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On the Use of Simple Analytic Mathematical Models of Communicable Diseases

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Briscoe J [present address: Ministério das Obras Públicas, CP 268, Maputo, Mozambique]. On the use of simple analytic mathematical models of communicable diseases. *International Journal of Epidemiology* 1980, 9: 265–270.
Complex simulation models of diseases are becoming widely used by researchers and planners. This paper shows how simple analytic models can explain some otherwise inexplicable aspects of the behaviour of both these complex models and of the diseases in the real world. A system for grouping communicable diseases on the basis of the mathematical representation of the disease aetiology is developed.

Complex mathematical models of diseases are becoming widely used. Research epidemiologists use such models as a formal method for organising complex ideas on a disease, and as a tool for testing hypotheses about the epidemiology of the disease. Planners are concerned with the rational allocation of resources and use such models to assess the effects of different intervention strategies.

The validity of these models is typically judged by 2 criteria. The 'structural' criterion assesses whether all the known micro characteristics of the disease have been included in the model. For example, in a model of typhoid fever the structure of the model may be examined to see if allowance has been made for the fact that after recovery from the disease a person may remain a temporary carrier. The second, or 'meta', criterion looks not at structure but performance, asking whether the output of the model accords with what is known about the epidemiology of the disease in the real world. For instance, the output of a typhoid fever model will be examined to see whether the epidemic curve is similar to that which has been observed in actual typhoid epidemics.

Concern with satisfying either of these 2 criteria inevitably leads to more and more detailed models which typically end up as complex, computer-based simulation models. It is the contention of this paper that in this process modellers have often 'lost sight of the woods for the trees'. An attempt to explain why certain epidemiological characteristics are observed has been replaced by a demonstration that when all the variables are 'plugged into' the model, the output reproduces the epidemiological characteristic of interest. This paper attempts to show how a set of extremely simple mathematical models which include only the central elements of the more complex models, can *explain* certain epidemiological phenomenon, while the complex simulation models cannot explain but only, apparently magically, *reproduce* these phenomena.

It should be emphasised that it is not suggested that complex simulation models are not useful. What is proposed is that formal disease models are likely to be most useful when a simple analytic model is used in conjunction with a complex simulation model. The analytic model can elucidate the consequences of the basic assumptions of the disease model and thus can help interpret the output of the more complex and realistic model. It will remain the task of the complex simulation models to take account of the full complexity of the aetiology of the disease and to satisfactorily reproduce the epidemiological features of the actual disease.

To demonstrate how such simple analytic models can serve as useful adjuncts to the more complex simulation models, 4 different groups of com-

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municable diseases are examined. All of the diseases in any one group share a common mathematical representation of their aetiologies.

THE MODELS

I: Models of diseases with no superinfection and with the force of infection determined by human environmental contamination.

Examples of the simulation models which have been developed for this category of disease are Cvjetanovic's[1] model for typhoid and Uemera's[2] model for cholera. The typhoid model is examined here. The detailed structure, as presented by Cvjetanovic, is given in Figure 1, while in Figure 2 the essential elements of the underlying model are presented in a simple didactic model.

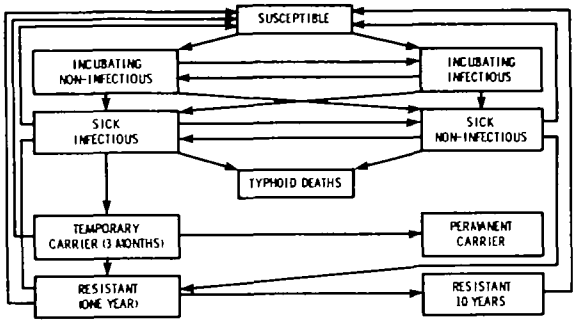

FIGURE 1 *Cvjetanovic's Model for Typhoid Fever*

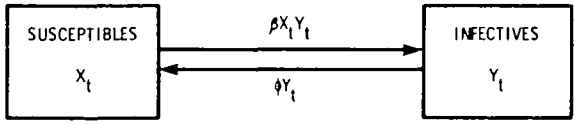

FIGURE 2 *Simplified Model of Disease Type I*

Assumptions incorporated in these models include:
(i) The infectivity of the environment is linearly related to the number of infective human hosts. (In the typhoid model the incubation differential is linearly related to the product of the number of susceptibles and the sum of the numbers of incubating infectious, sick infectious, temporary carriers and permanent carriers.) Therefore, the number of new infectives in each time period is related to the *product* of the number of susceptibles and infectives.
(ii) Superinfection, or the simultaneous presence of multiple infections in the host, is not permitted.
(iii) In the simulation model natural immunity to infection is taken into account, but in the analytic model no allowance is made for immunity.

