CHAPTER 5

Microparasite transmission and persistence

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The transmission dynamics of microparasites are an interplay between the spread of infection through a naïve population and the way in which the resulting post-epidemic population is returned to susceptibility through demographic processes.

Here we address questions like: What are the characteristics of the deterministic invasion threshold of infection? How do these differ from the stochastic fadeouts? How does host population density and transmission routes affect infection levels? What mechanisms do directly transmitted pathogens use to persist in small populations?

5.1 Background

Microparasites are those pathogens whose epidemiology can be usefully modelled with a classification of hosts into susceptible, immune, or recovered individuals. They generally include the viruses, bacteria, and protozoa. The epidemiology of microparasites of wildlife naturally has much in common with the better-established studies of microparasite dynamics in human and domestic animals. While much of the basic theory was established in the context of humans, there are a number of features of wildlife epidemiology that give it a particular flavour, including variability in host demography, such as seasonal variation in birth rates, and the significance of social structuring, such as territoriality versus group living.

Theory has been largely conducted in terms of two important concepts: threshold theory and fade out theory. Threshold theory relies on the notion of the basic reproductive number, R_0 and how changes in host demography change R_0 for the pathogen; it defines the necessary conditions for an epidemic to occur (see Box 3.4). By contrast, fadeout theory is about what happens in the aftermath of an epidemic and whether the pathogen has been so infectious as to run out of Susceptibles and thus become extinct.

5.2 The fundamental theory of microparasite transmission

The observed epidemiological patterns of microparasites have been reviewed at some length by Dobson (1995), and the mathematical models constructed to deal with them by Heesterbeek and Roberts (1995a). In this section we present only the simplest outline of the theory and the reader should refer either to these papers or Scott and Smith (1994). In particular, this chapter concentrates on how host densities affect parasite ecology, rather than the equally important and intertwined question of how parasites affect host abundance (Chapter 3; Grenfell and Dobson 1995).

A simple model of microparasite epidemiology, capable of demonstrating three important infection patterns, can be constructed by assuming that a host population is divided into: Susceptibles, S, who have never experienced infection; Infecteds, I, who are currently infectious; and Recovereds, R, who experienced infection in the past and are now immune. In addition, we assume that infection itself causes no mortality but that all individual hosts have a fixed mortality risk from other causes and that the birth rate is sufficient to maintain the total population size. Such a model can be summarized in the flow diagram shown in Fig. 5.1 and the basic mathematics are presented in Box 5.1.

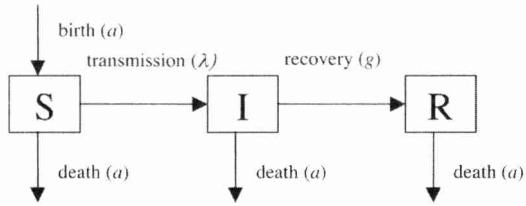

Figure 5.1 Flow diagram representing the basic SIR (Susceptible, Infected, and Recovered) model. Hosts are classified into one of three classes, young are born into the susceptible cohort, come into contact with an Infected then pass into this category and then either die from the infection or recover, usually with the development of life-long acquired immunity.

Three possible outcomes from this SIR model are illustrated in Fig. 5.2. The simplest infection pattern happens in a population when there are no births during the period of the epidemic (i.e. $a = 0$, Fig. 5.2(a)). This is the characteristic epidemic curve with an initial rapid epidemic growth, as the pathogen passes through the population, infecting and removing Susceptibles. The declines in the number of available Susceptibles leads to a decline in the growth rate, and then to a decline in the numbers infected, as the remaining Infecteds recover from infection without successfully infecting any Susceptibles.

When the host population has a turnover of births and deaths (i.e. $a > 0$, Fig. 5.2(c)), then a similar *initial* epidemic is observed in the wholly susceptible population. However, the births of new Susceptibles mean that not all of the later infections are dead-ends so the chain of transmission is maintained and the epidemic process can be repeated once Susceptibles are no longer too thinned out by the presence of Immunes (Fig. 5.2(c)). Eventually the infection settles down to an endemic equilibrium. An intermediate situation can also occur when birth rates are small but not quite negligible. We see the same oscillatory dynamics as in

Box 5.1 Mathematical formulation of the SIR microparasite model

A precise formulation of the SIR model for a population of size N can be created using differential equations for the sizes in each class S, I, and R. By assuming that the total birth rate aN is proportional to the total population size; that the death rates of Susceptibles, Infecteds, and Recovereds are aS, aI, and aR, respectively (so that the population size N is unchanging); that hosts recover from infection at rate gI; and that the rate of infection per susceptible given by the 'force of infection' $\lambda(I, N)$ we can produce the following linked differential equations:

$$\frac{dS}{dt} = aN - \lambda(I, N)S - aS \tag{5.1}$$

$$\frac{dI}{dt} = \lambda(I, N)S - gI - aI \tag{5.2}$$

$$\frac{dR}{dt} = gI - aR \tag{5.3}$$

A common assumption (discussed in Box 5.3), is that the force of infection λ has the form $\lambda(I, N) = bI/N$. It is then mathematically straightforward to show that this model can only support sustained infection when $R_0 > 1$, where R_0 is by definition the parameter combination $bI/(a + g)$. Biologically R_0 has a natural interpretation as the rate at which new cases are produced by a single infective ($b\,S/N$) multiplied by the average infectious period ($1/(a + g)$), when transmission is optimal for the parasite and almost the entire population is susceptible ($S = N$). It is the number of secondary cases produced by a single primary case in a wholly susceptible population. Other assumptions about the force of infection lead to different mathematical forms for R_0, but this biological interpretation remains. For further details see Heesterbeek and Roberts (1995a) and for a broad overview see Diekmann and Heeseterbeek (2000) or Anderson and May (1991).

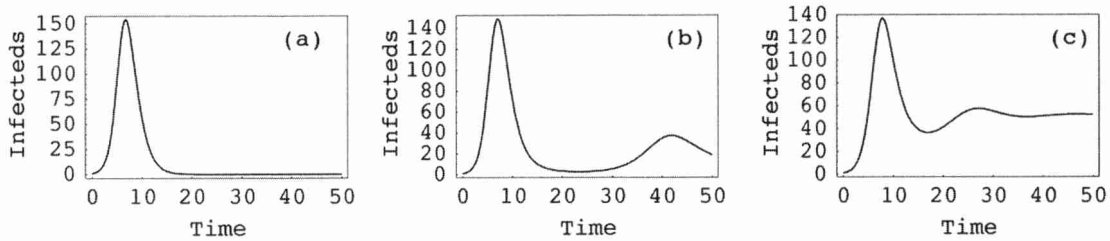

Figure 5.2 Three types of epidemic. Epidemic curves produced from the SIR model presented in Box 5.1, illustrating three scenarios of varying host birth rates. When there are no host births during the period of the epidemic curve (a), the number of Infecteds rises and falls as Susceptibles are removed from the population until the pathogen is finally eliminated and there are no Infecteds remaining. When host birth rate is high (c), then the birth of Susceptibles maintains the infection endemically and the pathogen persists. In the intermediate situation, with low host birth rates (b), the epidemic curve falls to a low level and it then becomes a matter of chance if the infection fades out or persists to generate a further oscillation.

Box 5.2 Phocine distemper virus (PDV) and harbour seals

During just a few months of 1988, about 20 000 harbour seals (*Phoca vitulina*) and a smaller number of grey seals (*Halichoerus grypus*) died in the North Sea following infection with phocine distemper virus (PDV) in one of the best-characterized epidemics in marine mammals (Heide-Jørgensen *et al.* 1992a, b; Heide-Jørgensen and Härkönen 1992; Barrett *et al.* 1995). PDV is a morbillivirus, closely related to canine distemper virus (CDV) and one of a family of viruses including measles (Barrett 1995). It takes several days for infectiousness to develop. Disease mortality is significant, although those animals that do not die recover within about a week and then appear immune for life (Harder *et al.* 1992b). In the PDV epidemic, transmission occurred at the seal haulouts, where the harbour seals congregate and come into close contact allowing direct transmission to occur. Within each of the single geographic regions, infection typically followed the epidemic pattern type shown in Fig. 5.2(a). Since seals only pup once a year, the infection had died out before new Susceptibles arrived, so there were no new Susceptibles born into the population.

Figure 5.3 (redrawn from Grenfell *et al.* 1994) shows the weekly seal mortality observed in a single bay, The Wash, off the East coast of England in the 4 months of the epidemic and compares this with the expected number from the SIR model. The model captures well the characteristic rise and fall of the morbillivirus in a small population but fails to capture the finer scale details observed. See also Box 3.3 and Box 6.4.

