The effects of cowpox virus on survival in natural rodent populations: increases and decreases

SANDRA TELFER*‡, MALCOLM BENNETT‡, KEVIN BOWN‡, RACHEL CAVANAGH*‡, LAURENT CRESPIN†, SARAH HAZEL*‡, TREVOR JONES*‡ and MICHAEL BEGON*

*School of Biological Sciences, Nicholson Building, The University of Liverpool, Liverpool L69 3BX, UK; ‡Department of Veterinary Pathology, The University of Liverpool L69 3BX, UK; and †Centre for Ecology and Hydrology Banchory, Hill of Brathens, Banchory AB31 4BW, UK

Summary

1. The effect of cowpox virus on survival in two rodent hosts was investigated using nearly 4 years of longitudinal data from two sites.
2. We investigated whether an individual's probability of infection influenced the probability of surviving the next month. We also investigated the effect at the population level, examining whether, in addition to seasonal effects, changes in cowpox prevalence explained further temporal variation in survival rates.
3. In bank voles, but not wood mice, individuals with high probabilities of infection survived better than uninfected animals.
4. At the level of the population, the effect of infection on survival varied through the year in both species. Survival rates in late summer increased with cowpox prevalence, whilst survival rates in winter decreased with cowpox prevalence.
5. We discuss why parasites such as cowpox virus may increase or decrease host survival and why the effect may depend on the time of year.

Key-words: Apodemus sylvaticus, capture–mark–recapture, Clethrionomys glareolus, endemic infection, pathogen.


Introduction

There is now increasing interest in the potential effects of parasites on the population dynamics of their hosts (Grenfell & Dobson 1995). The study of parasites circulating in wildlife is also important because some infections may pose a risk to humans, domestic stock or endangered species (Scott 1988). Much progress has been made in theoretical explorations, where models suggest that parasites may indeed regulate the abundance of host populations (Anderson 1995). Most empirical studies of disease in wildlife populations, however, involve epidemics and have been undertaken retrospectively, in cases where extensive mortality has occurred in a population (e.g. Osterhaus et al. 1995). In contrast to epidemic diseases, endemic infections tend to persist in populations for long periods and show relatively little fluctuation in prevalence (Anderson & May 1979). The effects of endemic infection can be considerably more difficult to predict. Parasite fitness is determined largely by transmission success and this may be maximized by increasing or decreasing the pathogenic effect on the host (Combes 1997). Some endemic parasites may not be pathogenic at all or influence a component of host fitness other than survival, such as reproduction (Gulland 1995). However, even apparently non-pathogenic parasites may become important when animal populations are malnourished or stressed or made more susceptible by infection with other pathogens (Scott 1988).

Crucial data from endemic infections in natural populations have recently been forthcoming (e.g. Hudson, Dobson & Newborn 1998; Begon et al. 1999). One element in the elaboration of the importance of parasites is the demonstration that infection may affect host survival (e.g. Hudson, Newborn & Dobson 1992). Although the clearest way of estimating parasite induced mortality is through field-scale experiments (McCallum 2000), the number and range of populations in which biological and practical difficulties can be overcome, and field experiments carried out, is likely to remain...
Effect of cowpox virus on rodent survival

Cowpox virus is found throughout much of Europe and western Asia (Baxby & Bennett 1999). In Great Britain, antibody has been found occasionally in house mice (Mus musculus L.) but the highest seroprevalence is in bank voles, wood mice and field voles (Microtus agrestis L.), and these species are believed to be the reservoir hosts (Chantrey et al. 1999). Although it does not cause obvious clinical signs or increase mortalities in voles or mice in the laboratory (Bennett et al. 1997), experimental studies have demonstrated that cowpox can affect fecundity by delaying the onset of reproduction (Feore et al. 1997). However, there are many reasons why infection may have a greater impact on survival in field conditions.

Recent advances in methodology and the development of appropriate software (e.g. Lebreton et al. 1992; White & Burnham 1999) have enabled survival analyses of capture–mark–recapture (CMR) data to account for variation in recapture rates. Several recent studies of demography in small mammals have used such an approach (e.g. Julliard et al. 1999). However, to our knowledge this is the first such analysis to look at the effects of a pathogen on survival.