If X_t is the proportion of the population which is susceptible to typhoid, ϕ the rate of recovery parameter, and β the infectivity parameter, then the differential equation describing the system is:

$$\frac{dx_t}{dt} = \phi Y_t - \beta X_t Y_t.$$

Noting that $Y_t = 1 - X_t$, the equation can be rewritten as:

$$\frac{dx_t}{dt} = \phi - (\phi+\beta)X_t + \beta X_t^2$$

which gives equilibrium values of X_t^* of $\frac{\phi}{\beta}$ and 1.

The meaning of the second equilibrium value is obvious: If there are no people infected, the force of infection is zero and the disease is eradicated (in this simplified world). The first equilibrium value, viz. $X_t^* = \frac{\phi}{\beta}$ is more interesting.

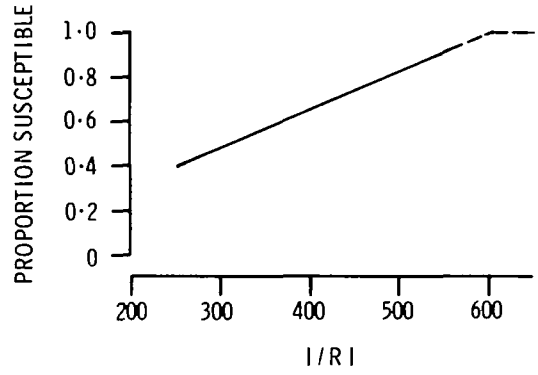

FIGURE 3 *The Effect of the Infective Factor (RI) in Cvjetanovic's Typhoid Model*

Cvjetanovic's simulation model has been used to generate the proportion of the population free from disease for a range of values of the 'infectivity parameter' (RI in Cvjetanovic's terminology, β in the present paper). The result presented in Figure 3 is striking: despite the considerable elaboration of the basic structure which Cvjetanovic's model represents (including the treatment of immunity), the linear inverse relationship, suggested by the analytic model, holds precisely. According to Cvjetanovic:

> It was found that the size of the epidemiological classes was almost linearly related to the reciprocal of the force of infection RI . . . It is thought that a stable level of endemicity can establish itself only if the rate RI remains above a certain critical value and that this value is a

function of the birth and death rates. Further study in this direction might be fruitful.

The simple analytic model, then, provides a clear explanation for a phenomenon which otherwise remains confusing.

This relationship between the proportion infected and the infectivity parameter has considerable utility in analysing health changes under different environmental conditions: from a given prevalence rate the implied value of the 'force of infection' can be inferred, and then the value of β at which the disease will be eradicated can be determined. For this class of diseases it is striking that β need not be reduced to zero for eradication.

While this result is in accordance with epidemiological experience with this category of disease,[3] a great deal of caution should be exercised in drawing inferences concering eradication. In reality the disease is, of course, much more complex a phenomenon, and the world is stochastic rather than deterministic as assumed in the model. This simple deterministic model, however, can be used to investigate how stable any 'equilibrium' will be in a stochastic world by examining the rate at which the system will approach equilibrium after a transitory perturbation away from the equilibrium position. This is done by examining the 'restoring force' which is the rate at which the system is returned to equilibrium and which is represented mathematically by $\Delta X_t / \Delta t$.