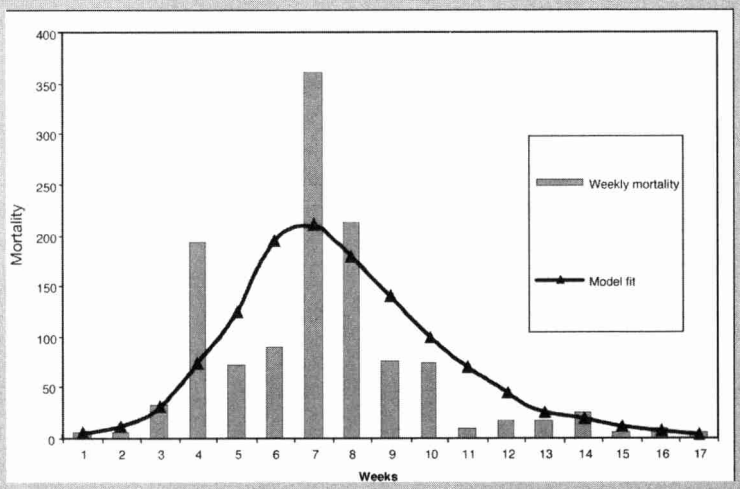

Figure 5.3 Course of PDV infection in seals in the Wash (UK) illustrated as the number of dead seals recovered by weeks after 1 August 1988, together with the fit of a simple SIR model (after Grenfell *et al.* 1992b).

Fig. 5.2(c), but the depth of the trough of infection is now much deeper (Fig. 5.2(b)). At this stage the model is in danger of breaking down because infection densities have dropped to a low level. Populations consist, in fact, of discrete individuals and the assumption that we can measure them by continuous densities, implicit in the use of the differential equation, is violated. In fact, what is likely to happen is that there will be one last infected individual who will recover without infecting any more newborns, and infection will *fadeout*. The subsequent pattern of infection will then be very different to that in the graph, and highly dependent on the pattern of subsequent re-introduction from outside the system (a so-called recurrent epidemic). For a detailed treatment of the intricacies involved in the three situations sketched here, see Diekmann and Heesterbeek (2000).

The simple SIR model outlined in Box 5.1 is enough to reproduce a number of observed epidemic behaviours, some of which have been observed in free-living populations. A nice example is the pattern of infection observed in the 1988 phocine distemper virus (PDV) seal epidemic illustrated in Box 5.2, with further details in Box 6.4.

5.3 Transmission of microparasites

A necessary condition for microparasites to persist for more than a few generations is that, under optimal conditions, the average infected host infects more than one Susceptible during the infectious period. In the context of the *SIR* model, in which infection is constrained only by the lack of Susceptibles, optimal conditions for parasite transmission requires a population composed almost entirely of Susceptibles. It is for this reason that the basic reproductive number, R_0, is defined in terms of what happens when a pathogen enters a new population (Box 5.1).

5.3.1 Threshold theory and host demography

The basic reproductive number, R_0, defines a threshold ($R_0 > 1$) for a pathogen to invade. If R_0 increases with host density or population size, it follows immediately that there must be some threshold host density or population size below which infection cannot persist. For typical *SIR*-type models, R_0 contains a factor describing the rate of contact between Susceptibles and Infecteds, and it is this factor that we expect to respond to host population density. Understanding the nature of this response is the key to understanding threshold theory. For many wildlife populations that extend continuously over habitat ranges (such as elm trees subject to Dutch elm disease), the natural unit of both measurement and population ecology is the number of individuals per unit area. For others (such as the harbour seal populations described in the PDV case study, Box 5.2), it is the total numbers observed at particular haulouts that form the relevant epidemiological and measurement unit. Once the relevant population variable has been identified it is then possible to consider how it influences the contact rate. There are a number of different paradigms in use for the influence of host demography on contact rate that are discussed in Box 5.3.

Which scaling actually occurs for a given system is best identified empirically. An analysis of the cowpox–rodent system carried out by Begon *et al.* (1998) is shown in Box 5.4. Given knowledge of the number of Susceptibles and Infecteds at each point in time, they use the numbers infected at the next time-point to derive the numbers infected in a time period. Using a regression analysis with this as response and numbers susceptible and infected as predictors, they demonstrated that explaining infection dynamics did require a non-linear interaction term and, more equivocally, that mass action was to be preferred over pseudo mass action in this context.

Another observation of infection-intensity scaling with population size comes from experiments with the gypsy moth *Lymantria dispar* and its nuclear polyhedrosis viruses (a baculovirus; Box 5.5). Here, the transmission parameter *declined* with increasing host and pathogen density (D'Amico *et al.* 1996). However, this pattern has proved difficult to interpret, although defoliation or behavioural changes have been suggested as possible explanations (D'Amico *et al.* 1996). Heterogeneities in susceptibility to infection may lead to a reduction in the transmission parameter with increasing pathogen density (§5.3.4; Dwyer *et al.* 1997), and density-dependent increases in patho-

Box 5.3 R_0 and the 'law' of mass-action

Suppose that the number of infectious individuals is I within a population of size N. The per capita rate at which Susceptibles become infected is the force of infection (λ). In Box 5.1 this was represented as a function of I and N. De Jong *et al.* (1995) named and contrasted two particular representations: first pseudo mass-action, with a force of infection $\lambda = \beta I$; and second, mass-action, with a force of infection of the form $\lambda = \beta I/N$. Pseudo mass-action can be interpreted as saying that a given Susceptible makes contacts at random with a fixed *fraction* of the individuals in the population, while mass-action can be interpreted as saying that given Susceptible makes contacts at random with a fixed *number* of individuals from the population, but only a fraction I/N of these can lead to a new case (Heesterbeek and Roberts 1995). The 'pseudo' prefix does not imply that the assumption is necessarily inappropriate; the same contrasts have also been labelled as those appropriate to vector-transmitted and directly-transmitted infection (Anderson and May 1991), or to sexually-transmitted and directly-transmitted infection (Thrall and Antonovics 1997). Yet another usage has been to label these contrasts as density-dependent and frequency-dependent transmission (Thrall *et al.* 1998). Moreover, these are just two possible scalings from many that may be relevant to different modelling settings.

One of the reasons that this distinction is important is that mass-action implies that the basic reproductive number R_0 (as defined in Box 5.1, where mass-action is assumed) is independent of N, while pseudo mass-action implies that R_0 is proportional to N. Since R_0 has a threshold for infection to be able to invade (i.e. $R_0 > 1$), it follows that mass-action implies that N has no effect on invasibility, while pseudo mass-action implies that there is a threshold N value below which infections cannot invade.

How should the modeller choose a plausible representation of the scaling of transmission? It is important to be careful about the definition of population 'size', distinguishing population numbers and population densities as variables. The choice of variable is likely to be dictated by the problem at hand. While a choice of scaling in either case is best empirically justified, the *interpretation* of mass-action in terms of a fixed contact acquisition rate is only really applicable when population size is used.

gen resistance may lead to reduction in the transmission parameter at high host densities (Wilson and Reeson 1998).

Transmission in the moth *Plodia interpunctella*, by contrast, occurs mainly through cannibalism of infectious cadavers, and so an increase in cannibalism at high host-densities should lead to an increase in the rate of contact between host and pathogen. Indeed, laboratory experiments using *P. interpunctella* and *Bacillus thuringiensis* showed that transmission increased with host density and decreased with pathogen density (Knell *et al.* 1996).

There is some evidence that stresses associated with high host-density can increase the host's susceptibility to infection. However, there is also evidence from Lepidoptera and Coleoptera that some insects may direct *more* resources into pathogen resistance when at high densities than at low (Kunimi and Yamada 1990; Goulson and Cory 1995; Wilson and Reeson 1998; Reeson *et al.* 1998; Barnes and Siva-Jothy 2000). These insects typically experience wide fluctuations in population density both within and between generations, and this is reflected in a phenotypically plastic life-history that responds to changes in host density. The high-density morphs of species like the African armyworm (*Spodoptera exempta*), exhibit a range of adaptations to the threats that accompany life at high densities; threats that include increased competition for food, increased predation risk, and, most importantly in the present context, increased risk of contracting disease (Wilson and Reeson 1998). These phenotypic changes may have a marked impact of pathogen transmission in the field and on the dynamics of the host-pathogen interaction (White and Wilson 1999).

