest to assess the effect on Figure 2 of changes in $m_{v,int}$ and q_v. A sensitivity analysis is reported in Figure 4

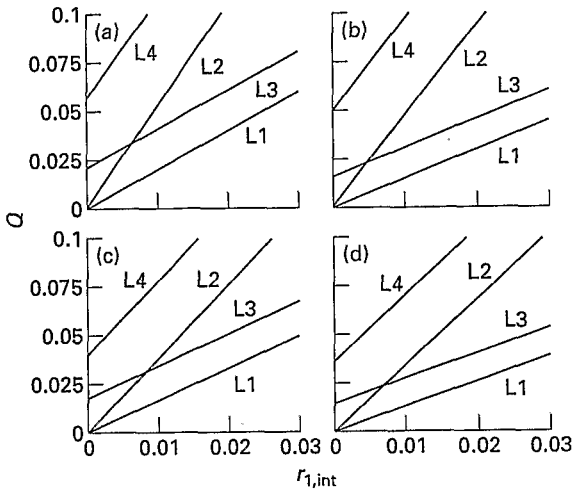

Figure 4 Sensitivity of the feasibility diagram to the fixed parameters $m_{v,int}$ and q_v. a, $m_{v,int}$=0.10, q_v=0.10; b, $m_{v,int}$=0.05, q_v=0.10; c, $m_{v,int}$=0.10, q_v=0.15; d, $m_{v,int}$=0.05, q_v=0.15.

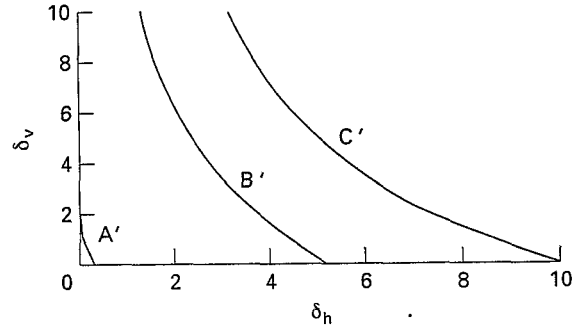

Figure 5 For scenarios A′, B′, C′, locus of points (δ_h, δ_v) (detection rate and added vector death rate) for which R_o=1. On right of curve R_o<1 (extinction) and on left R_o>1 (epidemic).

which depicts the four lines L1, L2, L3 and L4 for four pairs of values of ($m_{v,int}$, q_v): values of $m_{v,int}$ equal to 0.10 or 0.05 (i.e. a life expectancy of flies equal to 1 and 2 months) are combined with q_v=0.10 of 0.15 (fly incubation periods of 30 and 20 days). Figure 4 shows that the regions are not very sensitive to the parameter values chosen, and the broad areas outlined in Figure 3 remain valid for the ranges of parameter values considered.

Figures 5 and 6 give for scenarios A′–C′ (Figure 5) and scenarios D″–F″ (Figure 6) the actual values of (δ_h, δ_v) for which R_o is 1 (equation (5)). If a point

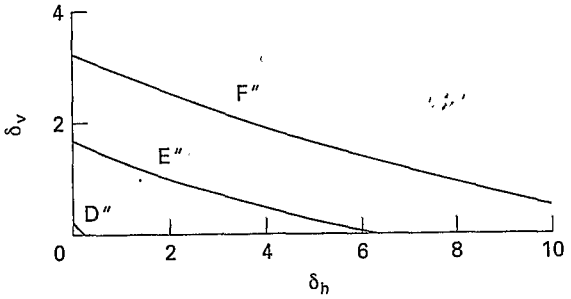

Figure 6 For scenarios D″, E″, F″, locus of points (δ_h, δ_v) (detection rate and added vector death rate) for which R_o=1. On right of curve R_o<1 (extinction) and on left R_o>1 (epidemic).

(δ_h, δ_v) is on the right side of the curve there is extinction; on the left side there is an epidemic.

