Bulletin of Mathematical Biology (1998) **60**, 585–596

Modelling the Spread of Phocine Distemper Virus among Harbour Seals

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Data presented in earlier publications on the 1988 epizootic among seals in North West Europe show a pattern that is somewhat inconsistent with the predictions of the standard mathematical model of epidemics. We argue that for animals living in herds or colonies, such as seals, the mutual contact behaviour is such that models for the transmission of infectious diseases should be applied with special care for the distinction between numbers and densities. This is demonstrated by using a mechanistic description of the contacts among seals, which leads to a slightly different formulation of the model. Results of the analysis of this formulation are more in line with the data.

The model introduced here can be applied to epidemics among all kinds of animals living in herds and in fact to any species with constant local density, independent of the total population size (i.e., occupying a variable area). Application of the traditional formulation, using different parameters for herds of different sizes, will give equally good results for non-lethal diseases. However, especially for diseases with a low R_0 *and* high death rates, such as the phocine distemper virus (PDV) disease, the two model formulations give quite different results.

Further analysis of the model is performed to determine the most important factors influencing such an epidemic. The survival of infected animals turns out to have a disproportionately great influence on the intensity of the epidemic. Therefore in the case of the PDV epizootic we conclude that marine pollution may not only have contributed to the high death rates, but, if so, it has intensified the epizootic as well.

1. INTRODUCTION

On a short timescale (weeks) one can think of seals inhabiting the coastal waters of Northern Europe as constituting a meta-population, a collection of many local subpopulations (colonies) loosely coupled by incidental migrations. Within a colony, contacts are probably at random.

0092-8240/98/030585 + 12 $25.00/0 bu970030

In the spring and summer of 1988 this meta-population was struck by an infectious disease that caused the death of a substantial fraction of all individuals (estimates vary from 40 to 60%). A morbilli virus, causing the disease, was identified by Osterhaus and Vedder (1988) and called phocine distemper virus (PDV).

The following characteristics appear from data acquired and analysed by Heide-Jørgensen and Härkönen (1992a).

- Almost all colonies in the studied area suffered from an outbreak.
- The fraction that caught the disease was more or less the same for all colonies, and in particular independent of the size of the colony (in Eastern Scotland this fraction was a bit lower). A more elaborate presentation of these data can be found in Tables 1–3.

While analysing the Kermack and McKendrick (1927) epidemic model in its traditional form, one arrives at the following conclusions.

- The basic reproduction ratio R_0, i.e., the expected number of secondary cases per primary case in the initial phase of an outbreak is proportional to the colony size. Hence, since R_0 has a threshold value 1, there exists a critical colony size below which the virus can only cause minor outbreaks affecting a negligible fraction.
- The final size, i.e., the fraction ultimately infected, increases (nonlinearly) with R_0, hence with colony size (the overshoot is stronger when the peak is higher, which is the case in larger colonies).

Clearly these general conclusions are at variance with the data [see the above and Heide-Jørgensen *et al.* (1992a)]. Harwood and Hall (1990) suggested that the traditional epidemic model might not be very suitable for this epizootic, because the periodical aggregation of seals would keep the contact rate rather high, although 'density' might become low. Nevertheless, the traditional model was applied both by Grenfell *et al.* (1992) and Heide-Jø rgensen and Härkönen (1992a). The latter authors achieved a correction of the results by adapting the key contact parameter to the colony size. They motivated such an adaptation by noting that 'seal density within a herd is relatively high regardless of population size'. A larger colony will simply occupy a larger area during haul-out, while the effective, local density remains constant. [See also Harada *et al.*, (1995).]

When disease always leads to immunity and never to death, an adaptation of the contact parameter to colony size is indeed all that is needed to take into account the fact that numbers may vary wildly while density remains constant and, more importantly in the present context, contact intensity remains constant. However, when, as in the case of PDV among seals, a substantial fraction of all cases ends with death, a slightly more complicated correction is required. In a sense the adaptation of the contact parameter has to be updated as the colony becomes smaller due to the virus making victims. In other words, as immunes

receive part of the contacts of infectives, they serve to protect susceptibles; when infected individuals die, rather than becoming immune, they do not contribute to this protection and a larger outbreak is to be expected. This argument suggests that the final size should not only depend on R_0, but also on the probability to survive an infection.

