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# Emerging infectious pathogens of wildlife

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The first part of this paper surveys emerging pathogens of wildlife recorded on the ProMED Web site for a 2-year period between 1998 and 2000. The majority of pathogens recorded as causing disease outbreaks in wildlife were viral in origin. Anthropogenic activities caused the outbreaks in a significant majority of cases. The second part of the paper develops some matrix models for quantifying the basic reproductive number, $R_0$, for a variety of potential types of emergent pathogen that cause outbreaks in wildlife. These analyses emphasize the sensitivity of $R_0$ to heterogeneities created by either the spatial structure of the host population, or the ability of the pathogens to utilize multiple host species. At each stage we illustrate how the approach provides insight into the initial dynamics of emergent pathogens such as canine parvovirus, Lyme disease, and West Nile virus in the United States.

**Keywords:** emerging disease; $R_0$; survey; mathematical model; epidemiology; West Nile virus

## 1. INTRODUCTION

Over the last decade a number of epidemics have caused large-scale declines in several wildlife species: an epidemic of phocine distemper reduced the seal population of the North Sea by nearly 30% (Heide-Jorgensen *et al*. 1992); the populations of Gyps vultures have declined in India by nearly 90% (Prakesh 1999); the Serengeti lion population has declined by 20% (Roelke-Parker *et al*. 1996); and a wide variety of frog species has been recorded as declining in Australia, Central America and the western United States (Blaustein & Wake 1990). Infectious diseases have been implicated in all these declines; in some cases the aetiological agent is unknown, in other cases pathogens have crossed species barriers, or geographical boundaries, to produce epidemics that devastate wildlife populations. Similar phenomena have been recorded in plant populations and in marine invertebrates. Here we will restrict our discussion to pathogens of vertebrates.

Emerging (or re-emerging) infectious diseases can be broadly defined as infectious diseases whose geographical range, host range or prevalence have been increasing in recent years. Although increased disease incidence can result from increased surveillance and awareness, mounting evidence suggests that wildlife epidemics are indeed a problem of increasing importance and urgency (Daszak *et al*. 2000; Harvell *et al*. 1999). Emerging wildlife pathogens have been identified at the present time all around the globe and no major ecosystem on Earth remains unaffected.

Emerging epidemics in wildlife fall into three categories. The first group consists of parasitic organisms that have recently invaded a wildlife population. Because of high host susceptibility the introduction of novel pathogens is often followed by explosive spread through the host population in what is termed a 'virgin ground epidemic'. Invading pathogens of this type most frequently originate in other wildlife species or in domestic or feral host populations. The pandemic of rinderpest that devastated Africa's wildlife in the 1890s is the classic example of this type of emergent disease outbreak (Plowright 1982).

A second type of emerging pathogen is those native to a specific host and geographical region that are currently spreading within the same host population as a result of new external factors. Such factors frequently alter environmental conditions in a way that facilitates parasite transmission. The spread of Lyme disease in the eastern USA is a classic example of this type of emerging pathogen (Ostfeld 1997). Alternatively, some environmental factors, like pollution, can stress hosts and reduce their ability to respond to existing parasite infections.

A final category of pathogens emerges as a result of a combination of the previously mentioned circumstances. Here we would include pathogens that have recently invaded an immunologically naive host population that is in addition stressed or immunocompromised because of existing environmental conditions. In a relatively recent example, phocine distemper virus (PDV) invaded the North Sea pinniped populations after the harp seal, its native host, shifted its range southward following human exploitation of Arctic fish stocks (Goodhard 1988). Ambiguous evidence suggests that the North Sea seals might also have been rendered particularly susceptible to the epidemic because of pollution with polychlorinated biphenyls (PCBs) (Hall *et al*. 1992; Heide-Jorgensen *et al*. 1992). Similarly, combined factors such as increased ultraviolet radiation and global climate change are associated with increased disease incidence in amphibian populations in the western USA (Kiesincher & Blaustein 1995).

This paper is organized into three sections: in the first we use an online database to examine broadscale taxonomic and habitat variation in recently recorded infectious disease outbreaks in wildlife. In the second section we outline some general models that may be used

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to examine the dynamics of emergent diseases in the early stages of their establishment in a new host population. In the third and final section we extend this general framework by applying the models to a number of specific examples of recently 'emerged' pathogens of wildlife.

## 2. SURVEY OF RECENTLY EMERGED PATHOGENS OF WILDLIFE

To obtain a better understanding of the origin, taxonomic affiliation and environmental correlates of emerging wildlife pathogens we conducted a survey of wildlife disease epidemic outbreaks reported on the Internet. A disease outbreak was loosely defined as a distinct cluster of vertebrate infections that resulted in sufficient host mortality and morbidity to have been reported.

Specifically, we surveyed the Web archives of ProMED-mail, a non-governmental, not-for-profit organization that acts as a clearing-house for reports on human, animal and plant diseases (ProMED-mail 2000). To ensure reporting consistency we restricted the survey to North America, defined as the terrestrial region north of the USA–Mexican border together with the associated coastal areas. In addition, the scope of the analysis was restricted to the 2-year period between June 1998 and June 2000. Although the use of Internet-based sources provides access to a wealth of new information, it may also introduce some biases into the analysis. Disease outbreaks reported tend to be from those vertebrate host species that are large-bodied and easily observable and/or of economic interest. Furthermore, because the identities of many parasites occurring in ectotherm vertebrates are not well known, the resulting epidemics cannot always be well characterized. Finally, a reporting bias exists towards those disease outbreaks that produce either high host mortality or clearly visible disease symptoms and which occur in regions easily accessible to humans. Despite these biases this survey represents a first attempt to determine the nature and the magnitude of the problem of emerging wildlife pathogens.

The survey focused on host identity, location, date of outbreak, life-history characteristics and environmental correlates of infectious pathogens of vertebrate wildlife and freshwater or saltwater fish. Although the pathogens reported primarily infected wildlife populations, in some circumstances they also affected domestic animals or humans.

## 3. RESULTS

### (a) *Taxonomic affiliation*

A wide taxonomic range of pathogenic organisms causes emerging wildlife diseases. For the period surveyed, we identified 31 different pathogens associated with outbreaks of new or emerging diseases (table 1). They constitute a diverse group of bacteria, viruses and protozoans as well as a few species of helminths, fungi and prions (see figure 1); this reflects the wide spectrum of parasites occurring in wild vertebrates. Nevertheless, this group of organisms causing wildlife epidemics is not a random sub-sample of all known vertebrate parasites. Instead, microparasites, such as viruses, bacteria and protozoans, are almost exclusively responsible for the observed wildlife epidemics and very few records exist of macroparasites (e.g. helminths, arthropods and tapeworms) associated with wildlife diseases.

