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Transmission dynamics of a zoonotic pathogen within and between wildlife host species

Michael Begon[1,2*], Sarah M. Hazel[1,2,3], Derrick Baxby[1,4], Kevin Bown[1,2,3], Rachel Cavanagh[1,2,3], Julian Chantrey[1,2,3], Trevor Jones[1,3] and Malcolm Bennett[1,3]

[1]*Centre for Comparative Infectious Diseases,* [2]*Population Biology Research Group, School of Biological Sciences, Nicholson Building,* [3]*Department of Veterinary Pathology, and* [4]*Department of Medical Microbiology, The University of Liverpool, Liverpool L69 3BX, UK*

The transmission dynamics of the cowpox virus infection have been quantified in two mixed populations of bank voles (*Clethrionomys glareolus*) and wood mice (*Apodemus sylvaticus*), through analyses of detailed time-series of the numbers of susceptible, infectious and newly infected individuals. The cowpox virus is a zoonosis which circulates in these rodent hosts and has been shown to have an adverse effect on reproductive output. The transmission dynamics within species is best described as frequency dependent rather than density dependent, contrary to the 'mass action' assumption of most previous studies, both theoretical and empirical. Estimation of a transmission coefficient for each species in each population also allows annual and seasonal variations in transmission dynamics to be investigated through an analysis of regression residuals. Transmission between host species is found to be negligible despite their close cohabitation. The consequences of this for the combining ability of hosts as zoonotic reservoirs, and for apparent competition between hosts, are discussed.

Keywords: cowpox; *Apodemus*; *Clethrionomys*; transmission dynamics; host–pathogen dynamics; apparent competition

1. INTRODUCTION

The dynamics of pathogens in natural populations, especially of wildlife, and the role of pathogens in the dynamics of these populations, are now major foci of interest in ecology (De Leo & Dobson 1996; Hudson *et al.* 1998), having long been neglected (Grenfell & Dobson 1995). Moreover, the role of such host populations as reservoirs of infection for domestic animals and/or zoonotic disease (disease transmissible to humans) is of great concern in medicine (Mills & Childs 1998), especially following the emergence of 'new' pathogens such as the hantaviruses (Niklasson *et al.* 1995), and *Borrelia burgdorferi*, the causative agent of Lyme disease (Ostfeld 1997). While recent progress in developing the theory of these interactions has been considerable, these theories largely lack related field data (Grenfell & Dobson 1995). Furthermore, most theoretical and empirical studies have focused on one-host-one-pathogen systems, and most empirical studies have been of pathogen epidemics (Hone *et al.* 1992; Grenfell & Dobson 1995), either of newly introduced pathogens such as myxoma virus, or within host populations otherwise not normally in contact with the pathogen, such as the phocine distemper virus epidemic of 1988 (Swinton *et al.* 1998). Yet most pathogens are endemic, circulate in more than one host species, and coexist with other pathogens. In seeking to redress these imbalances, we examine the dynamics of an endemic, zoonotic pathogen, the cowpox virus, in two natural, mixed populations of two reservoir hosts that can be adversely affected by the virus: the bank vole (*Clethrionomys glareolus*) and the wood mouse (*Apodemus sylvaticus*).

Cowpox virus is an orthopoxvirus (and thus related to smallpox and vaccinia viruses), endemic in Europe (Baxby & Bennett 1994; Robinson & Kerr 1999). Although natural infection and disease occur in domestic cats and, rarely, in man and cattle, the reservoir hosts are generally accepted to be wild rodents. In Great Britain, a high prevalence of cowpox virus antibody, and cowpox virus-specific DNA detected by polymerase chain reaction (PCR), suggest bank voles, wood mice and field voles (*Microtus agrestis*) as reservoir hosts (Crouch *et al.* 1995; Bennett & Baxby 1996; Chantrey *et al.* 1999). While the natural routes of cowpox virus transmission have not yet been confirmed experimentally, a variety of evidence from this and related orthopoxviruses indicates direct transmission between infectious and susceptible hosts (Robinson & Kerr 1999). Little obvious disease has been reported for rodents either in the field or in the laboratory, but infection, under standard animal house conditions at least, has a marked negative effect on reproductive rate in both bank voles and wood mice (Feore *et al.* 1997).

