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A mathematical model of common-cold epidemics on Tristan da Cunha

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SUMMARY

Records of seven common-cold outbreaks on the island of Tristan da Cunha are compared with the corresponding time courses given by the mathematical model of Kermack & McKendrick (1927) and with an alternative model that directly involves a constant average duration of individual infection. Using computer simulation techniques the latter model is shown to be preferred and is then closely matched to the field data to obtain values for the model parameters. Consideration is then given to the intensity of epidemics predicted by the model and to the distribution of the actual epidemics relative to the theoretical epidemic threshold.

INTRODUCTION

The occurrence of common-cold epidemics among the islanders of Tristan da Cunha has already been discussed in a previous paper (Shibli, Gooch, Lewis & Tyrrell, 1971). For the purpose of that study daily records of the development of upper respiratory infection were kept by individuals involved in each of the seven outbreaks that affected the community between 1964 and 1968. Several observations were made based upon a collation of these records but the data may also be used to provide information regarding the time course of each epidemic as a whole. For example, Fig. 1 shows the development of the outbreak in April 1966 and has been obtained from the individual record cards in the following manner.

The total number of individuals reporting the onset of symptomatic upper respiratory infection was found for each day and these totals then accumulated day-by-day to give the left-hand curve of Fig. 1. In general, any ordinate of this curve gives the number of individuals who have become involved in the epidemic during the corresponding period, but this number of individuals is uniquely fixed for only the beginning and end of each day. At intermediate times there is uncertainty as to the appropriate numbers that should be taken, but limits to this uncertainty are set by the opposing assumptions that the daily totals are achieved immediately at the beginning and end of each day. The representation of these two extreme assumptions in Fig. 1 gives rise to rectangles which are one unit wide and of heights equal to the daily totals. The figure thus embodies a statement of these uncertainty

limits. Identical arguments apply to the right-hand curve, which is composed of the daily totals of individuals reporting a last day of infection. Any ordinate of the latter curve gives the number of individuals who have recovered from symptomatic infection at the appropriate time whilst the numerical difference between the two curves gives the number of individuals who remain infected.

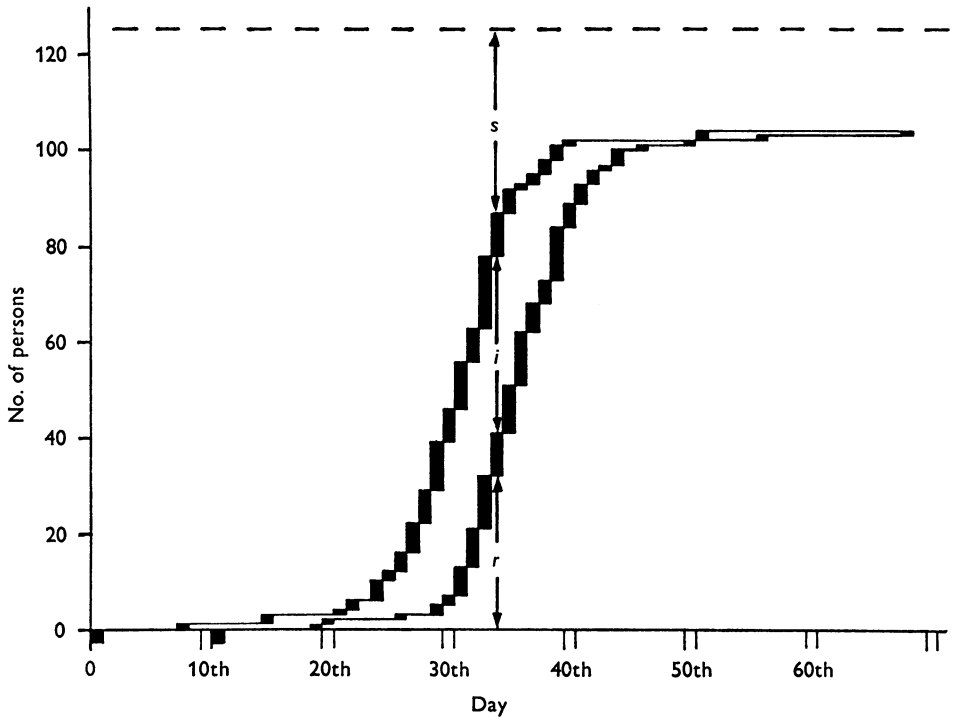

Fig. 1. The epidemic of April 1966 constructed by means described in the text. The number of individuals who have recovered from infection, the number who are infected and the number of susceptibles remaining are given by the quantities r, i and s respectively. The number of susceptibles at time zero is not known but is represented by the horizontal dashed line. The dates of ship arrivals are indicated by rectangles below the abscissa.

