Simple Models of Massive Epidemics of Herpesvirus in Australian (and New Zealand) Pilchards

Alexander G. Murray
Mike O'Callaghan
And
Brian Jones
1. CSIRO Division of Marine Research
Hobart, Tasmania
2. Eugowra, New South Wales
3. Fisheries WA
Perth, Western Australia

Abstract In March 1995 a mass mortality of pilchard started to occur in South Australia; this spread very rapidly throughout the Australian pilchard's range, later reaching New Zealand. In November 1998 a similar mass mortality broke out in South Australia and also spread, at a slower rate, throughout the Australian range. The mortality appeared to be caused by a herpesvirus. The mortality spread as a classical epidemic front, but its speed of progress and the brief duration of mortalities at a given location are extreme. We apply simple epidemic modelling techniques, SIR and SEIR modelling, to examine the factors behind the spread of this mortality and the differences between the 1995 and 1998/9 epidemics. We discuss biological factors influencing the critical processes of long-distance (D) and local (β) transmission of infection.

1. INTRODUCTION

In March 1995 mass mortality of pilchards (*Sardinops sagax*) occurred on the central South Australian coast (Whittington et al. [1997]). Over the next three months these mass mortality events then spread both east and west to cover the entire range of the Australian pilchard (Fig. 1). Similar mortality occurred in New Zealand from June.

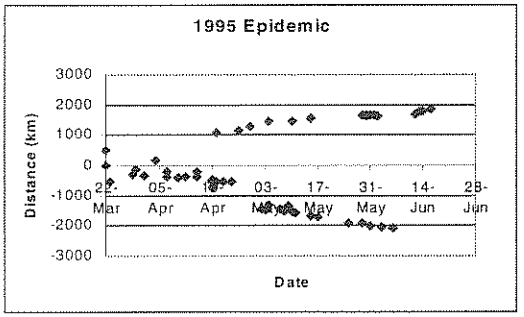

Figure 1. Radial distance from the site of the first mass mortality of subsequent reported events. Negative = eastward spread.

A second mortality event began in November 1998 and spread throughout the Australian range of the pilchard by mid 1999.

The mortality was not related to physical or biological oceanographic features (Griffin et al. [1997]) or to the occurrence of toxic algae (Fletcher et al. [1997]). The only common feature in the mortality events was the presence of herpesvirus in the gills of the fish; this virus was absent more than a few days before mortality (Whittington et al. [1997]).

The speed of the epidemic, at approximately 30 km d^{-1} in 1995, was remarkable. This is close to the maximum swimming speed of pilchards. The mortality lasted for only a few days at any given location, except in the first few weeks of the epidemic. The speed of the 1998/9 epidemic front was approximately half that of 1995, but this was still a spectacular rate of spread.

In spite of its spectacular nature, the mortality appeared to affect only a small proportion of the pilchards, even within a given school many individuals survived. Some estimates are as low

as 10 – 15% (Whittington et al. [1997]). Other estimates are substantially higher, but substantial numbers of pilchards survived.

The pilchard is an abundant fish in temperate coastal waters throughout the Southern Hemisphere, and the North Pacific (Parish et al. [1989]). It forms a critical link in the food chain, feeding on plankton (both zoo- and phyto-) and being food for larger fish, birds and mammals. In Australia, its range is largely restricted to a narrow band along the continental shelf.

In the following paper we describe the simple modelling methods which are applied to examine the spread of the epidemic. We also examine the influence of biology on model parameterisation and hence behaviour. These simple models are useful in themselves and also act as a guide for the analysis of more complex dynamic models, which may lack explicit analytical solutions.