The specific questions addressed here all concern pathogen transmission dynamics within the bank vole–wood mouse–cowpox virus system: transmission dynamics are the driving force underlying any interaction between host and pathogen populations. The questions are investigated through analyses of time-series of numbers of infected and susceptible hosts—an approach that has not apparently been possible with other systems. We ask first, within both species, whether the mode of

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transmission conventionally assumed, especially in modelling studies, is in fact appropriate. We then turn to a comparison of transmission rates within and between species. This is important, first, for the light it throws on whether coexisting wildlife hosts should be considered as joint or independent reservoirs of zoonotic infections, and second, because it allows an assessment of the strength of 'apparent competition' in a host–host–pathogen system to be made from field data, whereas previously this has largely been the subject of theoretical analysis (Holt & Pickering 1985; Begon & Bowers 1995; Greenman & Hudson 1997). Finally, computing single transmission coefficients for each host from extended (three-year) time-series allows shorter-term (seasonal) and longer-term (annual) variations in cowpox virus transmission rates to be investigated by examining patterns of residuals around overall regressions.

2. MATERIAL AND METHODS

(a) *An analytical framework*

We wish to understand the dynamics of the cowpox virus infection in mixed populations of hosts, comprising bank voles and wood mice. To do so, we seek an explanation for the changing numbers of new infections in terms of the interactions between susceptible and infectious hosts. Our basic model, following the usual conventions of infectious disease epidemiology (Anderson & May 1992; De Jong *et al.* 1995; Begon & Bowers 1995; Begon *et al.* 1998) is as follows:

$$I(t,t+1) = \left\{\begin{array}{l}\text{new infections}\\ \text{from within-species}\\ \text{transmission}\end{array}\right\} + \left\{\begin{array}{l}\text{new infections}\\ \text{from between-species}\\ \text{transmission}\end{array}\right\} + \left\{\begin{array}{l}\text{new infections}\\ \text{from elsewhere}\end{array}\right\},$$

where $I(t,t+1)$ refers to the number of new infections arising in the period $(t,t+1)$ in one of the host species, and each bracketed term on the right-hand side encapsulates an interaction between susceptible and infectious hosts. 'Within-' and 'between-species' refer here to transmission within bank voles or wood mice or between the two. 'Elsewhere', then, refers to the possibility of transmission from another host species or some other (unknown) source.

Broadly, two theoretical modes of infectious disease transmission have been proposed for each of the bracketed terms (De Jong *et al.* 1995). In 'density-dependent' transmission (also called 'pseudo mass action') susceptible hosts are assumed to contact other hosts throughout the whole of their population 'at random', such that the number of these contacts rises in proportion to the size of the population. (In the past, this has also often been called simply 'mass action', without either 'pseudo' or 'true' (see below) as qualifiers (De Jong *et al.* 1995); this is potentially misleading.) Such transmission has typically been assumed for infections, like cowpox, transmitted directly by 'homogeneous mixing' (i.e. not, for example, by sexual transmission). Here, the first two transmission terms in the model above would, for new bank vole infections, take the form $\beta'_{VV}S_V(t)I_V(t)$ and $\beta'_{MV}S_V(t)I_M(t)$, where $S(t)$ is the average number of susceptible, uninfected individuals over the period $(t, t+1)$, $I(t)$ is the average number of infectious individuals over that period, the subscripts V and M refer to bank voles and wood mice, respectively, and β'_{VV} and β'_{MV} are within- and between-species transmission coefficients (Holt & Pickering 1985; Begon & Bowers 1995; Greenman & Hudson 1997). Corresponding terms are readily deduced for new wood mouse infections.

The alternative is 'frequency-dependent' transmission (also called 'true mass action' or 'proportionate mixing'), where susceptible hosts are assumed to make a fixed number of contacts with other hosts, independent of the size of the population, such that the corresponding transmission terms are $\beta_{VV}S_V(t)I_V(t)/N_V(t)$ and $\beta_{MV}S_V(t)I_M(t)/N_M(t)$, where $N(t)$ refers to the average total population size over the period $(t, t+1)$, and the prime has been deleted from the transmission coefficients to indicate that they differ between the two modes of transmission: in frequency-dependent transmission, the coefficients are dimensionless, whereas in density-dependent transmission they are of the form $(\text{numbers})^{-1}$. Frequency-dependent transmission has mostly been associated with sexually transmitted diseases but has recently been suggested as having more widespread relevance (De Jong *et al.* 1995).

