Sensitivity Analysis of Simple Endemic Models

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I. Introduction

Simple mathematical models have had considerable success in explaining basic epidemiological features, such as threshold phenomena and cyclical outbreaks. This chapter presents a sensitivity analysis of some simple models for endemic diseases such as rabies, and shows that there are unresolved problems in making *quantitative* use of them, especially in the crucial area of evaluating control strategies.

This is not to say that it is wrong to look at simple models. On the contrary, what I try to do here is to go a step further in simplification and argue as far as possible in terms of the basic components which any model for endemic rabies must include. Such coarse data as exist for diseases like rabies can be used to confirm that we have included the essential components in our epidemic model, and to calibrate each such component correctly. It is much more difficult to get adequate data to determine the quantitative details of each component, yet these details are important if our model is to have predictive value.

I shall illustrate these problems mainly with reference to a basic differential equation model for endemic rabies introduced by Anderson *et al.* (1981; see also Anderson, 1981, 1982), and presented in this volume by Dr. Smith (Chapter 6); and particularly to the possibility of making quantitative use of this model, as

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suggested by those authors. This rabies model differs from standard epidemic models (see e.g. Bailey, 1975) chiefly in including a density-dependent population growth term. This is a welcome improvement, as such a term is clearly important for a proper discussion of diseases like fox rabies in which the disease itself regulates the population density.

Anderson *et al.* cite as support for their model its predictions relating to (1) threshold densities, (2) contact rates between infectious and susceptible foxes, (3) average levels of prevalence of infection, (4) the 3- to 5-year cycle sometimes observed in fox populations infected with rabies, and (5) an association between unstable (i.e. cyclical) endemic conditions and areas of high carrying capacity. Encouraged by this agreement, they base a quantitative discussion of possible control strategies on their model.

The crucial model component for consideration of control, whether by vaccination or culling, turns out to be the *infection term.* These authors follow conventional lines in using a multiplicative term, βXY, for the rate of infection between susceptible and infectious populations of respective densities X and Y. Unfortunately, as I shall show here, the use of a multiplicative infection term in the case of varying population density makes strong implicit assumptions, which critically influence the conclusions on control strategies. However, once the importance of the exact form of the infection term is recognised, we can look for relevant observational evidence which will allow us a more reliably based discussion of control strategies.

The other two main components of a basic rabies model are the terms representing *population growth* and the *generation gap* of the disease (see Section II). We find that the level of prevalence and period of oscillations of the disease are fairly robustly determined, but that conclusions on the stability of oscillations are very sensitive to the detailed assumptions concerning these components.

The considerations presented here should also be relevant to a wide range of applications of simple epidemic models, the main theme being that the quantitative assumptions implicit in such models need careful consideration, especially if we wish to draw quantitative conclusions. The problem of controlling tuberculosis in badgers (see e.g. Henderson, 1982) is similar to that of rabies in foxes. The estimation of required vaccination rates in non-fatal diseases, such as measles and whooping cough, is cited as another example.

I shall also refer more briefly to other simple epidemic models, and to some factors which all these models omit, particularly spatial, stochastic and seasonal effects.

II. Components of Basic Epidemic Models

I here identify three basic components essential for modelling the endemic state of a disease such as rabies: (1) the population dynamics in the absence of

disease, (2) the infectious contacts made by a diseased individual, and (3) the *generation gap* of the disease, that is the time interval between an individual's becoming infected and passing on the disease.

First are the population dynamics in the absence of disease. Diseases that are not usually fatal, such as human colds or measles, have little effect on population numbers; the latter can therefore be modelled separately. Often, it is reasonable to assume a constant equilibrium population, with deaths (from other causes) at a constant rate and births introducing fresh susceptibles occurring at the same constant rate.

In contrast, fatal diseases such as rabies will reduce a population below its usual level, and this may both increase the birth rate and decrease the death rate from other causes. We may reasonably assume that the *per capita net population growth rate* in the absence of disease, ϱ, is a decreasing function of the population density N, varying from a value r at low density to negative values at high densities. The population density K for which the net growth rate is zero defines the *carrying capacity* of the environment. For example, for their deterministic non-spatial model, Anderson *et al.* suggested $\varrho = r(1 - N/K)$, which yields the familiar logistic growth curve for a population below carrying capacity (in the absence of disease).

