Mathematical Modelling

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Thanks

INTRODUCTION

The basic problem that we are going to discussed in this project is to describe the spread of an infection within a population. As a canonical example one thinks of a small group of individuals who have a communicable infection being inserted into a large population of individuals capable of "catching" the disease. Then an attempt is made to describe the spread of the infection in the larger group. To do this, certain assumptions are required to describe the characteristics of the disease and the mixing of the population. From these assumptions a mathematical model is formulated. The model is analyzed, and the results of the analysis (hopefully) interpreted in epidemiological terms and thereby insight is gained into the nature of the phenomenon.

In the mathematical theory of epidemics a variety of different approaches are utilized. The models in this project are all deterministic rather than stochastic — that is, they use differential equations rather than stochastic processes to describe changes in the population.

SIMPLE DETERMINISTICS EPIDEMICS MODELS

We begin by looking at a sequence of three increasingly complicated mathematical models for the development of an epidemic of a contagious disease.

1. The first model is so simple as to be almost entirely unrealistic, however, its shortcomings suggest how it can be improved.

2. The second model, which results from modifying the first model, is considerably better , but still leads to unacceptable results.

3. The third model is likewise an outgrowth of the previous models. Although still imperfect, the third model manifests a property which was not built into the formulation explicitly, but which is in fact observable in an actual epidemic of a contagious disease.

Assumptions which will be common to all of the models:

a. The disease is transmitted by contact between an infected individual and a susceptible individual.

b. There is no latent period for the disease, hence the disease is transmitted instantaneously upon contact.

c. All susceptible individuals are equally susceptible and all infected individuals are equally infectious.

d. The population under consideration is fixed in size. This means that no births or migration occurs, and all deaths are taken into account.

I. The Trivial Model

Consider a population which is effectively infinite in size. Initially everyone in the population is susceptible to a contagious disease, with the exception of a small number of individuals who are already infected.

Let the independent variable be time, t, and also let:

$I(t)$ = number of infected individuals at time t

B = average number of contacts with susceptible individuals which lead to a new infective per unit time per infective in the population.

It is a simple matter to deduce the number of infected individuals at time in terms of the number of infectives at time t. Clearly, $I(t+\Delta t)$ is just the sum of the number of infectives at time t, I(t), plus the number of new infectives who contract the disease in the time interval from t to $t+\Delta t$ In mathematical notation,

$$I(t+\Delta t) = I(t) + B\, I(t)\, \Delta t$$

$$\frac{I(t+\Delta t) - I(t)}{\Delta t} = B\, I(t)$$

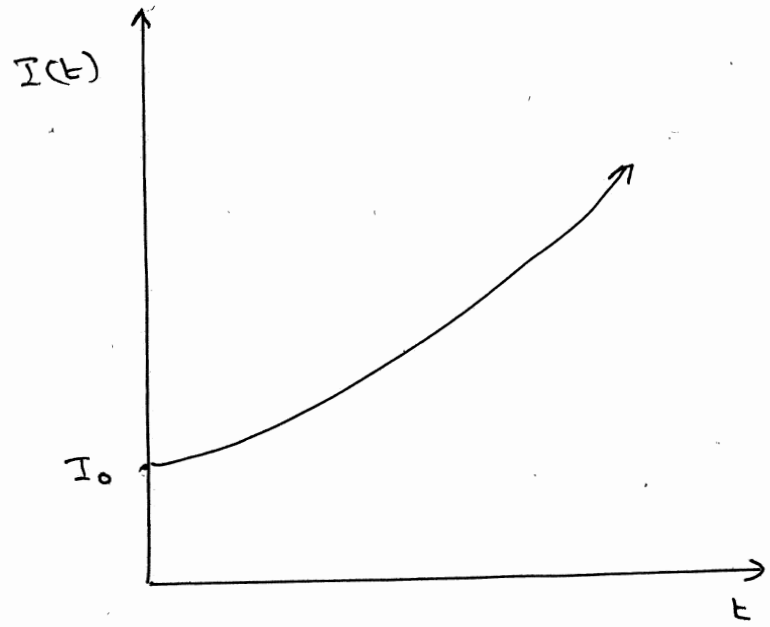
and then let $\Delta t \longrightarrow 0$