In seeking to understand cowpox virus dynamics, we require the most parsimonious form of our model with the greatest explanatory power (that is, the most appropriate terms in each of the brackets), placing particular emphasis on consistency between the populations in attributing biological significance to results.

(b) *Data*

The data reported here were obtained from two field sites in north-west England: Manor Wood and Rake Hey. Both are 1 ha plots in much larger areas of mixed woodland, supporting large populations of bank voles and wood mice plus the occasional field vole. Each was sampled every four weeks for more than three years from March–April 1995. When first captured all animals were given an electronic tag that allowed their individual recognition on recapture. At each sample, blood was taken from the tip of the tail, which allowed the detection of antibodies to cowpox virus. Hence, each individual at each sample could be characterized as either antibody-negative ('seronegative', denoted by '−'), seropositive (denoted by '+'), or not caught in that sample (denoted by '0'), and individuals were represented in the data set by a sequence of such symbols over time. Zeros both preceded and followed by a '−' or a '+', were converted to a '−' or a '+', respectively.

We define a 'seroconverter' as either (i) a recaptured seropositive animal which was seronegative in the previous sample, or (ii) a seropositive animal caught for the first time, which is young (low body weight) and therefore likely to have seroconverted in the previous six weeks, rather than being an adult immigrant that may have seroconverted at any time in the past. As explained fully elsewhere (Begon *et al.* 1998), the changing numbers of seroconverters in the populations can be interpreted in the light of the observation that infected animals remain infected (and therefore, to some degree, infectious) for approximately four weeks and seroconversion occurs approximately halfway through this period. This allowed the number of new infections, $I(t, t+1)$, the average number of susceptible hosts, $S(t)$, and the average number of infectious hosts, $I(t)$, to be estimated for both species in both populations for each inter-sample period.

3. RESULTS

The general patterns of disease dynamics—the numbers of susceptible and infectious individuals—are