Second are the infectious contacts made by an infectious individual. Not surprisingly, the total number of potentially infectious contacts made by an infectious individual, sometimes called the *basic reproductive rate, C,* of the epidemic, is a crucial parameter. Indeed, for non-spatial models, in which homogeneous mixing of infectives and susceptibles is assumed so that in the initial stage of an epidemic almost all infectious contacts are with susceptibles and therefore successful, the basic threshold result states simply that the disease has a chance of spreading widely if and only if C is greater than 1. In models with more realistic (local) mixing, the probability of contacting another infective cannot be neglected, even in the earliest stages of an epidemic; C is still a crucial parameter, but its threshold value may be significantly greater than 1.

Unfortunately, the basic reproductive rate does not usually feature explicitly in epidemic models, but enters indirectly through the overall rate of infectious contacts, which is of course an important variable in analysis of such models. The relation between the two is quite straightforward, at least in the case of models with homogeneous mixing, and is as follows.

We take $\tau_2 = 1/\alpha$ to be the mean infectious period, so that an individual makes contacts at average rate αC while infectious; and assume that contacts are made indiscriminately among the population so that their probability of success is equal to the proportion of susceptibles in the population, X/N. Multiplying by the density of infectious individuals Y, we have that the overall rate of infectious contacts (per unit area) is βXY, where $\beta = \alpha C/N$ is a constant which in general must depend on the population density and its relation to the carrying capacity, that is on N and K. Taking β to be a constant, as is often done (e.g. Bailey, 1975;

Anderson *et al.*, 1981), is equivalent to assuming that the reproductive rate $C = \beta N/\alpha$, i.e. that C is proportional to N and independent of K. [Indeed Bacon (see Chapter 7 of this volume) has explicitly used this relationship to produce a 'dimensionless' model, scaled relative to K.]

Third and last, is the *generation gap* T, defined as the time interval between an individual's becoming infected and passing on the disease. The generation gap's mean value τ is important in determining the speed with which an epidemic develops, and in endemic conditions is closely related to the level of prevalence, that is the mean proportion of the population suffering from the disease. Less obviously perhaps, the *variability* of the generation gap turns out to be important for such features as the dependence of an epidemic's velocity on population density, and for determining whether endemic conditions are stable or oscillatory.

It is important in principle to distinguish between the mean generation gap and the mean survival time after infection. However, the difference between the two in practical terms is usually small, at least for rabies where the infectious period is short compared with the latent period; and in several of the simplest models, including all those described in the next section (Equations 1–3), the generation gap and survival time are actually assumed to have the same distribution.

III. Some Basic Models and Their Assumptions

As described in the previous section, the models I shall discuss are each made from three basic components: *population growth, infection,* and the *generation gap* of the disease. In this section I shall first define some simple deterministic models, and then bring out some of the assumptions implicit in the particular form of components chosen for each of them.

In the model by Anderson *et al.* (1981) the densities of susceptible (X), incubating (I) and infectious (Y) individuals is as follows:

$$\begin{aligned} dX/dt &= \varrho X - \beta XY \\ dI/dt &= \beta XY - \sigma I - [(b+\gamma N)I] \\ dY/dt &= \sigma I - \alpha Y - [(b+\gamma N)Y] \end{aligned} \tag{1}$$

where $N = X+I+Y$ is the total population density, and α, β, γ, σ and b are constants; ϱ denotes the *per capita* net population growth rate, which Anderson *et al.* take equal to $r(1-N/K)$, where K denotes the carrying capacity of the fox habitat. An interpretation of the constants β, α, σ and r, and of the corresponding constants in the following models [Equations (2) and (3)] is given later; for estimates, appropriate to fox rabies, of the values of all these constants, see Section IV. The terms in square brackets (involving the constants γ and b) relate to mortality from natural causes of incubating and infectious individuals; their effect is negligible in most respects, and discussion of the model will be much clearer if we omit them.