Increasing host population size or density will make per capita contact rates increase under two broad circumstances (Heesterbeek and Metz 1993; Diekmann *et al.* 1996). First, when individuals contact other conspecifics within a given socio-spatial arena and crowding increases the number of individuals within that arena. For example, if badger population densities are correlated with social group size then overall transmission of tuberculosis may increase (White *et al.* 1997). Second, when the

Box 5.4 Cowpox in rodents: mass action in operation

Cowpox virus is a member of the genus *Orthopoxvirus*, and is endemic in Europe and some western states of the former USSR (Baxby and Bennett 1997). Although natural infection and disease occurs in cattle, man, and domestic cats, such cases are relatively uncommon, and the reservoir hosts are generally accepted to be wild rodents (reviewed by Bennett and Baxby 1996). Antibody and virus have been detected in wild ground squirrels (yellow suslicks) (*Citellus fulvus*) and gerbils (*Rhombomys opimus*, *Meriones libicus*, and *Meriones meridianus*) in Turkmenistan and Georgia (Marennikova *et al.* 1984; Tsanava *et al.* 1989), from root voles (*Microtus oeconomus*) on the Kolskiy Peninsula in northern Russia (Lvov *et al.* 1988), and evidence of infection has been obtained by PCR from various rodents in Norway (Tryland *et al.* 1998). In Great Britain, a high prevalence of cowpox virus antibody has been detected in wild bank voles, *Clethrionomys glareolus*, field voles, *Microtus agrestis*, and wood mice, *Apodemus sylvaticus* (Crouch *et al.* 1995) and cowpox virus-specific DNA in bank voles and wood mice detected by PCR (unpublished data).

Begon *et al.* (1998) studied cowpox dynamics in two field sites in north-west England and found annual cycles in the number of susceptible bank voles $S(t)$ (reflecting the annual arrival of newborn hosts) with corresponding but delayed cycles in the numbers seropositive for cowpox, $I(t)$ (Fig. 5.4).

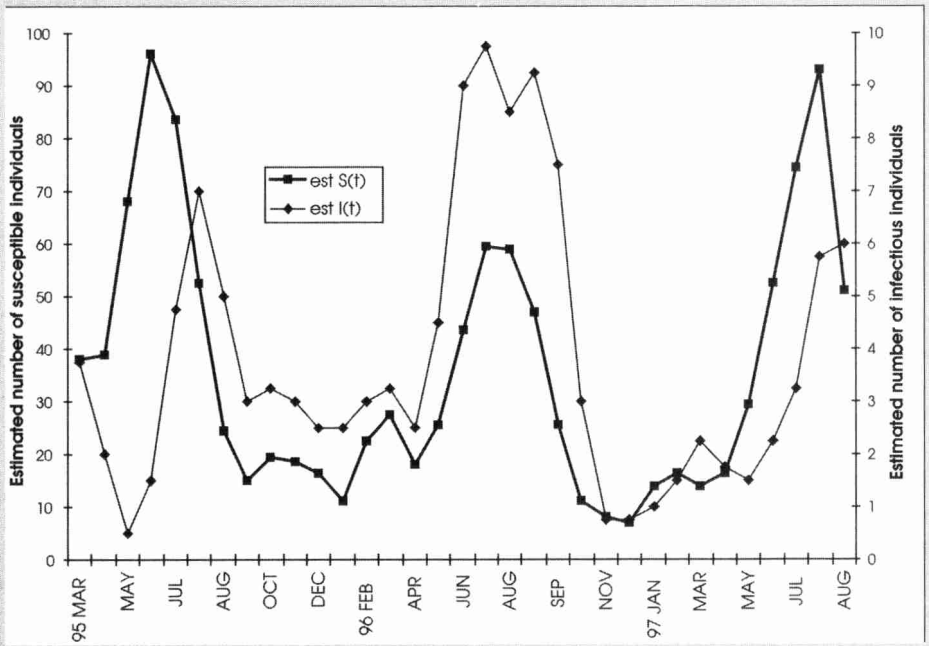

Figure 5.4 The estimated number of bank voles infected with, or susceptible to, cowpox virus in 4-weekly samples between March 1995 and September 1997 at Manor Wood, England (after Begon *et al.* 1998).

social structure of the population allows the contact with most of the other hosts over the lifetime of infection. For example, harbour seals with daily regrouping at the haulout might do this over the week of PDV infectiousness; pathogens with longer infectious periods would require less rapid mixing. In either case, population increases will lead to increased contact rate, and pseudo-mass action models may be applicable. By contrast, if population increases are associated with an increased number of groups over an expanded range (e.g. possums in New Zealand: Ryan *et al.* 1998), population increase at that scale will not significantly affect contact rates. As such, it is important to recognize that pathogen life-history determines the relevant features of host social structure. More-

Box 5.5 Insect baculoviruses

Baculoviruses, from the family Baculoviridae, are a large group of double-stranded DNA viruses that are restricted to arthropods, most having been isolated from lepidopteran insects. The two main groups are the nuclear polyhedrosis viruses (NPVs), which produce large structures called polyhedra containing many virus particles (virions), and the granulosis viruses (GVs), which produce smaller structures called granules, normally containing a single virion. Both groups infect their lepidopteran hosts when the larva ingests polyhedra or granules while feeding on their host plants. In the alkaline gut of the insect, the proteinaceous coat surrounding the virions breaks down, and they pass into the midgut epithelium. In most Lepidoptera there is a transient phase of infection in the midgut and from here the virus spreads to most larval tissues via the haemolymph, or via the tracheoles (Volkman 1997). Several days later, the insect host will be little more than a flaccid bag of virus (Fig. 5.5). Frequently, an infected larva climbs to the tips of shoots shortly before death (Vasconcelos *et al.* 1996). The body tissues then disintegrate, liberating the occlusion bodies (polyhedra or granules) over the foliage beneath, so distributing the virus particles in a suitable place to infect new susceptible hosts. This elevation-seeking behaviour of the host before death is just one of the many ways in which the baculovirus manipulates its host to facilitate transmission and persistence.

over the route of transmission can be very important and it clearly matters whether a pathogen is sexually transmitted or food-borne.

5.3.2 Threshold theory and disease management

If one believed that pseudo mass-action was appropriate for a particular pathogen system, then simple models will suggest that the population threshold exists and (in the simplest case) is the observed size of the susceptible population at the endemic equilibrium (e.g. Anderson *et al.* 1981; Lyles and Dobson 1993; Barlow 1995; Fromont *et al.* 1998a, b). For many infections this is a rather small fraction of the population (e.g. possums: Barlow 1993, 1996) so this may predict that disease eradication can be achieved through substantial populations reduction. However, this conclusion should be treated with caution. Trivially, mass-action and pseudo mass-action make identical predictions when host population sizes are unchanging. So, in this situation, empirical comparisons of any scaling laws are impossible. This is particularly serious when it is proposed to make a radical change in population density and when the system has not been previously observed at a wide range of densities. In addition to the uncertainties about population scaling of transmission, it has also been suggested that the social perturbation arising from such

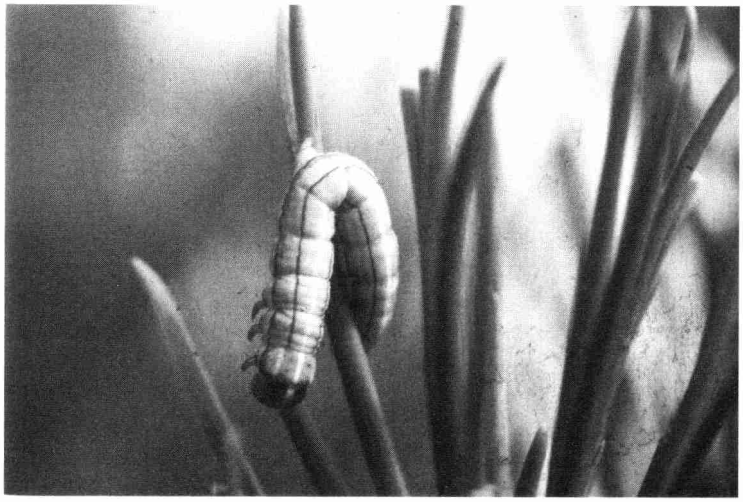

Figure 5.5 The pine beauty moth, *Panolis flammea*, in the advanced stages of a nucleopolyhedrovirus (NPV) infection. Note that the larva has climbed to the top of the plant before releasing the virus occlusion bodies that fall onto vegetation being eaten by other larva. (Courtesy of Jenny Cory.)

major intervention may itself promote dispersal and enhance transmission, thus working against the desired effect, e.g. bovine tuberculosis in badgers (Box 5.8; Swinton *et al.* 1997).