### (b) *Life-history characteristics of emerging pathogens*

Pathogens responsible for wildlife epidemics are frequently characterized by particular life-history traits that facilitate emergence. We found that the majority of these pathogens are microparasites that lack intermediate stages and have a direct life cycle (figure 1). Because they only require a single host species to complete their development, they can generally persist in a wide range of environmental conditions. In contrast, macroparasites with complex life cycles depend on multiple hosts and a constellation of appropriate habitats and conditions to complete their development. Absence of a single factor can therefore result in interruption of transmission.

In addition, many emerging pathogens have catholic preferences regarding host suitability and can reproduce within a variety of related host species. Emerging pathogens appear to have high transmission rates and are spread directly, either through contact between infected and uninfected hosts or indirectly through vectors. Finally, some pathogens have the capacity to remain infective for long periods of time. As a result, the life-history traits of emerging pathogens show interesting parallels to those of weedy plants that have been selected to spread rapidly and persist under a broad range of environmental circumstances.

For example, *Batrachochytrium dendrobatidis*, a chytrid fungus that has been implicated in the declines of many amphibian populations, possesses a typical suite of life-history traits that are characteristic of emerging pathogens. The pathogen has a very broad host range and the capacity to reproduce rapidly in a susceptible population. In addition, it survives saprophytically in the soil and in the keratinized mouthparts of asymptomatic but infectious tadpoles. This suite of traits enhances the pathogen's persistence and prevents the long-term recovery of infected populations. Chytridiomycosis has now been identified as the cause of mass deaths and severe declines in amphibian populations around the globe (see Dazsak *et al*. 1999). The pathogen has also been hypothesized to be linked to the global extinction of several species of frogs and toads in Australia (*Rheobatrachus* spp.) and in Central America (*Bufo periglenes*) (Dazsak *et al*. 1999).

### (c) *Origin of pathogens*

Pathogens responsible for recent wildlife epidemics were categorized based on their area of origin. We created three categories of pathogen origin: native, exotic and likely exotic. 'Native' indicates that the parasite has been in long-term coexistence with the afflicted host population. 'Exotic' indicates that the pathogen originated either from a different geographical region or from a different population in the same area. A parasite was also assigned to this category if an exotic strain of an otherwise local pathogen was responsible for the reported epidemic. The third category, 'likely exotic', was reserved for parasites for which we could find no conclusive origin information but for which circumstantial evidence, such as association

Table 1. List of emerging and re-emerging pathogens with hosts, taxonomic affiliation, origin, and anthropogenic factors (other than pathogen introduction).

| pathogen or disease | host species | taxonomic affiliation | origin | anthropogenic factors? |
|---|---|---|---|---|
| *Heterosporis* infection | lake perch | protozoal | likely exotic | not clear |
| whirling disease | various salmon and trout species | protozoal | exotic | probably, hatcheries |
| infectious salmon anaemia | Atlantic salmon | viral | likely exotic | probably, hatcheries |
| salmon sarcoma virus | Atlantic salmon | viral | likely exotic | probably, hatcheries |
| furunculosis | trout | bacterial | likely exotic | probably, hatcheries |
| undetermined bass virus | largemouth bass | viral | likely exotic | not clear |
| chytridiomycosis | various amphibian taxa | fungal | exotic | probably, habitat modification |
| upper respiratory tract disease | desert tortoises | bacterial | likely exotic | probably, habitat modification |
| eastern equine encephalitis | various bird species | viral | native | not probable |
| western equine encephalitis | various bird species | viral | native | not probable |
| St Louis encephalitis | various bird species | viral | native | not probable |
| avian botulism | waterfowl | bacterial | native | probably, habitat modification |
| duck plague | waterfowl | viral | exotic | probably, habitat modification |
| avian cholera | waterfowl | bacterial | exotic | probably, habitat modification |
| West Nile encephalitis | various bird species | viral | exotic | not probable |
| salmonellosis | various passerine species | bacterial | native? | probably, feeding stations |
| avian malaria | Hawaiian honeycreepers | protozooal | exotic | not clear |
| avian pox | Hawaiian honeycreepers | viral | exotic | not clear |
| mycoplasma conjunctivitis | various passerine species | bacterial | likely exotic | probably, feeding stations |
| neurotropic velogenic Newcastle disease | double-crested cormorants | viral | exotic | not clear |
| canine distemper | foxes, racoons | viral | likely exotic | probably, feral animals |
| rabies | wide range of mammalian taxa | viral | native (at least some strains) | probably, animal transfers, feral animals |
| Sylvatic plague | various rodent, canid species | bacterial | exotic | not probable |
| leptospirosis | various rodent species | bacterial | not clear | not clear |
| toxoplasmosis | sea otters | protozooal | not clear | not clear |
| coccidioidomycosis | sea otters | fungal | native | probably, habitat modification |
| acanthocephaliasis | sea otters | helminthic | native? | not clear |
| chronic wasting disease | mule deer, white-tailed deer, elk | prion? | native? | probably, animal transfers |
| bovine tuberculosis | wild cervids, canids, bovids | bacterial | exotic | probably, animal transfers, feeding stations |
| brucellosis | elk, mule deer, buffalo | bacterial | exotic | probably, animal transfers, feeding stations |
| epizootic haemorrhagic disease | deer, bighorn sheep | viral | native | not probable |

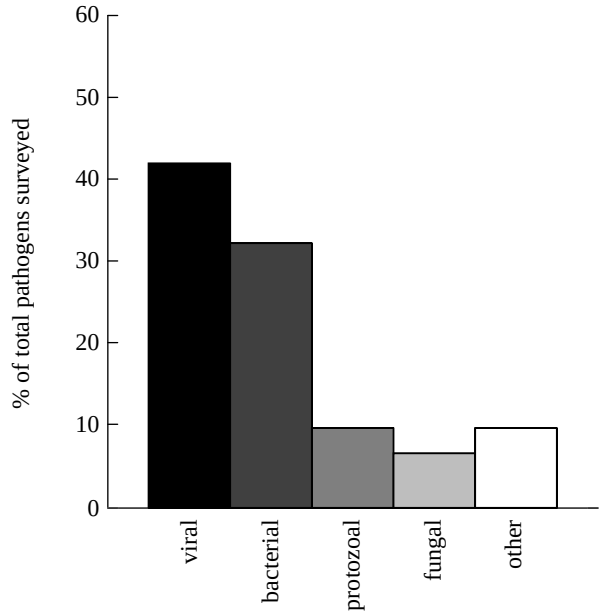


Figure 1. Taxonomic affiliation of emerging wildlife pathogens expressed as percentages of total sample surveyed.