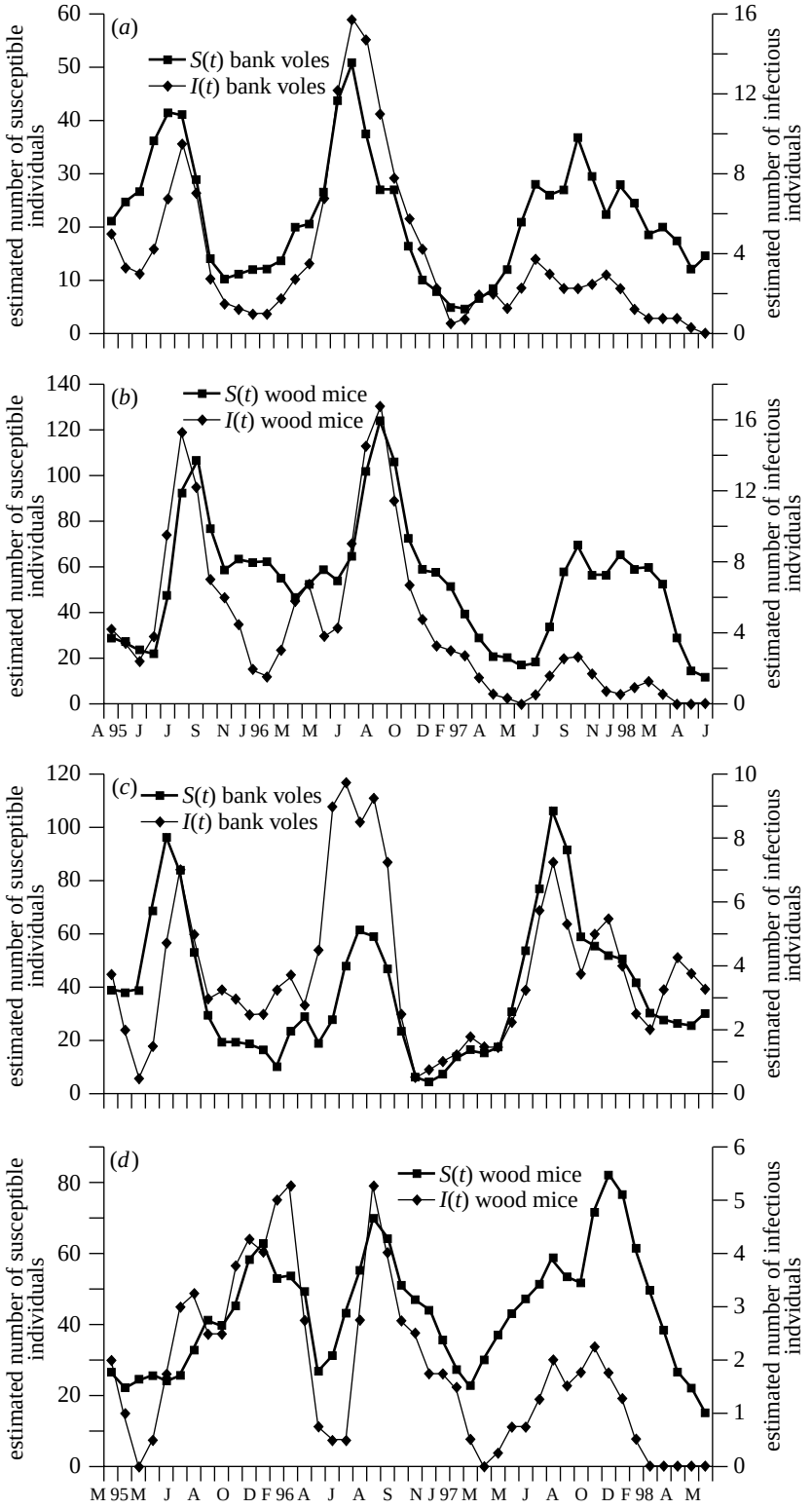

Figure 1. Host–pathogen dynamics of the cowpox virus in bank voles and wood mice, as indicated by time-series of the numbers of susceptible and infectious hosts. (*a*) Bank voles at Rake Hey; (*b*) wood mice at Rake Hey; (*c*) bank voles at Manor Wood; (*d*) wood mice at Manor Wood.

shown for both species in both populations in figure 1. The picture, superficially at least, is of these two closely coexisting host species exhibiting broadly parallel patterns of dynamics. The peaks of susceptible and infectious individuals coincide, each year, with the peak period of breeding from late summer to early winter, although the wood mouse peak in Manor Wood in the winter of 1995–1996 occurred substantially after the bank vole peak.

Turning to the analytical framework, we consider first whether density- or frequency-dependent transmission has greater explanatory power for the dynamics of

Table 1. *Parameter estimates (obtained by generalized linear model analysis) for the transmission dynamics of cowpox virus in bank voles and wood mice at two sites*

(Those for $\beta' SI$ and $\beta SI/N$ refer to the transmission coefficients ($\pm$s.e.) for density- and frequency-dependent transmission, respectively, when each species is considered in isolation; those in the succeeding columns refer to the coefficients and the intercepts ($\pm$s.e.) when transmission other than from conspecifics is assumed (encapsulated in the intercept). 'dev' in each case refers to the residual deviances in the analyses (with residual degrees of freedom as a subscript), which may be used to compare different models within a row. *F*-values refer to a comparison with the fitting of a simple mean and can therefore only be calculated when an intercept is assumed and an additional degree of freedom used.)