Control analysis does not necessarily require good answers to these difficult scaling questions. In particular, when considering the impact of vaccination, a good model assumption is that contact structures remain completely unchanged, except that the proportion of infectious contacts is reduced. Indeed, one advantage of vaccination is that, whatever its impact is relative to other forms of disease control, such as culling or immuno-contraception, the impact of vaccination is likely to be more predictable in advance, since it is less sensitive to the uncertainties about the population scaling of transmission.

5.3.3 Ecological complexities in disease management

Complexities such as density-dependent processes that act on the birth and death rate of the host will also influence the efficacy of the different control methods (Barlow 1996). An unusual example of this could occur in the control of swine fever in wild boars (Box 5.6). In some areas, hunting selectively removes the older, immune boars and this mortality may be rapidly balanced by compensatory birth rates that lead to an increase in the number of young susceptible animals that in turn promote transmission. An intriguing theoretical possibility is that a pathogen may even benefit from enhancing its own virulence, so as to increase its access to Susceptibles in this way. This idea was examined in the phocine distemper case study (Boxes 5.2, 6.4) but the relatively slow intrinsic growth rates of seal populations prevents sufficient compensation for re-infection. Nevertheless, the idea could be tested further in a fast breeding host with density dependent birth rate.

When disease management involves the control of infection in a wildlife population with the objective of reducing the risk of infection in an economically important domestic population (e.g. swine fever in wild boar and pigs, tuberculosis in badgers and cattle) then it is important to recognize that disease risk is likely to be related, not only to the prevalence in the wild population, but also to the total numbers infected. A crude analysis that ignored the epidemiology may assume that killing half the wildlife population will halve the risk of infection but the non-linearities discussed above will often modify this conclusion in significant ways. When the goal is disease eradication, rather than mere control, then a clear understanding of these complexities becomes more important.

Such considerations are also relevant when one attempts to map disease risk through GIS-based prediction of host densities from satellite derived environmental data (Box 6.1). For example, Boone *et al.* (1998) found that hantavirus infection of deer mice (*Peromyscus maniculatus*) was less likely where rodent densities were below a threshold value, but that density had little effect on prevalence above threshold.

5.3.4 Host heterogeneity

Heterogeneities in host susceptibility can also significantly affect transmission (Woolhouse *et al.* 1997). Dwyer *et al.* (1997) has shown in insect baculoviruses that incorporating variation between hosts in their susceptibility to pathogens into mathematical models of *L. dispar*-NPV improved the fit of the models to data from field experiments. Such variation can act in a density-dependent manner. Another heterogeneity that has been found to be important in a number of human disease is age-structured mixing, where transmission is more likely to be between similarly aged people than between age groups (Anderson and May 1991). Another heterogeneity of particular importance to conservation biology is the relationship between host genetic variability and small population viability in the presence of parasites (Lyles and Dobson 1993).

5.4 Persistence of microparasites

The previous section concentrated on the transmission of microparasite infection after a pathogen invaded a population of susceptible hosts and investigated this using the concept of the basic reproductive number, R_0. However, such conditions are not sufficient for pathogen persistence. For example, each sub-figure of Fig. 5.2 represents

an epidemic with $R_0 > 1$; yet only one corresponds to the long-term persistence of an infection. This section now examines the mechanisms that directly-transmitted microparasites use in order to persist.

Pathogens that develop the means of persisting, after most susceptible hosts have been lost from the host population, will clearly be at a selective advantage. Some pathogens, such as feline immunodeficiency virus (FIV) persists in feral populations of domestic cats *Felis catus* simply by inducing lifelong infectivity (Courchamp *et al.* 1995). Others remain in the host species but develop a 'carrier state' amongst some of the recovered individuals, where certain individuals continue to shed virus after recovery. In some long-lived hosts, the infection may have a long incubation period before the full-blown infection develops, such as in the transmissible spongiform encephalopathies (§5.4.9). A more common strategy is to use a biological reservoir of one kind or another. Some use vectors (Chapter 7) or a 'reservoir' host species, as in the case of tuberculosis in cattle and badgers (§5.4.7) or canine diseases in Ethiopian wolves and domestic dogs (§5.4.5; §8.2). Directly transmitted macroparasites often have long-lived free-living stages and while the microparasites do not have special infective stages, viruses such as the baculoviruses can be sustained in an environmental reservoir (§5.4.8).

Spatial structuring of the host population may also allow pathogen persistence (§5.4.4). This may be simply a consequence of the way the hosts are socially structured, such as brucellosis in ruminants (§5.4.6), or how the population is divided into sub-populations. Here, the pathogen invades a host sub-population and then jumps to another susceptible population, leaving the original population to recover through the immigration and birth of Susceptibles, thus making it a suitable habitat for future invasion. This may provide the key to understanding both the non-persistence of phocine distemper virus in harbour seals (Boxes 5.2, 3.3, 6.4) and the apparent persistence of caliciviruses (Box 5.7).

5.4.1 Fadeout theory and host demography

In those highly infectious pathogens with a short duration of infectiousness and a lack of specialized persistence mechanisms, the dynamics of microparasites are dominated by the deterministic consequences of invasion and the stochastic conditions that lead to fadeout. The probability of fadeout is influenced predominantly by the critical community size.

For pathogens like the morbilliviruses, a reasonable first approximation of the epidemic curve is that almost every member of a population will get infected and then become immune. This leads to a post-epidemic trough, from which infection can only recover through the input of new Susceptibles, usually through birth. Initially, all of these new Susceptibles will be diluted amongst the Immunes, and the chance of new transmission will remain small. Not until the number of Susceptibles has increased sufficiently can a subsequent epidemic re-occur. The input of Susceptibles depends directly on the birth rate and thus, via host ecology, on population size. However the risk of fadeout during this period is largely independent of population size and is controlled by the behaviour of the small number of non-immune individuals. The combination of these two factors, one population-independent and one population-dependent, leads once more to a population threshold. This is an effect that cannot be simply captured in continuously based models, since they allow arbitrarily low numbers of Infectives in the troughs which can then reseed the infection, and is much harder to analyse mathematically beyond the initial work of Bartlett (1957) (see Nåsell 1999a, b).

One example of infection fadeout in wildlife is the loss of phocine distemper virus (PDV) in the North Sea seal epidemic (Boxes 5.2, 3.3, 6.4). Although the infection had no difficulty in spreading ($R_0 > 1$) it could probably not persist because the epidemic ceased before sufficient new Susceptibles were introduced at the annual pupping season. Serological evidence for the continuing transmission of PDV after 1988 in North Sea harbour seals is equivocal. Seropositive samples were reported from Dutch seals born after 1988 (Visser *et al.* 1993), but none from Germany (Harder *et al.* 1993), the Wash (Hughes *et al.* 1992) or the Moray Firth (Thompson *et al.* 1992), There are no reports of continued excess mortality at any of these sites. As we saw in Figure 5.3, observed mass mortality

in Wash harbour seals ceased after a few months, and the same pattern was repeated around the North Sea (Box 3.3). It appears that, even if transmission did continue beyond early 1989, it was of a strain of greatly reduced virulence and different transmission characteristics. Thus it seems likely that, if there is a critical community size for PDV in North Sea harbour seals, it will be greater than 50 000 individuals.

5.4.2 Fadeout and persistence: classical swine fever

The range of epidemic patterns, from fadeout to persistence of infection, and how this pattern is influenced by host demography, is nicely illustrated by the case of classical swine fever (Box 5.6) in the wild boars of Italy. This also provides a possible example of the role of compensatory reproduction in enhancing disease persistence.

The introduction of swine fever into the wild boar populations of Italy has come about through three routes: contact with infected captive wild boars, illegal restocking with infected wild boars, and shared habitat with infected free-ranging pigs (Lowings *et al.* 1999). Three different types of infection dynamics have followed these outbreaks. Infection in small populations (Lunigiana, 800 animals/304 km^2; Piacenza: 400 animals/75 km^2) has resulted in rapid fadeout from 45% seroprevalence to 4.5% within 12 months. In large populations (Maremma, 8000 head/3800 km^2) of which about 35% of animals are culled each year, virus was detected for 5 years and seropositive animals for 8 years (Fig. 5.6(a)). A third type of dynamics has been observed in eastern Sardinia, where infection is endemic and has persisted for at least 17 years with a low seroprevalence (Fig. 5.6(b)). The age-stratified serological data suggest a small endemic area out of which the infection spreads unpredictably from year to year and this spread is influenced by wild boar dynamics. In order to eradicate infection in this area, strong hunting pressure has been encouraged so that 45% of the population has been killed each year.