The difference equation may be written as:

$$\frac{\Delta X_t}{\Delta t} = B((X_\infty - X_t).(1 - X_t)).$$

When the equilibrium value ($X_\infty = \frac{\phi}{\beta}$) is small, $(1 - X_t)$ will be approximately constant as X_t approaches X_∞ and the restoring force will be approximately linearly related to $(X_\infty - X_t)$. When the equilibrium value is large (i.e. X_∞ is slightly less than or equal to unity), as equilibrium is approached $(1 - X_t)$ becomes progressively smaller and the restoring force becomes progressively weaker. This has important stability implications when considering eradication of the disease in a biological system subject to incessant perturbations. If $\bar{\beta}$, the mean value of β, is less then ϕ, the deterministic model indicated eradication of the disease. If β is a stochastic variable, however, we would have: (i) a slow approach to the state $X_t = 1$ for those cases in which $\beta < \phi$; and (ii) a rapid approach to $X_t = \frac{\phi}{\beta}$ when $\beta > \phi$. Thus when $\beta < \phi$ but β is considered to be a stochastic rather than a deterministic variable, eradication may never be attained.

It is noteworthy that the complementary nature of the size of the infective and susceptible populations, and the relationship between these population sizes and the rate of infection, ensure the establishment of an equilibrium in this class of diseases. The prevalence values at equilibrium are not dependent on the invocation of an immune response or other density-dependent effect.

II: Models of diseases with no superinfection and with the force of infection not primarily determined by human environmental contamination.

Cvjetanovic et al[4] have presented a simulation model for tetanus (Figure 4). The essential difference

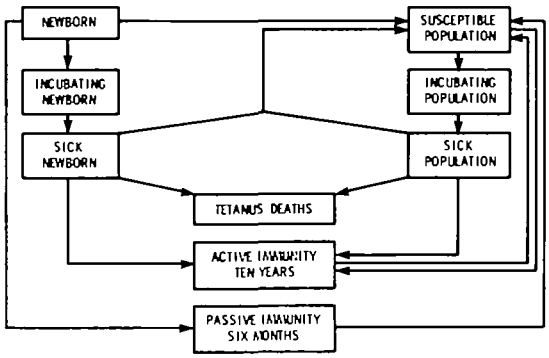

FIGURE 4 *Cvjetanovic's Tetanus Model*

between this model and the communicable disease models in group I above is that the human host is, relative to the soil and the intestinal canals of animals, an unimportant source of the tetanus spore. Thus in Figure 4 the force of infection is independent of the size of the human epidemiological classes.

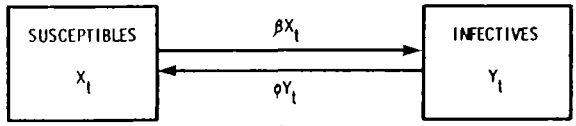

FIGURE 5 *Simplified Model of Disease Type II*

The analytic analogue to the simulation model is presented in Figure 5. The differential equation describing the model is:

$$\frac{dX_t}{dt} = \phi Y_t - \beta X_t,$$

or, since $Y_t = 1 - X_t$,

$$\frac{dX_t}{dt} = \phi - X_t(\phi + \beta).$$

The solution to this differential equation is:

$$X_t = \frac{\phi}{\beta+\phi} + (X_0 - \frac{\phi}{\beta+\phi})e^{-(\beta+\phi)t},$$

whence $X_\infty = \frac{\phi}{\phi+\beta}$.

Interesting distinctions between the typhoid and tetanus models become clear with the use of the analytic framework. The nature of the equilibriating mechanisms is quite different. In the tetanus model the differential equation is linear and there is, thus, only one equilibrium point. This point is never an end-point for a finite β, implying that eradication can take place only when β, the infectivity parameter, is reduced to zero.

With respect to the approach to equilibrium, the case of tetanus is less complicated than that of typhoid. In this case the difference equation can be written as:

$$\frac{\Delta X_t}{\Delta t} = (\phi+\beta).(X_\infty - X_t).$$

The restoring force is linearly related to $(X_\infty - X_t)$ and thus the disease prevalence is likely to be stable in the vicinity of the equilibrium point. It is important to note that, despite the linearity of the model, equilibrium is established without the invocation of acquired immunity.

III: Models of diseases with superinfection and with the force of infection not determined by environmental contamination.

MacDonald has developed 2 models – for an arthropod-transmitted protozoal infection, malaria,[5] and a zoonotic helminthic infection, schistosomiasis[6] – which fall into this category. These models are examined in this section.

In his malaria model MacDonald assumed that the amount of infective material to which the population is exposed is not affected by the proportion of the population harbouring the parasite, and that the existence of infection is no barrier to superinfection. The analytic model is given in Figure 6.