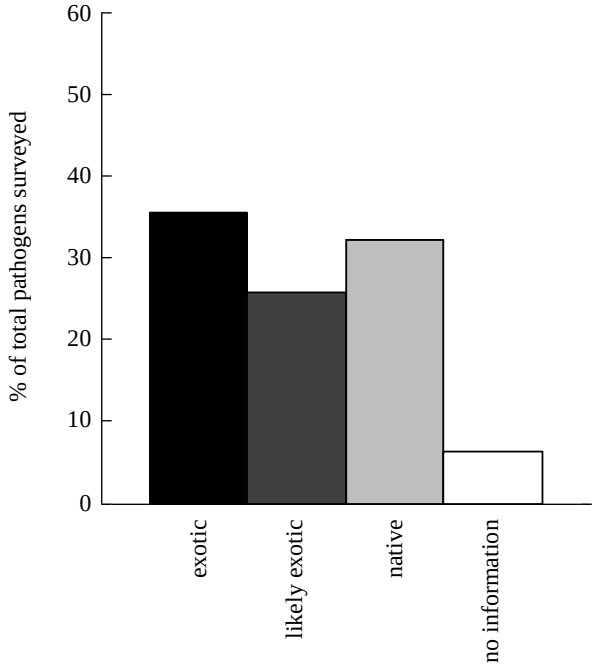


Figure 2. Probable geographical origin of emerging wildlife pathogens expressed as percentages of total sample surveyed.

of the disease with feral animals or human activities, indicated a non-native origin. A final category was created for those cases in which no definite assignment could be made because of the paucity of information regarding the origin and nature of an outbreak.

The majority of the causative pathogens were of exotic or likely exotic origin (see figure 2). In contrast, only a minority of outbreaks could be traced to local pathogens. This suggests that it is more likely that an exotic pathogen will produce a severe wildlife epidemic than a pathogen locally co-evolved with its host. Nevertheless, we did identify several examples of exclusively viral pathogens that apparently produce regular epidemics in wildlife populations. These included various encephalitides, rabies and epizootic haemorrhagic disease in ungulates.

### (d) *Anthropogenic factors*

Humans can influence the outcome of a host–parasite interaction in multiple ways. We found that in a slight majority of pathogens (17 out of 31), human involvement facilitated the outbreak of an epidemic. Only in 6 out of 31 cases could we find no evidence of human influence. In the remaining cases, no clear conclusions could be drawn.

The most important anthropogenic activity associated with wildlife disease outbreaks was environmental degradation (figure 3). This degradation has a multitude of forms such as atmospheric pollution, habitat fragmentation or eutrophication of freshwater and estuarine habitats. For example, mounting evidence suggests that eutrophication contributes to the spread of avian cholera (caused by the bacterium *Pasteurella multocida*) in waterfowl populations in freshwater ecosystems (Friend 1987). In the estuaries along the east coast of the USA, run-off from agricultural and urban areas has facilitated the spread of *Pfiesteria piscicida*, an aggressive fish-killing pathogen (Harvell *et al*. 1999). Last but not least, natural habitat fragmentation is perhaps the most important anthropogenic factor associated with wildlife pathogen outbreaks. Habitat fragmentation increases the contact between wildlife surviving in undisturbed habitat and other host taxa living in the disturbed matrix and hence facilitates the cross-species transmission of pathogens. In either case environmental degradation is often the hallmark of disease either because environmental pollution stresses vertebrate hosts, and subsequently reduces their ability to resist infection, or because pathogen transmission is facilitated under altered environmental conditions.

A second factor associated with the emergence of wildlife diseases was transport of wild animals by humans. Transported animals are often crowded and stressed and are therefore particularly susceptible to infection even if only a few individuals are infected. Chronic wasting disease (CWD), a transmissible spongiform encephalopathy of wild ungulates, appears to be spreading through the transport of infected but unsymptomatic elk from one game ranch to the other (ProMED-mail 2000; Miller *et al*. 2000). In another classic example illustrating this point, racoon rabies was introduced into the middle Atlantic seaboard of the USA through the release, for hunting purposes, of infected racoons (Childs *et al*. 2000; Dobson 2000). Duck plague and avian cholera, which constitute perhaps the most important emerging diseases in North American wildfowl, were also introduced into the continent through the import of infected domestic waterfowl (Brand 1987; Friend 1987; Leibovitz & Hwang 1968).

Feeding stations or food supplementation programmes, alone or in conjunction with the previous factors, were also identified as being associated with the emergence of wildlife diseases. Because wildlife tends to concentrate in such areas, feeding stations can exacerbate transmission of disease either within or across species boundaries and therefore facilitate epidemics in susceptible host populations. This problem tends to be worst in charismatic or economically important species such as songbirds or wild ungulates. Currently, several diseases including *Salmonella*

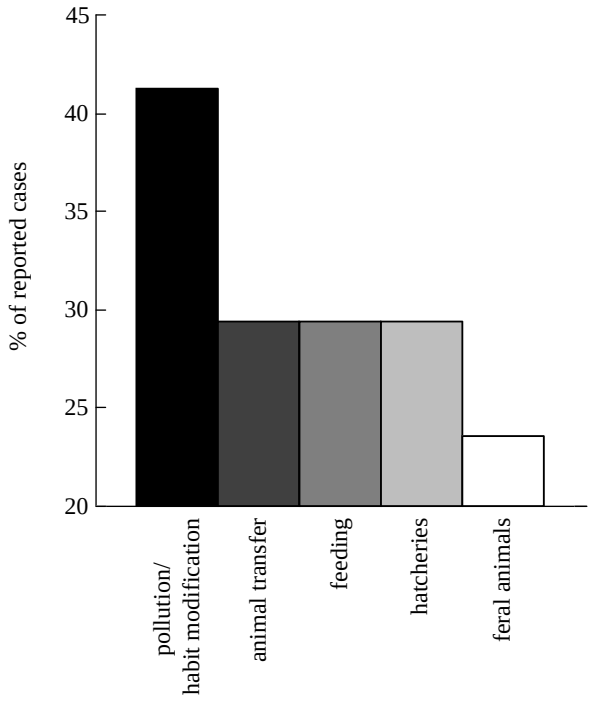


Figure 3. Environmental factors associated with the emergence of wildlife pathogens expressed as percentages of the total sample surveyed. Note that multiple factors may be associated with the emergence of a particular pathogen.

*typhi* infections, avian mycoplasmosis and trichomoniasis are spreading through North American passerine bird populations that are attracted to bird-feeders. Similarly, deer and elk congregating at deer stations in the Upper Midwest have increasingly been infected with bovine tuberculosis, a disease that appears to be spilling over from cattle into wildlife populations. A similar situation occurs in the National Elk Refuge and other parts of Wyoming, USA, where winter feeding of elk concentrates their numbers and increases rates of transmission of brucellosis (Boyce 1990; Thorne *et al*. 1979).