The aim of this paper is to present the final size equation for a situation of constant local density as described above and to analyse the data on the PDV epidemic with this equation as the main tool.

2. MATERIALS AND METHODS

Usually the harbour seal (*Phoca vitulina*) is solitary in the water, where they have their own private fishing routes. Social life, if at all, takes place on haul-out sites; in the Wadden Sea these are the tidal sand banks. When the tide is out and the banks appear, seals aggregate (and more or less form a row) on the shore. The virus is thought to spread during this resting period on the banks, so to formulate a model we will only consider this period.

On the sand banks of the Dutch Wadden Sea the seals typically lie down along the waterline, thus forming a sort of row. Morbilli viruses are usually transferred by aerosols secreted while coughing and snarling. In such a system the viruses are thought not to be able to 'fly' very far; only near neighbours of the infectious animals can be reached. As long as space is not a limiting factor, the typical nearest-neighbour distance is constant, that is, independent of colony size. When the colony is not too small boundary effects do not matter very much. Hence, the *per capita* contact intensity does not depend on the number of seals hauling out at the sand bank and in particular it will remain constant when the colony size decreases during an epidemic. As a consequence, the force of infection (the probability per susceptible per unit of time of becoming infected) is proportional to the *fraction* of seals that is infectious and *not* to their absolute number. This is the keypoint underlying the model.

2.1. ***The model.*** Morbilli viruses usually induce lifelong immunity, so we will assume that when a seal recovers from PDV infection, it is fully immunized. Choose S to represent the number of susceptible seals in the colony. Let I denote the number of infectious and R denote the number of resistant (immune) animals. N denotes the total number of seals in the colony, therefore $N = S + I + R$. Note that we describe numbers now, not densities.

Let α denote the average number of contacts of one infectious animal per unit of time, multiplied by the probability of spreading the infection indeed during such a contact. β denotes the probability of removal from the infectious class in one tide period, and f is the (average) survival probability for animals that reach the end of the infectious period. Then an epidemic in the seal population can be

described by the following set of differential equations:

$$\frac{dS}{dt} = -\alpha S\frac{I}{N} \tag{1}$$

$$\frac{dI}{dt} = \alpha S\frac{I}{N} - \beta I \tag{2}$$

$$\frac{dR}{dt} = f\beta I \qquad f \in [0..1] \tag{3}$$

$$\frac{dN}{dt} = -(1-f)\beta I. \tag{4}$$

The third equation could actually be left out, as it gives the same information as the fourth one. Note that for $f \neq 1$, N is a dynamic variable. For $f = 1$ we recover the traditional ordinary differential equation (ODE) form of the Kermack–McKendrick model.

We derived and analysed this system (De Koeijer, 1993) simultaneously with Lefèvre and Picard (1993) and Picard and Lefèvre (1993), who gave a detailed analysis of the model. A more elaborate mathematical study of a general version of the model can be found in Diekmann *et al*. (1996). They described the model in the spirit of the general Kermack–McKendrick model of 1927, which is (it cannot be stated often enough) far more general than the special case described by the ODE system.

3. Results

3.1. ***Analysis.*** Important information on the initial phase of an epidemic is given by R_0 (by definition, the average number of new infections caused by an infectious seal living in a completely susceptible population). In this model the expected infection time is $1/\beta$ during which the infectious individual makes new victims at rate α, therefore R_0 is equal to α/β (and independent of population size). If R_0 is smaller than or equal to 1, the infection will soon disappear from the population. If R_0 is larger than 1 an epidemic outbreak may occur.