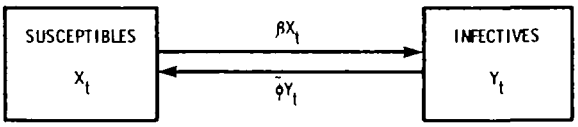

FIGURE 6 *Simplified Model of Disease Type III*

The central point made by MacDonald is that the rate at which individuals move from the state 'infective' to the state 'susceptible', or the 'effective recovery rate', $\tilde{\phi}$, is not equivalent to ϕ, the recovery rate from a single infection.

The differential equation describing Figure 6 is

$$\frac{dX_t}{dt} = \tilde{\phi}Y_t - \beta X_t,$$

whence $X_\infty = \frac{\tilde{\phi}}{\tilde{\phi}+\beta}$.

To investigate the relationship between $\tilde{\phi}$ and ϕ, we note that the mechanism underlying this disease type may be considered as a classic immigration-death process, giving an equilibrium value of:

$$X_\infty = 1 - e^{-\frac{\beta}{\tilde{\phi}}} \quad (\text{see}^7).$$

The relationship between $\tilde{\phi}$ and ϕ is thus defined by the equality:

$$\frac{\tilde{\phi}}{\tilde{\phi}+\beta} = 1 - e^{-\frac{\beta}{\phi}}$$

When the possibility of the host carrying more than two infections simultaneously is neglected, the equilibrium value of the immigration-death process becomes $X_\infty = 1 - \beta/\phi$, whence $\tilde{\phi} = \phi - \beta$. This was the relationship between $\tilde{\phi}$ and ϕ determined by MacDonald, who apparently did not realise that this relationship held only when the possibility of more than 2 infections was ignored.

In MacDonald's schistosomiasis model, the assumptions of central importance pertain to the quantitative relationships between the number of hatched larvae (mericidiae), the snail population, and the number of free-swimming larvae (cercariae). MacDonald assumes that the possibility of superinfection of the alternative (snail) host may be ignored, with the result that the infectivity of the alternative host becomes independent of the number of infections it has received. The second crucial factor is that the mean load is generally such that the mericidiae are much more numerous than the susceptible snails. The result is that modification in the number of mericidiae within a very wide range produces an insignificant change in the ultimate number of infective snails.

Under the above assumptions, the force of infection is unrelated to the worm load in the community, and the resulting model structure is essentially that presented for malaria.

In contrast to malaria, however, superinfection of the human host is the rule in schistosomiasis. The 'susceptible'-'infective' dichotomy is no longer useful since the relevant measure of infestation is now the number of worms harboured by the indivi-

dual. If ω is the average number of worms carried by an individual,

$$\frac{d\omega}{dt} = \beta - \phi\omega,$$

whence $\omega = \beta/\phi$.

Again, the simple formulation provides insights into the results emerging from the simulation model. Examining the results of his simulation model, MacDonald concluded that 'the ultimate level of endemicity attained is almost exclusively dependent on the number of snails, the frequency of entry to water and the longevity of the worm'.[9] Why this is so is obvious from the simple analytic formulation and the equilibrium value emerging from it: It is the first two factors which are the determinants of β, while the longevity of the worm is represented by ϕ.

Again the simple analytic form can be used to examine the likely behaviour of the system in a stochastic world. Rewriting the difference equation as:

$$\frac{\Delta\omega}{\Delta t} = \frac{1}{\phi}(\omega_\infty - \omega_t),$$

suggests that the system is likely to be stable in the vicinity of the equilibrium point.

It should be noted that while no account is taken of immunity, it is possible to obtain intuitively plausible results. In particular, equilibrium is attained without the invocation of immunity.

IV: Models of diseases with superinfection and with the force of infection determined by environmental contamination.

Until recently,[10] there have been no epidemiological models of helminthic infections in which the force of infection is determined by the degree of human environmental contamination. Inferences concerning the dynamics of this class of diseases (ancylostomiasis, ascariasis, trichuriasis and strongyloidiasis) have been made on the basis of epidemiological models of other diseases (e.g. schistosomiasis). The important differences in the nature of relationships between different epidemiological classes make such extrapolations inappropriate.