A comparison of control strategies can be illustrated on Figure 5 for scenario C′. This figure shows that in this case (with Q=0.018) detection alone can work at the maximum monthly 10% detection rate (C′ is just above the L3 line in Figure 2). Vector control alone will not work, but the combinations of both strategies that work can be read off the graph for C′. The figure also shows the impact of a lowered Q: if a decrease of τ_1 or V lowers Q to 0.010 (scenario B′ in A_3) then a 5% monthly detection rate becomes sufficient to bring about extinction. Vector control alone still cannot produce the desired result. If Q can be lowered to 0.02 (scenario A′ in A_4) then an added vector mortality rate of only 2% or a detection rate of about 0.5% per month is sufficient.

The fact that in Figure 5 (endemic focus) the curves are steeper than in Figure 6 (epidemic focus) confirms that in an endemic situation detection is more efficient, while vector control is more efficient during an epidemic.

Application

We tested the model with data obtained in two typical sleeping sickness foci of Central Africa: the Niari focus (circa 1980) in a savanna area in the Republic of Congo (Frezil *et al.* 1980) and the historic focus of Nola Bilolo in a forest area (circa 1940) in the M'Bimou area, Central African Republic (Lotte 1953; Gouteux *et al.* 1993a,b). In both cases the vector is Glossina *palpalis palpalis*.

In order to test our model in these foci, we need to get rough estimates of $r_{1,int}$ and Q and investigate whether the results obtained in the field are consistent with the model (at least in broad terms).

The parameter $r_{1,int}$ is estimated by noting that in an equilibrium situation without intervention the ratio $r_{1,int}/r_2$ is equal to the ratio MI of the population in the second stage to that in the first stage; MI is called the 'Muraz index' (Lotte 1953). In the Nola-Bilolo focus MI is about 0.15 (Lotte 1953), and we estimate the sojourn time in the removed compartment to be roughly 2 months, which corresponds to $r_2=1/20$. Therefore in this case $r_{1,int}$ is equal to $0.15 \times (1/20)=0.0075$ which corresponds to an average sojourn time of 13.33 months in the first stage. This agrees with Lotte's (1953) observation that the time spent in the first stage is slightly greater than one year. As in the M'Bomo focus in Congo (Frezil *et al.* 19891), this relatively long time in the first stage is an indication of high trypanotolerance of forest populations (Frezil *et al.* 1981; Frezil 1983).

Data from the Niari focus show that MI is about 0.54 in that area (Gouteux *et al.* 1988). With the same r_2 of 1/20 we get an estimate of $r_{1,int}$ that is equal to $0.54 \times (1/20)=0.027$ (which corresponds to an average sojourn time of 3.7 months in the first stage). The higher virulence of the parasite in this focus has been observed by Frezil *et al.* (1979).

The four parameters m_h, $m_{v,int}$, q_v, and q_h are kept equal to their previous values. In order to estimate Q we assume as before that $H/V=300/5000$, $\tau_2=0.1$ and $\tau_3=0.62$. The difference in the values of Q between the two sites will reside in different values of τ_1. In the forest area of Nola-Bilolo we take $\tau_1=0.15$, and in the savanna area of Niari we take $\tau_1=0.25$. These figures, which are rough estimates obtained from villages without pig-rearing, are based on the assumption that in the absence of pigs there are more tsetse hosts (e.g. game) in forests and a higher man–fly contact in a savanna focus. The corresponding values of Q are 0.023 for Nola-Bilolo and 0.065 in the Niari focus.

For each one of the two foci we have drawn in Figure 2 a black square at the corresponding value ($r_{1,int}$, Q). Figure 7 depicts the (δ_v, δ_h) loci.

Figure 2 shows that Nola Bilolo is in A_4 which means that one or the other strategy can be used alone. Figure 7 shows the corresponding values of $\delta_v \sim 5.5\%$ (for $\delta_h=0$) and $\delta_h \sim 6.5\%$ (for $\delta_v=0$). In 1946 the 'Service Général d'Hygiène Mobile et de Prophylaxie' (SGHMP) was set up to efficiently find and treat infected people in that focus. Dr Jamot's method of mobile detection units resulted in detection rates probably well above 6.5% per month and incidence rates dropped rapidly to values close to 0 by 1949 (Lotte 1953). Vector control was not attempted in Nola Bilolo but the model suggests that an added death rate of flies above 5.5% per day (or any combination of δ_v and δ_h on the curve) would have resulted in extinction.