Application of a simple SIR model has identified how the dynamics of the infected population could influence the maintenance of the infection in the eastern Sardinian population (Guberti *et al.* 1998). This showed that the large number of young animals could form a reservoir of Susceptibles. Increased hunting of the wild boar population increased the number and the survival of the newborn Susceptibles, so the virus had enough susceptible animals to be maintained in the wild. Four main factors determine the persistence of the infection in the wild:

1 the size of the susceptible wild boar population;
2 the presence of domestic herds of pig or wild herds in the area;
3 depopulation or very high hunting pressure promoting persistence by increased population turnover through compensatory reproduction;
4 the presence or the selection of low virulence strains (Guberti *et al.* 1998).

5.4.3 Persistence of highly virulent pathogens: caliciviruses

The newly emerging lagomorph caliciviruses, European brown hare syndrome virus (EBHSV) and

Box 5.6 Classical swine fever

Classical swine fever is an RNA pestivirus in the Togaviridae. Infection typically results in high morbidity and mortality, though infections with low-virulence virus do exist. Suidae are the sole natural hosts, and direct contact between infected and susceptible animals is the principal means of viral transmission—though in domestic pigs, swill feed has also been identified as a source of infection. Infected animals shed large amounts of virus for up to 40 days, sometimes intermittently. The virus is excreted in oronasal and lacrimal secretions, urine, and faeces. Recovered animals show specific antibody and lifelong immunity. European Union pig protection programmes have shown that swine fever outbreaks in wild boars cause severe economic losses to domestic pigs. Oral vaccination does not induce durable protection and depopulation of wild pigs is considered the only suitable approach.

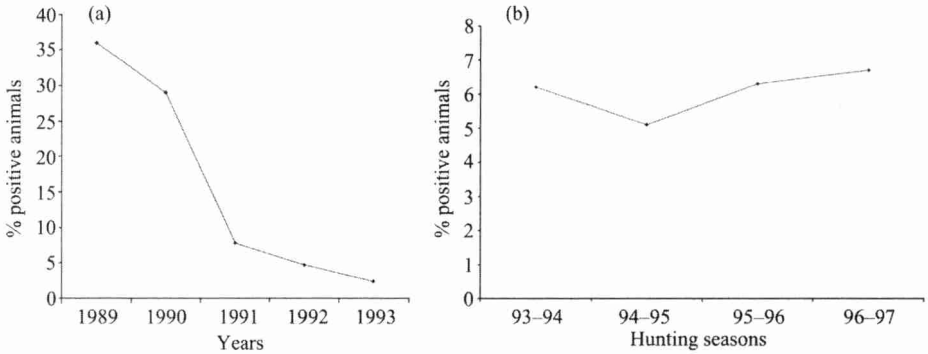

Figure 5.6 Longitudinal serology to classical swine fever in wild boars showing (a) slow decline of seroprevalence at Maremma (Tuscany) from initial infection in June 1983 and (b) long-term persistence in Eastern Sardinia, Italy where infection has been present since 1981 in this population (after Lowings *et al.* 1998).

rabbit haemorrhagic disease virus (RHDV) (see Box 5.7), are highly pathogenic infectious pathogens that could be of great significance both ecologically and economically. Their impact is very variable, and probably highly sensitive to host demography.

Host population density affects the rate of transmission and the host age structure determines the size of the susceptible and refractory juvenile populations, which vary greatly over the year. In a study of hares in the Modena region of Italy, Lavazza *et al.* (1997) found that mortality due to EBHSV was negligible at high densities (>15 hares/ha) due to rapid transmission, meaning that most hares were exposed whilst still very young. At lower densities (<8/ha) juveniles were more likely to become exposed after their refractory period and hence to

Box 5.7 Lagomorph caliciviruses

Rabbit haemorrhagic disease virus (RHDV) and European brown hare syndrome virus (EBHSV) constitute a novel and distinct subgroup of *Caliciviridae* (Wirblich *et al.* 1994). They are both host-specific, the former infecting only European rabbits (*Oryctolagus cuniculus*) (Lenghaus *et al.* 1994), and the latter infecting both brown hares (*Lepus europaeus*) and mountain hares (*Lepus timidus*). Both viruses are highly infectious and have case-fatality rates of up to 97% for RHD and over 50% for EBHS, with death occurring within 2 days. An interesting feature of EBHS is the 'juvenile refractory period': hares less than 8 weeks old are infectious and become immune, but do not suffer symptoms (Lenghaus *et al.* 1994, Lavazza *et al.* 1997). Additionally, EBHSV is highly robust and has been found to remain infectious for 3–4 months in the field in Italy.

First identified in China in 1984, RHDV spread rapidly throughout Europe and North Africa in the late 1980s and early 1990s. It was imported into Australia and New Zealand for use as a biological control agent (Coman 1997) because of its host-specificity, coupled with its rapid and, relative to myxomatosis, humane killing ability. But these lagomorph caliciviruses also pose a threat for conservation of high-quality, rabbit-grazed swards, and the loss of an important food source for threatened predators.

RHDV's epidemic dynamics vary greatly, in terms of seasonal timing, speed of spread, mortality, and persistence. In arid areas of Australia, epidemics tend to be very intense, peaking 2–3 days after introduction and lasting for a few weeks (Barlow and Kean 1998). Mortality is high and local fadeout of infection is likely. In more temperate areas, epidemics are usually less intense, last for months, and mortality is much lower. In Spain, RHDV may have become endemic, limiting the rabbit population to around a third of its former level and removing important food sources for predators such as kites and the endangered Spanish lynx.

A further interesting factor is the discovery of a non-pathogenic strain of RHDV, which does not cause symptoms but confers immunity to pathogenic RHDV. This strain may be widespread and highly prevalent in parts of the UK (Trout *et al.* 1997) and Europe.

succumb to infection. At low density, host extinction is a possibility, and it was recommended that populations be maintained above 8–15/ha to avoid this. Barlow and Kean (1998) developed a simple homogeneous-mixing model for RHDV, and found that the juvenile refractory period reduced the epidemic intensity and enhanced subsequent population recovery. In areas with a long breeding season the population may have a chance to recover. Thus the local population dynamics in terms of the length, timing, and intensity of the breeding season are important.

Given its propensity for intense epidemics with fast mortality rates, how does a pathogen such as RHDV persist? There is no evidence of a reservoir species and experimental data from Australia could not identify a carrier state (Lenghaus *et al.* 1994). Barlow and Kean (1998) considered that local persistence is unlikely to occur and that after fadeout, subsequent outbreaks are caused by re-infection. However, epidemics can exhibit very fine spatial heterogeneity, killing all rabbits in a warren, whilst leaving those in a neighbouring one unaffected; an unbroken 'epidemic wave' probably does not occur often (B. Richardson, personal communication). In the UK, data from Ramsey Island also support this view (R. Trout, personal communication). If RHDV is as robust as EBHSV (Box 5.7), then some burrows could act as an environmental reservoirs triggering another outbreak.

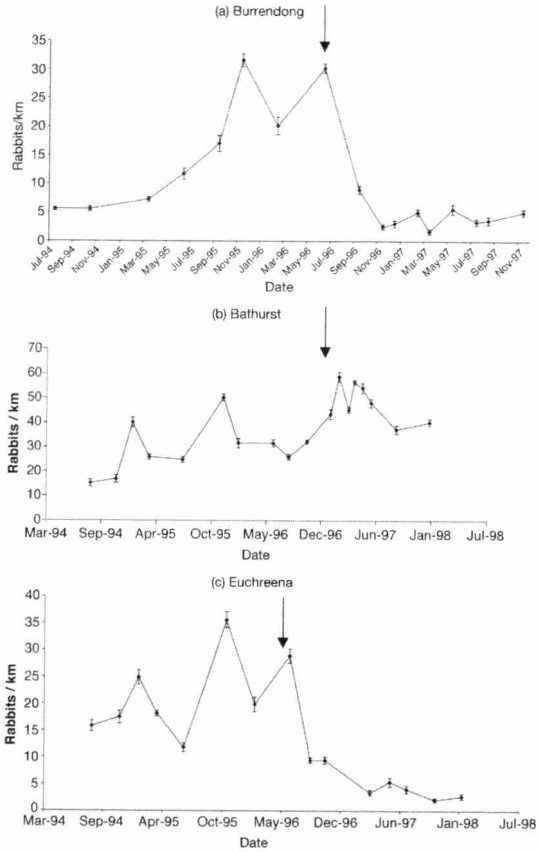

Figure 5.7 The impact of RHD on rabbit abundance. Figures show numbers of rabbits at three sites in central-western New South Wales, Australia in 1996–97. *Arrows* indicate the arrival of RHD. Infection appears to have little impact in site (b), the most densely populated: the difference may be due to the presence of juveniles (refractory to symptoms) at the time of the outbreak (after Saunders *et al.* 1999).