We recognize this as a simple ordinary differential equation. By virtue of its form it is easily solved by separation of variables. All that is needed is an initial condition. This is provided by the fact that at time t = 0 when the model begins, the initial number of infectives is $I(0) = I_0$. Separating and integrating leads to

$$\int_{I_0}^{I(t)} \frac{dI}{I} = B \int_0^t dt$$

$$= \ln I \Big|_{I_0}^{I(t)} = Bt + I_0$$

$$\therefore I(t) = I_0 \exp(Bt)$$



The defects of the trivial model

1. The basic defect of the model is easily seen from the graph above. As time passes, the number of infectives is seen to grow without bound. This property is easily traced to the initial premise on which the model is based. Specifically, that the population at risk of catching the disease is effectively infinite in size. A more realistic model will take into account that there are only a finite number of susceptible individuals.

2. It should be clear that we have already encountered a small inconsistency. In general, one would not expect formula (1) to be an integer even if I(t) was an integer. Instead of trying to cope with this problem, we will recognize that our model is inexact, and will interpret I(t) to the nearest integer. Since we will discover that the number of infectives grows without bound, this imprecision will not be serious.

II. The Classical Simple Epidemic Model

To overcome the problem encountered in the previous model, it is next assumed that at all times the population under consideration numbers N individuals. Everyone in the population is either susceptible to the disease or else infected with the disease.

In addition to the variables defined for the previous model, let:

$S(t)$ = number of susceptible individuals at time t.The susceptible class, i.e., those individuals who are not infective but who are capable of contracting the disease and becoming infective

β = average number of contacts between susceptible and infected individual which lead to a new infective per unit of time per infective per susceptible in the population

By comparing the definitions of B and it should be clear that
$B = \beta S(t)$.
Although B was treated as a constant in the first model, it is now vary with the number of susceptibles.

Note that the total population size never entered into the derivation of the equation for the number of infectives in the first model, the same argument with B replaced by $\beta S(t)$ leads to

$B \neq \beta$, $B = \beta S(t)$

$$\frac{dI(t)}{dt} = \beta S(t) I(t)$$

The logistic Law.

In addition, since the total population size is always N, and since all individuals are either susceptible or infected,

$$S(t) + I(t) = N$$

$$\frac{dS}{dt} + \frac{dI}{dt} = 0 \quad , \text{ since } N \text{ is a constant.}$$

$$\frac{dS}{dt} = -\frac{dI}{dt} = -\beta S(t) I(t)$$

However, since S(t) can be eliminated using $S(t) = N - I(t)$ in the differential equation for I(t), one need only solve

$$\frac{dI(t)}{dt} = \beta I(t) [N - I(t)]$$

We have substituted $S(t)$, by $N - I(t)$

Although this differential equation is non-linear, it submits to the same method of solution as the linear differential equation in the previous section. As before, the initial number of infectives is $I(0) = I_0$, where $0 < I_0 < N$, and typically, $I_0 << N$. Separating variables leads to

$$\int_{I_0}^{I(t)} \frac{dI}{I(N-I)} = \beta \int_0^t dt$$

Expanding the denominator of the integrand on the left-hand side using partial fractions, integrating and rearranging provides .

$$I(t) = \frac{I_0 \exp(N\beta t)}{1 - \frac{I_0}{N}(1 - \exp(N\beta t))}$$

The limiting behaviour of this solution:

1. In the limit as $N \to \infty$ the denominator becomes unity and (with the proviso that $\beta N \to B$) the solution is identical with the solution to the first model.

2. In the limit as $t \to \infty$, since $N > 0$ and $\beta > 0$, the exponentials dominate both the numerator and the denominator, so $I(t)$ goes to N.

So, $\beta N \longrightarrow B$, $N \longrightarrow \infty$

So, $I(t) \longrightarrow N$

Taken together, these two asymptotic observations suggest that in a large population with a small initial number of infectives, at first the epidemic (as measured by the total number of infectives) grows exponentially. Then, as fewer susceptibles are available, the rate of growth decreases, but the epidemic does not end until everyone in the population has contracted the disease.