A somewhat simpler family of models is described by the equations

$$\begin{aligned} dX/dt &= \varrho X - \beta' XV \\ dV/dt &= \beta' XV - \alpha' V \end{aligned} \tag{2}$$

This equation covers several well-known models, in each case keeping β' and α' as constants. First, we can regard it as an epidemic model in which we fail to distinguish between incubating and infectious individuals; thus V replaces $I+Y$. If $\varrho = c/X$ we obtain a standard model for diseases such as measles (Bartlett, 1960) in which we assume the 'immigration' of susceptibles at constant rate c. For rabies it would be more appropriate to follow Anderson *et al.* in taking $\varrho = r(1-N/K)$. If we take the slightly different formula $\varrho = r(1-X/K)$, we have a special case of Verhulst's model, with V representing predators and X prey; while the simpler formula $\varrho = r$ similarly yields a special case of Lotka and Volterra's classic predator–prey model (see e.g. May, 1974, or Chapter 7, this volume).

So far, I have referred only to differential equation models. A possible alternative is to use a discrete-time model, such as the following, in which we have discrete generations of infectious individuals, at time intervals of fixed length τ:

$$\begin{aligned} X_{t+\tau} &= X_t + (\rho X_t - \beta' X_t Y_t)\tau \\ Y_{t+\tau} &= \beta' X_t Y_t \tau \end{aligned} \tag{3}$$

For *infection*, each of these models includes a conventional multiplicative term, βXY. As described in the previous section, this essentially amounts to taking the reproductive rate $C = \beta N/\alpha$; while the *effective reproduction rate*, the mean number of successful contacts, is $R = C.\ (X/N) = \beta X/\alpha$. Similarly, for Equation (2) we obtain $C = \beta' N/\alpha'$; for Equation (3), $C = \beta' \tau N$. Thus if we take β (or β') to be a constant, we are assuming that the reproductive rate C of the epidemic is proportional to N, and independent of K. These are strong assumptions, which go well beyond the observational evidence. The dependence of C on N and K is crucial for the evaluation of control strategies, as will be discussed in Section IV.

Each of the three models also includes a net *population growth* term ϱX, representing the excess of births over deaths from natural mortality. As already mentioned, Anderson *et al.* take $\varrho = r(1-N/K)$. The qualitative assumption here, that ϱ decreases from a value r in low-density populations to zero at the carrying capacity, is very reasonable and a welcome improvement on standard models. The quantitative assumption, that this decrease is linear with increasing population density N, has no particular justification, and we must be sceptical of any conclusions which depend on it.

Last is the distribution of the disease's *generation gap*. Here the three models make different detailed assumptions, in each case chosen to give the simplest mathematical equations. In each case the transfer rates out of certain states are assumed proportional to the numbers in those states. In the differential equation

models, this amounts to assuming that the sojourn times in each state are exponentially distributed; while in discrete-time models they are assumed to be of fixed length or geometrically distributed.

Thus for Equation (2), the generation gap has exponential distribution with mean $\tau = 1/\alpha'$. For Equation (1), the terms σI and αY essentially assume exponential distributions for the incubation and infectious periods, respectively, with means $\tau_1 = 1/\sigma$ and $\tau_2 = 1/\alpha$; then the generation gap T has mean $\tau = \tau_1 + \tau_2$, and probability density function

$$[\alpha\sigma/(\alpha-\sigma)](e^{-\sigma t} - e^{-\alpha t}) \tag{4}$$

The discrete-time model [Equation (3)] assumes a fixed incubation period of length τ and an instantaneous infection period, so that the generation gap is of fixed length τ. This is clearly an extreme case; a more realistic discrete-time model for rabies will be mentioned in the discussion of Section V.

To sum up, the *infection term* involves a parameter β, which has traditionally been assumed to be a constant. The consequences of this assumption in the context of fox rabies will be examined in Section IV. The models discussed also include basic parameters r (the net *population growth rate* in low-density populations) and τ (the mean *generation gap*), which can both be estimated fairly reliably from observations. The detailed forms of the population growth and generation gap terms are less easy to estimate from data, and all the models considered here make simple assumptions based on mathematical convenience. As we shall see in Section V, some features of the models depend principally on r and τ and are thus insensitive to the modelling details, while others are not.