Persistence through re-infection from neighbouring populations will be facilitated by the high natural mortality of rabbits (typically 60% per annum in adults) leading to rapid replacement of immune individuals by Susceptibles. Additionally, maternal antibodies, which last for longer than the juvenile refractory period, may inhibit the development of immunity to RHDV, thus depriving the offspring of surviving females of the opportunity to become immune whilst refractory to symptoms, and so enhance the supply of new Susceptibles following an epidemic.

The robustness of the viruses means that they may be transmitted via a number of routes and apparently over long distances. Whilst experimental conditions have shown that it can be transmitted by close contact, indirect transmission probably predominates in the field. Due to rabbits' restricted home range, this is likely to be mainly short-range transmission. Short-range transmission could be vector-borne transmission via the flea, *Spilopsyllus cuniculi*, as well as direct transmission from cadavers and through the oro-faecal route. Vector transmission by mosquitoes is another potential transmission route that would operate over longer distances. However, since mortality is so rapid there is only a short window of opportunity prior to death during which the host is viraemic and so direct transmission from cadavers and via carrion-feeding animals may be more important. Infectious virus has been detected in the droppings of some predators.

5.4.4 Spatial structure and critical meta-population distributions

Host populations that are structured into sub-populations promote persistence of microparasites by allowing epidemics to occur asynchronously in the various sub-populations and avoiding deep global troughs (Bolker and Grenfell 1996). However, if the sub-populations are small and isolated, then infection to fadeout will occur and some form of intermediate coupling is required for persistence (Rohani *et al.* 1996). The notion of the critical community size, in fact, needs to be generalized to the critical meta-population distribution to accommodate the conditions when there are a number of different host patches of different sizes and connectivities. Indeed, this is particularly important for infections of wild-mammal populations that are frequently at low and variable densities, with low reproductive rates.

This approach may be particularly important to conservation problems (Chapter 6 and 8), such as canine distemper virus in black-footed ferrets (Forrest *et al.* 1988) or Ethiopan wolves (*Canis simensis*) in the Bali mountains (Laurenson *et al.* 1998) or rabies in the Serengeti (Gascoyne *et al.* 1993)—see Chapter 8. All these are situations in which generalist pathogens are freshly re-introduced to susceptible populations by chance or through changing species distributions (McCallum and Dobson 1995; Woodroffe 1998). Models, and their theoretical and empirical underpinnings, clearly need to be developed for these settings in which a single pathogen can affect several different species in many different patches.

5.4.5 Reservoir hosts and inter-species transmission

There are a number of key examples in which infection has spread from one host species within which it appears to be endemic to another in which it cannot persist, though there have been few systematic tests of such hypotheses. Cleaveland and Dye (1995) suggested three conditions to test the hypothesis that a reservoir host is acting as a source of infection to other species:

1 that reservoir host populations should show evidence of persistent infection;
2 that cases should occur in the reservoir host in the absence of cases in the other species;
3 that outbreaks in the other species should follow cases in the reservoir host.

On this basis, they demonstrated that domestic dogs were the likely reservoir of rabies infection in the Serengeti. Similarly, Rhodes *et al.* (1998) suggested, on the basis of a density model, that side-striped jackal (*Canis adustus*) populations in Zimbabwe were unable to sustain endemic infection with rabies and, by implication, that domestic dogs were re-introducing infection into the population.

Further examples in which inter-species transmission have been studied are brucellosis, bovine tuberculosis, and the transmissible spongiform encephalopathies. We now consider each of these pathogens.

5.4.6 Inter-species transmission: brucellosis

An example of inter-species transmission is provided by brucellosis, which is present in a number of well-studied wildlife and livestock systems, including bison in Yellowstone, USA, and chamois in the Italian Alps.

Brucella abortus has been present in the Yellowstone bison herd since its introduction by infected cattle in the early years of this century (Dobson and Meagher 1996; Meyer and Meagher 1997). Ironically, it is now perceived to be a threat to the local cattle industry (Baskin 1998). Determining the risk of transmission of *B. abortus* from wildlife to cattle requires a quantitative understanding of the transmission dynamics of pathogens within the host population. Three routes of transmission between bison have been described (Fig. 5.8), these are vertical (mother to calf), horizontal as a sexually transmitted disease, and what Heesterbeek has called 'diagonal' when an infected bison cow aborts and contaminates the environment (Williams *et al.* 1997). It is only this latter route that could transmit *B. abortus* to cattle but, in contrast to cattle, brucellosis-induced abortion is rare in bison (Meyer and Meagher 1997). In addition, the vertical and horizontal routes of transmission are frequency-dependent, hence systematic culling of

the Yellowstone bison herd will not lead to the eradication of the disease.

By contrast with the Yellowstone experience, the primary issue with brucellosis in the Western Italian Alps is the risk from livestock to wildlife populations. The species of concern are the chamois (*Rupicapra rupicapra*) that suffered an outbreak between 1994 and 1996 in the Western Italian Alps. Since the first case in Switzerland in 1950, *B. abortus* infection has been reported from only six other animals, and it was suspected that infection arose from infected bovine herds. No other cases were recorded until 1988 when *B. melitensis* was isolated in the French Alps in an area of relatively high (10%) prevalence of brucellosis in sheep (Garin-Bastuji *et al.* 1990; Garin-Bastuji 1993). Since then a further ten cases have been recorded. The sporadic nature of brucellosis in chamois is confirmed by serological surveys that show infection is either sporadic (Corti *et al.* 1984) or absent (Tolari *et al.* 1987; Gauthier 1991; Gennero 1993)

Circumstantial evidence for inter-species transmission comes from the Susa valley where *Brucella abortus* was first recorded in chamois in December 1994. This followed an outbreak in a bovine herd in the valley and chamois were presumably exposed when they grazed on the contaminated pasture (Ferroglio 1998). Prevalence in chamois subsequently decreased from 28% in 1995, to 18% in 1996, and 8% in 1997. All the infected animals were adult and exhibited classic clinical signs of chronic disease. More males were positive than females, probably because males tend to use low pastures more than females and were more exposed to the infected pasture. Confirmation that chamois are just a spill-over host comes from the observation that when brucellosis is eradicated from livestock it also disappears from wildlife (Rementzova 1964; Leon-Vizcaino 1991).

The high mortality of the disease in chamois could be why chamois epidemics appear self-limiting (Bouvier and Burgisser 1958). However it is interesting to note that the infection also fades out in the solitary moose (Corner and Connell 1958; Forbes *et al.* 1996) but is endemic in many of the gregarious ruminants such as bison (*Bison bison*), elk (*Cervus canadiensis*), and caribou (*Rangifer tarandus*). This may be partly due to the higher rate of induced mortality but may also be because of increased transmission from aborted foetuses in the herding species. Indeed diagonal transmission could be the way to explain persistence in species where abortion occurs, such as elk and caribou (Thorne and Morton 1978; Tessaro and Forbes 1986).

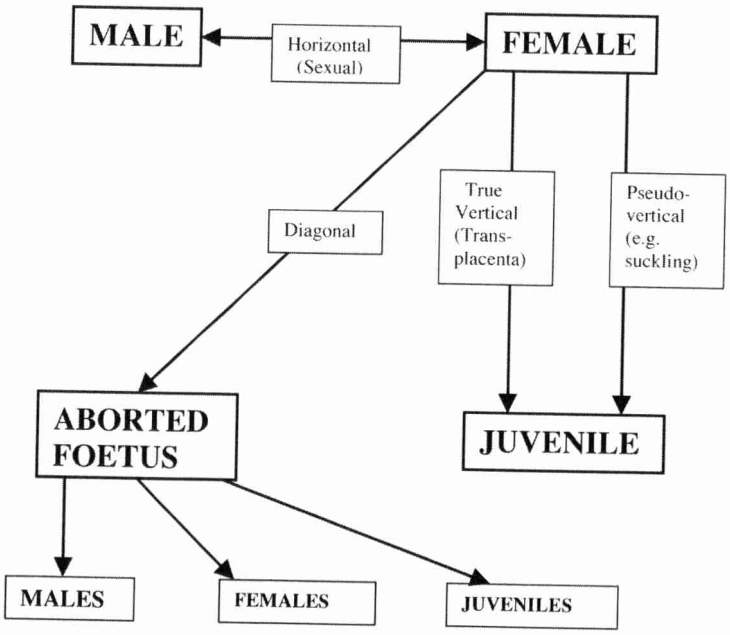

Figure 5.8 Transmission routes of *Brucella abortus* in bison. Note that cross-infection to cattle can not occur through the vertical or horizontal routes, and can only occur through diagonal transmission via abortion. Interestingly, the prevalence of abortion in bison is rare.