In common with other helminthic infections, the unit of infectivity of the host is the number of parasites harboured, whereas in most other infections infectivity is a 'zero–one' phenomenon. The crucial systemic distinctions between the infections of this group (e.g. hookworm) and those of Group III (such as schistosomiasis) is that whereas in the schistosomiasis model the force of infection was effectively unrelated to the egg output, in the hookworm model the force of infection is directly related to the egg output in the faeces and thus to the worm load in the population. If non-linearities in the host are ignored, the following differential equation describes the change in the average number of worms harboured:

$$\frac{d\omega}{dt} = \beta\omega - \phi\omega$$
$$= 0 \text{ only for } \beta = \phi$$
and then at any (the initial)
worm load; or $\omega = 0$, for all ϕ and β.

For $\beta = \phi + \epsilon$ we have an infinite increase in the worm load for $\epsilon > 0$ and complete elimination of infection for $\epsilon < 0$. In short, the nature of the equilibrium conditions makes it clear that the above model does not represent the realities of hookworm infection adequately. As has been shown[10] by the development of a complex simulation model (Figure

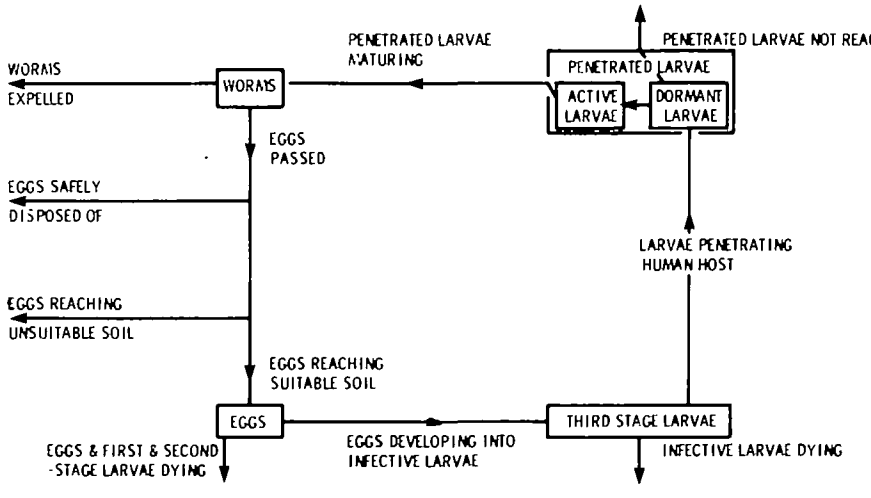

FIGURE 7 *Briscoe's Model for Hookworm*

7), it is only when non-linearities in the soil as a result of competition and soil heterogeneity, and acquired immunity in the host, are taken into account that plausible results may be obtained.

This class of diseases is thus rather different from those diseases in the first 3 groups. For the diseases in Groups I, II and III, the simple analytic models ignore immunity and other non-linearities and yet show the broad system characteristics as the more complex simulation models which *do* include immunity. For Groups I, II and III, then, the inference is that immunity does not play a central role in maintaining an equilibrium, while in the diseases of Group IV the role of immunity and other non-linearities is central to the stability of the system.

It is interesting to note that the particular importance of immunity to the equilibrium of this class of diseases has been stressed by helminthologists with extensive field experience. Darling, for instance, 'was accustomed to stress the discrepancies between the level of hookworm infection in the population groups he had studied and their very great exposure to infection, and repeatedly stated in conversation that the development of an acquired immunity in these populations seemed to him the only explanation of the failure of their worm burdens to increase until they were all killed by their hookworms'.[11]

CONCLUSION

The simple analytic models developed in this paper provide useful insights into the dynamics of more complex simulation models and insights into the nature of the equilibriating mechanisms in these models. The classification of the models indicates that there are 2 primary criteria on which the communicable diseases are to be grouped. Firstly, can the individual be adequately described as 'infected' or 'free from infection' or does super-infection take place; and, secondly, is the force of infection dependent on the degree of human environmental contamination or not? The classification system is potentially useful in suggesting which infectious diseases may respond similarly to, say, changes in water supply or excreta disposal conditions. Thus in a study of the effect of environmental changes on health, the classification system may be used to select 'indicator diseases' from the wide range of diseases of possible interest.

ACKNOWLEDGMENTS

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