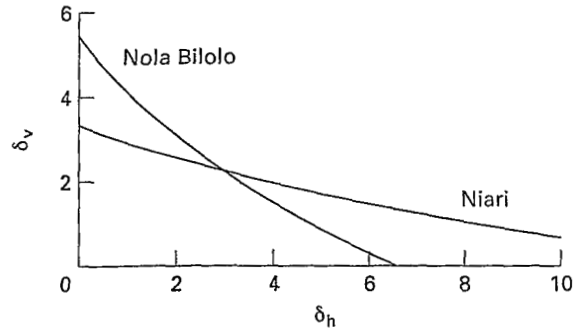

Figure 7 For the two Central African foci considered in the text, locus of points (δ_h, δ_v) (detection rate and added vector death rate) for which $R_o=1$. On right of curve $R_o<1$ (extinction) and on left $R_o>1$ (epidemic).

In Figure 2 the square corresponding to the Niari focus is in A_5 where vector control alone should bring about extinction but detection alone cannot. This conclusion, arrived at on the basis of the model, is in agreement with field observations. Indeed, in this savanna focus detection and annual screenings of the population did not stop the epidemic. However, a more than 50% drop in the vector population was obtained in a few weeks (Gouteux *et al.* 1986) and this implies a 50% drop in Q. (This is a case where vector control was achieved through a decrease in V, and thus of Q.) The black square for Niari then moves into A_4 or even A_6 (Figure 2). In this context the prevalence of the disease decreased from an average 2.7% during the period 1983–1985 to about 0.4% in 1986–1987 (Gouteux & Sinda 1990). The model suggests that even without detection (which is always used for ethical reasons) the 50% drop in V would probably have resulted in extinction.

Given the great uncertainty surrounding our estimates of $r_{1,int}$ and Q in those two foci we would not claim to have truly validated the model with those examples. However, results are generally consistent with field observations which suggests that our simple model is at least a plausible approximation to a complicated biological system.

Conclusion

Our goal was to compare two control strategies for sleeping sickness in Central Africa. A detailed analysis of the basic reproduction rate of a compartmental model has shown that the optimal control strategy depends on two important parameters: the intrinsic removal rate $r_{1,int}$ which captures the pathogenicity for the population of the particular trypanosome strain, and the intrinsic contamination rate Q which reflects the potential spread of the epidemic. The crucial role played by Q shows that greater efforts need to be made to obtain better estimates of its components, i.e. the epidemiologic parameters τ_1, τ_2, τ_3 and the ratio V/H. It is noteworthy that τ_1, τ_2 and τ_3 enter together into Q and that total populations enter only in the form of the ratio V/H. Because τ_1 (the proportion of blood meals on humans) is squared in Q, it is the most sensitive parameter but also one that can be estimated by entomologists on the basis of gorged flies caught in transmission zones.

In an endemic situation with a small $r_{1,int}$ there is a large infected population in the first stage and the detection and treatment of these sick individuals is critical and more efficient than vector control. In an epidemic characterized by a large $r_{1,int}$ the situation is reversed: there are fewer infected individuals and vector control becomes more efficient. In all cases a value δ_v for extinction (Figures 5–7) that is calculated on the assumption that V (and therefore Q) does not decrease, will yield a *conservative* estimate of the vector death rate needed for extinction. This insight can be useful when the impact of vector control on the total vector population cannot be measured accurately.

The fact that the optimal control strategy depends on $r_{1,int}$ (the endemicity) suggests a typology of sleeping sickness foci that needs to be further investigated: endemic-type foci with a long first stage for which detection may be more efficient and epidemic-type foci with a short first stage for which vector control may yield better results.

The model can be generalized and extended in several ways. First, our analysis of the basic reproduction rate could be applied to a model that would incorporate animal reservoirs. This would produce results applicable to the Gambian sleeping sickness that affects Western Africa. An extension of the model could include economic and social variables essential in the search for optimal control strategies when resources are limited.