The most important human activity associated with disease in fish is hatcheries (Kennedy 1994*a*). Here multiple factors have contributed to the outbreaks of various pathogens (Kennedy 1994*b*). Because fish of different populations are sometimes kept together, the possibility exists for pathogens to invade previously unexposed fish stock. Hatchery fish are also kept under crowded conditions and hence may be stressed, facilitating rapid parasite dissemination. When multiple waterbodies are stocked with infected fish a pathogen can rapidly colonize a wide geographical range. Fishery biologists in both government hatcheries and private fish breeding operations are aware of these circumstances and employ preventive measures—nonetheless the problem remains acute. We identified several pathogens that are currently emerging in wild fish populations because of human fish-breeding activities. The most important is the protozoan *Myxobolus cerebralis*, which produces whirling disease in salmonids and which has caused extensive damage to the recreational fisheries in the mountainous west of the USA. In addition, infectious salmon anaemia, salmon sarcoma virus and furunculosis are all diseases that are currently in the process of spreading through North American fish populations (ProMED-mail 2000).

The final factor that we found to be associated with wildlife disease emergence was the presence of feral animals in a region. Because feral animals come in contact with both domestic animals and wildlife they can act as conduits for pathogen exchange between otherwise isolated host populations. As a result they pose a threat not only to wildlife but also to domestic animals and ultimately to humans. It is very difficult to determine the true frequency of disease transmission between domestic or feral animals and wildlife, as very little is known about the actual probabilities of pathogen 'crossover'. These probabilities depend on a number of other external factors such as environmental conditions and encounter frequency, but it is likely that only a minority of wildlife–domestic animal interactions result in pathogen transmission. Nevertheless, we identified several cases where the presence of feral dogs and cats were linked to distemper, plague, rabies, leptospirosis and toxoplasmosis outbreaks in wild predator populations. Ducks and geese—ranging from completely sedentary domesticated birds through escaped, feral individuals to completely wild animals—occur in a continuum of dependency on humans that also facilitates the spread of pathogens. Not surprisingly, they provide some of the best-documented examples of feral animals transmitting pathogens to wild populations.

## 4. THE POPULATION DYNAMICS OF EMERGING PATHOGENS

When a pathogen first appears in a population of naive hosts its dynamics will follow one of two trajectories: it will either die out or it will initiate an epidemic. A considerable body of epidemiological theory has shown that the population dynamics of emergent pathogens when they first enter a new host population will be strongly dependent upon their basic reproductive number, $R_0$. This is formally defined as the number of secondary infections produced by the first infective individual to appear in the population (Anderson & May 1982; Dietz 1993). When $R_0$ is less than unity the pathogen ceases to maintain itself and declines to local extinction. In contrast, when $R_0$ is greater than one, an epidemic outbreak occurs. If we can derive an expression for $R_0$, then it is possible to estimate the proportion of hosts that escapes infection during the course of the epidemic. The magnitude of $R_0$ also determines the proportion of hosts that has to be treated to eradicate the pathogen.

A number of different methods have been developed for deriving expressions for $R_0$ (Anderson & May 1991; Dietz 1993); they all explicitly assume that $R_0$ can be defined as the number of new infections produced by an infected individual during the period of time for which they are infectious. A particularly useful approach to deriving expressions for $R_0$ has been developed by Diekmann *et al*. (1990) and by Hasibeder & Dye (1988). This approach is particularly useful in cases where a variety of sources of heterogeneity exists in the host population. The technique assumes that we can divide the host population, or populations, into discrete classes and that we can compare the rates of transmission from one class

to any other class of host. The host classes are then arranged as a 'next generation' matrix, each element of which consists of the product of the rate of transmission from one host class to another and the duration of time for which an individual in this class is infectious (e.g. the reciprocal of the mortality and recovery rates of individuals in that class). Expressions for $R_0$ are obtained by deriving an analytical or numerical expression for the spectral radius (dominant eigenvalue) of this matrix.

A simple example best illustrates the approach and creates a framework to which we will return when we consider more complex cases. Consider the standard model for malaria as first proposed by Ross (Ross 1916) and MacDonald (MacDonald 1952) and later modified by Aron & May (1982). The model assumes that the dynamics of malaria may be characterized by two equations. The model captures the basic features of the interaction between the infected proportions of the human host population and the mosquito vector population. It is defined as follows:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \left(\frac{abM}{N}\right)(1-x)y - rx, \tag{4.1}$$

where $x$ is the proportion of the human population infected, $y$ is the proportion of the female mosquito population infected, $N$ is the size of the human population, and $M$ is the size of female mosquito population.

$$\frac{\mathrm{d}y}{\mathrm{d}t} = ax(1-y) - \mu y. \tag{4.2}$$

Here $m = M/N$ is the number of female mosquitoes per human host; $a$ is the rate of biting on man by a single mosquito (bites per unit time); $b$ is the proportion of bites on man that produces an infection; $r$ is the per capita recovery rate for humans ($1/r$ is the average duration of infection in the human host); $\mu$ is the per capita mortality rate for mosquitoes ($1/\mu$ is the average life expectancy of a mosquito). If we set equations (4.1) and (4.2) to 0, and rearrange to provide equations that describe two zero-growth isoclines along which each population will remain at equilibrium:

$$y = ax(1-y)\mu \tag{4.3}$$

$$y = rx/abm(1-x). \tag{4.4}$$

The initial slopes of the lines, when $x$ and $y$ are very small, are given by $y = r/abm$ and $y = a/u$. If the two lines are to intersect then the initial slope of $\mathrm{d}y/\mathrm{d}t = 0$ has to be larger than $\mathrm{d}x/\mathrm{d}t = 0$; this means that $a/u > r/abm$. This can be rearranged to give us an expression for $R_0$:

$$R_0 = \frac{a^2bm}{r\mu}. \tag{4.5}$$

If we were to apply the next-generation matrix approach to this calculation, we would first write down the matrix that describes the duration of time for which humans and mosquitoes are infectious and the rate of transmission of malaria from humans to mosquitoes and vice versa. No transmission occurs between mosquitoes, or between humans, so the diagonal elements of the matrix are zero. This gives the following matrix:

$$M = \begin{pmatrix} 0 & \frac{abm}{r} \\ \frac{a}{\mu} & 0 \end{pmatrix}. \tag{4.6}$$

The dominant eigenvalue of this matrix will provide an expression for $R_0$:

$$R_0 = \sqrt{\frac{a^2bm}{r\mu}} \text{ or } \sqrt{R_\mathrm{H}R_\mathrm{V}}. \tag{4.7}$$

Notice that this is only identical to the expression derived above when $R_0$ equals unity, but this is the property of $R_0$ that we are most interested in. By inspection we can see that this expression is the geometric mean number of new infections produced in the next stage of the life cycle for the duration of time that each host in the life cycle is infected (e.g. $R_\mathrm{H}$ for the human section of the life cycle and $R_\mathrm{V}$ for the vector stage of the life cycle). Most importantly, the expression illustrates the sensitivity of $R_0$ to each of the parameters that determine the initial dynamics of the epidemic.