2. A SIMPLE EPIDEMIC MODEL

A standard SIR epidemic model divides the host population into susceptible (S), infected (I) and removed (R) sub-populations (Anderson and May [1979]). Transmission of the virus to new hosts occurs at a rate β, I^{-1} d^{-1}. Infected individuals recover (or die) at a rate α d^{-1}. A simple version of this model is:

$$dS/dt = -\beta IS \quad (1)$$

$$d\,I/dt = \beta IS - \alpha I \quad (2)$$

$$dR/dt = \alpha I \quad (3)$$

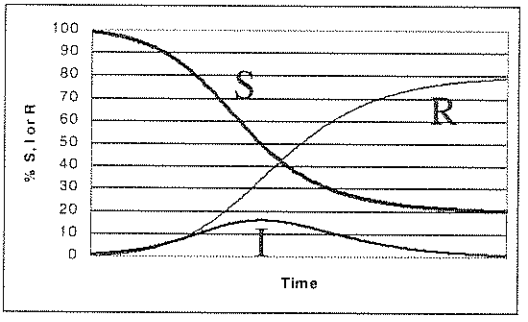

Figure 2. Development of an SIR epidemic at single location.

Populations are normalised to the average initial total population and are initially entirely susceptible, i.e. $N_0 = S_0 = 1$. Gradually the S become infected I, which in turn are removed to R (Fig. 2). R includes both deaths and recovery, in either case these fish are no longer involved in the epidemic. Because the pilchard mortality lasts for only a short period at a given location, factors such as background mortality or births are insignificant during the passage of the disease.

Such models have a threshold population of susceptible that is required for an epidemic to be initiated:

$$S_t = \alpha/\beta \quad (4)$$

Since there is a 2 – 4 day period between the onset of lesions and mortality the value of α is approximately 0.25 d^{-1}. To account for survival of 85% by avoidance of the infection would require β of <0.3 d^{-1}. This level of production of infection (particularly the net production) is incompatible with the observed local mortality, which generally occurred over a few days. Therefore, significant numbers of the survivors appear to have been infected but then recovered.

The model can be extended to include an incubation phase of infection during which viruses accumulate in the infected pilchard but are not yet released. This incubation phase E, which turns over at rate σ d^{-1}, leads to the extended model:

$$dS/dt = -\beta IS \quad (5)$$

$$dE/dt = \beta IS - \sigma E \quad (6)$$

$$d\,I/dt = \sigma E - \alpha I \quad (7)$$

$$dR/dt = \alpha I \quad (8)$$

This adoption of an SEIR model does not change the threshold population in this case. There is negligible mortality of E, given the brief duration of the epidemic, and hence it is still true that $\beta IS = \alpha I$. Addition of this phase does, however, tend to increase the time required for the infection to build up.

3. SPATIAL EPIDEMIC SPREAD

Perhaps the most outstanding feature of the 1995 and 1998/9 epidemics was the extremely rapid speed with which they spread over 1000's of km. We add a Fickian diffusion term to the equations to replicate this spread. Because the pilchards are restricted to a continental shelf that is much longer than it is wide, we use a 1 D diffusion model to describe flux.

Biological waves of the spread of populations and epidemics (pathogen populations) are well

known. The simplest such wave, for a single invading population N with initial growth rate r d^{-1} and diffusion coefficient D (km^2 d^{-1}), is derived from the Fisher equation. This equation (in 1-D) has the formula

$$dN/dt = rN(1 - N) + D\partial^2N/\partial x^2 \quad (9)$$

It generates a population that spreads as an invasive wave with a velocity of

$$V = 2\sqrt{(rD)}. \quad (10)$$

Note that this wave's speed is independent of time and depends rather simply on diffusion and the local population growth rate at low N.

Epidemics too can travel as spatial waves. With diffusion the SIR model becomes:

$$dS/dt = -\beta IS + D\partial^2S/\partial x^2 \quad (11)$$

$$dI/dt = \beta IS - \alpha I + D\partial^2I/\partial x^2 \quad (12)$$

$$dR/dt = \alpha I + D\partial^2R/\partial x^2 \quad (13)$$

This model generates a travelling wave of infection (Fig. 3). As in the Fisher equation, the wave speed is driven by diffusion and the local transmission of infection. The wave has a constant velocity and the value of this velocity can also be derived analytically.