Methods

STUDY AREA AND TRAPPING DESIGN

Bank voles and wood mice were trapped within 1 ha plots at two mixed woodland sites (Rake Hey: N53°20′02″ and Manor Wood: N53°19′03″) from April 1995 to December 1998. The plot in Manor Wood is located within a much larger area of woodland, while the plot in Rake Hey is surrounded on two sides by pasture. Each site was trapped approximately monthly for a period of 2–3 days, with traps checked daily on a 10×10 grid with 100 trap stations at 10 m intervals, as described previously (Begon et al. 1998; Begon et al. 1999; Hazel et al. 2000). Individual animals were identified using subcutaneous microchip transponders. On first capture animals were assigned to one of three age categories on the basis of mass. Using monthly growth rates estimated from field data and laboratory information on mass at 2 weeks we calculated mass thresholds for juvenile (j: < 6 weeks), subadult (s: 6–10 weeks) and adult (a: > 10 weeks) age categories (S. Telfer, unpublished data). Thresholds used were as follows: wood mice, April–July j: < 15 g, s:15–18 g, a: > 18 g; wood mouse, August–December j: < 14 g, s:14–17 g, a: > 17 g; bank voles, April–July j: < 14 g, s:14–17 g, a: > 17 g; bank voles, August–December j: < 12 g, s:12–14 g, a: > 14 g.

On first capture within a monthly trapping session, sex and mass were recorded and a 20–40 µl blood sample was taken from the tip of the tail. Antibody to cowpox virus was detected in sera by immunofluorescence (IF) assay (Crouch et al. 1995).

OUTLINE OF MODELLING APPROACH

We carried out the analysis in steps in order to maximize the power for both the general analysis of survival and the investigation of the effect of cowpox (Lebreton et al. 1992). First, we assessed the goodness of fit of the global model, testing the assumptions of independence and homogeneity of individuals within groups. Next we modelled recapture and survival independently and then varied them together to ensure selection of the best base model. Finally, using this base model, we investigated whether cowpox infection affected survival and recapture probabilities. Model notation is based on Lebreton et al. (1992), with the model structure for each parameter type given by subscripts. Interaction terms are denoted by an asterisk; additive effects are denoted by a plus sign. Subscripts used are listed in Table 1.

CAPTURE–MARK–RECAPTURE DATA SET

As the two sites were to be combined and analysed together, both had to have similar time intervals between corresponding trap sessions. Although trapping occurred approximately monthly, one session at each site was missed due to snow. In such months, dummy capture opportunities with recapture rates fixed at zero were inserted (see Viallefont 1996). Additional variation in trapping interval made it necessary to drop three trapping sessions from each site. The resulting capture histories had 46 capture sessions with one intersession time interval of 54 days, one intersession time interval of 81 days and the remaining 43 intersession time intervals lasting an average of 25±2 days (SE 0·22). Survival rates were estimated over 4-week periods.

GOODNESS OF FIT TESTS

Individual capture histories were classified by sex, age, site and position on grid. Age was treated as a group effect and subadults and adults were grouped together as preliminary analyses showed no differences in their recapture and survival rates. Capture histories of individuals caught as both juveniles and adults were split into two independent sections, with the juvenile section coded to indicate that the individual was not released upon last capture (Julliard et al. 1999). Position on the grid was included to investigate a possible ‘edge effect’, which would result in individuals with only part of their home range on the grid having a lower capture probability (Julliard et al. 1999). ‘Edge’ individuals had 75% or more of their captures in the traps on the outer edge of the grid. ‘Edge’ was used as a grouping variable in the
goodness of fit tests, but to simplify model construction, as a binary covariate for model selection (see below).