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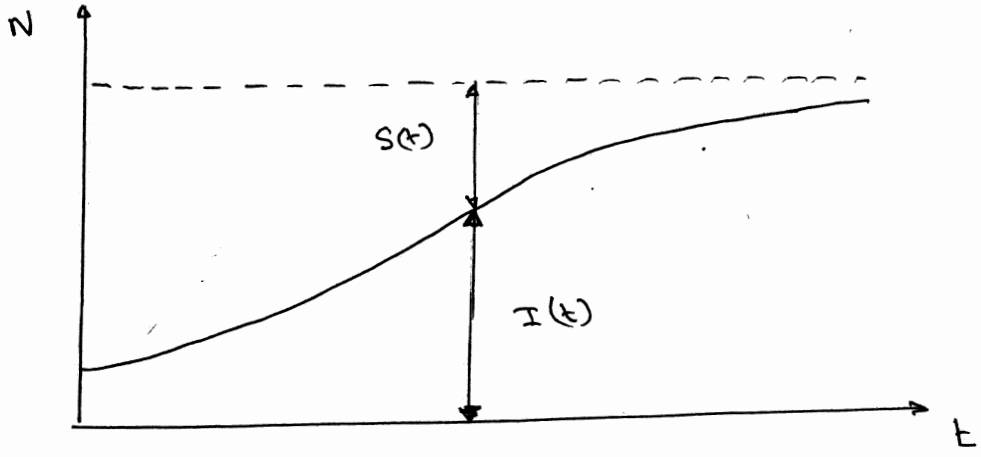
A typical solution as a function of time is shown below



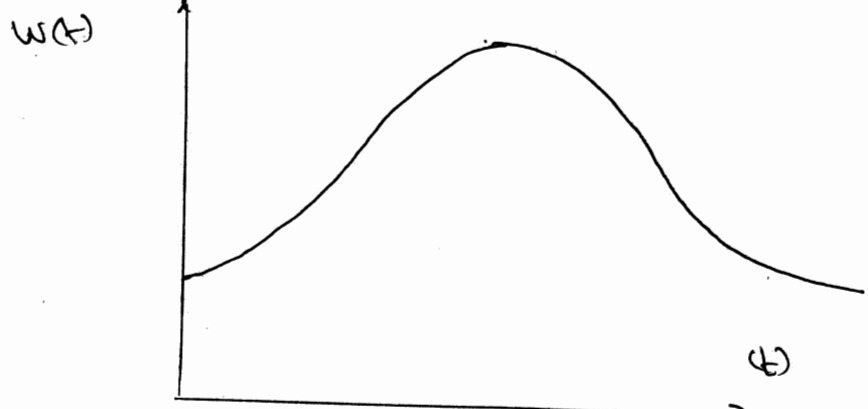
Although the analytic form of I(t) is not known, and a similar expression for S(t) follows immediately from the fact that S(t) = N - I(t), in practice these are not the observed quantities in an epidemic. The more usual quantity to report is the 'epidemic curve' which records the rate at which the disease spreads in the population. For the present model the epidemic curve, W(t), is the rate of change in the number of infectives, thus

$$W(t) = \frac{dI(t)}{d(t)} = \beta S(t) I(t)$$

$$= \frac{\beta (N - I_0) I_0 \exp(N\beta t)}{\left[1 - \frac{I_0}{N}(1 - \exp(N\beta t)\right]^2}$$

Typically, this function looks like:

A graph of $W(t)$ against t



It is not difficult to show that W(t) is symmetrical about its maximum and this is not a priority at this time.

General remarks of the second model

1.The second model is considerably better than the first, but still has one rather unrealistic aspect. Notice that whenever an epidemic gets started, everyone in the population ultimately contracts the disease. The reason for this can be traced to the fact that infectives remain infected forever. A more realistic model must take into account that for most diseases infectives either recover or else they die.

III. The Classical General Epidemic Model with permanent removal(Kermack-McKendrick)

In order to overcome the problem encountered in the previous models, it is assumed that infectives are removed from circulation at a rate which is proportional to the current number of infectives. Since for many diseases a natural immunity occurs, it is further assumed that former infectives enter a new class which is not susceptible to the disease.

By introducing a class of removed individuals, we have managed to avoid a precise statement of the severity of the disease being modeled. The removals may be recovered and immune, or they may be quarantined and thus out of circulation or they may be dead. All that is necessary is that the disease not be available to any individual more than once.

