A mathematical approach to epidemic control

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SUMMARY. A mathematical model of an influenza epidemic which occurred in 1961 is suggested. The mathematics imply conclusions on the practical control of similar outbreaks. This is a technique applicable to one general practice.

Introduction

Neither complete immunisation of a whole population, nor total control of the methods of transmission is necessary to eliminate the possibility of an epidemic developing.

We have attempted to calculate the percentage of the susceptible population which would have required immunisation to check an actual influenza outbreak. We discuss the general principles involved and conclusions to be drawn, which may prove useful in the future.

An increasingly important concept—in such widely differing fields as aircraft design and university staffing—is that of creating and using mathematical models. Even if imperfect, the use of such models can save time and the expense of many experiments.

We believe that the particular model we have used is the most successful in fitting the observed course of an epidemic of the size likely to be seen in one practice.

We suggest that those general practitioners who keep records should have some knowledge of the subject if their records are to be collected in the most useful way, i.e. the waves shown in our model would not have appeared in our observations if our records had been kept at weekly, rather than daily intervals. The presence of waves in a graph greatly increases the amount of information it contains compared with that contained in a smooth curve.

Bailey (1957) has described the early work on epidemic models. We believe that the choice of a simple epidemic model giving reasonable interpretation to the data available is more important to general practitioners than sophisticated mathematical treatment.

General formula

A formula describing the chain reaction of an epidemic is given below.

$$C = R \times I \times S$$

where: R = Infectivity factor (effectiveness of transmission).

I = The number of infectives in a particular wave.

S = The number of susceptibles in the same wave.

C = The number of new cases created from the susceptibles in this wave by the interaction of the I and S. These new cases are the infectives of the next wave.

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This equation is a discrete time version of that of Bailey (1957). In any wave, say wave i (i = 1,2, . . .), where the population consists one infective and two susceptibles, if R = 1 then there are $1 \times 1 \times 2 = 2$ new infectives created for the next wave leaving no susceptibles in the population. If R = $\frac{1}{2}$ then there are $\frac{1}{2} \times 1 \times 2 = 1$ new infectives created for the next wave leaving one of the original susceptibles in the population.

In using this formula certain assumptions must be made about the epidemic. It must be assumed that infectives are capable of spreading infection during only one wave of the epidemic and that they are then removed from circulation until they have recovered. Once recovered these individuals may be considered to be immune to further infection for the remainder of the epidemic. The new cases, susceptibles infected, in one wave become the infectives of the next wave after the lapse of the incubation period for the infection (the time-lag between waves). It must also be assumed that the population is constant, i.e. no immigration or emigration of new susceptibles or infectives.

Explanation of R

The presence of a large number of malarial mosquitoes gives a high value of R for malaria—the vector is effective.

In a tightly packed community with a sterilised milk supply, bovine tuberculosis does not spread; R has a low value.

Ventilation reduces R for airborne diseases, for example in operating theatres.

R has a time factor involved. Longer exposure to an infection implies more risk to the susceptible.

Explanation of S and I

Let S_0 and I_0 represent the initial state of the population, S_0 and I_0 both non-zero. S will be decreasing over time, however, if R is large enough for an epidemic to be created, I will increase from I_0 to a maximum value and then decrease as the epidemic dies out or is controlled.

Numerical results for the general formula

Figure A shows plottings of the formula for different values of R with the same initial state of the population. These graphs demonstrate that, making R, the infectivity factor, three times as effective, the epidemic can be changed from one which is dying out from its inception into one which will infect the entire population in just four waves.

The critical value of R

If the sole interest in the study of an epidemic disease is in its prevention, then the critical value of R which determines its progression or regression is the only factor requiring consideration.

An observed epidemic with the characteristics of waves occurring at fixed intervals suggests that the criteria stated as assumptions for the model are satisfied and that the formula may be used as a model to form the starting point for a mathematical investigation of observations.