Our global model involved a Cormack–Jolly Seber model applied to each group (i.e. model \( \phi_{a,sx,stm,seas,year}^{t} \), for model notation see Table 1). Goodness of fit was assessed through tests provided by a modified version (Pradel 1993) of the program \textsc{release} (Burnham et al. 1987). The CJS model was rejected strongly for all groups (see Results), particularly suggesting ‘trap dependence’: the probability of capturing an animal depends on its previous capture history (Pradel 1993). Such an effect is likely to be strongest immediately after a capture. Consequently, we used immediate trap dependency models (Pradel 1993) that allow for recapture estimates on the first occasion following a capture to differ from recapture on subsequent occasions. Although this improved the fit of the global model considerably, the goodness of fit tests were still significant (see Results). Hence we used QAICc for model selection and estimation of the sampling variance of the parameters. QAICc is a measure that provides a compromise between bias and precision when the global model does not fit the data (Anderson, Burnham & White 1994) and incorporates a variance inflation factor \( c \). We estimated \( c \) from the goodness of fit chi-square statistic and its degrees of freedom (\( \chi^2 \) d.f.) (Anderson et al. 1994). Values of \( c \) between 1 and 3 are generally considered acceptable (Anderson & Burnham 1999). Goodness of fit tests are not available for global models that include individual covariates and therefore the global models tested did not include any effect of cowpox infection. As using values of \( c > 1 \) in model selection tends to select against complex models, by using estimates of \( c \) derived for models without any cowpox effect, our tests for a cowpox effect are conservative. Models with differences in QAICc of < 2 were considered similar in their ability to describe the data (Burnham & Anderson 1992). The analysis was carried out in program \textsc{mark} (White & Burnham 1999).

### Table 1. Subscripts used in model notation

<table>
<thead>
<tr>
<th>Subscript</th>
<th>Description</th>
<th>Parameter type</th>
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<tbody>
<tr>
<td>a</td>
<td>Two age classes (juvenile (&lt; 6 weeks); adult (&gt; 6 weeks))</td>
<td>( \phi, p )</td>
</tr>
<tr>
<td>t</td>
<td>Full time-dependence</td>
<td>( \phi, p )</td>
</tr>
<tr>
<td>sx</td>
<td>Sex-effect</td>
<td>( \phi, p )</td>
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<tr>
<td>st</td>
<td>Site-effect</td>
<td>( \phi, p )</td>
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<tr>
<td>mo</td>
<td>Month effect</td>
<td>( \phi, p )</td>
</tr>
<tr>
<td>seas</td>
<td>Season effect (April–July; August–November; December–March)</td>
<td>( \phi, p )</td>
</tr>
<tr>
<td>year</td>
<td>Year effect</td>
<td>( \phi, p )</td>
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<tr>
<td>m</td>
<td>Trap-dependency effect</td>
<td>p</td>
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**Individual covariates**

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<td>n</td>
<td>Binary covariate denoting months with reduced trapping effort</td>
</tr>
<tr>
<td>r</td>
<td>Average rainfall during trapping sessions</td>
</tr>
<tr>
<td>tm</td>
<td>Average temperature during trapping sessions</td>
</tr>
<tr>
<td>cp</td>
<td>Prevalence of cowpox</td>
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</table>

**Time-specific individual covariates**

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<tr>
<td>e</td>
<td>Binary covariate denoting individuals from the edge of the grid</td>
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**Subscripts used in model notation**

<table>
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<th>Subscript</th>
<th>Description</th>
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<td>a</td>
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<td>t</td>
<td>Full time-dependence</td>
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<td>sx</td>
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<td>mo</td>
<td>Month effect</td>
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<tr>
<td>seas</td>
<td>Season effect (April–July; August–November; December–March)</td>
</tr>
<tr>
<td>year</td>
<td>Year effect</td>
</tr>
<tr>
<td>m</td>
<td>Trap-dependency effect</td>
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</table>

**Covariates**

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<th>Description</th>
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</thead>
<tbody>
<tr>
<td>psc</td>
<td>Average probability of infection during time interval after observed seroconversion</td>
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</table>

**Modelling recapture and survival**

We first modelled the effect of trap dependency on recapture and then examined whether recapture rate varied with time, site and age. Preliminary analyses showed no effect of sex on recapture. Consequently, we present only analyses with no sex effect. We then investigated whether the temporal component of the best recapture model could be described adequately by combinations of monthly, seasonal (three seasons: April–July; August–November; December–March), yearly (January–December), climatic or trapping effort effects. In some months, traps were set for less than three nights and we investigated a binary covariate that denoted such months. Weather data were provided by the UK Meteorological Office and were recorded at Ness Gardens weather station, located 6.2 km and 7.3 km south of Manor Wood and Rake Hey, respectively. For each trapping session we calculated the average temperature and average rainfall over the period of trapping. Field experience suggested that these climatic factors might have influenced trappability. Lastly, we examined whether an individual’s location on the grid (edge or centre) influenced recapture rates.