The data for all seven epidemics, when prepared as for Fig. 1, show broadly similar characteristics although the form of the smaller outbreaks tends to be less distinctive. However, the data seem sufficiently consistent to serve as a set of empirical functions against which the performance of a mathematical model of the epidemic process could be checked, and it is with this approach that the present paper is concerned.

Formulation of mathematical models

The smooth progress of the two curves in Fig. 1 suggests that the main phase of an epidemic in the present situation could well be described by a deterministic process. At the beginning and end of the epidemic, however, when the number of infected individuals is small, the curves show the sort of irregularity associated with a more stochastic process. In these circumstances an approach using a deter-

ministic model was adopted and the epidemic data were suitably truncated to exclude the two extreme phases.

Certain characteristics of the Tristan community allow the corresponding epidemic model to be somewhat simplified. Firstly, the moderate size and free social mixing of the community (Shibli *et al.* 1971) suggests that topographical or sociological groupings may not significantly affect the progress of the epidemic; and secondly, the isolation of the community rules out the effects of emigration and immigration. The Tristanian community would in fact seem to approach very closely the ideal homogeneous and closed society whose theoretical consideration has provided a basis for epidemic theory since its inception.

In conformity with the classic deterministic approach, the following three classes of individuals are recognized within the community at any time: (*a*) the class, numbering s individuals, who are susceptible to infection; (*b*) the class, numbering i individuals, who are infected and are also assumed to be infectious; (*c*) the class, numbering r individuals, who have recovered from infection and are assumed to be immune from reinfection. The number of individuals who are susceptible at the outbreak of infection, $s(o)$, must also be considered, and this unknown number is represented in Fig. 1 as the horizontal dashed line, which then allows all three of the above classes to be related to the epidemic field data.

Statements concerning the transfer of individuals between classes are now required and a suitable law for the process of infection is derived from the hypothesis that the rate of infection is proportional to the probability of contact between infected and susceptible individuals. In a randomly mixing society the deterministic infection rate is then given by Iis, where I is a constant which may be termed 'infectivity'. The rate of recovery may be taken as proportional to the number of infected individuals at any time, that is equated to Ri, where R is a recovery rate constant. These laws of infection and recovery then give the differential equations which constitute the model due to Kermack & McKendrick (1927):

MODEL 1

$$\begin{aligned} ds/dt &= -Iis, \\ di/dt &= Iis - Ri, \\ dr/dt &= Ri. \end{aligned}$$

An alternative to the above model arises with a modified recovery law that corresponds with the assumption of a constant duration of infection. In this case the recovery rate at a time $(t+D)$ may be equated to the infection rate at time t, where the time interval, D, represents the average duration of individual infection. The function Iis, when delayed by a period D, may be written as $I[is]$, then

MODEL 2

$$\begin{aligned} ds/dt &= -Iis, \\ di/dt &= Iis - I[is], \\ dr/dt &= I[is] \end{aligned} \quad \text{where} \quad \begin{aligned} [is] &= i(t-D)\, s(t-D), \; t \geqslant D \\ [is] &= 0, \; t < D \end{aligned}$$

METHODS

Preliminary examination of the above models was carried out using a Pace TR 48 analogue computer and more detailed studies on the second model were then undertaken by coupling the analogue computer to a Honeywell DDP 516 digital computer to form a hybrid computer system. The main object of the later studies was to determine the sets of values for $s(o)$, I and D that gave rise to best agreement with the seven recorded epidemics.