The critical value of R around which a small change gives an epidemic which is spreading or dying out, is given by $R = \frac{\text{one.}}{S}$ If at any wave (a) $R > \frac{\text{one,}}{S}$ the number of infectives is increasing, (b) $R = \frac{\text{one,}}{S}$ the number of infectives is unchanged for the next wave and then decreasing, (c) $R < \frac{\text{one,}}{S}$ the number of infectives is decreasing. This can be seen by inspection of the formula. This applies to any wave of an epidemic, so whereas a small reduction of R or one at the beginning of the sequence can

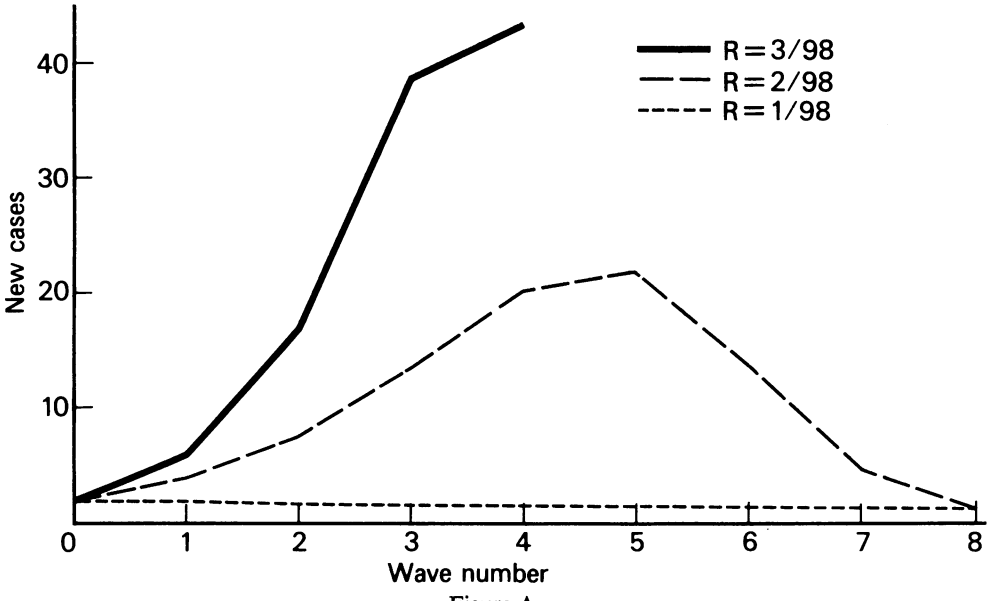

Figure A
C = R.I.S. $I_0 = 2$ $S_0 = 98$ Examples of plots with different values of R

eliminate the development of the epidemic, obviously a much larger change is required later if it is to be worthwhile.

Relation between theory and observations

(a) The existence of a critical value gives an explanation of the capriciousness of epidemics—a good example of this behaviour was the epidemic of influenza expected in 1968–69, which came to nothing, only to reappear more seriously in 1969–70. Small variations in R would explain this.

(b) $R = 1/S$ as a critical value can explain why the common cold dies out in small communities: if S is sufficiently small, it is below the critical limit. In an experimentally induced epidemic in mice, those which were divided into smaller groups (ten groups of ten) showed a mortality rate much less than those kept in one group of 100 (Topley and Wilson, 1955).

(c) The presence of a long " tail " to the histogram where R is near 1/S (figure A) explains why an epidemic of measles may continue through the summer of an off-peak year, only to be ready to detonate the next outbreak when sufficient new susceptibles have been born for the critical level to be exceeded.

(d) An example of an explosive influenza epidemic was given by Lee (1961) and resembles that in figure A.

The 1961 influenza epidemic

Daily doctor/patient contacts were recorded routinely in an urban practice of 3,800 patients. During the period 7 January, to 7 February 1961, 414 new calls were received, of which 289 were attributed to the influenza epidemic. Since patients tend to defer sending for the doctor until Monday, when they require a National Insurance Certificate, an average of the Sunday–Monday cases has been recorded. The uncorrected and corrected numbers are shown in figure B.