Once an adequate model of recapture had been obtained, we modelled survival. Again, we first modelled survival in terms of time, site, sex and age and secondly sought to simplify the temporal component of the model using month, season and year effects.

**Investigating the effect of cowpox on survival at the individual level**

As cowpox virus is most likely to affect survival during the period of infection and infection of an individual is only detected upon seroconversion, we modelled the effect of cowpox using a time-specific individual covariate that allowed survival immediately after observed seroconversion to depend on an individual’s average
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The raw data for cowpox virus infection were in the form of animals being seropositive, seronegative or not caught at each sampling period. From this we could estimate the probability that an individual was infected in each sample and then the average probability of being infected during the following time period (Fig. 1a). Some individuals may be recorded as seropositive at their first capture. For such individuals the estimated average probability of being infected depended on the age at first capture (Fig. 1b).

Results

INVESTIGATING THE EFFECT OF COWPOX ON SURVIVAL AT THE POPULATION LEVEL

For reasons examined in the discussion, investigating the effect of a pathogen on survival at the individual level using longitudinal data of the kind presented, here can underestimate any negative effect. We therefore also investigated whether cowpox prevalence explained temporal variation in survival rates, in addition to monthly and yearly effects. To calculate cowpox prevalence we summed the probabilities of infection across all individuals and divided by population size, as estimated by the minimum number alive method (Krebs 1966).

At both the individual and population level we examined whether the effect of cowpox varied between groups (age, sex, site) or between months or seasons by including up to two-way interactions.

SUMMARY OF DATA

Between April 1995 and December 1998 there were substantially more wood mice trapped at Rake Hey than bank voles: 884 wood mice (502 males, 382 females) and 427 bank voles (250 males, 177 females). At Manor Wood numbers of the two species were similar: 753 wood mice (430 males, 323 females) and 752 bank voles (390 males, 362 females). Cowpox was more prevalent at Rake Hey than Manor Wood and more prevalent in bank voles than in wood mice. At Rake Hey 39% of bank voles (166/427) and 21% of wood mice (183/884) tested seropositive at least once. In comparison, 23% of...
bank voles (175/752) and 10% of wood mice (78/753) at Manor Wood tested seropositive. Overall, out of 163 bank voles that seroconverted after initial capture, 24 had one missing sample prior to the time of observed seroconversion (see Fig. 1). A further 14 had more than one missing sample. Similarly, out of 161 wood mice that seroconverted after initial capture, 15 had one missing sample at the time of seroconversion and 15 had more than one missing sample.

Figure 2 shows temporal changes in the rodent population sizes and cowpox virus prevalence at the two sites. The annual peak population size of bank voles ranged from 30 in August 1998 at Rake Hey to 126 in September 1997 at Manor Wood. Variation in the annual peak population size of wood mice ranged from 62 in November 1998 at Manor Wood to 167 in October 1996. Peaks in the number of infected individuals tended to correspond with peaks in rodent population size. The proportion of individuals infected with cowpox virus also tended to peak in the autumn, although this is more pronounced at Rake Hey than Manor Wood (Fig. 2). In wood mice at both sites, infection was most prevalent in 1995 and 1996 and almost disappeared in 1998. In bank voles, the prevalence of cowpox was highest in 1996. The proportion of individuals infected with cowpox peaked at 15% and 17% for wood mice and bank voles, respectively.

GOODNESS OF FIT TESTS

The release goodness of fit test of the global model without the inclusion of trap dependence ($\phi_{at^*at^*ct^*}$, $p_{at^*at^*ct^*}$) was highly significant for both species (wood mice: $\chi^2_{300} = 906.7, P < 0.0001$; bank voles: $\chi^2_{300} = 822.0, P < 0.0001$). Much of the lack of fit was found in test component 2.Ct (wood mice: $\chi^2_{124} = 346.2, P < 0.0001$; bank voles: $\chi^2_{118} = 241.7, P < 0.0001$), which can be interpreted as evidence for trap dependence. Although global models that included trap dependency ($\phi_{at^*at^*ct^*}, p_{at^*at^*ct^*}$) fitted better, goodness of fit tests still showed significant deviation from the assumption that the global model adequately fitted the data (wood mice: $\chi^2_{376} = 560.4, P < 0.0001$; bank voles: $\chi^2_{395} = 580.2, P < 0.0001$). The variance inflation factors ($c$) were estimated as 1.49 for wood mice and 1.51 for bank voles. These values are well within the range allowable from CMR data (Anderson et al. 1994).