To aid the search for best agreement a special hybrid program was written which allowed use of the teletype keyboard for prespecification of eight values for each of the model parameters, and which then supervised the implementation of the 512 resulting combinations. For each combination of the parameter values the program compared the performance of the model with the epidemic under study by calculating the sum-square-error between the appropriate variables of the model and the daily epidemic data. These error values were automatically printed out in eight by eight arrays corresponding with increasing values of the first parameter from column to column and increasing values of the second parameter from row to row. The third parameter was incremented between successive arrays. This format allowed the error to be visualized as a three-dimensional function and rapid location of the minimum was made possible. Determination of the parameter values to two significant figures usually demanded repetition of the procedure with successively finer increments between the parameters. A further facility of the hybrid program allowed sets of values for $s(o)$, I and D to be specified using the computer teletype and the resultant time-courses of the variables s, i and r were then automatically typed out.

RESULTS

Implementation of the Kermack and McKendrick model on the analogue computer revealed a discrepancy between the performance of the model and the form of the recorded epidemics. This is illustrated in Fig. 2(d), where the dashed lines show the solution of the model which gives minimum error when compared with the corresponding epidemic data. The failure of the model evidently arises from the recovery law, which imposes an unduly high recovery rate in the early part of an epidemic. The second model was shown by the analogue computer to promise better agreement with the epidemic records and this model was therefore pursued in preference to the former. Using the hybrid computer as previously described, least-squared-error solutions were obtained for five of the seven epidemics and the daily values given by these solutions are shown in Fig. 2 together with their corresponding sets of field data.

The time courses of the two remaining epidemics were not satisfactorily matched by model 2 owing to discontinuities which appear in the later phases of each epidemic. The form of these discontinuities is apparent in Fig. 3 and their possible cause was considered in some detail. First, the epidemics were split into five components corresponding with the five social groups distinguished during a sociological survey in 1965 (P. A. Munch, personal communication). However, no significant difference

in the time courses of these components could be distinguished. Secondly, the locations of houses in which new infections occurred were annotated on a map of the island's residential area, a different map being used for each day. By scanning the completed sequence of maps the spread of the epidemics could be followed and several possibly significant groupings of houses could be distinguished. However, examination failed to reveal any relevant differences between the epidemic components associated with various combinations of these groups. It became apparent from these first two investigations that neither sociological nor topographical grouping could be indicted as the cause of the observed discontinuities.

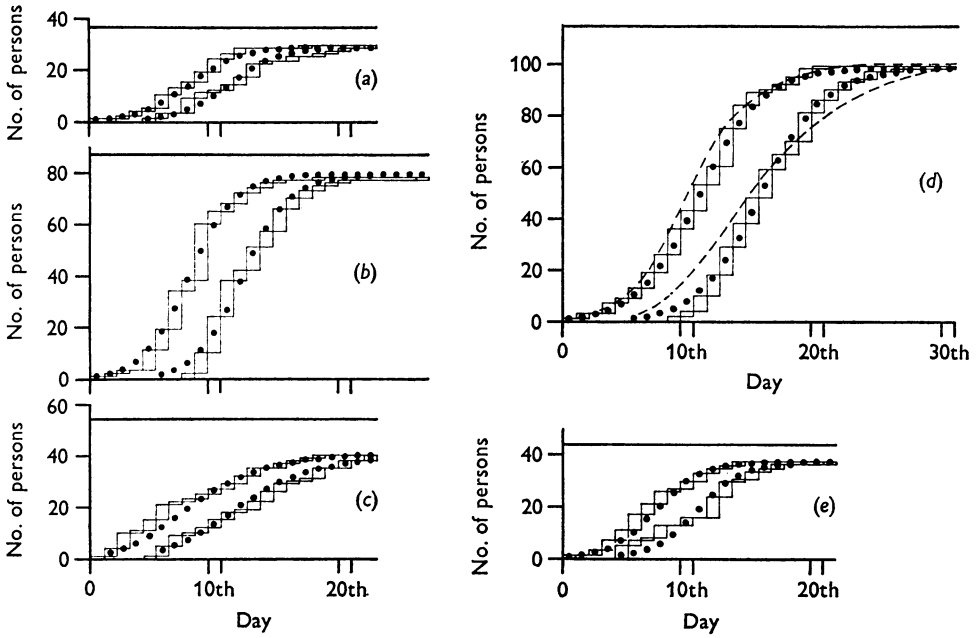

Fig. 2. The epidemic records for September 1964, January 1965, January 1966, April 1966 and October 1967 correspond with letters (*a*)–(*e*) consecutively. The dashed lines in (*d*) represent the solution of model 1 that is in closest agreement with the data. The solid circles in each figure give the solutions of model 2 that are in closest agreement with each set of field data and the upper horizontal lines show the corresponding levels of susceptibles at time zero.