		transmission dynamics			
site	species	$\beta' SI$	$\beta' SI$ + intercept	$\beta SI/N$	$\beta SI/N$ + intercept
Rake Hey	bank vole	**0.033 ± 0.003**	**0.026 ± 0.003**	**1.49 ± 0.12**	**1.36 ± 0.15**
		$dev_{41} = 36.0$	**0.89 ± 0.26**	$dev_{41} = 19.9$	**0.35 ± 0.26**
			$dev_{40} = 18.1$		$dev_{40} = 17.4$
			$F = 271.6$		$F = 284.1$
			$p < 0.01$		$p < 0.01$
	wood mouse	**0.013 ± 0.001**	**0.010 ± 0.001**	**1.28 ± 0.10**	**1.29 ± 0.12**
		$dev_{38} = 60.6$	**1.11 ± 0.30**	$dev_{38} = 18.7$	**−0.02 ± 0.25**
			$dev_{37} = 44.1$		$dev_{37} = 18.7$
			$F = 118.8$		$F = 332.4$
			$p < 0.01$		$p < 0.01$
Manor Wood	bank vole	**0.021 ± 0.002**	**0.012 ± 0.002**	**1.29 ± 0.10**	**1.12 ± 0.14**
		$dev_{43} = 71.2$	**1.66 ± 0.33**	$dev_{43} = 17.4$	**0.48 ± 0.34**
			$dev_{42} = 30.7$		$dev_{42} = 14.3$
			$F = 60.7$		$F = 178.6$
			$p < 0.01$		$p < 0.01$
	wood mouse	**0.020 ± 0.002**	**0.016 ± 0.003**	**1.15 ± 0.13**	**1.15 ± 0.19**
		$dev_{36} = 18.9$	**0.36 ± 0.26**	$dev_{36} = 9.5$	**0.00 ± 0.25**
			$dev_{35} = 16.7$		$dev_{35} = 9.5$
			$F = 62.2$		$F = 136.4$
			$p < 0.01$		$p < 0.01$

cowpox virus infection. To do this, the regression of $I(t, t+1)$ on the appropriate within-species transmission term has been determined (through generalized linear models with Poisson errors and an identity link function) for each species in each population considered alone (i.e. conventionally, as a single host–pathogen system). This has been done assuming the relationship to pass through the origin (i.e. the host–pathogen system is self-contained: in the absence of infectious individuals of that species, there can be no new infections), and also with an intercept to take account of between-species transmission (a significant intercept suggesting transmission from 'outside' the single host–pathogen system). (Note that error terms may be temporally correlated within sites, but that this should not present a serious problem as the purpose is model fitting rather than hypothesis testing.) In all cases, as measured by the scaled deviance remaining after a model has been fitted (table 1), frequency-dependent transmission ($\beta SI/N$) is clearly superior to density-dependent transmission as a descriptor of the transmission dynamics.

The analysis may now be extended to include both within- and between-species transmission (table 2). Frequency-dependent transmission has been assumed (but see below), and the multiple regression of $I(t, t+1)$ on the two transmission terms has been determined as before, both assuming the relationship to pass through the origin and with an intercept to take account of transmission from 'elsewhere'. For wood mice, there is clearly no need to take account of transmission 'from elsewhere' (table 2). Moreover, including vole-to-mouse transmission adds either negligibly (Manor Wood) or very little (Rake Hey) to the explanatory power of the model: the rate of transmission from bank voles to wood mice was apparently extremely low (0.0003 ± 0.06 and -0.03 ± 0.09, compared to 1.14 ± 0.17 and 1.33 ± 0.19 ($\pm$s.e.) for within-wood-mouse transmission).

For bank voles, too, between-species transmission rates were extremely low compared to those within the species (-0.13 ± 0.24 and -0.03 ± 0.36, compared to 1.19 ± 0.19 and 1.37 ± 0.26 ($\pm$s.e.)), and their inclusion adds little to the explanatory power of the model for either population. However, in this case, models for both populations are improved significantly by the inclusion of an intercept, suggesting strongly that there were more new infections in bank voles than could be accounted for by transmission either from infectious conspecifics or infectious wood mice. (For both species, results of similar or less explanatory power were obtained assuming density-dependent transmission between species.)

The four optimal regression models in table 2 (two species in both of two populations) capture the overall pictures of cowpox virus transmission in each case. Examining the residuals around each regression may now reveal whether there were differences in transmission rates between the three years of the time-series, or consistent seasonal differences in transmission rates across years. Analysis of variance of the residuals was therefore carried out in each case, with 'year' and 'sample' (time within year) as factors. (In view of the non-independence

Table 2. *Parameter estimates (obtained by generalized linear model analysis) for the transmission dynamics of the cowpox virus within and between species in bank voles and wood mice at two sites, assuming frequency-dependent transmission (see table 1)*

(Estimates in the first data column refer to within- and between-species transmission coefficients (s.e.) when the two species are considered in isolation; those in the next column refer to the coefficients and the intercepts (s.e.) when transmission other than from these species is assumed (encapsulated in the intercept). 'dev' in each case refers to the residual deviances in the analyses (with residual degrees of freedom as a subscript), which may be used to compare different models within a row; values in brackets refer to corresponding values for within-species transmission alone (table 1). *F*-values refer to a comparison of models with and without an intercept.)