The situation at the end of the epidemic can be derived from equations (1) and (4) by integration. We assume that at the start of the epidemic all seals are susceptible to the disease. Then a relation between the fraction of the population that survives the epidemic (x), and the fraction of the initial population that does not get infected at all (y), can be calculated for any combination of the parameters f and R_0 from equations (5) and (6):

$$\frac{(1-f)}{R_0}\ln y = \ln x \tag{5}$$

$$(1-x) = (1-y)(1-f). \tag{6}$$

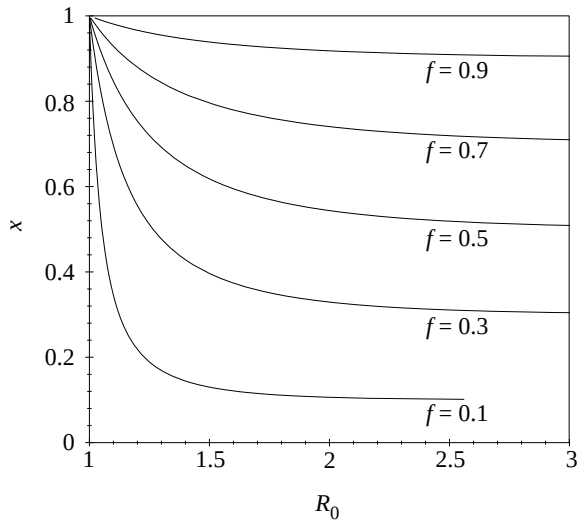

Figure 1. The final fraction of survival of the population, x, as it depends on R_0, the reproduction number of the virus, for several different survival rates f.

We see that the final situation is independent of population size N but only depends on the parameters f and R_0. Note that equation (6) has a clear interpretation: the fraction of seals dying as a result of the infection must be equal to the total fraction that got infected during the epidemic multiplied with the probability to die due to the infection.

When, conversely, x and y can be estimated from data of a certain epidemic, then the disease-specific parameters f and R_0 can be calculated from:

$$f = \frac{x - y}{1 - y} \tag{7}$$

$$R_0 = \frac{(1 - f)\ln y}{\ln x}. \tag{8}$$

In the case of the PDV-seal epizootic, these results are valid for one subpopulation, i.e., one herd. However, during this epizootic all the different herds in the area of the Wadden Sea, Kattegat and Skagerrak were affected. In all these herds the epizootic will give equal final fractions, because the size of the (sub)population does not make any difference, hence the same fractions apply to the metapopulation.

Graphical representations of the final fractions under varying parameter values (Figs 1 and 2) show the influence of the parameters f and R_0 on the outcome of the epidemic. As to be expected, f is the parameter that influences the final fractions x and y the most. For an R_0 smaller than 2 we can see that there is quite a substantial influence of the precise value of R_0, but for higher values only the value of f really makes a difference.

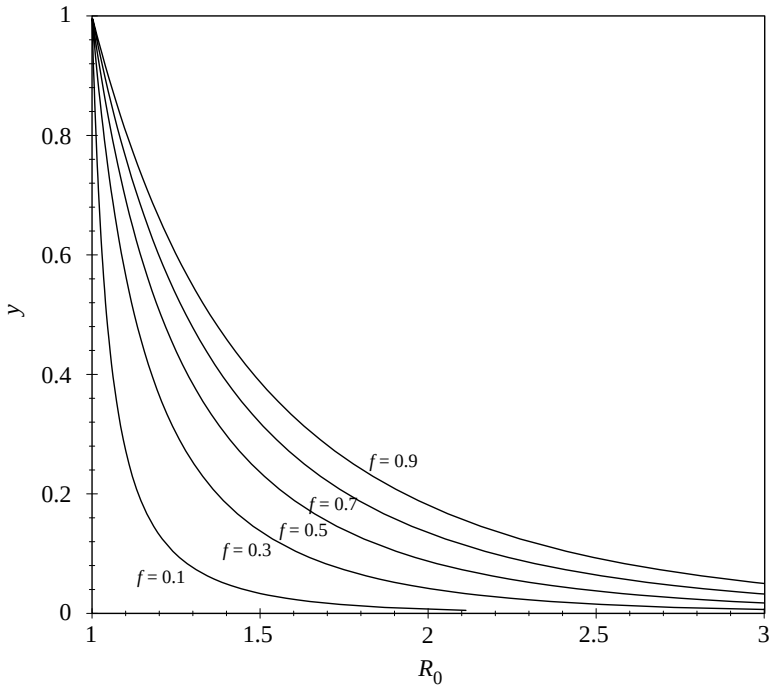

Figure 2. The fraction of the population that remains susceptible, y, as it depends on R_0, the reproduction number of the virus, for several different survival rates f.