Another cause of irregular epidemics could be a sudden change in infectivity related, for example, to temperature or even possibly to an increase in the inherent virulence of the infective agent itself. However, when such a change was implemented in the analogue computer simulation, agreement with the data was only marginally improved and the hypothesis of changed infectivity was abandoned. A final hypothesis considered the data of Fig. 3 to arise from two independent epidemics involving different viral agents. It may be noted in this respect that both epidemics were associated with the arrival at Tristan da Cunha of two ships and that contact with infected passengers has been identified as the origin of common-cold epidemics on the island (Shibli *et al.* 1971). In the case of the May 1967 outbreak one ship arrived 2 days before the first notified infection and another ship

arrived 1 week later; in February 1968 two ships arrived at the island on the day preceding the first notification of infection. The hybrid simulation of model 2 was extended to include a second and concurrent epidemic whose form was determined by an independent set of the parameters $s(o)$, I and D. The start of the second epidemic was delayed by a period whose duration gave a seventh parameter that it was necessary to adjust in matching the double infection model to the irregular epidemics. The daily values corresponding with the least-squared-error solutions that were eventually obtained are shown in Fig. 3.

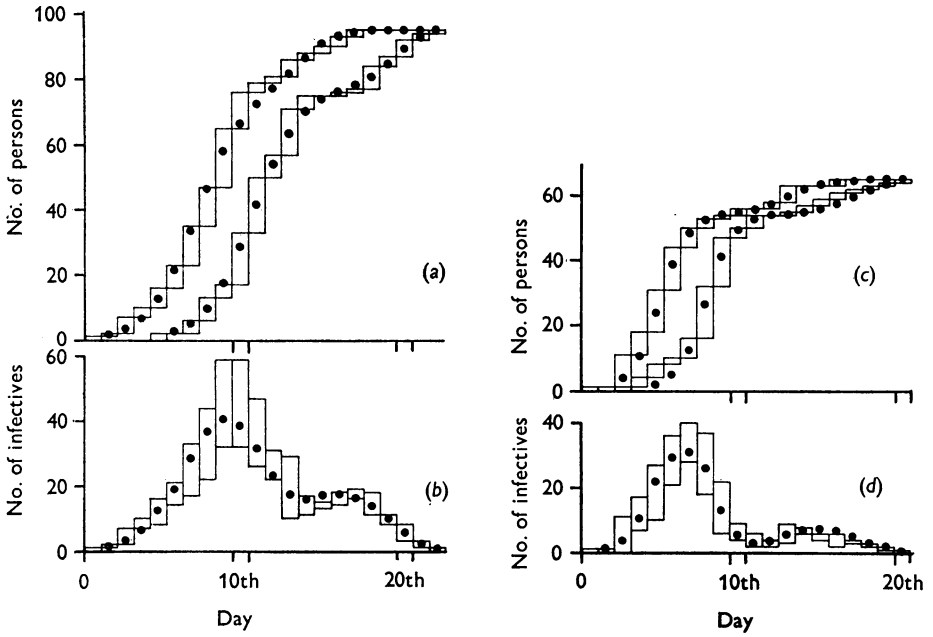

Fig. 3. The epidemic records for May 1967 and February 1968 correspond with (*a*) and (*c*) respectively. The lower figures (*b*) and (*d*) in each case give the number of individuals infected at any time. The solid circles in each figure give the solutions of model 2 that are closest in agreement with each set of field data.

Table 1.

Date of epidemic	Ident no.	$s(o)$ (inds.)	I (ind./day)	D (days)	N'	$s(o)\,ID$
Sept. 1964	1	36	0·018	3·2	0·78	2·1
Jan. 1965	2	87	0·0072	4·0	0·91	2·5
Jan. 1966	3	54	0·0086	3·6	0·74	1·7
Apr. 1966	4	114	0·0043	4·6	0·87	2·3
May 1967	5*a*	88	0·0084	3·4	0·90	2·5
May 1967	5*b*	16	0·074	5·5	1·00	6·5
Oct. 1967	6	44	0·016	3·2	0·84	2·3
Feb. 1968	7*a*	56	0·22	2·8	0·96	3·4
Feb. 1968	7*b*	10	0·067	4·2	0·95	2·8

The values of $s(o)$, I and D are the parameter values for model 2 that give best agreement with the records of the corresponding epidemics; in stating units 'individuals' is abbreviated to 'inds'. Double infections are indicated by the use of letters following a common reference number. The last two columns give values of epidemic constants as discussed in the text.