IV. Control Strategies and the Reproductive Rate

The first two points of observational evidence cited by Anderson *et al.* (1981) relate to threshold densities, and contact rates between infectious and susceptible foxes.

Firstly, they note evidence that there exists a threshold value K_T for the carrying capacity K, below which rabies cannot become endemic (their estimate is $K_T \approx 1$ per km^2). This supports the common assumption that the contact rate between foxes increases with K, but not necessarily the further assumptions implicit in the βXY infection term, i.e. that the reproductive rate $C = N/K_T$.

Secondly, the authors cite observations suggesting that the contact rate between normal foxes at around the threshold population density, βK_T, is approximately equal to the death rate α of infectious foxes, as predicted by their model. However, it is axiomatic that at the threshold population density (if such exists) each infected fox gives rise on average to one secondary case. Thus if foxes are rabid for an average period of 5 days, they must in these conditions contact on

average one susceptible every 5 days. The prediction that $\beta K_T = \alpha$ is thus not dependent on their particular model.

Two notes of caution should be sounded here. Firstly, we really need data on the rates of contacts by rabid rather than normal foxes. Secondly, if we take a model which more accurately reflects the local structure of the population, e.g. a stochastic lattice model, we will find that the deterministic model's assumption that $R \approx C$ when $N \approx K$, i.e. that initially almost all infectious contacts are with susceptibles, is incorrect; in fact R may be significantly lower than C because the few infectious cases tend to be clumped together. Thus $\beta K_T = \alpha$ is not strictly correct, the threshold value of C being rather greater than unity for a more accurate model (see Mollison, 1981, or Chapter 12, this volume). In this context, it should be noted that the definition of Anderson *et al.* of the basic reproductive rate is also unsatisfactory in that it ignores the difference between contacts within and outwith a fox's family.

However, ignoring these complications, we may sum up by saying that the evidence of the existence of a threshold population density, together with '$\beta K_T \approx \alpha$', support the general form of the infection term, but not necessarily its quantitative detail, especially its implicit assumption that β does not depend on N or K. But if we do assume the quantitative form, this evidence serves to calibrate our model.

This is a convenient point at which to summarise the calibration of all three models [Equations (1–3)] for the case of fox rabies. For Equation (1), Anderson *et al.* estimate $r \approx \frac{1}{2}$ year^{-1}. They take $\tau_1 = 28$ days and $\tau_2 = 5$ days for the mean incubation and infectious periods, respectively, leading to $\sigma = 1/\tau_1 = 13$ year^{-1}, $\alpha = 1/\tau_2 = 73$ year^{-1}, and $\tau = \tau_1 + \tau_2 = \frac{1}{11}$ years. The threshold population density K_T is estimated ≈ 1 per km^2, as mentioned previously, so that using $\beta K_T \approx \alpha$ we have that $\beta \approx \alpha = 73$. For Equations (2) and (3), the corresponding estimates are given by $\alpha' = 1/\tau = 11$ year^{-1}, and $\beta' K_T \approx \alpha'$, so that $\beta' \approx \alpha' = 11$.

We now turn to the discussion of control strategies. Simply put, the aim of any control strategy must be to reduce the effective reproductive rate R to less than unity. As we have seen, the use of a βXY infection term by Anderson *et al.* implicitly assumes that $R = X/K_T$ and, thus, immediately implies the core of their conclusions, namely that a control policy will succeed if and only if it reduces the density of susceptibles below the threshold carrying capacity K_T.