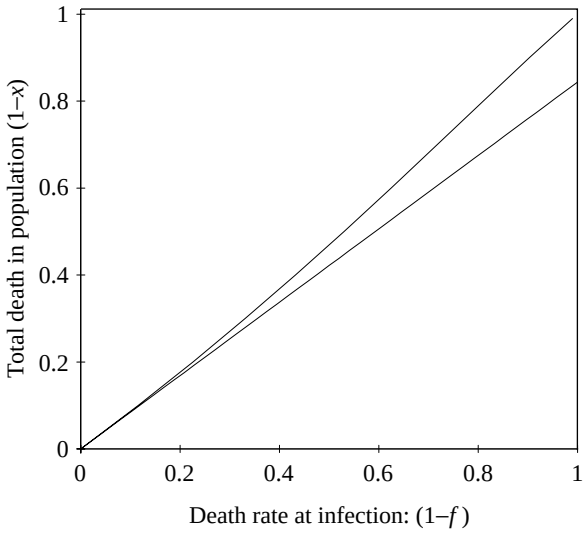

Figure 3. Total deaths in the population with different modelling assumptions while $R_0 = 2.2$. The straight line takes only account of the direct effect, as it simply multiplies the final size for $f = 1$ by the probability $1 - f$ to die. The curved upper line gives the fraction of the population that dies from the disease, according to (2.10) and (2.11) and so takes account of both effects. We see that the indirect effect is quite important for low survival (i.e., when $1 - f$ is large).

The main difference between the predictions of the current model and those of the more traditional variant lies in the influence of the survival probability. If all animals survive the disease ($f = 1$), then N will be constant and the traditional formulation is obtained. For diseases inducing high mortalities, the difference can be quite substantial. This is shown in Fig. 3, which illustrates the (different) final fractions in one plot: the total fraction of the population that died due to the disease ($1 - x$) as it depends on the value of f. For very small R_0 and low f the difference is very large, so obviously in such cases it is really important to make the right assumptions. For R_0 higher than 3, the difference in the total number of deaths is very small.

However, for very high death rates, the influence depends on what is considered the most important factor: the fraction that died or the fraction that survived the epidemic. Under certain conditions survival may be estimated at 1% under the current model and 2% for the traditional model, a substantial difference, while the total fraction of deaths in these cases, 98% or 99% are almost equal. The survival seems to be more important from a conservation biology point of view, while farmers might consider the fraction of deaths more important.

3.2. ***Parameter estimates.*** To see what new information this model can supply in the case of the PDV epidemic, we analysed available data from literature, which leads to the parameter estimates as displayed in Tables 1–3. Unfortunately there was a limited amount of data available, coming from many sources and collected with different aims and methods, so large variance in the results is to be expected.

Table 1. Denmark. Values for f and R_0 are calculated from x (overall survival) and y (fraction escaping infection) estimates. These estimates are taken from the literature.

Location	x	y	f	R_0
Koster	0.38	0.05	0.33	2.1
Varberg	0.38	—	—	—
Hesselø	0.40	0.01	0.39	3.0
Anholt	0.33	0.03	0.31	2.4
Måkläppen	0.41	<0.03	0.4	>2.3

Table 2. Kattegat and Waddensea area. Values for f and R_0 are calculated from x (overall survival) and y (fraction escaping infection) estimates. These estimates are taken from the literature.

Location	x	y	f	R_0
Netherlands	0.44	0.03	0.42	2.5
Niedersachsen	0.50	0.03	0.48	2.6
Schlesw.H	0.39	0.03	0.37	2.3
Denmark	0.49	0.03	0.47	2.6

Table 3. Great Britain. Values for f and R_0 are calculated from x (overall survival) and y (fraction escaping infection) estimates. These estimates are taken from the literature.