The corrected numbers show a pattern of nine waves of infection ascending at four-day intervals and descending at three-day intervals. Not all cases in any wave will be

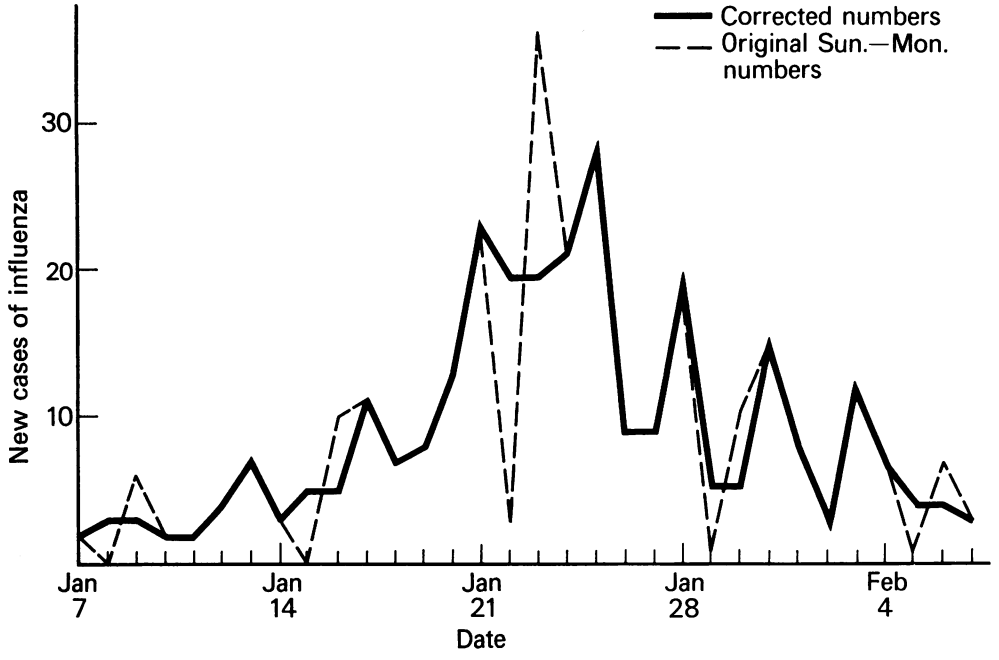

Figure B
Asian influenza 1961. Saturday 7 January to Tuesday 7 February 1961.

reported on the same day. Hence, the number of cases in each wave is not just the cases at the peak of the wave, but includes those on either side of the peak. On a three-day wave the cases on the day before and after peak day were added in to give total for the wave; for four-day waves the cases for day before and after peak day and half the midwave day cases were included to give the total number of cases for the wave.

Figure C shows the totals for the nine waves. The susceptible population for this practice is taken of those who become infectious and require medical treatment. Hence, the initial state of the population used in order to estimate R to fit the model C = R.I.S. is I = 10, S = 280.

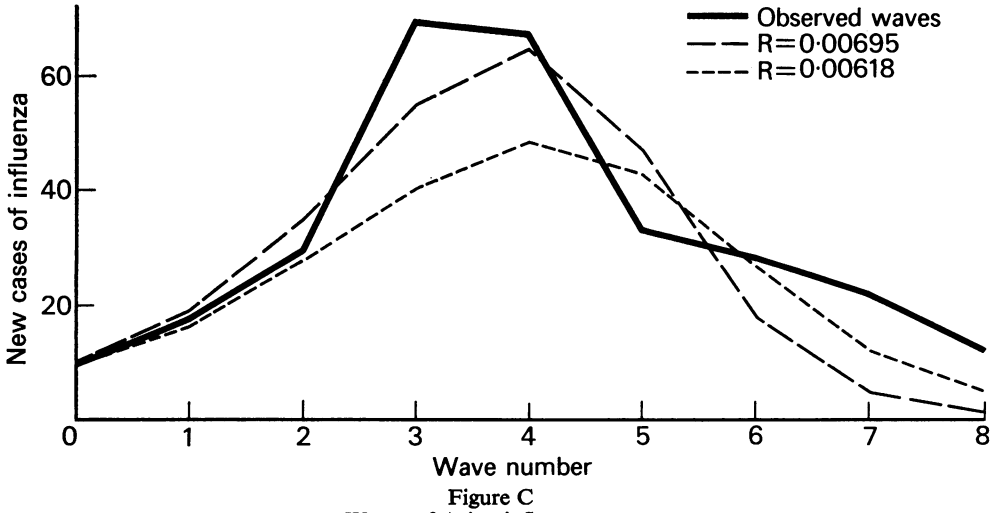

Figure C
Waves of Asian influenza.