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In addition to the variables defined in the previous models, let:

R(t) = number of removed individuals at time t.The removed class, i.e., those individuals who have had the disease and are dead, or have recovered and are permanently immune, or are isolated until recovery and permanent immunity occur.

λ = average rate of removal of infectives from circulation per unit time per infective in the population.

Since the new class of individuals, the removals, in no way interacts with the susceptibles, the governing equation for the susceptibles is unchanged from the second model. Thus the differential equation is

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \lambda I(t)$$

The individuals who are removed from the ranks of the infectives then contribute to the number of removed individuals according to the relation

$$\frac{dR(t)}{dt} = \lambda I(t)$$

Since all individuals in the population are either susceptible, infected or removed, it follows that since the population is constant in size,

$$S(t) + I(t) + R(t) = N$$

Remarks: By differentiating this last expression with respect to time, it follows that the sum of the three governing equations must sum to zero . In addition, the last expression guarantees that once the size of any two of the classes is known, the size of the third follows by simple arithmetic.

To complete the specification of the model it is necessary to know the initial state of the population. Assume that at time t = 0 there are no removed individuals, a very small number, I_0, of infectives, and the remainder of the population, S_0, is susceptible. Thus,

$$S(0) = S_0 = N - I_0$$
$$I(0) = I_0 << N;$$
$$R(0) = 0$$

Before attempting to find a solution to the set of governing equations, it is informative to look carefully at the equations. Specifically, look at the equation for the number of infectives in the form

$$\frac{dI(t)}{dt} = \beta [S(t) - P] I(t)$$

where $P = \frac{\lambda}{\beta}$

Not to confuse B to β

Clearly, since I(t) >= 0, the sign of the term in square brackets is the same as the sign of $\frac{dI(t)}{dt}$, hence

$$\frac{dI(t)}{dt} > 0 \quad \text{if and only if} \quad S(t) > p$$

Further, since S(t) is a monotonically decreasing function of time (since susceptibles become infected and no new susceptibles are made)

if S(0) < p then

S(t) < p for all t > 0 and $\frac{dI}{dt} < 0$ for all future time.

In other words, if the initial number of susceptibles is smaller than some critical number, p, there will not be an epidemic..

We proceed to analyze the model in detail. To do so, begin by eliminating the explicit dependence on I(t) between the first and the third of the governing differential equation to get

$$\frac{dS(t)}{dR(t)} = \frac{dS(t)}{dt} \times \frac{dt}{dR(t)} \qquad \text{Chain Rule.}$$

$$\frac{dS(t)}{dt} = -\frac{S(t)}{p} \frac{dR(t)}{dt}$$

Separating variables, multiplying through by _t and integrating leads to

$$S(t) = S_0 \exp\left[\frac{-R(t)}{p}\right]$$

Next, make use of the relation S(t) + I(t) + R(t) = N in the equation for R(t):

$$\frac{dR(t)}{dt} = \lambda I(t) = \lambda [N - R(t) - S(t)]$$

Since $S(t) = S_0 \exp\left(-\frac{R(t)}{P}\right)$

$$\frac{dR(t)}{dt} = \lambda\left[N - R(t) - S_0 \exp\left(\frac{-R(t)}{P}\right)\right]$$

and then use the expression just derived to eliminate S(t); thus

$$\frac{dR(t)}{dt} = \lambda\left[N - R(t) - S_0 \exp\left(\frac{-R(t)}{P}\right)\right]$$

Note that R(t) is the only one of the dependent variables which appears in this equation.

Since this difficulty in solving the equation results from the presence of the exponential term, we proceed to replace the exponentials by a polynomial. To do so we expand the exponential in a Taylor Series about the only point at which we know the value of R(t). Specifically, we expand about R(0) = 0; this leads to:

$$\exp\left\{\frac{-R(t)}{P}\right\} = 1 - \left(\frac{R(t)}{P}\right) + \frac{1}{2}\left(\frac{R(t)}{P}\right)^2 - \frac{1}{6}\left(\frac{R(t)}{P}\right)^3 + \text{- - - - - -}$$

Clearly, if one attempts to retain the entire infinite series, nothing has been gained. By truncating the series after the first few terms, a separable differential equation which is fairly easily solved will result. The question remains, how many terms should be retained? It is not difficult to show that if only terms up to linear one are kept, only an absurd answer is possible. On the other hand, if terms up to the cubic one are kept, the resulting integration is very hard. We therefore, choose to keep terms up to the quadratic one, thereby balancing realism against solvability. Following a bit of rearranging, the resulting equation is:

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$$\frac{dR(t)}{dt} = \lambda\left[I_0 + \left(\frac{S_0}{P} - 1\right)R(t) - \frac{S_0}{2P^2}R(t)^2\right]$$

Separating variables and integrating leads to the expression:

$$R(t) = \frac{P^2}{S_0}\left[\frac{S_0}{P} - 1 + \alpha \tanh\left(\frac{\alpha \lambda t}{2} - \phi\right)\right]$$

where

$$\alpha = \sqrt{\left(\frac{S_0}{P} - 1\right)^2 + \frac{2 S_0 I_0}{P^2}} \quad \text{and} \quad \phi = \tanh^{-1}\left[\left(\frac{S_0}{P} - 1\right)\alpha\right]$$

As with the second model, we are really more interested in knowing the shape of the predicted epidemic curve, W(t), than the cumulative number of removals, R(t). Since cases of the disease are counted as victims seek medical attention, and this is also the time at which individuals are removed from active circulation, it is customary to assume that

$$W(t) = \frac{dR(t)}{dt} = \frac{\lambda \alpha^2 P^2}{2 S_0} \operatorname{sech}^2\left(\frac{\alpha \lambda t}{2} - \phi\right)$$

Note that this expression describes a function which rises to a single maximum at time

$$t = \frac{2\phi}{\alpha \lambda}$$

and then dies away symmetrically. This is very similar to the result for the epidemic curve in the second model; however, in this model not all susceptibles need to be infected as we will now see.

Asymptotic behaviour of the epidemic as t (formula

Since there are only a finite number of individuals in the population and since none can contract the disease more than once, the epidemic must eventually die out. Further, once the epidemic has ended, all individuals will be either still susceptible or else removed. None are still infected.

$$\lim_{t \to \infty} R(t) \equiv R_\infty = \frac{p^2}{s_0}\left[\frac{s_0}{p} - 1 + \alpha\right]$$

If it is further assumed that the epidemic is started by a very small group of infectives, so that

$$\frac{2 s_0 i_0}{p^2} \ll \frac{s_0}{p} - 1 \qquad s_0 > p$$

it then follows from the definition of α that

and $$\alpha = \frac{s_0}{p} - 1$$

$$R_\infty = 2p\left(1 - \frac{p}{s_0}\right)$$

The condition for an epidemic outbreak of the disease is $S_0 > p$.

Assume that $\hat{s}_0 = p + \varepsilon$ where $\hat{0 < \varepsilon \ll p}$ Substitute this into the equation for R_∞ to get

$$R_\infty = 2p\left(\frac{\varepsilon}{p+\varepsilon}\right) = 2\varepsilon$$

This means that for a population which initially has $\hat{s}_0 = p + \varepsilon$ susceptibles, after the epidemic has subsided, there will be about $s_\infty = p - \varepsilon$ susceptibles remaining. In other words, the final number of susceptibles is as far below the threshold for an epidemic as the initial number was above the threshold. <u>This result is called the Kermack-McKendrick Threshold Theorem.</u>

A Two POPULATIONS THRESHOLD MODEL

We now discuss very briefly a more complicated model involving two populations and an infection which is communicated between them. An example would be **males** and **females** as the populations and a venereal disease, or mosquito and man as the populations and malaria as the disease. Each population is divided into the four classes, which we denote respectively by

what is E?

(S),(E), (I), (R) and **(S1), (E1), (I1), (R1),**

The infection is presumed to spread according to the following rules where S(t) indicates the number of susceptibles of the first population at time t; S1(t), the second population; etc:

(i) The rate of exposure of susceptibles to infectives at time t is given by $-r(t)\,S(t)\,I_1(t)$ and $-\bar{r}_1(t)\,S_1(t)\,I(t)$

(ii) An individual who is first exposed at time T become infective at time t if

$$\int_T^t \left[P_1(x) + P_2(x)\,I_1(x)\right] dx = m$$

?