Let us now apply this approach to a more complex and characteristic problem in the emergence of new pathogens. A central problem here is the population dynamics of pathogens that infect multiple species of hosts. A number of authors have examined a number of aspects of this problem (Anderson & May 1986; Begon *et al*. 1992; Norman *et al*. 1994). Models for these systems have to consider two components of transmission: within-species transmission and between-species transmission. The structure of the transmission matrices for these models will be similar to the structure of transmission matrices for pathogens in host populations that are subdivided into different age, sex or sexual activity classes (Anderson & May 1984; Anderson *et al*. 1989; Gupta *et al*. 1989).

When extending these models to examine the transmission dynamics of pathogens that infect multiple host species we initially ignore heterogeneities due to social organization, or age and sex considerations within each species, and focus on the consequences of simple within- and between-host species transmission. Here we need to acknowledge that between-host species transmission will have three different components: (i) the spatial distribution of each host species; (ii) the within- and between-species contact rates; (iii and iv) two physiological components that determine both susceptibility when exposed to infection and the rate at which infective fomites are produced.

Initially, we assume that all of the different components of transmission from individuals of host species '$j$' to host species '$i$' can be captured by a single transmission parameter, $\beta_{ij}$. This allows us to construct a matrix of transmission values termed a WAIFW matrix (Who Acquires Infection From Whom) (Anderson & May 1985; Schenzle 1984). In the case of a simple three-species system, this matrix takes the form

$$W = \begin{pmatrix} \beta_{i,i} & \beta_{j,i} & \beta_{k,i} \\ \beta_{i,j} & \beta_{j,j} & \beta_{k,j} \\ \beta_{i,k} & \beta_{j,k} & \beta_{k,k} \end{pmatrix}. \tag{4.8}$$

The elements of the matrix characterize the rates of infection between all possible combinations of species (e.g. $\beta_{ij}$ corresponds to transmission from species '$j$' to species '$i$').

Plainly it would be possible to modify each of the $\beta_{ij}$ terms to consider explicitly the contact rates between species, which will be complex functions of the overlap in their spatial distributions and the behavioural and physiological components of susceptibility and transmission.

The approach by Diekmann *et al*. (1990) allows us to modify this WAIFW matrix and produce an estimate of the basic reproductive rate of the pathogen, $R_0$. In order to do this we need to multiply each term in the matrix by the average duration of infection for an individual of the species transmitting the pathogen. This would give a new matrix, $R$:

$$R = \begin{pmatrix} \frac{\beta_{i,i}\, p_{i,i}}{(\alpha_i + \mu_i + b_i)} & \frac{\beta_{j,i}\, p_{j,i}}{(\alpha_i + \mu_i + b_i)} & \frac{\beta_{k,i}\, p_{k,i}}{(\alpha_i + \mu_i + b_i)} \\ \frac{\beta_{i,j}\, p_{i,j}}{(\alpha_j + \mu_j + b_j)} & \frac{\beta_{j,j}\, p_{j,j}}{(\alpha_j + \mu_j + b_j)} & \frac{\beta_{k,i}\, p_{k,i}}{(\alpha_j + \mu_j + b_j)} \\ \frac{\beta_{i,k}\, p_{i,k}}{(\alpha_k + \mu_k + b_k)} & \frac{\beta_{j,k}\, p_{j,k}}{(\alpha_k + \mu_k + b_k)} & \frac{\beta_{k,k}\, p_{k,k}}{(\alpha_k + \mu_k + b_k)} \end{pmatrix}. \tag{4.9}$$

Here $b_i$ is the mortality rate of host species $i$, $\alpha_i$ is the parasite induced host mortality rate of host species $i$, and $\mu_i$ is the recovery rate of an infected individual of host species $i$. The '$p_{ij}$' terms determine whether transmission is density dependent (pseudo mass action), or frequency dependent (true mass action) (*sensu* de Jong *et al*. 1995). Where transmission is pure mass action the '$p_{ij}$' terms are unity (times the relative proportion of interspecific contacts). Where transmission is density dependent, then the '$p_{ij}$' terms correspond to the product of the density of species $j$ and the proportion of total contacts that species $j$ has with species $i$.

These matrices allow us to explore some important properties of the dynamics of pathogens that infect multiple species of hosts. For example, a central question in the field of biodiversity and conservation biology is whether increased diversity of host species tends to either buffer or amplify disease outbreaks (Ostfeld & Keesing 2000*a*,*b*; Schmidt & Ostfeld 2000). In the simplest case the potential for disease outbreaks will be determined by the magnitude of $R_0$. In cases where increases in species diversity lead to increases in the number of contacts between infected individuals and potentially susceptible hosts, then increased host diversity will always lead to increased values of $R_0$ and a greater potential for disease outbreaks. In contrast, where increases in interspecific transmission lead to reductions in within-species transmission, then it is possible for increased host species diversity to lead to reductions in $R_0$. Where transmission between species is density dependent, then increasing the number of hosts will always increase $R_0$. This will not necessarily be the case for frequency-dependent transmission, particularly where some hosts act as 'dead-ends' for the pathogen. Under these circumstances increases in the diversity of potential host species may reduce $R_0$ and the potential for an epidemic outbreak.

### (a) *Force of infection experienced by each host species*

The $R_0$ matrices have several other important properties: the sum of each column provides an index of the relative force of infection experienced by each species, whereas, in contrast, the sum of each row reflects the relative force of infection exerted by a species. The species that exert the largest force of infection are likely to be the ones against which control might most effectively be introduced. Those that experience the strongest force of infection may be the ones that receive the most significant impact from the presence of the pathogen, particularly in cases where these species experience high rates of mortality, $\alpha$. Finally we note that it is possible to use the matrices to examine the efficacy of possible control by either vaccination or culling of one or more host species. Here all the terms in the row corresponding to species $i$ should be multiplied by $(1-v_{\mathrm{I}})$, where $v_{\mathrm{I}}$ is the proportion of individuals of that species that are either vaccinated or removed. A principal goal here will be to determine the minimum value (or combination of values) of $v_{\mathrm{I}}$ that reduces $R_0$ below unity. In cases where ethical or logistical reasons prevent the application of control methods to one particular species, then this approach may be valuable in examining whether it is possible to eradicate the pathogen by applying control methods to other host species.