		transmission dynamics	
site	species (host 1)	$\beta_{11}S_1I_1/N_1 + \beta_{21}S_1I_2/N_2$	$\beta_{11}S_1I_1/N_1 + \beta_{21}S_1I_2/N_2$ + intercept
Rake Hey	bank vole	$\beta_{11}S_1I_1/N_1$: **1.49 ± 0.24** $\beta_{21}S_1I_2/N_2$: **0.008 ± 0.36** $\text{dev}_{40} = 19.9$ (19.9)	$\beta_{11}S_1I_1/N_1$: **1.37 ± 0.26** $\beta_{21}S_1I_2/N_2$: **−0.03 ± 0.36** intercept: **0.35 ± 0.26** $\text{dev}_{39} = 17.3$ (17.4) $F = 5.9$; $p < 0.05$
	wood mouse	$\beta_{11}S_1I_1/N_1$: **1.33 ± 0.19** $\beta_{21}S_1I_2/N_2$: **−0.03 ± 0.09** $\text{dev}_{37} = 18.6$ (18.7)	$\beta_{11}S_1I_1/N_1$: **1.33 ± 0.19** $\beta_{21}S_1I_2/N_2$: **−0.03 ± 0.11** intercept: **0.03 ± 0.30** $\text{dev}_{36} = 18.6$ (18.7) $F = 0.01$; n.s.
Manor Wood	bank vole	$\beta_{11}S_1I_1/N_1$: **1.35 ± 0.16** $\beta_{21}S_1I_2/N_2$: **−0.12 − 0.24** $\text{dev}_{42} = 17.1$ (17.4)	$\beta_{11}S_1I_1/N_1$: **1.19 ± 0.19** $\beta_{21}S_1I_2/N_2$: **−0.13 ± 0.24** intercept: **0.48 ± 0.34** $\text{dev}_{41} = 14.0$ (14.3) $F = 9.1$; $p < 0.01$
	wood mouse	$\beta_{11}S_1I_1/N_1$: **1.14 ± 0.17** $\beta_{21}S_1I_2/N_2$: **0.0003 ± 0.06** $\text{dev}_{35} = 9.5$ (9.5)	$\beta_{11}S_1I_1/N_1$: **1.14 ± 0.18** $\beta_{21}S_1I_2/N_2$: **0.0002 ± 0.06** intercept: **0.00 ± 0.26** $\text{dev}_{34} = 9.5$ (9.5) $F = 0.02$; n.s.

of errors mentioned above, *p*-values should be treated cautiously, as a guide only.) For bank voles, the only significant effect was that of 'year' at Rake Hey ($F_{2,24} = 4.86$; $p \approx 0.03$). This was the result of the transmission rate being higher towards the middle of the series than at either end (figure 2*a*). For wood mice, on the other hand, 'sample' had a significant effect at Manor Wood ($F_{12,24} = 2.90$; $p \approx 0.03$) and an effect which came close to significance at Rake Hey ($F_{12,24} = 2.15$; $p \approx 0.10$). In both of these cases this was associated with low rates of transmission around September and perhaps April–May, and high rates around June–July (figure 2*b*,*c*).

4. DISCUSSION

Within the confines of this study, these results indicate that the transmission efficiency of the cowpox virus is similar overall within wood mouse and bank vole populations. However, for both species it appears to be higher in the Rake Hey than in the Manor Wood population, which is most likely to be the result of habitat differences promoting differences in contact rates (a suggestion currently under investigation). Also, while wood mice at both sites are apparently unaffected by transmission of the cowpox virus from any other species, bank voles at both sites, although unaffected by transmission from wood mice, appear to become infected not solely through contact with conspecifics. The intercept values (table 2) suggest that by this route there is roughly one new infection in a population every ten weeks, on average. One possible source is field voles. These were too rare in traps for an analysis of dynamics, but were always seropositive for the cowpox virus when captured, and bank voles and field voles, of the three species present, are the pair most likely to interact behaviourally (Corbet & Harris 1996).