The values of $s(o)$, I and D that give best agreement between model 2 and the seven recorded epidemics are listed in Table 1, where statement to two significant figures is made possible by the sensitivity of the error-squared function to changes in parameter values. The sensitivity was different for each epidemic but at worst gave a 10 % change in the sum of squares of errors corresponding with unit change in the second significant figure of each parameter. Typically the change was in excess of 50 %. The method used to determine these values required the model to be expressed in terms of numbers of individuals, but it is of more general value to

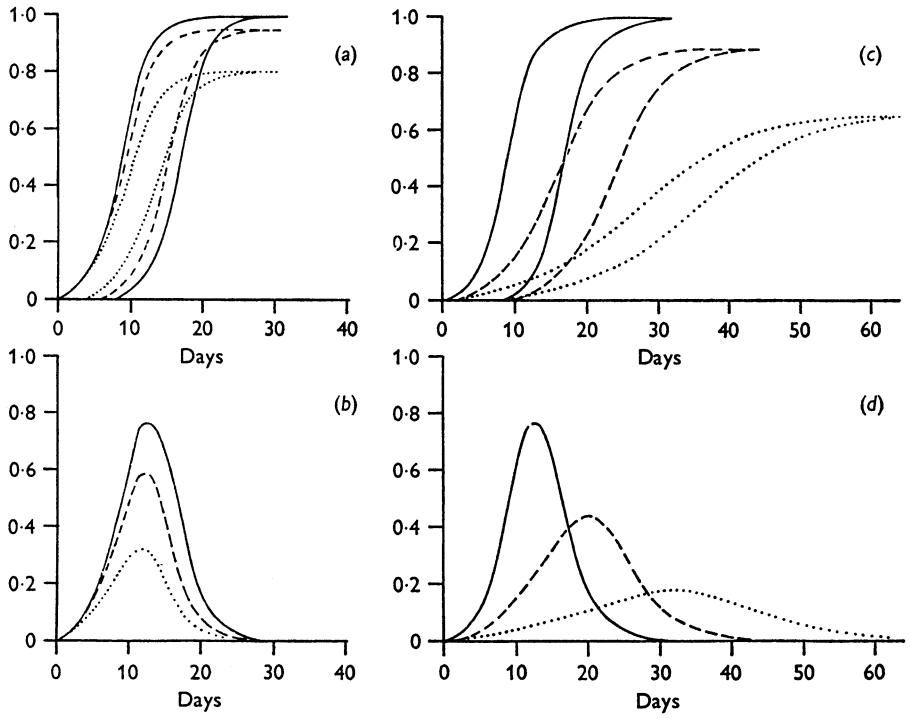

Fig. 4. Theoretical epidemics produced by model 2. In (*a*) and (*c*) the left-hand curves give the number who have been infected as a fraction of the initial number of susceptibles; the right-hand curves give the fraction who have recovered. The difference between any pairs of curves gives the fraction who remain infected at any time and these values are plotted in the lower figures. In (*a*) and (*b*) the product $s(o)I$ is kept at 1/day and D has the values, 4 days (—), 3 days (– – –) and 2 days (. . . .). In (*c*) and (*d*) the value of D is kept constant at 4 days and the product $s(o)I$ has the values 1·0/day (—), 0·6/day (– – –) and 0·4/day (. . . .).

consider the model in a normalized form where the variables are expressed as fractions of the initial number of susceptibles $s(o)$. Thus, let

$$s' = s/s(o), \qquad ds'/dt = -f(t),$$
$$i' = i/s(o), \quad \text{then} \quad di'/dt = f(t)-f(t-D),$$
$$\text{and } r' = r/s(o), \qquad dr'/dt = f(t-D),$$
$$\text{where } f(t) = s(o)Ii's'.$$

It becomes apparent from the normalized model that the resulting temporal forms of the predicted epidemics are dependent solely upon two factors: first, the product of infectivity with initial number of susceptibles, and secondly, the average duration of individual infection. As is shown in Fig. 4, both these factors affect the size of an epidemic, but in addition the value of $s(o)I$ has a profound effect upon the time at which an epidemic reaches its peak.