Two statistical methods are used to estimate R from the data. The first method gives R = 0·00618, the second R = 0·00695. Figure C shows graphs of theoretical data. The methods are described in appendix 2.

Theoretical control of an epidemic

From the general formula some conclusions can be drawn about the basic methods of control:

(1) *Reducing R*

By reducing R, i.e. the " degree of contact " between individuals. Lessening the density of the population is one way of doing this.

An epidemic showing many waves to reach a peak indicates that controlling methods of transmission will succeed, since the value of R for that epidemic will be close 1/S. An epidemic with few waves to reach a peak suggests that controlling transmission will be ineffectual since R will be large relative to 1/S.

(2) *Reducing I*

By reducing I. This will slow down the development of an epidemic. It will not control it completely, unless it is brought down to zero. Ring vaccination has the advantage of giving time for permanent action, i.e. reducing R or S; it has the danger of complete failure. So far this method appears to work only under veterinary conditions, i.e. rabies and foot-and-mouth disease; even here it causes considerable worry.

(3) *Reducing S*

By reducing S. The obvious way to reduce the number of susceptibles is by immunisation.

With R = 0·00618 for the epidemic under consideration, in order to have controlled the epidemic the susceptible population would have needed to have been reduced from 280 to 1/R = 162, i.e. by 42 per cent, by immunisation.

With R = 0·00695 the necessary reduction in the susceptible population would have been 48 per cent.

It will be seen that reducing S will not give permanent control. If fresh non-immune subjects are continually introduced, as in measles, there would simply be an epidemic of the previous size, but after a longer period once the critical concentration is reached. The definition of susceptibles depends not merely on the possibility of being non-immune, but also on the chances of coming into contact with the infection.

People who move a great deal with others and come into close proximity, as far as method of transmission are concerned, can either be rated as having a high value of susceptibility, or as having a high personal value of R; so far as disease control is concerned, these are the people one would like to have priority of immunisation in influenza. Old, debilitated and housebound people play little part in the transmission of an epidemic.

Bus conductors (Damms, 1959), school teachers, and people in contact with the public in confined spaces should be immunised early, or allowed to work under conditions of better ventilation, and thus make an epidemic "pocket" (as in the mouse experiment), so as to produce, in effect, a number of small S communities instead of one large one. According to Fry (1969), other things being equal young people are more susceptible to influenza, and one should thus attempt to immunise them preferentially.

Appendix 1

The formula C = R.I.S. may be written in more mathematical notation.

Let I_o = Initial number of infectives
P = Population size
$P-I_o$ = Initial number of susceptibles
I_n = Number of infectives in the n^{th} wave $n = 1,2, \ldots$

$$\text{then } I_n = R.\ I_{n-1}\left[P-\sum_{j=0}^{n-1} I_j\right]$$

Appendix 2

Let I_n^* = Observed number of infectives in the n^{th} wave
I_n = Number of infectives in the n^{th} wave predicted by the above equation.

$R = 0{\cdot}00618$ is such that

$$\sum_{j=0}^{8} (I_j^*-I_j)^2/I_j \text{ is minimised}$$

$R = 0{\cdot}00695$ is such that

$$\sum_{j=0}^{8} (I_j^*-I_j)^2 \text{ is minimised}$$

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NEW BRITISH NATIONAL FORMULARY PROCEDURE FOR INCOMPLETE SCRIPTS FROM 1 JUNE 1976

A new procedure for dealing with prescriptions for British National Formulary preparations where the prescriber has omitted to state the quantity or strength to be supplied came into effect with the new *British National Formulary* on 1 June 1976.

The most important innovation is that where the prescriber cannot be contacted and the pharmacist has sufficient information to make a professional judgement he may dispense up to five days' supply of a BNF preparation for systemic use and endorse the prescription accordingly. The new arrangement does not apply to controlled drugs or, in general, S4A preparations. And where the prescription is for a combination pack, an oral contraceptive, or a liquid antibiotic preparation which needs to be supplied in an unopened container, the smallest pack should be dispensed. The old arrangements will apply to non-systemic preparations.

Details of the new procedure are set out in a family practitioner notice (FPN114) which will shortly be issued by the Department of Health and the Welsh Office.

REFERENCE

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