Brucellosis also provides an example of density-dependent transmission. Where elk receive supplementary feed, herd size may reach several thousand and the prevalence of brucellosis is high (37%, Herriges *et al.* 1992); while in areas where elk herd size is not artificially increased, the observed prevalence is less than 3% (Merrell and Wright 1978; Rhyan *et al.* 1997). For comparison, in Yellowstone, bison brucellosis is present whenever herd sizes exceed about 200 animals (Dobson and Meagher 1996).

5.4.7 Inter-species transmission and reservoirs: bovine tuberculosis

Another pathogen found in both wildlife and cattle is bovine tuberculosis. As tuberculosis control in cattle has become increasingly effective, areas of control failure have been attributed to wildlife reservoirs of infection, most notably in possums in New Zealand and badgers in the south-west of England (Box 5.8). One lesson that epidemiologists have learned in the past decades is how difficult it has been to identify any one 'reservoir' species with certainty: authors disagree, for example, on whether wild deer *Cervus elaphus* also function as a reservoir in New Zealand (Hickling 1995; Wobeser 1995). Emerging molecular techniques, have the potential to offer much in this area (Clifton-Hadley 1998), especially when combined with the rigorous approach of Cleaveland and Dye (1995) discussed in §5.4.5.

5.4.8 Persistence and environmental reservoirs

Baculoviruses persist in the natural environment between epidemic outbreaks in their invertebrate hosts, although the actual mechanism of persistence still remains a mystery (Box 5.9). New isolates of baculovirus are usually found when the host population is at high density, but how they persist during periods of low host-density is unknown. One possibility is that they may be present as sublethal or latent infections. There is limited evidence that a very slow, replicating infection persists in a laboratory culture of *Mamestra brassicae* (Hughes *et al.* 1993, 1997), though similar infections are yet to be found in field populations. Alternatively, they may frequently go locally extinct, but persist globally through the action of long-distance dispersers, such as birds (Entwistle *et al.* 1993). However, whilst it has been demonstrated that birds have the potential to disperse baculoviruses, few data are available to enable an assessment of how frequently this occurs. Even so, there is considerable empirical evidence that baculoviruses can persist locally in sheltered microhabitats, such as the soil or crevices on the bark of trees, for weeks, months, and even years (McLeod *et al.* 1982), they die quite quickly when exposed to sunlight. As such, local persistence is very much dependent upon microhabitat.

5.4.9 Long incubation period: transmissible spongiform encephalopathies

In contrast to environmental reservoirs, there are a wide range of biological reservoirs. Microparasites use their hosts as reservoirs in different ways. For example, an infection may be sustained simply as a chronic infection within a host, a strategy associated with sexually transmitted diseases (Smith and Dobson 1992), such as chlamydia in koalas *Phascolarctos cinereus* (Augustine 1998). A further strategy is to develop a long incubation period, a particularly good strategy in hosts with low mortality rate and in pathogens where no alternative biological or environmental reservoir is used. One group that has a long incubation period are the transmissible spongiform encephalopathies that are examined in this section.

Transmissible spongiform encephalopathies (TSEs) are neurological diseases affecting a wide range of mammals, including humans (Table 5.1). Those of major importance include: scrapie in sheep; bovine spongiform encephalopathy (BSE) in cattle; and Creutzfeld–Jakob disease (CJD), especially the 'new variant' form (vCJD) in humans. Transmissible mink encephalopathy (TME) is known as a disease problem on fur farms. The only known TSE in wildlife is chronic wasting disease (CWD) in mule, deer, elk, and white-tailed deer in Colorado and Wyoming in the USA. However, TSEs have been widely reported from zoo animals in the UK in recent years. These cases were mostly due to BSE transmitted via contaminated meat or commercial feedstuffs. BSE is

Box 5.8 Badgers, possums, and tuberculosis

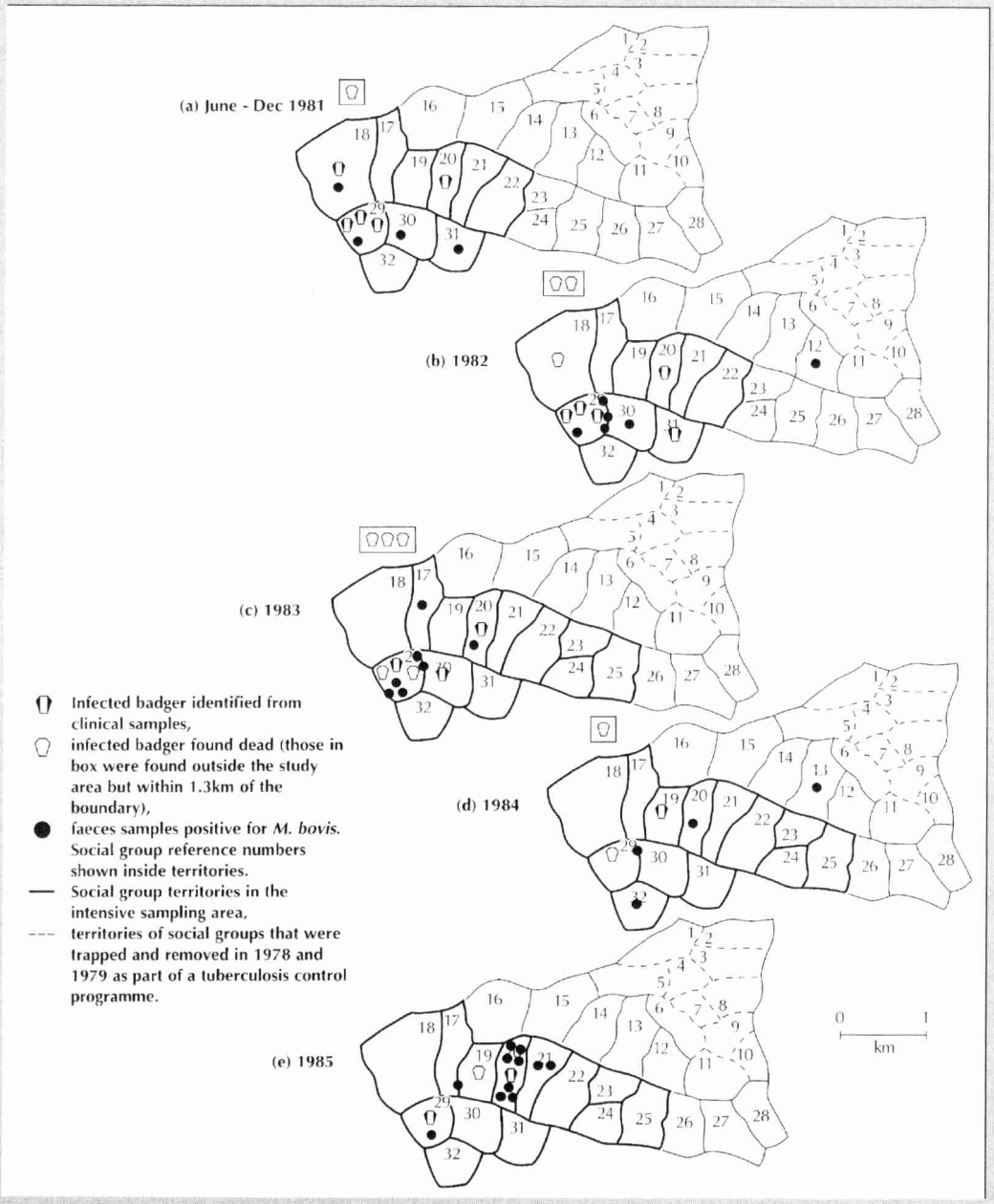

Figure 5.9 Spatial pattern of bovine tuberculosis at Woodchester Park, showing long-term infection localized within a few social groups (after Cheeseman *et al.* 1988a, b).

continued

Bovine tuberculosis (Tb) is caused by the bacterium *Mycobacterium bovis* and while the pathogen is of little threat to humans there is an international effort in Europe to try and eradicate the pathogen from domestic cattle herds. Overall, cases are relatively uncommon in cattle in Great Britain, although most cases are concentrated in the south-west of England and coincide with high densities of badgers *Meles meles*. More recently, the disease has spread spatially and moved into new parts of central and western Britain, causing increased concern amongst farmers. Cattle in other countries, notably New Zealand, the Republic of Ireland, Italy, and Spain also have *M. bovis*. In Britain, badgers have been implicated as a significant source of infection in cattle (Clifton-Hadley *et al.* 1995). Badger removal has been followed by reduced rates of herd breakdown and while the evidence is largely circumstantial and controversial, a committee of scientists found it compelling (Krebs 1997). Direct contact between badgers and cattle appears to be unusual, and pasture contamination with faeces and urine has been proposed as the main route of infection, simply because badgers shed large numbers of bacilli in their urine (Krebs 1997). While it is generally considered that the badgers are a source of infection, there is little evidence to quantify the extent to which badgers receive spill-over infection from cattle. Simple husbandry methods to separate badgers and cattle could have a significant role in reducing risk of infection to either or both species. However, other wildlife species may also carry the pathogen and be an important cause of initial breakdown. Interestingly, some badger social groups remain chronically infected for many years, while neighbouring groups remain uninfected (Smith *et al.* 1995). This pattern of temporally continuous but spatially patchy infection is thought to be caracteristic of maintenance wildlife hosts (Morris and Pfeiffer 1995).