Appendix 1. Model's equations

With V and H the total populations of vectors and humans, $V_s(t)$ and $H_s(t)$ are the susceptible populations; $V_i(t)$ and $H_i(t)$ the incubating populations; $H_a(t)$ is the human population in the first (asymptomatic) stage and $V_a(t)$ the fly population in the active infection stage; $H_r(t)$ is the number of removed humans. We thus have $V=V_i(t)+V_a(t)+V_s(t)$ and $H=H_i(t)+H_a(t)+H_r(t)+H_s(t)$ for all t. The system of differential equations is:

$$\frac{dV_i(t)}{dt}=Vm_v\tau_1\tau_2\frac{H_a(t)}{H-H_r(t)}-V_i(t)(q_v+m_v) \quad (A.1)$$

$$\frac{dV_a(t)}{dt}=V_i(t)q_v-V_a(t)m_v \quad (A.2)$$

$$\frac{dH_i(t)}{dt}=\tau_1\tau_3V_a(t)\left(\frac{H-H_i(t)-H_a(t)-H_r(t)}{H-H_r(t)}\right)-H_i(t)(q_h+m_h) \quad (A.3)$$

$$\frac{dH_a(t)}{dt}=H_i(t)q_h-H_a(t)(r_1+m_h) \quad (A.4)$$

$$\frac{dH_r(t)}{dt}=H_a(t)r_1-H_r(t)(m_h+r_2) \quad (A.5)$$

Because total populations are assumed to be constant, the susceptibles are obtained as:

$$V_s(t)=V-[V_{in}(t)+V_a(t)] \quad (A.6)$$

$$H_s(t)=H-[H_{in}+H_a(t)+H_r(t)] \quad (A.7)$$

The critical transitions are those from the susceptible compartments to the incubating ones (equations (A.1) and (A.3)). To approximate the fact that a fly can become infected only during the very early stages of its life we will assume that only flies in the

first age-group (i.e. aged less than 3 days) are actually susceptible to infection. This means that they can become infected only during their first blood meal since the unit of time was taken equal to 3 days (the average time between meals). Given that all flies (including the infected ones) are assumed to have the same birth and death rates m_v and are assumed to give birth to uninfected flies, there will be at all times Vm_v uninfected flies in the first age-group. Each one of these Vm_v flies will have a blood meal which will lead to an infection on an actively infected human, with probability $\tau_1\tau_2 H_a(t)/(H-H_r(t))$. (The $H_r(t)$ removed individuals cannot be bitten.) The second term on the right-hand side of equation (A.1) expresses losses of incubating flies to active infection and death.

Equation (A.3) expresses the fact that to become infected a given susceptible human must be bitten by (at least) one of the $V_a(t)$ actively infected flies (which occurs with probability $\tau_1 \times V_a(t) \times (t) \times (H-H_i(t)-H_a(t)-H_r(t))/(H-H_r(t))$); this bite must also lead to an infection (probability τ_3). The second term on the right-hand side of equation (3) expresses losses to active infection and death. Equations (A.2), (A.4) and (A.5) are routine balance equations. More details on the model are described in Artzrouni and Gouteux (1996).

Appendix 2. Derivation of basic reproduction rate R_0

The parameter R_0 is a product R_1R_2 where R_1 is the average number of flies infected by one infected human and R_2 is the number of humans each infected fly will infect in turn. One newly infected human has a probability $q_h/(m_h+q_h)$ of reaching the active infection stage (this number is essentially 1, as the probability of death is negligible compared to that of a transition to active infection). In one unit of time each one of the $\tau_1 Vm_v$ young susceptible flies that will have a blood meal on a human has a probability $1/H$ of biting the infected human and a probability τ_2 that this bite will lead to an infection. Finally the average duration of the active infection stage during which the one infected human can contaminate flies is $1/(r_1+m_h)$: the human leaves this stage through death or a transition to the removed compartment. Hence $R_1=\tau_1\tau_2 q_h Vm_v/[(r_1+m_h)(m_h+q_h)H]$.

Similarly, R_2 (the number of humans each infected fly will infect) will be $\tau_1\tau_3 q_v/[m_v(m_v+q_v)]$: $q_v/(m_v+q_v)$ is the probability of reaching the active infection stage; $1/m_v$ is the average duration of that stage during which an infected fly can spread the disease, and $\tau_1\tau_3$ is the average number of humans such a fly will infect per unit of time. Therefore

$$R_0=R_1R_2=\frac{\tau_1^2\tau_2\tau_3 q_h V q_v}{(m_v+q_v)(r_1+m_h)(m_h+q_h)H}.$$

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