An important additional result can be obtained when we examine the consequences of adding additional host species. In the case examined here, where transmission between species is frequency dependent, then addition of more species tends to reduce $R_0$, particularly when the additional species are less suitable hosts for the pathogen than those already in the system. This effect occurs predominantly because transmission to these species leads to 'dead-end' infections that make no further contribution to the growth of the epidemic. They are also 'wasted' infections that are subtracted from the total that are made upon the host species that can amplify the epidemic. This situation corresponds closely to the effect described by Ostfeld and co-workers for Lyme disease in the eastern USA (Schmidt & Ostfeld 2000). Simulations of the dynamics of Lyme disease in the species-rich southern part of its range exhibit reduced rates of spread when compared with the dynamics in the less diverse northern parts of its range (Ostfeld & Keesing 2000*b*).

It is important to notice that the opposite result is obtained when either additional hosts have large population sizes, or transmission between species is density dependent (pseudo mass action) and shows no tendency to saturate. Under these conditions, the addition of more species leads to increases in $R_0$ and increased host diversity (and abundance) leads to increases in the magnitude of epidemic outbreaks.

### (b) *Emergence due to anthropogenic change*

Daszak *et al*. (2000) and Harvell *et al*. (1999) provide important reviews of the emergence of novel pathogens of wildlife in both terrestrial and marine environments. The epidemic of PDV in seals in the North Sea provided a detailed example of the spread of a pathogen through a host population with little or no previous experience of the pathogen (Heide-Jorgensen *et al*. 1992). The virus that causes the phocine distemper is endemic to the harp seal populations in the Gulf of Labrador. There were almost no records of harp seal sighting in the eastern Atlantic until the late 1980s when a number of different individuals were observed (Goodhard 1988). Two possible

explanations were proposed to explain these appearances: one, that warmer waters off the coast of Labrador may force the seals to change their foraging range or, alternatively, the collapse of the Labrador banks cod fishery may force harp seals to disperse further in their search for food (Goodhard 1988). The latter seems the more parsimonious of these two explanations because if the ocean warming were the reason for a change in distribution it seems more likely that harp seals would disperse further north to the richer waters that border the polar ice cap. In contrast, if their feeding supply collapses due to anthropogenic overexploitation, seals will then disperse in all possible directions, the easiest of which is to use the North Atlantic currents, which would drift them into the eastern North Atlantic and the North Sea.

The epidemic of PDV spread rapidly through the common and grey seal populations of the North Sea and seemed to have died out within 2 years of its first appearance. Although there are some reports that it spread as far as the Mediterranean monk seal populations in the Eastern Mediterranean and the Canary Islands (Osterhaus *et al*. 1997), these seem to be misidentifications due to poor sampling techniques (Harwood *et al*. 1998). The dynamics of PDV in the North Sea has been examined in detail using a metapopulation model developed by Swinton *et al*. (1998). Their approach specifically focused on how the spatial substructure of the population affects the persistence of the pathogen and eloquently demonstrates that the population of seals in the North Sea is insufficiently large to sustain an endemic infection with PDV. Here we paraphrase their work using the techniques described above and simply examine how the spatial structure of the population affects pathogen establishment. Let us assume that the host population is subdivided into $n$ sub-populations, each of size $H_i$. Transmission within each of these sub-populations is assumed to occur by pure mass action (*sensu* de Jong *et al*. 1995; see Swinton *et al*. 1998). Let us also assume that the sub-populations are arranged in a roughly linear fashion around a circle such that transmission between groups is dominated by transmission between adjacent sub-populations. Under these circumstances the transmission matrix will take the general form:

$$\begin{bmatrix} \frac{\beta_w T}{M} & \frac{\beta_a T}{M} & 0 & \frac{\beta_a T}{M} \\ \frac{\beta_a T}{M} & \frac{\beta_w T}{M} & \frac{\beta_a T}{M} & 0 \\ 0 & \frac{\beta_a T}{M} & \frac{\beta_w T}{M} & \frac{\beta_a T}{M} \\ \frac{\beta_a T}{M} & 0 & \frac{\beta_a T}{M} & \frac{\beta_w T}{M} \end{bmatrix}. \tag{4.10}$$

Here $\beta_w$ is within patch contact rate and $\beta_a$ is contact between adjacent patches, $M$ represents the combined mortality and recovery rates of infected individuals (thus $1/M$ is the duration of time for which an individual is infectious) and $T$ represents the transmission and population size components within the patch (as described by $p_{ij}$ in equation (4.9) above). It can readily be shown that the basic reproductive rate of a pathogen in a population with this structure will be given by the dominant eigenvalue of this matrix:

$$R_0 = \frac{(\beta_w + 2\beta_a)T}{M}. \tag{4.11}$$

Provided that transmission only occurs within a patch or between adjacent patches, this expression for $R_0$ holds however large we make the number of patches. We can obtain one more general result if we replace the zero terms in the above matrix with expressions for 'background' transmission from patches non-adjacent to any patch—if we call this term $\beta_b$, then a second, more general, expression may be derived for $R_0$ a population of $n$ patches, where $n > 3$,

$$R_0 = \frac{(\beta_w + 2\beta_a + (n-3)\beta_b)T}{M} \tag{4.12}$$

Here we assume that each patch is adjacent to two other patches, but this may be readily modified for $c$ adjacent patches (when $(n-3)$ in equation (4.12) is replaced by $(n-(c+1))$. In both these cases, the pathogen will only establish and cause an initial epidemic if there is sufficient between-group (or colony) transmission to balance the constant extinction of the pathogen in each local sub-population (group or colony). The result is directly comparable with one derived by May and Anderson for the emergence of HIV in human populations in Africa (May & Anderson 1990). Here it is assumed that HIV establishes by always colonizing another village while exhausting its supply of susceptibles in previously infected villages. The duration of infectiousness, the spatial distribution of the host sub-populations and the movement patterns of infected individuals between these sub-populations determine the time between when the pathogen first arrives in the new host population and when a full epidemic is detected. In the case of HIV, a major epidemic was only detected when the pathogen established itself in large urban centres, far from its original source.

The framework we have derived here is one that applies to emergent (and endemic) pathogens of hosts whose populations are subdivided by either social organization or habitat fragmentation. More detailed stochastic and deterministic models that examine the persistence and transient dynamics of pathogens in subdivided host populations have been developed by Ball (1999), Swinton (1998) and Foley *et al*. (1999). The population dynamics described by these systems will apply to a variety of systems including the spread of canine distemper virus (CDV) into the lion population of Serengeti National Park in Tanzania (Roelke-Parker *et al*. 1996), and the spread of rabies and CDV into the hunting dogs in this region.