DISCUSSION

Mathematical epidemiology really began with the work of Kermack & McKendrick (1927), and in particular with the simple deterministic model reproduced as model 1 in this paper. Considering a closed homogeneous society and this simple three-state infection, the time course of an epidemic is determined by the laws that are assumed for the rates at which individuals enter and leave the infected state. The product law describing the rate at which new infectives are generated is based upon the probability of a susceptible coming into effective contact with an infectious individual in a randomly mixing society, and this law has been adopted by most later workers in application to both deterministic and stochastic models. On the other hand, the law stating that the rate of removal is proportional to the number of infectives has been less readily accepted and alternatives have arisen; for example, in models of the Reed-Frost variety, first examined by Abbey (1952). In these models infectives are removed after a given period of infection and the recovery rate at any time is thus implied by the duration of individual infection. The fundamental laws of infection and recovery are obviously of vital importance to the body of mathematical epidemiology as summarized by Bailey (1957) and Bartlett (1960). These studies have been largely theoretical and the data from Tristan da Cunha now make it possible to test more thoroughly than was previously possible whether the fundamental laws adequately describe real epidemics.

In view of the above comments, the basic field data were processed so that as much as possible of the relevant information was retained for comparison with the performance of the models. In particular this allowed the simultaneous matching of the time courses for all three groups of individuals rather than the more common procedure of using some selected feature such as infection rate as the sole criterion for the performance of the model. In addition, Figs. 2 and 3 show, as previously described, the uncertainty arising from the use of daily totals of first and last days of infection. It is also known that, owing to less than complete co-operation of the islanders, the data sets are not complete records of an epidemic. The degree of co-operation has been estimated by one of the island's Medical Officers as about 80 %, but provided that under-reporting does not distort the shape of the epidemic record it does not affect the general agreement between model and data. This retention of agreement arises as a property seen in the equations of the normalized model whereby epidemics of different sizes but of identical shape are obtained provided that any change in $s(o)$ is compensated by an opposite change in I. In this respect it should be noted that no allowance for under-reporting has been made in obtaining the values given in Table 1, and in particular that the values given for I will be proportionately high.

Despite a measure of uncertainty in the field data, an inconsistency has been shown between the data and the epidemic model of Kermack & McKendrick. This inconsistency is removed when the recovery law is replaced by one based directly on a constant duration of infection and embodied in the revised formulation of model 2. The revised law would also seem to be more reasonable on the common-sense ground that the progress of a patient's infection is independent of other infectives and that in summating the infectives the individual infections will only lose their identities as the number of infectives rises. In considering the improved agreement with present epidemic data provided by model 2 it should, however, be borne in mind that the extent and number of epidemics are too small for statistical validification of the model.

An expression for the final size of an epidemic as predicted by the new model may readily be obtained by integration of its first equation,

$$\int_{s(o)}^{s(\infty)} 1/s\,ds = -I\int_0^{\infty} i\,dt,$$

but

$$\int_0^{\infty} i\,dt = ND,$$

where N is the final number of individuals involved in the epidemic, and

$$s(\infty) = s(o) - N.$$

Thus

$$\frac{ln\,(1-N')}{N'} = -s(o)ID,$$

where N' is the intensity of the epidemic, i.e. the proportion of susceptibles affected, and is given by $N/s(o)$. This result may be compared with that for model 1 obtained by Kendall (1956), which in present terminology gives

$$\frac{ln\,(1-N')}{N'} = \frac{-s(o)I}{R}.$$

These two predictions become identical if the duration of infection in model 2 is taken to correspond with the reciprocal of the removal rate constant in model 1. This relationship may be readily accepted since each quantity then implies the same removal rate of infectives over any time increment during the central phase of an epidemic.

The relationship between epidemic intensity and the triple product $s(o)ID$ is plotted in Fig. 5 and clearly shows an epidemic threshold at unity value of the triple product. This threshold, below which epidemics do not occur, is equivalent to that first discussed by Kermack & McKendrick (1927) in relation to their deterministic model and subsequently demonstrated in stochastic models by Whittle (1955) and Kendall (1956). The intensities and triple products of the present epidemics are given in Table 1 and these values locate each epidemic in Fig. 5, where the closeness of each point to the calculated intensity curve reflects the overall accuracy of the hybrid simulation by which $s(o)$, I and D were determined. The epidemics are clustered well above the theoretical threshold; if the secondary epidemics of May 1967 and February 1968 are discounted as involving too few individuals for

realistic analyses, the mean value of $s(o)ID$ for the epidemics is 2·40 with a standard deviation of 0·48.