Consider first a vaccination programme among an undisturbed population, where the density N is equal to the carrying capacity K, and K is greater than K_T. If we vaccinate a proportion p, the density of susceptibles will be $(1-p)K$, so that according to Anderson *et al.* (1981) the vaccination programme will succeed if and only if $p > 1 - K_T/K$. (Note that the more complex spatial simulation model of Berger (1976) also assumes a βXY infection term, and therefore not surprisingly leads to numerical conclusions in good agreement with this.) Experiments

cited by Anderson *et al.* suggest that the maximum achievable value of p for foxes is about $\frac{2}{3}$, leading to the conclusion that vaccination alone can only be effective if K is less than about $3K_T$. However this conclusion depends on the assumption that contact rates are proportional to density ($C = N/K_T$). This does not seem a realistic assumption for territorial animals such as foxes, since the number of *neighbours* of a fox family will increase only slightly if at all as the population density increases. If, for instance, we take C proportional to $\sqrt{N}$ [i.e. $C = \sqrt{(N/K_T)}$], we find that vaccination will be successful if $p > 1-\sqrt{(K_T/K)}$; so that for the same vaccination success rate ($p = \frac{2}{3}$), we would predict that the disease can be prevented in populations of density up to $9K_T$ rather than $3K_T$.

The effects of culling (or of a mixed programme of vaccination and culling) are more difficult to assess. Anderson *et al.* (1981) consider two types of culling policy, of which the 'constant effort' strategy seems the most relevant, the alternative of quota culling being more appropriate to red herring (May, 1981). In any case, their main conclusion is that control by culling will succeed if and only if the population density is held down below K_T. This assumes that contact numbers in a population held down to density K_T will be the same as in an undisturbed population in territory of carrying capacity K_T. There are obvious ecological reasons why this might not be so. For instance, when $N = K_T << K$, competition between foxes for available food will be much reduced, tending to reduce contacts; while on the other hand, families will be broken up by the culling, and this social disturbance is likely to cause more contacts. The poor record of practical attempts at control by culling, to which Anderson *et al.* refer, suggests that the latter may be the stronger effect. Of course, rabies is itself a culling policy of sorts, so that observations of equilibrium densities in endemic areas will be of use, especially in areas where the carrying capacity can be estimated. However, the effect on the contact rate will depend on the method of culling: whether it kills one fox at a time or whole families, and whether it selects relatively more itinerant or settled foxes. Quantitative conclusions clearly require more evidence.

V. Endemic Equilibrium and Oscillations about It

Anderson *et al.* (1981) cite three pieces of evidence relating to the population growth rate and generation gap: namely, the observed level of prevalence, the period of oscillations, and their stability. The first of these concerns the *level of prevalence,* that is the proportion of incubating plus infected cases when the disease is in endemic equilibrium. This can be more simply explained without reference to any particular model as follows: in equilibrium, the net population growth rate ϱX (in their model $\varrho = r(1-N/K)$), and the transition rates from susceptible to incubating, incubating to infectious, and infectious to dead, must

all be equal. It is easily deduced that the ratio $X:I:Y$ (susceptibles : incubating : infectious) must be approximately $\varrho^{-1}:\sigma^{-1}:\alpha^{-1}$ (approximately because natural mortality among infected cases is here neglected). If we let τ denote the mean generation gap (as previously), we then have that the level of prevalence is approximately $\varrho\tau$. Thus we need only the qualitative assumption, that ϱ varies from a value r when $N << K$ down to 0 when $N = K$, to predict that levels of prevalence in endemic areas will vary up to a maximum of $r\tau$. In fact, the cited observation that levels of prevalence in endemic areas lie in the range 3–7%, together with the relatively exact estimate for τ, $\approx \frac{1}{11}$ (years), suggests values of r up to about $\frac{3}{4}$ (per head per year), slightly higher than the authors' estimate of $r \approx \frac{1}{2}$. However, the evidence available does not appear adequate to determine the detailed form of ϱ.

The period of oscillations also turns out to depend principally on the two parameters r and τ (rather than primarily on r alone as suggested by Anderson *et al.*). For instance, for all the models defined previously [Equations (1) to (3)], we find that oscillations close to the equilibrium point have period approximately $T_0 = 2\pi\sqrt{(\tau/\varrho)}$, $\approx 2\pi\sqrt{(\tau/r)}$ for endemic areas of stable rabies where we may assume $\varrho \approx r$ and for oscillations further from equilibrium the period rises in each model. Taking the authors' figures ($r = \frac{1}{2}$, $\tau = \frac{1}{11}$), we find that periods of around 3 years upwards are predicted in each case.