### (c) *Emergence of a pathogen in an introduced species*

Introduced or alien, non-native species are an increasingly important source of disruption to ecological communities and ecosystems (Cox 1999; Elton 1958; Mooney & Hobbs 2000). A potential reason that these species are so successful is that they may have escaped from the natural enemies that reduce their abundance in their native habitats (Dobson 1988). Alternatively, introduced species may cause enhanced damage when they act as reservoirs for novel pathogens that impact their potential competitors. Possibly the best wildlife example of this occurred when avian malaria was introduced into

Hawaii (Van Riper *et al*. 1986; Warner 1968). Here the introduction of birds from the Far East and North America led to the introduction of avian malaria that has completely eliminated native Hawaiian forest birds from most habitats below 1200 m.

The introduction of a previously unknown strain of *Mycoplasmosa gallisepticum* into the house finch (*Carpodacus mexicanus*) population of the eastern USA provides an important example of the introduction of a pathogen into an introduced host species (Dhondt *et al*. 1998). House finches were introduced into the eastern USA from the western USA in 1940s (Elliott & Arbib 1953). After a few years at relatively low abundance, the population expanded rapidly and is at present beginning to meet the eastern edge of its natural range. Mycoplasmosis was introduced into the eastern population from commercial poultry populations in the Baltimore region; birds in the suburbs were first reported with lesions in January 1994. The pathogen causes conjunctivitis in infected birds, which reduces their ability to detect and escape predators and may increase their dependence upon bird-feeders, which may in turn act as vectors for the transmission of the pathogen. The spread of the conjunctivitis through the house finch population has been monitored using detailed records obtained from the 'feeder watch' programme. This programme provides broadscale monitoring of birds visiting bird feeders throughout the USA. Analyses of these data illustrate that the pathogen has spread rapidly throughout the introduced eastern population of the house finch; by March 1995 the epidemic covered an area of approximately one million square kilometres. The presence of *M. gallisepticum* has reduced local densities of the hosts to 40% of their density prior to its introduction. The spatial spread of mycoplasmosis could be examined by assuming the host population to exhibit a metapopulation structure and then using a simple modification of the framework described above for seals in the North Sea.

### (d) *Emergence of a potential human pathogen from transportation of a wildlife pathogen*

West Nile virus is an important zoonotic disease that first appeared in the USA in 1999 (Anderson *et al*. 1999). Disease outbreaks were sequentially detected in birds, predominantly American crows (*Corvus brachyrhynchos*), and then humans in the northern part of New York City. Although these were initially thought to be separate disease outbreaks, it was quickly realized that they were both caused by the same pathogen (Lanciotti *et al*. 1999). West Nile virus is a mosquito-transmitted virus. A large epidemic of West Nile virus occurred in Israel in 1999. At least 1000 people travel by plane from Israel to the New York area on any given day and it thus seems likely that the introduction was made by an infected human who returned to New York while incubating a viral infection. The pathogen was then spread by at least two species of mosquitoes (*Culex pipiens* and *Aedes vexans*) to birds and humans. The presence of the pathogen led to broadscale mosquito control programmes throughout the five boroughs of New York City. Within 1 year of the initial outbreak, infections have been recorded from birds from a large area of the eastern USA.

Interesting insights into the dynamics of West Nile virus may be obtained by deriving simplified expressions for $R_0$ using the next-generation matrices described above. Two approaches may be adopted for modelling the dynamics of this pathogen. In the first case we will assume the dynamics of the vector stage are sufficiently fast that they can be represented by simple mass action dynamics. We will, however, acknowledge that under this form of transmission, any transmission to one host reduces the potential for transmission to another host. This acknowledges that arthropod vectors are only capable of taking a limited number of blood meals and feeding on one host precludes them from feeding on another at that time. We will then extend this framework and include some aspects of the vector's dynamics. This framework will also apply to a number of other emergent pathogens, in particular applying to Lyme disease and other tick-transmitted pathogens.

Initially let us consider a hypothetical three-species case where the hosts may be considered to be humans and two different bird species. Let us assume that one of the bird species experiences high pathogen-induced mortality while the second is relatively resistant. Here the former may apply to North American crow species, which have no prior evolutionary experience of the pathogen. The latter may apply to house sparrows, whose European ancestors may have been exposed to West Nile virus. Using $T$ and $M$ as we did in the previous matrix to describe birth and mixing, and mortality and loss of infection by each host, respectively, and using $\beta_{ij}$ to designate transmission from host species $j$ to host species $i$, we may write down a matrix for the spread of a pathogen through a community of three host species, humans (h), crows (c) and sparrows (s):

$$\begin{bmatrix} \frac{\beta_{hh}T}{M_h} & \frac{\beta_{hc}T}{M_c} & \frac{\beta_{hs}T}{M_s} \\ \frac{\beta_{ch}T}{M_h} & \frac{\beta_{cc}T}{M_c} & \frac{\beta_{cs}T}{M_s} \\ \frac{\beta_{sh}T}{M_h} & \frac{\beta_{sc}T}{M_c} & \frac{\beta_{ss}T}{M_s} \end{bmatrix}. \tag{4.13}$$

Several important insights emerge from this simple exercise. First recall that the sum of each column provides an index of the relative contribution each species makes to the overall growth rate of the epidemic. In contrast, the sum of each row describes the relative 'force of infection' experienced by each species. A key insight to emerge here is that species that experience high levels of parasite-induced mortality (large $M_i$) tend only to make a large contribution to the net force of infection if they have large population sizes. In contrast, species that exhibit little or no parasite-induced host mortality will act as important reservoirs for the pathogen. This suggests that crows may operate as an important sentinel species, as large numbers of infected birds have been found dead. However, they may not be important as reservoirs. In contrast, very few dead, infected house sparrows have been recorded, though prevalence levels in the wild are quite high. An important caveat here is that smaller birds are less likely to be located when they die than larger birds. Nevertheless, the huge population size of house sparrows in the eastern USA suggests they may be a key reservoir of the pathogen.