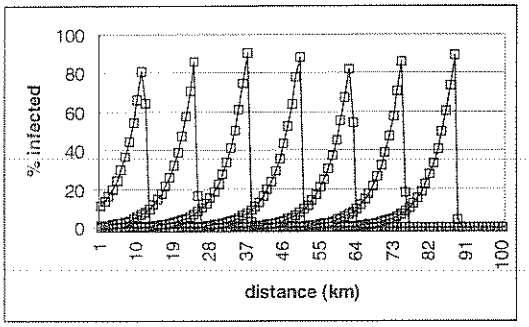

Figure 3. The numerically calculated passage of an epidemic at 10 day intervals, found using an SIR model.

This model has the travelling wave solution (see Murray [1993] for derivation):

$$V = 2\sqrt{(\beta S_0 D)} \times \sqrt{(1 - \alpha/\beta S_0)} \quad (14)$$

Provided the initial susceptible population, S_0, is greater than α/β, i.e. the threshold population for epidemics to occur. If the initial S population is substantially greater than the threshold then the speed of the front tends to the Fisher travelling wave solution $2\sqrt{(rD)}$, production of new infection βS_0 being equivalent to r. Therefore the wave speed is equally sensitive to changes in local and long-distance transmission.

Addition of the incubation phase of infection complicates transmission. Yachi et al. [1989] derived the following velocity for waves of rabies, in which the incubation is long relative to the infectious, rabid, phase.

$$V = \sqrt{(2D\{\sqrt{[(\sigma - \alpha)^2 + 4\sigma\beta K)]} - (\sigma + \alpha + 2a)\})} \quad (15)$$

In this case K is the carrying capacity, equivalent to S_0, and a is background mortality, which is negligible for pilchards given the rapid passage of the front. We can also note that both σ and α are small, given this rapid turnover, and hence $(\sigma - \alpha)^2$ is very small; particularly if σ and α are comparable in size. The equation approximates to:

$$V = \sqrt{(2D\{\sqrt{[4\sigma\beta S_0)]} - \sigma - \alpha\})} \quad (16)$$

The wave speed V (km d^{-1}) is thus dependent upon $\sqrt{D}$ and $\sqrt[4]{4\sigma\beta S_0}$, when V is not small. This equation also has a threshold for epidemic transmission that is determined by σ and α.

The speed of the wave is thus driven by relatively simple processes and, in simple cases, exact dependence on parameters can be found. More complex models may not have such simple solutions, but similar processes underlie the wave's velocity. These simple models can be used to guide experimental analysis.

4. DISPERSION AND THE ROLES OF FISH AND BIRDS

The parameter D, long-distance diffusion, plays a critical role in the epidemic's spread. The extreme rapidity of the spread of infection (30 km d^{-1} in 1995) means that physical mixing processes cannot account for the spread of infection (Griffin et al. [1997]). Therefore the movement of animals must drive the infections spread.

There are 2 potential means of viral spread, the pilchards themselves or carrier organisms, probably birds (or both). The different carriers are not simply interchangeable; they can give different responses to the spread of the epidemic in the case of changes in the nature of the virus.

If local viral transmission (β) is increased the diffusion-based models predict increased epidemic wave speed without limit. The observed 30 km d^{-1} spread of the epidemic is close to the pilchard maximum swimming speed

(more on this shortly). This imposes a limit on epidemic transmission speed. Birds, on the other hand, can travel much faster than 30 km d^{-1}, and therefore the epidemic speed would indeed be expected to increase if local transmission increased. The nature of the long-distance transport vector is therefore important in predicting the response of the epidemic to change in local transmission.