$$\int_{T_1}^t \left[\bar{P}_1(x) + \bar{P}_2(x)\,I(x)\right] dx = \bar{m}$$

where $p_1(x)$, $p_2(x)$, $\bar{p_1}(x)$, $\bar{p_2}(x)$ are non-negative functions,

(iii) An individual who becomes infective at time t recovers from the infection a time $t+\sigma(t+\bar{\sigma})$ where $\sigma, \bar{\sigma}$ are given

positive constants,

(iv) An individual who recovers from the infection at time t is immune until t+ w ($t+\bar{w}$), at which time he becomes susceptible again, where w, $\bar{w}$ are non-negative constants,

(v) Each population is constant with

$$I(t) + S(t) + E(t) + R(t) = N$$

$$(\bar{I}(t) + \bar{S}(t) + \bar{E}(t) + \bar{R}(t) = \bar{N}).$$

In this model the model the infection is spread from infectives in the first population to susceptibles in the second; from infectives in the second to susceptibles in the first. The equations can be derived exactly as before , except that where infectives appear, it will be infectives of the other population. The model as presented is entirely symmetric, only the constants differ. This would be the case, for example, in the spread of a venereal disease. However, different assumptions could be made in each population. In parasite-borne infections, $\sigma = +\infty$ is a common assumption, for example. One could also derive a model using more than two distinct populations, or one could also make a model where the infection spreads due to infectives within its own population as well as infectives in the other.

As initial conditions, it will be assumed that S_0 , $\bar{S}_0$ are given constants and are two given monotone increasing functions, defined on $-\sigma \le t \le 0$, $-\bar{\sigma} \le t \le 0$ respectively, with $I_0(-\sigma) = \bar{I}_0(-\bar{\sigma}) = 0$, $\bar{I}_0(t)$, $-\bar{\sigma} \le t \le 0$ is the past history of the $I_0(0)$ infectives inserted into the susceptible population at time $t = 0$

. SOME SIMPLE CONTROL ASPECTS

we now consider the problem of attempting to control a predicted epidemic. Suppose, using the current initial state in one of the previously described models, a large outbreak of the infection is predicted. There are two immediate possible courses of action — **vaccination and quarantine.**
In the context of the models, **vaccination is taking an individual from susceptible class and putting him in the removed class (or a special class) without passing through the infective stage while quarantine (isolation) is removing an individual from the infective class before the disease has run its course.**

The model will be the simplest model, with the addition of Class (V), the **vaccinated individuals.** Let $\alpha(t)$ denote the vaccination rate as a function of time. The model then is

$$S'(t) = -rIS - \alpha$$

$$I'(t) = rIS - \lambda I$$

$$R'(t) = \lambda I$$

$$V'(t) = \alpha$$

$$S(0) = S_0, \quad I(0) = I_0, \quad R(0) = V(0) = 0$$

It is explicitly assumed that only susceptibles are vaccinated and that the inoculation is effective immediately. The first of these presupposes some sort of test for susceptibility before inoculation to prevent "wasted" vaccination of infectives. This could be corrected by using $\frac{\alpha S(t)}{N}$ (where N is the total population)
as the effect of vaccination on the susceptible class. The methods here still apply, although some "short cuts" used in the computer program to account for the class (v) would need to be eliminated. However, we note that all of the models we have used ignore those individuals who are naturally immune. On these vaccination is also "wasted" if given generally. The presumed "test" for susceptibility covers these while the above modification of the vaccination rate does not. We are also implicitly assuming that the vaccination rate is not applied over a time period sufficient to make

$$S(t) < 0.$$

This restriction was "built in" all of the computations. If the vaccine is not 100% effective, $\alpha(t)$ denotes the effective rate.

If, with the initial conditions (S_0, I_0), the model with $\alpha(t)=0$ predicts the spread of the infection through the population with results that are unacceptable, the course of spread of the infection is to be altered by introducing a vaccination program, that is,

introducing a non-trivial function $\alpha(t)$ in the model above.

If the infection causes serious harm to the individuals, it is desirable to reduce the total number infected to an "acceptable" amount. (The level of acceptability is a trade-off between expenditure of resources and discomfort to individuals or damage to society). On the other hand, it may in some circumstances be important only to limit the number of individuals infected at any one time. As an example of the latter case one thinks of a group maintaining an important installation and a minor infection acting in that group. Here the important consideration may be to keep enough of the population healthy at any one time so that the installation can be maintained rather than to limit the total number infected. "Preventing an epidemic" is defined to be controlling these two quantities: the peak of the number infected at any particular time, and the total number infected in the given time interval. Of course, doing something to prevent the spread involves a cost (dollar costs and perhaps social costs). The control objective is to minimize this cost.