Location	x	y	f	R_0
East Anglia	0.52	0.03	0.51	2.6
Irish Sea	0.60	0.03	0.59	2.8
Scotland	0.90	0.16	0.88	2.1

The data, used to determine x in the different regions, come from estimated numbers before and after the epidemic. The number of carcasses found in different areas was a second, though equally unreliable, indicator for x. Estimates for y come from other sources: Heide-Jø rgensen and Härkönen (1992a) offered information on pup survival rates, which supplies an estimate for the fraction of seals that escaped infection, assuming that if a mother gets infected, its pup will surely die. This death rate, of course, has to be related to 'normal' pup survival rates.

Their detailed data on several different colonies are embodied in Table 1 (see Dietz *et al.*, 1989; Heide-Jø rgensen and Härkönen, 1992a; Heide-Jø rgensen *et al.*, 1992b). In Table 2, x estimates from our own data (Reijnders and Lankester, 1990) are combined with an overall estimate for y, an average of all the relevant data we could find. Table 3 shows data and parameter estimates for Great Britain only. Antibody tests on blood samples collected in 1989 supply good information to estimate y in that area, Harwood *et al.* (1989). Here y can be calculated from the data as $y = \hat{y}x$, where $\hat{y}$ denotes the fraction of seals with antibodies in the (sampled) group of survivors.

Using the more traditional formulation, one would determine f exactly as we did in (6) and (7). In that situation R_0 would be as follows

$$R_0 = \frac{1 - x\ln(y)}{1 - y\ln(x)}. \tag{9}$$

Then, when comparing the data of the outbreak in the Wadden Sea and Kattegat area with the Scottish data, under these model assumptions, survival rate f is also estimated half as high in the Wadden Sea but R_0 is estimated about 50% higher (3.6 vs. 2.2) in the Wadden Sea area. The difference with the parameter estimates from the model formulation as described in this article lies in the R_0 estimate only. Our R_0 estimates are almost equal for all the different regions.

3.3. ***Sensitivity analysis.*** For the data gathered on the seal epizootic (tables 1–3), we cannot really give a proper confidence interval, because the unreliability of these estimates is mostly in the methods used to determine them. However, a sensitivity analysis of the parameter estimates for R_0 and f will reveal their dependence on x and y, and hence their sensitivity to variation in these variables. The matrix A of partial derivatives of f and R_0 with respect to x and y is given

by (10)

$$\mathsf{A} = \begin{pmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \frac{\partial R_0}{\partial x} & \frac{\partial R_0}{\partial y} \end{pmatrix} = \begin{pmatrix} \frac{1}{1-y} & \frac{x-1}{(1-y)^2} \\ \frac{(x-1-x\ln x)\ln y}{(1-y)x\ln^2 x} & \frac{(1-x)(1-y+y\ln y)}{(1-y)^2 y\ln x} \end{pmatrix}. \tag{10}$$

For the Wadden Sea area, with $x = 0.4$ and $y = 0.03$ (and local estimates $f = 0.38$ and $R_0 = 2.4$), we find:

$$\mathsf{A} = \begin{pmatrix} 1.0 & -0.64 \\ 2.5 & -20 \end{pmatrix}. \tag{11}$$

We see that for the relevant magnitude of x and y, the error in the estimate of f has a contribution which is more or less equal to the error in x and a contribution less than the error in y (but reversed, increase of y gives decrease of f). The error in the estimate of R_0 depends strongly on y, but as R_0 is also an order 100 larger, the final error due to y remains relatively small.

This can be seen better from the matrix with relative sensitivities again evaluated at $x = 0.4$ and $y = 0.03$:

$$\begin{pmatrix} \frac{x}{f}\frac{\partial f}{\partial x} & \frac{y}{f}\frac{\partial f}{\partial y} \\ \frac{x}{R_0}\frac{\partial R_0}{\partial x} & \frac{y}{R_0}\frac{\partial R_0}{\partial y} \end{pmatrix} = \begin{pmatrix} 1.1 & -0.050 \\ 0.42 & -0.25 \end{pmatrix}. \tag{12}$$

This shows that the relative error in x is slightly amplified (1.1 times) in the estimate of f and is reduced in the estimate of R_0. The error in y reduces strongly for both estimates, f and R_0. Thus we see that the estimates of the parameters f and R_0 are not very sensitive to errors in the collected data.