Holmes [1993] has looked at an alternative model, the telegraph model. This model has the property that the maximum wave speed is indeed restricted to the maximum speed of the organism. She derived the following relationship between velocities predicted under the two models (based on the Fisher equation).

$$V_t/V_d = 1/(rD/\gamma^2 + 1) \qquad (17)$$

In this case V_t = telegraph velocity, V_d = diffusion based velocity, r is local increase (equivalent to bS_0), D is the diffusion coefficient and γ is the organisms velocity.

As $2\sqrt{(rD)}$ tends to γ, i.e. the Fisher waves speed calculated by diffusion tends to the maximum swimming speed, this ratio tends to 0.8 (Fig. 4). Thus, only when the epidemic's speed is very close to γ is there significant distortion introduced by the use of diffusion-based transmission equations.

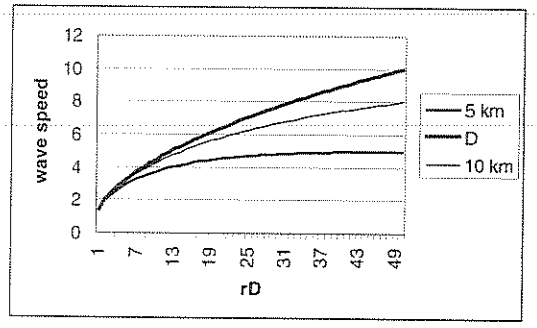

Figure 4. Daily progress of a Fisher wave calculated by diffusion D or by telegraph models with g of 5 km and 10 km d^{-1}.

The clarity with which the speed of the wave is shown to be dependent upon D in a simple model is a very good illustration of the value of such simple models. Without simplification it would be easy to miss this constraint on the use of diffusion equations. Because such equations are the standard means of modelling biological transport processes they are often used without reflection on their limitations.

The extent of diffusion, and hence the value of D, depends upon not only the velocity of the diffusing organisms but also on their pattern of motion. The formula giving this dependence is

$$D = L^2/2T \qquad (18)$$

We consider the fish to swim in legs of a given length before changing direction at random. L is the length of a leg and T is the time over which it is swum. Leg length depends upon time taken and swimming speed: $L = \gamma T$, so $D = 0.5\gamma^2 T$. As wave speed depends upon $\sqrt{D}$ it depends linearly upon the velocity of the organism and with $\sqrt{T}$, the time between changes in direction.

Maximum pilchard swimming speed is about 3 km h^{-1}, although this probably cannot be maintained for long periods (Blaxter and Hunter [1982], Beamish [1984]). A minimum value for the maximum speed is 1.25 km h^{-1}, given the epidemic's observed velocity of 30 km d^{-1}, provided that fish are the principle means of spread. If this fish motion is accounted for by 1 hour legs of swimming in a given direction then D = 18 to 108 km^2 d^{-1}, for 1.25 to 3 km h^{-1} swimming speed. If the legs are swum for between 15 minutes and 3 hours then a total range of D = 4.7 - 324 km^2 d^{-1}. If bird vectors account for dispersal then much larger diffusion coefficients are possible. However, large D with small β is not consistent with the brief local duration of the epidemic.

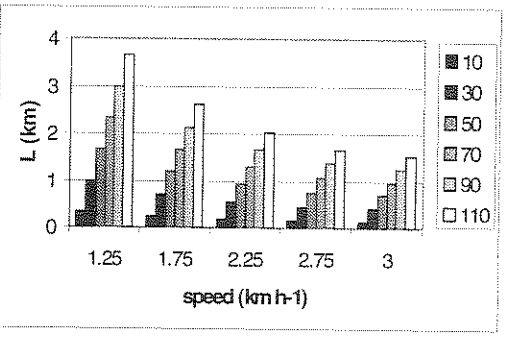

Figure 5. Lengths of legs required to generate D of 10 to 110 km^2 d^{-1}.