Comparable results are obtained in the slightly more complicated case where we explicitly add in the vectors. The simplest ways to do this is to assume that vectors exhibit no preference for any of the potential host species, but simply select them in direct proportion to their relative abundance in the environment. This also requires us to make an assumption about how important each host species is as a resource contributing to the size of the vector population. Here we will assume that each host contributes an equal amount per unit time but that its net contribution scales with its life expectancy. The transmission matrix can be readily modified to include a term for the vectors:

$$\begin{bmatrix} 0 & 0 & 0 & \frac{\beta_{\mathrm{mh}} T_{\mathrm{h}}}{M_{\mathrm{h}}} \\ 0 & 0 & 0 & \frac{\beta_{\mathrm{mc}} T_{\mathrm{c}}}{M_{\mathrm{c}}} \\ 0 & 0 & 0 & \frac{\beta_{\mathrm{ms}} T_{\mathrm{s}}}{M_{\mathrm{s}}} \\ \frac{\beta_{\mathrm{hm}} H_{\mathrm{h}}}{\mu \sum_{\mathrm{h=allhosts}} H_{\mathrm{h}}} & \frac{\beta_{\mathrm{cm}} H_{\mathrm{c}}}{\mu \sum_{\mathrm{h=allhosts}} H_{\mathrm{h}}} & \frac{\beta_{\mathrm{shm}} H_{\mathrm{s}}}{\mu \sum_{\mathrm{h=allhosts}} H_{\mathrm{h}}} & 0 \end{bmatrix}. \tag{4.14}$$

Ironically this can simplify the equations because in the earliest stages of the epidemic we have ignored interspecific transmission by the vectors and have assumed that each individual vector specializes on only one host species. An analytical expression can again be derived for the basic reproductive number of the pathogen (this again will generalize to one for $n$ potential host species):

$$R_0 = \sqrt{\frac{1}{\mu \sum_{\mathrm{h=allhosts}} H_{\mathrm{h}}} \sum_{\mathrm{h=allhosts}} \frac{\beta_{\mathrm{mi}} \beta_{\mathrm{im}} H_{\mathrm{i}} T_{\mathrm{i}}}{M_{\mathrm{i}}}}. \tag{4.15}$$

This expression has similar properties to the simpler case described above for Ross's original malaria model. At first sight mosquito biting rate still appears to be the key variable in determining $R_0$. However, the addition of more host species increases the denominator in the first summation; when these species act as sinks for the infection, this will tend to buffer epidemic outbreaks (particularly if those added have very large population sizes). In contrast, the addition of host species in which individual infections last for different periods of time may aid in establishment of the pathogen. This will be particularly important in the case of vector-transmitted pathogens where, on the one hand, increased host diversity leads to increases in the resources available to the vector population (e.g. more blood meals). As most vectors take a finite number of blood meals per lifetime, this will lead to an increased proportion of bites wasted on hosts that may be less viable resources for the pathogen. Whether or not the pathogen is buffered or amplified by the increased host diversity will depend on whether increases in the size of the vector population are sufficient to compensate for the 'wasted bites' on less viable hosts (Ostfeld & Keesing 2000*b*; Schmidt & Ostfeld 2000).

It is also important to realize that equation (4.14) ignores interspecific transmission by the vector. This could be included by adding an additional row for the subset of the vector population that specializes on each particular host species, but occasionally takes a bite from another host. A simple two-host one-vector version of this has been examined by Hasibeder & Dye (1988); the expressions for $R_0$ quickly become rather murky. So it should be borne in mind that equation (4.15) provides only an approximation for $R_0$ in the very early stages of the outbreak, in cases where vectors have only a low probability of switching between hosts.

### (e) *Emergence of a new wildlife disease through mutation*

Canine parvovirus (CPV) appeared almost simultaneously in litters of puppies at a number of locations during the 1970s as a new disease of domestic dogs. The earliest CPV-positive sera samples were collected in Greece in 1974; other samples were collected in Belgium and the Netherlands in 1976 and 1977. By the early 1980s it had spread throughout the world, including coyote populations from throughout the USA and wild wolves in Alaska (Parrish 1990). Wolf populations throughout the world were impacted by CPV. The best-documented cases of this came from studies in Minnesota (Mech & Goyal 1993, 1995) and particularly on Isle Royale in Lake Michigan (Peterson & Page 1988).

CPV provides the best example of a new pathogen of domestic animals and wildlife that evolved through mutation. The disease is similar to a common infection of cats, feline panleukopaenia virus (FPV), which was shown to be a filterable virus in the 1920s. In 1947 a new variant of FPV was described as mink parvovirus (MPV) from minks in Canada. In each case it took some time to isolate and identify the virus as it only replicates in dividing cells and exhibits only slow and subtle pathology in infected cell cultures. All of these viruses are characterized by high titres of virus in the faeces that are relatively resistant to the environment and can thus persist as infective fomites for several months or more. Genetic mapping studies of FPV, MPV and CPV indicate only three- or four-sequence differences between CPV and MPV, which in turn came from FPV. These all correspond to specific differences between the pathogens (e.g. pH dependence, which may be sufficient to explain the specificity for canid versus feline cells) (Parrish 1990).

## 5. DISCUSSION AND CONCLUSIONS

We have attempted to do two things in this paper. In the first part we examined emerging pathogens of wildlife using an online database. The main results of this section suggest that emerging pathogens of wildlife tend to be directly transmitted viruses and bacteria that have crossed species barriers due to anthropogenic disturbance. The debate continues on whether or not we are seeing an increase in the rate of emergence of new pathogens (Daszak *et al*. 2000; Epstein *et al*. 1997; Harvell *et al*. 1999; Levins *et al*. 1994). As long as humans continue to alter the natural environment dramatically, it is likely that we will see further outbreaks on novel and 'emergent' pathogens in wildlife. As estimates of background rates of emergence are inherently flawed for lack of basic data we think it unlikely that this debate will ever be resolved.

In the second part of the paper we suggest for all 'emerging' infectious diseases the most important aid to understanding their dynamics is $R_0$. This can formally be defined as the initial rate of increase when the pathogen first establishes itself in a naive host population. The appearance of any new pathogen (or the accidental introduction of an old pathogen into a new (or old) host species) creates a situation that is identical to that which is envisioned in many of the mathematical models that are central to the theoretical study of infectious disease dynamics. We have used a framework for deriving expressions for $R_0$ to examine a subset of the conditions under which emergent pathogens have invaded new host populations. Throughout this second section of the paper we have attempted to minimize the mathematical detail in order to make the techniques accessible to veterinarians and field biologists with a more limited understanding of mathematics. While apologizing for our lack of mathematical eloquence, we emphasize a desire to see more interactions and collaborations between empiricists and theoreticians in the study of wildlife disease.

Many 'emerging' pathogens have the potential to reduce significantly the abundance of threatened and endangered species that already face an excess of environmental insults. The emergence (or introduction) in human populations of West Nile virus, Ebola virus, Lyme disease and particularly HIV all illustrate how susceptible humans still are to infectious diseases. The rapid declines of Australian and Central American frog populations, seals in the North Sea, and vultures in India, suggest wild animal populations are also experiencing increased rates of challenge by new or re-emerging infectious diseases. As we write these conclusions, Britain's livestock industry is suffering a major outbreak of foot-and-mouth disease. All of this suggests that the current vogue for studies of 'emergent' disease is one that is justified as an area of research in need of a significant increase in funding. New diagnostic tools, which may contribute to the increased rate of discovery, also provide new and important ways to study the dynamics of pathogens in wild populations. Such studies create not only an important opportunity to test and develop some of the central tenets of theoretical epidemiology, but also to suggest ways to focus control schemes that might help prevent the spread of these new and emergent pathogens.

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