All these models share the authors' assumption that the disease's effective reproduction rate R is proportional to the density of susceptibles, $R = X/K_T$. It is easy to analyse oscillations near equilibrium without making this assumption, and it is found that their period is approximately $T_0 g^{-\frac{1}{2}}$, where $T_0 = 2\pi\sqrt{(\tau/\varrho)}$ as previously, and $g = (X/R)(dR/dX)$, evaluated at the equilibrium value X_0. For instance, if R is proportional to $X^{1/n}$ instead of to X, the period is increased by a factor of $\sqrt{n}$. Thus observed periods of 3–5 years suggest that R does indeed increase with population density, but are also equally consistent with a considerably slower than linear dependence of R on X.

The form of the population growth term ϱX has much less influence on the period. Whether we assume $\varrho = r(1-N/K)$, or take any of the three alternative forms for ϱ mentioned following Equation (2), makes very little difference to the period, at least for small oscillations.

Lastly, Anderson *et al.* cite evidence of a tendency for unstable, i.e. cyclical, dynamic behaviour to be associated with areas of high carrying capacity, $K >> K_T$. This supports the use of a density-dependent growth term, as in their model or Verhulst's equations, rather than the constant birth rate of the Lotka–Volterra model or the constant growth term of the epidemic with immigration. Qualitatively, their use of a more realistic growth term thus appears to be an improvement on previous deterministic epidemic models, though it should be noted that cyclical behaviour can arise through the seasonal and stochastic factors which they neglect (Bartlett, 1960; Stirzaker, 1975). However, the quantitative

details of their model are very sensitive to their precise assumptions concerning both the population growth rate and the distribution of the generation gap. For instance, while their model is unstable for K greater than $K_c \approx 9K_T$, the discrete-time model [Equation (3)] is unstable when $K > K_c = 2K_T$. It is not clear that the discrete-time model, with its fixed generation gap, is a worse approximation than their model, which assigns a probability of about $\frac{1}{4}$ to the generation gap's being shorter than the minimum observed value (12 days). Clearly we need to model the distribution of the generation gap better if we are interested in the conditions for stable population dynamics. A more realistic generation gap distribution, intermediate between the fixed gap of the discrete-time model and Equation (4), will presumably lead to intermediate values for K_c. (For instance, a discrete-time model with geometrically distributed incubation period, and constant infection period of 1 week so that the minimum generation gap is 2 weeks—yields $K_c \approx 5.6K_T$.)

Unfortunately, the value of K_c is also sensitive to the form of the per capita growth rate ϱ, which is difficult to estimate from observations. For instance, K_c will be significantly lower if ϱ, instead of declining linearly as the population density N increases, is near constant for low values of N, decreasing rapidly to zero as N nears K. In the extreme case, where $\varrho = r$ for $N < K$, and $\varrho = 0$ for $N > K$, we find that $K_c = K_T$, i.e. that endemic conditions are always unstable. The formula $\varrho = r(1 - (N/K)^z$, is suggested by R. M. May (personal communication), with values of z perhaps between 2 and 3. Figure 1 shows the dependence of K_c/K_T on z for Equation (1). Remembering that seasonal and stochastic factors may also tend to increase instability, K_c does seem likely to be less than Ander-