More generally, these results call into serious question the assumption that susceptible and infectious hosts mix at random and hence that transmission of the cowpox virus is 'density dependent'. This is made conventionally both in theoretical studies of non-sexually transmitted diseases, and in the rare studies of infection in wildlife (Anderson & May 1992; Grenfell & Dobson 1995). Here, by contrast, the analysis of each species in isolation (table 1) indicates that frequency-dependent transmission is a clearly superior descriptor (though does not of course indicate that transmission *is*, simply, frequency dependent); while the analysis of the species together indicates that between-species transmission is rare (table 2), in spite of them occupying not only the same general habitat but often, for example, sharing burrows. Recent results for farm animals (Moerman *et al.* 1993; De Jong & Kimman 1994; Bouma *et al.* 1995; De Jong *et al.* 1995) have cast doubt on the conventional assumption of density dependence, but the behaviour of such animals is severely constrained by human structuring of their environment. Frequency-dependent transmission has also been suggested as a likely mode of transmission in populations of domestic cats (Courchamp *et al.* 1995; Fromont *et al.* 1997). The present results for free-living wildlife populations therefore go further in suggesting that, generally,

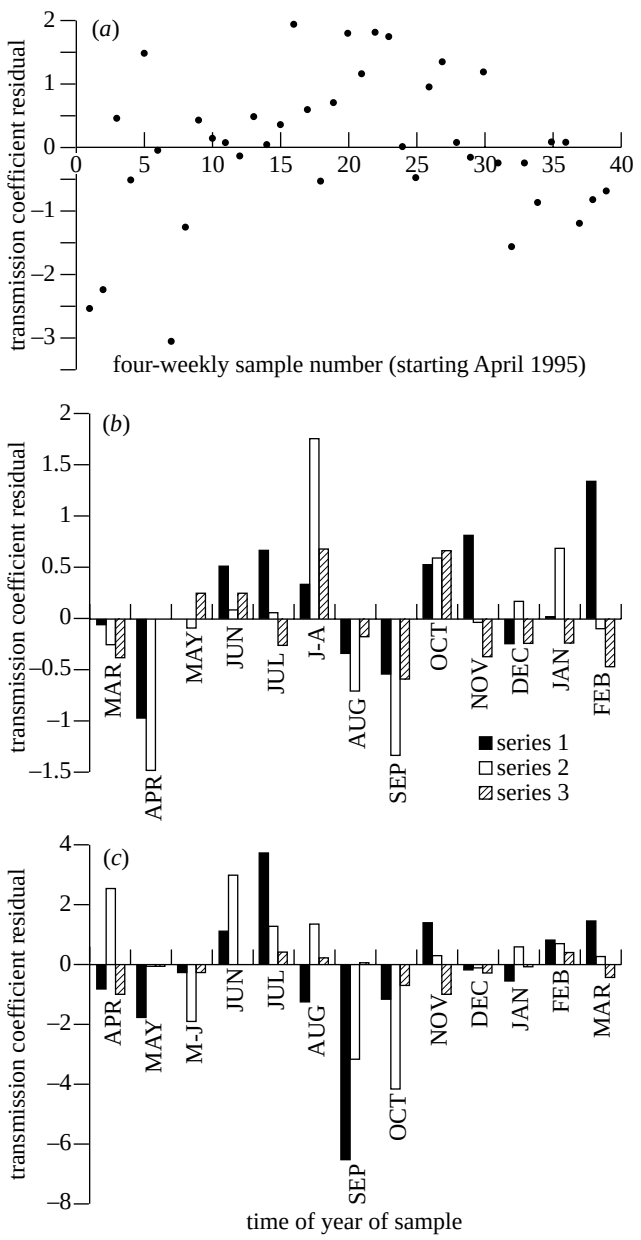

Figure 2. The distribution of transmission coefficient residuals where analysis of variance revealed a significant or near-significant effect. (*a*) Variation over the whole trapping period for bank voles at Rake Hey. (*b*) Seasonal variation for wood mice at Manor Wood. (*c*) Seasonal variation for wood mice at Rake Hey. (Series 1, 2 and 3 refer to the three years of the study.)

random mixing may have been too readily assumed as a basis for transmission dynamics, and that the dynamics of many other non-sexually transmitted diseases may reflect detailed patterns and frequencies of contact between hosts, which may be independent of overall density. In brief, many diseases that are not sexually transmitted may nonetheless be socially transmitted, with essentially the same transmission dynamics.