A population may be described as subcritical to a particular infection at any time that its triple product lies below the threshold value of unity; that is, when the number of its susceptibles is less than $1/ID$. However, the birth of new susceptibles, coupled with any loss of immunity by previously infected individuals, will steadily increase the number of susceptibles. The regular progress of the triple product may be envisaged as the movement of a point along the abscissa of Fig. 5,

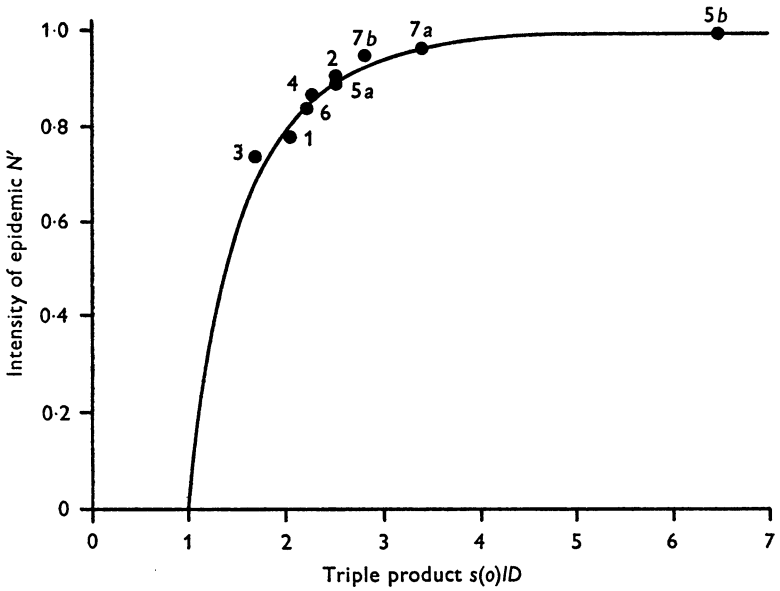

Fig. 5. The solid line gives the intensity of an epidemic predicted by model 2 as a function of the triple product $s(o)ID$. The solid circles show the positions of the analysed epidemics, which may be identified by the numbers given in Table 1.

the point reaching unity as the population achieves the critical condition and passing beyond it as the population becomes increasingly supercritical. The velocity of the point is given by the product ID, which for the present epidemics may be determined from the values given in Table 1. Excluding the secondary epidemics the velocities range from 0·020 to 0·058 per susceptible. An epidemic may be caused by the chance presentation of an infective agent when its corresponding point is at any position beyond the threshold and it is therefore surprising to find that the epidemics are not evenly distributed beyond the threshold. Furthermore, the clustering of the epidemics is not explained by assuming more frequent presentation of infective agent since in this case the epidemics would tend to cluster near to the threshold.

An explanation of this behaviour could be that theoretical epidemics of an intensity less than 0·7 involve fewer infectives than is required in practice for the maintenance of the level of infection. The predicted reduction in the number of infectives as intensity is decreased may be seen in Fig. 4 and the effect would seem

sufficiently marked to cast doubt on the applicability of the present deterministic infection law, and hence the model, under conditions which would lead to low-intensity epidemics. The present results therefore seem to argue for the existence of an empirical threshold below which infections follow stochastic paths to extinction without causing an epidemic. In the case of common-cold epidemics on Tristan da Cunha this empirical threshold lies between one-and-a-half times and twice the level of the theoretical threshold.

We hope to make further checks on the validity of the model, in particular to determine whether it adequately describes the epidemics that occur in other closed communities, such as residential schools, and also to obtain independent evidence on epidemic intensities by serological studies.

The authors wish to acknowledge the contribution made to the present work by Mr F. G. Tattam of the National Institute for Medical Research, who originated and developed the hybrid computer program. A debt is also owed to the MRC Tristan da Cunha Working Party for their assistance in this study. Finally, we wish to express our gratitude to the Tristanian community, whose co-operation made the present study possible.

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