For computational reasons, it is convenient to normalize the dependent variables and treat the proportion of susceptible, infective, removed, and vaccinated individuals.
If we let

$$\bar{S} = \frac{S}{N}, \quad \bar{R} = \frac{R}{N}, \quad \bar{V} = \frac{V}{N}, \quad \bar{\beta} = \frac{\beta}{N}, \quad \bar{S}_0 = \frac{S_0}{N}$$

and $\bar{I}_0 = \frac{I_0}{N}$, the above equations becomes.

$$\bar{S}' = \overline{rSI} - \bar{\alpha}$$

$$\bar{I}' = \overline{rSI} - \lambda I$$

$$\bar{R}' = \lambda \bar{I}$$

$$\bar{V}' = \bar{\alpha}$$

$$\bar{S}(0) = \bar{S}_0, \quad \bar{I}(0) = \bar{I}_0, \quad \bar{R}(0) = \bar{V}(0) = 0.$$

where $\bar{S}_0 + \bar{I}_0 = 1$, $\bar{S}(t) + \bar{I}(t) + \bar{R}(t) + \bar{V}(t) = 1$

. The time dimension could also be scaled but is not for computational reasons as will be noted below. Since the above system is formally the same as the original one with N normalized to 1, we will use the obove system of equation with N=1 and think of S, I, R, and V as the proportion of the population in the various classes. Note that the function and the parameter r have changed their original meaning and are now dependent on the total population size, N.

The effort expended in "preventing an epidemic" by vaccination is assumed to be proportional to the vaccination rate α, i.e., achieving a higher vaccination rate means that more equipment, personnel, supplies, etc., must be brought to the locale.

Let the expenditure (money, equipment, personnel, supplies, disruption of health care elsewhere, etc.) be described by a (nonlinear) cost functional will be restricted to be a step function; for example, α can be thought of as being constant for one time period (a day or a work shift).

The two measures of the size of the epidemic are the total proportion, R(T) + I(T), of the population affected by the infection in the time interval (0,T) and the maximum number infected at the peak,

$$\max_{t \in (0,T)} I(t)$$

The problem can now be stated formally.

PROBLEM: Given a cost functional C(a), positive constants I_0, S_0, A, B, T, and a class of allowable range points of the step functions

a, choose a function a(t) such that the solution of (8.1) with initial conditions I_0, S_0, and this a(t), yields a solution such that

(i) $R(T) + I(T) \leq A$

(ii) $\max_{[0,T]} I(t) \leq B.$

and

$C(\alpha) =$ minimum.

In more concrete terms this says that, given the achievable vaccination rates, a cost functional , and the current situation (I_0, S_0), select a pattern of vaccination that will achieve:

(i) no more than A of the population succumbs to the infection by time T, and

(ii) no more than B of the population is infective at any one time.

(111) We at the same time want to mininize cost..

A solution to this problem can be constructed using the techniques of. dynamics programming.

How the models can be improved

1 The definition for the class "S" should be modified to be "susceptible and unexposed to the infection".

2 There should be another class "E" of "exposed but not yet infective" individual that must be added to the models. With some diseases there is a latent period where the individual may be considered to "have" the disease but is not able to communicate it to others.

3 The length of the infection period was something not taken into consideration before .

4 In the previous models it was assumed that contracting the desease provided permanent immmunity and hence the class 'R' of removed individual was the final resting place for all individuals who become infective. With many deseases,however, the individuals after recovering from an infection, may become susceptible again after recovering from an infection.

5 The Models that we discussed earlier assumed a constant; closed total population or ; from another point of view, birth ;death ;and migration was in exact balance. This is not true in practice.

Conclusion

If we take those five points above into consideration ;it is more likely that we are going to have better understanding of the spread of epidemics. Actually F. Hoppensteadt describe a model in which birth; death; migration are allowed to vary and a futher complication is permitted is that age dependent rates of exposure.vilility, etc are also allowed. The name of the model is "A Model with age dependence and an open population"

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