Furthermore, while a number of modelling studies have examined host–host–pathogen dynamics and their dependence on both within- and between-species transmission coefficients (Holt & Pickering 1985; Begon & Bowers 1995; Bowers & Turner 1997; Greenman & Hudson 1997), the present estimates of coefficients are the first to have been made from an analysis of field data. One of the insights from such models concerns the manner in which host species may be combined as a viable resource for support of a pathogen, in the sense of exceeding a critical threshold together when neither of them could support the pathogen alone. Understanding this combining ability is a particularly pressing need for systems in which wildlife populations act as reservoirs of infections that may also affect man or domestic or endangered species. To take just one example, *C. glareolus* is the main reservoir for Puumula virus (a hantavirus) in Sweden and elsewhere, where Puumula virus causes nephropathia epidemica in humans (annual incidence reaching 20 per 100 000 in some areas), but the virus also circulates in several other rodent species of lower density and with lower antibody prevalence (Niklasson *et al.* 1995). If the various species are effectively independent reservoirs, then research effort can focus on *C. glareolus*, and the remaining species more safely be ignored; whereas if the species represent a combined reservoir, then all should be considered together.

The present results indicate that for the cowpox virus at least, bank voles and wood mice do not 'combine' to any significant extent: the between-species coefficients are too low. Each species acts as an effectively independent reservoir: whether or not bank voles act as a reservoir for the cowpox virus is independent of wood mouse numbers, and similarly the other way round. Moreover, the more general message—that the importance of contact structure in wildlife disease transmission has been underestimated, and random mixing too readily assumed—suggests that similar conclusions may be appropriate for many other infections, zoonotic and otherwise.

Host–host–pathogen models have also helped raise the profile of an ecological force that has received much recent attention called 'apparent competition'—an interaction between two 'prey' (in this case host) species, in which both suffer as a result of their shared interaction with a common predator or pathogen (Holt & Lawton 1994; Bonsall & Hassell 1997; Hudson & Greenman 1998). Here, though, while the potential for apparent competition between bank voles and wood mice mediated by the cowpox virus undoubtedly exists, since the virus depresses the birth rate of both host species (Feore *et al.* 1997), it is likely to be insignificant in practice because the pathogen is so rarely transmitted from one species to the other. This raises the intriguing possibility that a mature assessment of apparent competition may be reminiscent of that often reached for conventional interspecific competition for resources (Begon *et al.* 1996). That is, it is a process of clear potential importance as evidenced by the results of theory and of laboratory experiments, but one which may not always display that full potential in practice, in the field, especially for taxa where 'transmission' is through social interaction (here, directly transmitted pathogens).

The year-to-year and seasonal variations in transmission rates suggested by the analysis of residuals are difficult to interpret with confidence, but do emphasize the potential of this type of analysis for pinpointing fertile areas for the further study of transmission dynamics. The increased transmission rate in bank voles in the second year at Rake Hey (figure 2*a*) was associated with the highest vole densities at this site (figure 1*a*), and may be

taken to support the idea that actual transmission dynamics combine elements of both frequency dependence and density dependence (Begon *et al*. 1998). Against this, bank vole densities were higher at Manor Wood (figure 1*c*) but transmission rates were lower, though it is important to emphasize again that it is the contact rate that is important (which may increase with density but vary from site to site) rather than density *per se*. The seasonal variations in transmission rates among wood mice observed at both sites, with high transmission rates around June–July and low rates around September, and perhaps April–May, may reflect the reported high levels of aggregation in early summer (among overwintered adults and especially juveniles when they first appear in the trappable population), with less aggregation both earlier (prior to the appearance of juveniles) and later (when the territorial adult females especially become less aggregated in their distribution) (Montgomery 1989).

Finally, while this study concerns a zoonotic infection circulating in wildlife populations which is of less medical importance than many that have received much recent publicity (Niklasson *et al*. 1995; Ostfeld 1997; Mills & Childs 1998), it does demonstrate that the dynamics of such infections are amenable to quantification and to being matched against the very largely untested assumptions and predictions of theoretical models.

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