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Simplifying simple epidemic models

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Interest has recently revived in the use of simple models for epidemic diseases. In particular, Anderson *et al.*[1] have introduced an improved simple differential equation model for diseases such as fox rabies which regulate the population density of their host. Here I describe how such apparently simple models can be dissected into their basic components. This dissection facilitates a structural sensitivity analysis in which we explore the dependence of features of a model's behaviour on the assumptions regarding each component. I report that particular features can be related to particular components, for example, oscillations depend mainly on population growth and the generation gap of the disease, while estimates of the effect of potential control strategies such as vaccination or culling can be related directly to assumptions concerning the infection term and the way it changes with population density. Some features, for example, the level of prevalence of the disease and the period of any oscillations, turn out to be robust, depending mainly on basic ecological parameters. Others, including the crucial estimates regarding control, prove very sensitive to the details of the model. This is unfortunate, as the detailed form of the components is to a large extent chosen, not for ecological reasons, but to keep models simple, for example, the infectious period of a disease is often assumed to have an exponential distribution because this implies a constant death or recovery rate for infectious individuals which is mathematically very convenient for a continuous-time model. Because our dissection is in terms of components with straightforward ecological interpretations, any required improvements in modelling can be related to observational evidence which either exists or for which experiments can be suggested[2,3].

The three basic components essential for modelling the endemic state of a host-regulating disease are: (1) the population growth term, describing the population dynamics in the absence of disease; (2) the infection term, describing 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 his passing on the disease.

The model presented by Anderson *et al.*[1] for fox rabies is about as simple as a complete model incorporating all three components can be, but it nevertheless consists of a set of three differential equations in which the relationships between individual components and the model's behaviour are not easy to discern. These equations, slightly simplified, for the densities of susceptible (X), incubating (I) and infectious (Y) individuals, are:

$$\begin{aligned} \partial X/\partial t &= \rho X - \beta XY \\ \partial I/\partial t &= \beta XY - \sigma I \\ \partial Y/\partial t &= \sigma I - \alpha Y \end{aligned} \tag{1}$$

where β, σ and α are constants. In this model, ρX defines the population growth term, βXY the infection term, and σI and αY the distribution of the generation gap. The per capita net growth rate ρ may be density-dependent; usually it is reasonable to assume that it decreases with density, from a value r in low-density populations to zero at the carrying capacity K of the habitat.

A number of such complete models, including a difference equation alternative, with time step equal to the mean generation gap, are analysed in work described elsewhere[2]. Here I shall concentrate on the results and understanding that can be obtained by considering the basic components on their own.

First I shall discuss the infection term in isolation, showing how conclusions on control depend directly on assumptions concerning this term. It is common in simple epidemic models for the infection term to be specified in terms of the overall rate at which infectious contacts occur; for example, the infection rate is commonly assumed to have a multiplicative form, βXY, as in equation (1). However, a better understanding is achieved if we work in terms of the mean number of potentially infectious contacts made by an infectious individual, R_0 (often called the 'basic reproductive rate' of the epidemic, although 'ratio' would be more accurate). In most cases it is reasonable to assume (i) that R_0 does not depend on the density of infectives Y, so that the overall contact rate is $(R_0/\tau_2)Y$, where τ_2 denotes the mean infectious period [$\tau_2 = 1/\alpha$ in the model of equation (1)]. If we also assume (ii) that a proportion X/N of such contacts are successful, as will be the case if a population of density N mixes homogeneously (here $N = X + I + Y$), the mean number of successful infectious contacts (the 'effective reproductive ratio') will be $R = R_0X/N$. The overall infection rate will then be $(R/\tau_2)Y = \beta XY$, where $\beta = R_0/(N\tau_2)$.