In New Zealand the possum is the major reservoir, with deer, ferrets, and pigs. The transmission of tuberculosis between possums is believed to be largely due to den-sharing, fighting, and mating (Roberts 1996; Kao and Roberts 1999). As such, other mechanisms are necessary to explain transmission to cattle. In one experiment, a possum was semi-anaesthetized and introduced into a field of cattle (Sauter and Morris 1995). The cattle approached the possum and investigated it by nuzzling and licking, so it is likely that if the possum had Tb, the cattle would have become exposed. When the experiment was repeated with a semi-anaesthetized ferret, the cattle avoided it. These observations demonstrate a potential route of infection and imply that ferrets might be less important as a reservoir of infection.

particularly adept at jumping species. For example, there was an epidemic of feline spongiform encephalopathy in domestic cats in the United Kingdom associated with the BSE epidemic in cattle. However, there have been no reports of BSE infection in wildlife to date.

TSEs have long incubation periods and progressive pathologies and are invariably fatal once clinical signs have developed. There appears to be no effective immune response, there is no cure, and diagnostic tests for pre-clinical infections are still under development. The nature of the infectious agent remains controversial but the leading proposal is the 'prion' hypothesis that suggests that TSEs are caused by the introduction of an abnormal form of the prion protein (PrP), which spreads by recruiting normal protein molecules to the abnormal state. Certainly, the late pathology of TSEs is characterized by accumulating plaques of abnormal PrP in the tissues, especially the central nervous system. TSEs are transmitted by many and varying routes: some, such as scrapie in sheep, are clearly horizontally transmitted, although the precise route is uncertain and scrapie may also persist in the environment. BSE is transmitted via ingestion of infected tissues or of commercial feedstuffs prepared from infected tissues. Some TSEs might be vertically transmitted from mother to offspring and several TSEs have been transmitted iatrogenically (i.e. during medical treatments involving infected tissues).

The epidemiology of chronic wasting disease (CWD) is described in detail in Williams and Miller (2000) and Spraker *et al.* (1997). CWD was first recognized in 1967 in captive animals and subsequent outbreaks have affected up to 90% of adult animals at some sites. Forty-nine cases had been reported in wild animals by 1995; annual incidences are increasing but this may simply reflect improved reporting. Cases are confined to adults more than one-and-a-half years old. Transmission routes are uncertain but the high incidences in captive animals are suggestive of horizontal transmission—there is no evidence of exposure to contaminated feed and no evidence of a genetic component to susceptibility. Vertical transmission is possible but hard to distinguish from high rates of horizontal

Box 5.9 Modelling baculovirus persistence

Hochberg (1989) incorporated heterogeneity in baculovirus persistence in a model where the occlusion bodies (OBs) in the environment were divided between those on the leaf surfaces exposed to sunlight and hence with high mortality, yet available to infect susceptible hosts, and those in a protected microhabitat, which were not available to Susceptibles. The relative importance of the reservoir to persistence depended on the rate of movement of OBs from leaves to soil by rainfall or invertebrates, the input of OBs directly into the soil, for example, by infected insects falling off the plant, the loss of OBs through decay and then the translocation of OBs from the soil back up to transmissible surfaces. The presence of a reservoir was irrelevant if either the rate of translocation was so high that the OBs returned from the reservoir as soon as they entered it, or so low that the soil acted as a sink. However, at intermediate rates of translocation, the reservoir acted as a buffer. At times of high virus-density on the leaves, there was net movement into the protected habitat, so enhancing the persistence of the virus. Conversely, at times of low virus-density on the leaves, there was net movement out of the reservoir back to the leaf surfaces. This heterogeneity in the pathogen population stabilized the pathogen host system to produce more constant host abundance and persistence of the pathogen. This raises the question of whether the movement of pathogen particles out of the protected microhabitats back to transmissible surfaces is sufficient for the presence of a reservoir to have any impact on the dynamics. Manipulative experiments have provided estimates for the 'translocation rate' and suggested that under some conditions reservoirs can be ecologically important (Hails, unpublished). The study in question involved wild-type baculoviruses in agricultural habitats where the habitats are considered ephemeral and cultivation destroyed the reservoir each year. Even so, such virus movement could act to buffer the within season dynamics, and could be of greater importance in more stable habitats.

transmission. Transmission between captive and wild animals may have occurred at boundary fences. Consistent with the minimum age of cases, the incubation period is at least 1.5 years, based on the occurrence of cases after the introduction of new stock into a CWD-free population. Efforts to eradicate CWD from captive populations by culling and decontamination have failed and the need to limit the spread of CWD and have led to movement restrictions. It is not known whether CWD can persist endemically in wild populations.

Since the real impact of TSEs on individuals is so unclear, it is not surprising that we do not know whether they have a significant impact on population dynamics. Outbreaks of scrapie in domestic sheep can cause mortalities exceeding 25% per year (Elsen *et al.* 1999; Woolhouse *et al.* 1999). However, such high mortalities due to TSEs are unusual because the incubation period is typically long in relation to the host's life expectancy. Most infected animals, therefore, die before showing clinical signs. A crucial question is whether there is mortality associated with pre-clinical infection? Diagnostic tests for pre-clinical TSE infection are only now being developed.

In general, risk factors for the possible occurrence of TSEs in wildlife will reflect the transmission routes of these diseases. Cannibalism is clearly a potential risk factor. Also, feeding on carcasses and ingestion of placental tissue (which may apply to herbivores in nutritionally poor habitats) may facilitate TSE transmission. Cross-species transmission is obviously most likely to be possible from prey to their predators.

5.5 Synthesis

This chapter has attempted to survey a wide range of patterns of microparasite dynamics under the dual approach of transmission and persistence. We have argued that each can be associated with a threshold phenomenon: one for invasion, with deterministic R_0 based-analyses, and the second for fadeout, with stochastic analyses of the critical community size. These two kinds of threshold phenomena are undoubtedly both important but, as with human infections, invasion phenomena are easier to characterize theoretically. The two are alternative sides of the coin of the violent recurrent epidemic: probably rare in 'established' coevolved infections (with exceptions such as the morbilliviruses), but important in some novel pathogens.

Understanding these density-dependent infection processes is essential for a rational approach

Table 5.1 Species that have been naturally or experimentally infected with transmissible spongiform encephalopathies

Human	Cattle	Mule deer
Chimpanzee	Sheep	Elk
Macaque	Goat	White-tailed deer
	Moufflon	Nyala
Puma		Gemsbok
Cheetah	Rat	Arabian oryx
Ocelot	Mouse	Scimitar-horned oryx
Tiger	Hamster	Greater Kudu
Cat		
Mink		

to the practice of ecologically managing disease. For example, under what circumstances will infection be promoted rather than reduced by host culls because of compensatory reproduction as suggested in the classical swine fever example? Can the same kind of transmission scaling (approximately mass-action in population numbers) seen in the cowpox study also be expected for the insect baculoviruses that have no recovered or immune class and are indirectly transmitted? Developing this approach depends on improvement in biological understanding. For some pathogens like TSEs, many of the appropriate experiments are under way, but results may take years to obtain. Mathematical models can, therefore, be extremely valuable in identifying, or at least confirming, research priorities.

Another theme that emerged from the case studies is the difficulty of assessing the significance of inter-species transmission assigning species as 'reservoirs' of infection. There has been much recent progress in understanding the dynamics of deterministic models of multi-species transmission (Hudson and Greenman 1998) and there are many theoretical challenges in extending these insights to the stochastic models needed to consider the dynamics of fadeout and persistence.