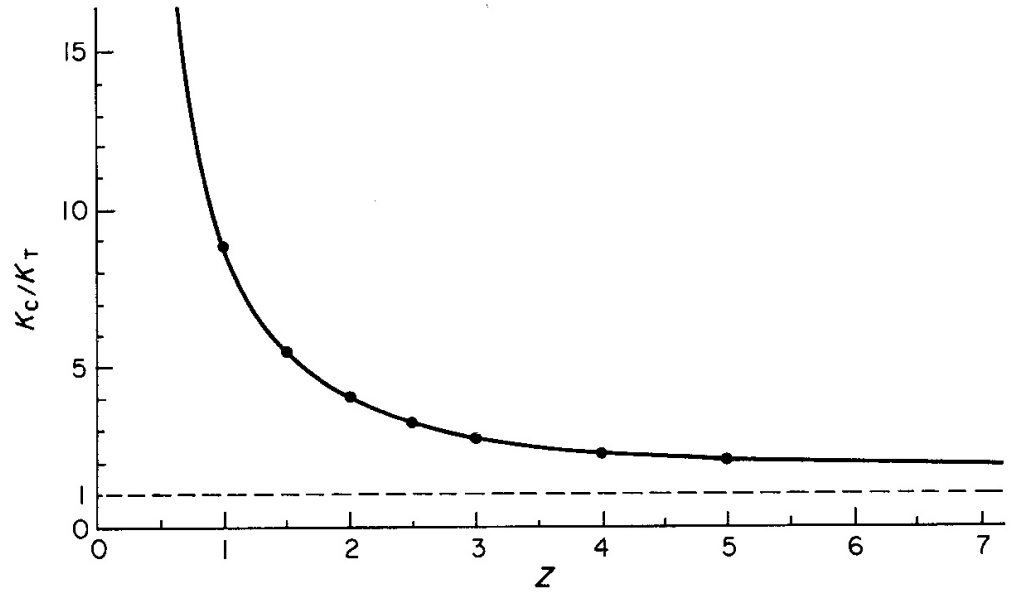

Fig. 1. The dependence of K_c/K_T on z for Equation (1), when $\rho = r[1-(N/K)^z]$ (values of r, α, β and σ as given in Section III).

son *et al.*'s value of approximately $9K_T$, but it is clear that no quantitative conclusions can be drawn at present.

VI. Conclusions

The cardinal virtue of a simple model is that it should be possible to see clearly which assumptions lead to which conclusions. Judged by this criterion, even the simplest models for endemic disease are too complex when considered as a whole.

What I have tried to do here is to show how such models can be dissected into their basic components, and that much of the discussion of their behaviour can be conducted in terms of these components. This dissection clarifies the implicit assumptions which are present in even the simplest models, and makes it easier to assess the dependence of any conclusions on those assumptions.

The most crucial questions concern the likely success of various possible control strategies. This turns out to depend almost entirely on the infection term alone and in particular on its assumptions as to how the basic reproductive rate C will change under the strategy considered. It becomes clear that if we are to make reliable predictions for the control of fox rabies, we need more information on the dependence of C on the population density N and the carrying capacity K. It should not be too difficult to investigate these factors, except that, ideally, studies of rabid foxes are required.

Further difficulties may however arise when we consider the effects of heterogeneous mixing. This is perhaps best illustrated by the example of non-fatal diseases, such as measles and whooping cough, where the population density is not affected by the disease, so that the dependence of C on N and K is of less importance. For such cases, a simple argument due to Dietz (1975) suggests that, when the disease is in endemic equilibrium, C can be estimated as $\approx 1+L/A$, where L is the mean lifetime and A the mean age of contracting the disease. It is easy to construct a model in which the population consists of groups relatively isolated from each other, where the apparent reproductive rate as estimated from Dietz's formula is essentially determined by the contacts between groups rather than between individuals. The true reproductive rate can be much lower, since it only takes $C \approx 3$ to ensure that the introduction of the disease to a 'virgin' group will infect practically all ($> 95\%$) of it (see also Chapter 8; this volume).

Returning to rabies models, we have seen that both the mean level of prevalence and the period of any oscillations about it are determined fairly robustly by the net population growth rate at low densities, r, and the mean generation gap, τ; being $\approx r\tau$ and $2\pi\sqrt{(\tau/r)}$; respectively. The stability of oscillations is a much less robust phenomenon, being particularly sensitive to the way the net popula-

tion growth rate depends on population density, an aspect on which it is difficult to find adequate data.

Even the more robust features considered here may also be sensitive to the effects of heterogeneous mixing associated with the spatial factor omitted from our present discussions (see Chapter 12, this volume).

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