If, as is conventional[1,4], we make the further assumption (iii) that β is a constant, we are effectively assuming that R_0 is proportional to the population density N. An immediate consequence of this assumption is that a control policy, whether by vaccination or culling, will eliminate the disease if and only if the susceptible population is kept at or below the threshold population density K_T defined by $R_0 = 1$, that is, $K_T = 1/(\beta\tau_2)$ (refs 1, 2, 5). However, there are few diseases for which the assumption is quantitatively plausible. In many cases, and especially among territorial animals such as foxes, it seems reasonable to assume that R_0 will rise more slowly than linearly with population density. (R_0 would rise linearly with population density if the area over which an animal ranges were independent of density, while on a strict territorial model, R_0 could be independent of N. It seems reasonable to conjecture that the truth lies somewhere between: that is, that R_0 rises with N, but more slowly than linearly.) This has favourable implications for a vaccination control strategy, because the criterion for elimination of the disease is that the proportion unvaccinated should be less than $1/R_0$, and this can be met in habitats of greater carrying capacity if R_0 rises more slowly with density.

When we consider culling, the basic threshold result still holds: we need to achieve $R_0 \leqslant 1$, and if we make the conventional assumption of a βXY infection term, with β constant, the conclusion is that we must reduce the population density to below the threshold carrying capacity K_T. Our analysis in terms of model components here has an advantage of a rather negative kind. By revealing that control depends on a single easily understood ecological parameter, R_0, our analysis makes it much easier to appreciate that our model on its own is inadequate for a consideration of culling: we cannot expect a population held down to density K_T by culling to behave like a natural population at the same density. Indeed, how it does behave will depend on the culling strategy. There is evidence that a strategy which disrupts the social pattern can be counterproductive (Ross, reported in ref. 3), increasing R_0 even as it reduces the population density. On the other hand, a relatively modest culling strategy might succeed if aimed selectively at the types of individual who make most contacts.

Second, I shall discuss some aspects which depend principally on the population growth and generation gap terms. In endemic equilibrium the net growth rate ρX must be equal to the infection rate [βXY in equation (1)], which in turn must equal the turnover rates of the incubating and infectious classes, I/τ_1 and Y/τ_2, respectively [here τ_1 is the mean incubation period, which equals $1/\sigma$ for equation (1)]. Hence, in equilibrium the 'level of prevalence', defined as $(I + Y)/X$, will be equal to $\rho(\tau_1 + \tau_2)$. For

strongly endemic areas we may take $\rho \approx r$; also $\tau_1 + \tau_2$ is approximately (for some simple models exactly[2]) equal to the mean generation gap τ. Hence, the level of prevalence should be approximately equal to $\rho\tau$, and thus vary from zero in near-threshold habitats up to $r\tau$ in areas where the disease holds the population down well below the carrying capacity. This simple argument does not depend on the detailed form of any of our three epidemic model components (it is sensitive, though, to spatial heterogeneity[6]).

The period of any oscillations about equilibrium also seems to be insensitive to the detailed form of the population growth and generation gap terms, being approximately equal to $2\pi\sqrt{(\tau/\rho)}$ for models with widely varying details[2]. (It does, however, depend on the relationship between R_0 and the population density: if this is less than linear, as suggested above, the period would be somewhat longer.) On the other hand, the stability of oscillations is found to be very sensitive to the form of both terms: a net population growth rate which falls steadily as the population density rises (for example, linearly[1]), and a generation gap with considerable variation [for example, a sum of two exponentials, as in equation (1)], are both conducive to stability. Other factors will also affect stability, for instance, seasonal and stochastic variation (both probably destabilizing[7,8]) and local rather than homogeneous mixing (probably stabilizing[6]).

Although ostensibly restricted to host-regulating diseases, the analysis presented here, especially the discussion of control, will have wider applications to models incorporating similar components. For example, in endemic equilibrium we must still have $R = 1$, and hence $X = N/R_0$ if we still assume homogeneous mixing (assumption (ii) in the discussion of the infection term). Thus, in a non-fatal disease such as measles, where N and hence R_0 will be unchanged, the equilibrium proportion of susceptibles will also be unchanged. Our approach makes it clear that this result is not related to the dependence of R_0 on N, but depends only on the success probability of contacts remaining the same before and after vaccination.

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