The length of the legs that are swum by the fish can be derived for a given value of D and a specific swimming speed. Because pilchards swim in schools, it is these schools which diffuse, not individual fish. If pilchards seek out patches

of zooplankton separated by a few km (2.5 km in the model of Nonacs et al. [1998]), then leg lengths of this order would be a reasonable pattern for the fish to adopt. Such a pattern is not consistent with lower diffusion rates, given the maximum swimming speed is at least 1.25 km h^{-1} (Fig. 5). Appropriate swimming leg lengths fit most closely with the lower range of possible swimming speeds of 1.25 – 2 km h^{-1}, or with very high diffusion coefficients.

5. TRANSMISSION AND LOCAL INFECTION, β AND σ

The other critical factor controlling the epidemic's rate of spread is the local development of infection. This is controlled largely by the value of the local transmission coefficient β, and the rate at which infections develop within the host σ. As we will discuss, viral parameters, particularly β, are the most likely to evolve with time.

Mathematically, the SEIR epidemic front speed is more sensitive to D than to β. D is particularly sensitive to changes in velocity, γ. However, for D to change requires major changes in the behaviour of fish or birds. In different parts of Australia, different pilchard stocks spawn every month (Fletcher et al. [1997]) so a nationwide change in pilchard behaviour is unlikely. Seabirds do tend to breed in spring and the extra fishing effort required could enhance D in spring 1995 relative to autumn/winter 1998/9.

Change in the nature of the virus, particularly the value of β, is biologically most likely to explain the observed differences in the speeds of the epidemic of 1995 and 1998/9. Except at low V, it is difficult to separate the effects of σ and β on wave speed and so we will consider the combined value $\beta\sigma$. The value of α appears to play relatively minor role and there is no evidence of a large decline in S_0. Change in β requires a change in the local transmission of the virus. This could be due to reduced viral production or infectivity or to increased viral resistance by the pilchards. Change in σ could similarly be due to reduced viral production or increased host resistance. Viruses often show rapid evolution of properties such as virulence (Ebert [1998]), whereas evolution of fish is likely to be slower.

The value of $\beta\sigma$ can be derived for a given D value in a given model, given that the other parameters are known. Under the SEIR model the local transmission is equivalent to:

$$\beta\sigma = (V^2/2D + \sigma + \alpha)^2/4S_0 \qquad (18)$$

Given observed V of 30 km d^{-1} and α of 0.25 d^{-1}, we can estimate the value of $\beta\sigma$ for a given value of D at the normalised population density $S_0 = 1$, provided that σ is small relative to $V^2/2D$.

The range of D values, derived in the previous section for pilchard swimming, was 4.7 to 324 $km^2\ d^{-1}$ from which is derived $\beta\sigma$ of 3.6 – 9000 d^{-2} (normalised to N_0). A restricted range of D = 18 to 108 $km^2\ d^{-1}$ gives $\beta\sigma$ 22 – 600 d^{-2}. Lower values of $\beta\sigma$ apply if higher D values result from bird-based transmission.

The rate of progression of the 1998/9 epidemic was about half that of the 1995 epidemic. This drop in V indicates $\beta\sigma$ (which varies with $\sqrt[4]{V}$) fell by a factor of 16 during the period. Because there is no evidence that the length of the infection period changed to such a large degree, it is likely that β accounted for most of this change. Changes in these two parameters are likely to compliment each other.

The 1998/9 epidemic remained locally short-lived and so even the reduced 1998/9 value of $\beta\sigma$ was still high. The lower limits of $\beta\sigma$ are the subject of continuing numerical experimentation.

6. DISCUSSION

The simple models presented show a constant spatial rate of spread of an epidemic, provided the initial host population exceeds a calculable threshold. This constant speed is dependent upon local and long-distance transmission processes in simple ways.

Conversely, for a known rate of spread and a given model we can use the model parameters to provide constraints upon each other. In particular, the values of the most critical parameters D and $\beta\sigma$ (or β in the SIR model) are closely constrained by each other.