4. Discussion and Conclusions

The model we describe here is, we admit, very crude and superficial. It certainly does not describe exactly what happens in 'real life', but it offers a convenient frame to organize one's thoughts about the key issues of a certain epidemic. Therefore we think that this model will be a good tool in the study of infectious diseases in species with gregarious behaviour.

From Figs 1 and 2 we can see that the most important parameter in the development of the epizootic is f, the survival probability of infected seals. If survival f is small, obviously more seals will die as a consequence of the infection. However, as can be seen in Fig. 3, the total number of deaths will be disproportionately larger, because the total fraction $(1 - y)$ of seals that become infected during the epizootic is higher, due to a positive feedback in the system. If the survival rate f is low, then the *fraction* of susceptible seals will remain high during the epidemic and therefore the force of infection will also remain at a higher level. With higher survival rates, a susceptible will have more contacts with immunized (recovered) animals, thus reducing the number of contacts with

infectious individuals and lowering the force of infection. This feature of such an epidemic is supported by data of the PDV-epizootic from Scotland, where, compared with the Wadden Sea, higher survival x was found in combination with lower prevalence of PDV antibodies, i.e., lower y (Harwood *et al.*, 1989).

The importance of careful modelling of contact behaviour is shown by the different results that are obtained when making a (seemingly) minor change in modelling these contacts. We repeat that, in populations with gregarious behaviour, local density should be used in modelling contacts, because local density may divert enormously from the overall density of the species.

The previously described contradictions between model and data (Heide-Jø rgensen and Härkönen, 1992a) are explained by applying this new model to the data. The parameter estimates show little variation over the different colonies, although the difficulty of estimating y results in a rather low precision of R_0. A minimal group *size* needed to allow for an epidemic does not exist, but all seals seem to live at local densities well above the minimal *density* needed to sustain an epidemic. An epidemic according to this model will follow the same pattern in all colonies and (sub)populations, independent of their size. In an equal time interval, an equal fraction of the population will become infected. Obviously, stochastic differences will cause small differences between those colonies, but these will be reduced by averaging over several colonies in a region. As none of the colonies in the affected area managed to escape from a large outbreak, we conclude that the contact rate between colonies must have been high. More distant colonies in Norway and the Baltic Sea remained free from infection; very low local density or low migration to and from the affected area may explain their lucky escape.

Although colonies in the Wadden Sea, Kattegat and Skagerrak seem to be affected equally, data from Great Britain display different results (Table 3). Only about 15% of the Scottish population died during the epidemic, but even there the intensity of the epidemic was still quite high (Thompson and Miller, 1992). Previously suggested explanations for this include the timing of the infection in relation to seasonal behaviour and the presence of secondary infections (Kennedy, 1990). Thompson and Miller (1992) concluded that it must have been due to either a mutation of the virus or higher resistance of the Scottish seals against the infection.

Comparison of our parameter estimates in the different areas shows that survival f is much higher in Scotland, while R_0 estimates are almost equal in all areas. The differences in survival could be explained by the different levels of pollution. Hall *et al.* (1992) postulated that high organochlorine levels were associated with higher mortality from PDV, although a direct link could not be established. Reduction of immune functions of seals feeding from the heavily polluted Baltic sea has been shown by De Swart *et al.* (1994), Ross *et al.* (1995) and De Swart (1995). These reduced immune functions may explain higher case mortality $(1 - f)$ in more polluted areas as the Wadden Sea, Irish Sea, Kattegat and Skagerrak. Parameter estimates show that survival f in Scotland is much higher.

As, under our model assumptions, R_0 turns out to be quite constant in all areas, mutation of the virus during the epizootic seems unlikely.

Although other suggested influences, as mentioned above, should not be neglected altogether, we conclude that the model presented here, explains the striking features of the PDV-seal epizootic very well.

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Received 1 January 1997 and accepted 9 November 1997