Because viruses can evolve rapidly, changes in β, enhanced by changes in σ, are likely to explain

the different speeds of the 1995 and 1998/9 epidemics. However, changes in bird-based D might also contribute.

The models show there are important differences between fish-base and bird-based processes for the long-distance spread of the epidemic. If the pilchards are the main carriers then the epidemic has a limit to its speed that is close to that observed in 1995. In this case the wave speed could not respond to increased viral virulence. With birds, a far higher speed is possible and so increased virulence could result in increased epidemic speed. Spring breeding in birds may cause seasonal changes in a bird-based D. Different pilchard populations breed at different times of year and so no Australia-wide seasonal pattern in pilchard-based D is likely.

With only 2 epidemics we cannot definitively resolve the transport agent using these simple models. However, values of D which generate appropriate epidemic speed, which are implied by the fairly high values of β that are required to generate observed rapid local turnover, are consistent with fish-base transmission. Indeed, constraints on the estimation of D that are provided by the epidemic model may provide a new insight into pilchard movement patterns.

These analytical solutions of simple models do not capture the dynamic behaviour of the infection. They are not intended to. Dynamic features include the original development of the epidemic in the South Australian initial focus of infection. Application of dynamic modelling is required to look at these dynamic processes.

More sophisticated models that incorporate factors such as multiple transmission vectors, fixed infection phase lengths (instead of continuous turnover) and the effects of non-uniform populations are in the process of development. These will allow us to look at spatial and temporal variation within the epidemics. These models may not all have analytical solutions, but can use the analytical solutions derived from these simple models as a guide for numerical experimentation.

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Anderson, R. M., R. M. May. Population biology of infectious diseases: part 1. *Nature* 280, 361-367, 1979

Beamish, F. W. H. Swimming performance of three southwest Pacific fishes. *Mar. Biol.* 79, 311-313, 1984

Blaxter, J. H. S, J. R. Hunter. The biology of clupeoid fish. *Adv. Mar. Biol.* 20, 1-223, 1982

Ebert, D. Experimental evolution of parasites. *Science* 282, 1432-1435, 1998

Fletcher, W. J., B. Jones, A. F. Pearce, W. Hosja. *Environmental and biological aspects of the mass mortality of pilchards (Autumn 1995) in Western Australia.* Fisheries Research Report 106. Fisheries WA. 1997

Griffin, D. A., P. A. Thompson, N. J. Bax, R. W. Bradford, G. M. Hallengreff. The 1995 mass mortality of pilchards: no role found for physical or biological oceanographic factors in Australia. *Mar. Freshwater Res.* 48, 27-42, 1997

Holmes, E. E. Are diffusion models too simple? A comparison with telegraph models of invasion. *Am. Nat.* 142, 779-795, 1993

Murray, J. D. *Mathematical Biology, 2nd Edition.* Springer (Berlin) 1993

Nonacs, P., P. E. Smith, M. Mangel. Modelling foraging in the northern anchovy (*Engraulis mordax):* individual behaviour can predict school dynamics and population biology. *Can. J. Fish. Aquat. Sci.* 55, 1179-1188, 1998

Parrish, R. H., R. Serra, W. S. Grant. The morphotypic sardines *Sardina* and *Sardinops*: their taxonomy distribution stock structure and zoogeography. *Can. J. Fish. Aquat. Sci.* 46, 2019-2036, 1989

Whittington, R. J., J. B. Jones, P. W. Hine, A. D. Hyatt. Epizootic mortality in pilchard *Sardinops sagax neopilchardus* in Australia and New Zealand in 1995. I. Pathology and epizootiology. *Dis. Aquat. Org.* 28, 1-16, 1997

Yachi, S., K. Kawasaki, N. Shigesada, E. Teramoto. Spatial patterns of propagating waves of fox rabies. *Forma* 4, 3-12, 1989