MODEL SELECTION

A simple additive model of trap dependency, with a constant effect across all groups, was adequate for both species: individuals caught in one month were more likely to be caught in the next month than missed individuals. Table 2 presents the best models in each of the stages of modelling recapture. The best model structures for recapture were similar for both wood mice and bank voles, having an interaction between site and year and an interaction between season and year. However, in wood mice a model with a simple additive effect of season was similar in QAICc (difference $< 2$; Table 2). Increased trapping effort also increased recapture rates in both species. In addition, bank voles were more trappable during relatively warm spells. In both species individuals living at the edge of the grid had lower recapture rates.
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Using the best model for recapture probabilities we then modelled survival probabilities (Table 3). Again, the best models were broadly similar between the two species. In wood mice, adults of both sexes and juvenile males (less than 10 weeks old) survived better than juvenile females. In bank voles, juveniles of both sexes had lower survival probabilities than adults. Survival rates in both species varied monthly but there were no significant differences between years. Once the temporal variation had been simplified to a monthly effect, there was evidence of a site effect in wood mice, with individuals from Rake Hey surviving better than individuals from Manor Wood.

Additional modelling where survival and recapture were varied together did not reveal any further models with lower QAICc values for bank voles. However, for wood mice, inclusion of an interaction between season and year in the recapture model resulted in a lower QAICc (Table 4) and consequently this model was used as a base for investigating the effect of cowpox on survival (Table 4). Using these base models, recapture rates in months immediately following a capture ranged from 0·23 to 0·99 and from 0·41 to 0·95 for bank voles and wood mice, respectively. The probability of catching an individual that had not been caught the previous month ranged from 0·07 to 0·96 for bank voles and 0·14–0·82 for wood mice. Estimates of survival rates are shown in Fig. 3.

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EFFECT OF COWPOX ON SURVIVAL AT THE INDIVIDUAL LEVEL

In wood mice, the model including an additive effect of the average probability of being infected was marginally better than the model without such an effect.
In bank voles, the model with a simple additive effect of cowpox prevalence had the lowest QAICc (Table 4). Again, cowpox infection appeared to increase survival, as months with higher prevalence had higher survival rates (parameter estimate for effect of cowpox prevalence (cp) = 8.49; 95% CI 4.55–12.42). For example, survival rates for adults in October ranged from 0.62 (95% CI 0.52–0.71) in Manor Wood in 1998, when the estimated prevalence of cowpox was 0.015, to 0.82 (95% CI 0.75–0.88) in Rake Hey in 1996, when the estimated prevalence of cowpox was 0.14.

In wood mice, the model with an interaction between month and cowpox prevalence had the lowest QAICc (Table 4). Effect of cowpox on survival at the population level

In bank voles, the model with a simple additive effect of cowpox prevalence had the lowest QAICc (Table 4). Again, cowpox infection appeared to increase survival, as months with higher prevalence had higher survival rates (parameter estimate for effect of cowpox prevalence (cp) = 8.49; 95% CI 4.55–12.42). For example, survival rates for adults in October ranged from 0.62 (95% CI 0.52–0.71) in Manor Wood in 1998, when the estimated prevalence of cowpox was 0.015, to 0.82 (95% CI 0.75–0.88) in Rake Hey in 1996, when the estimated prevalence of cowpox was 0.14.

In wood mice, the model with an interaction between month and cowpox prevalence had the lowest QAICc (difference from base model of 6·2). Examination of the parameter estimates indicated that in general the effect of cowpox infection in spring and summer (April–September) was positive, while in winter (October–March) the effect was negative (Fig. 4a).

### Table 4. Effect of cowpox on survival and recapture. The effect of cowpox on survival was investigated at both the individual and population level (see Methods). The base model is the best model selected from initial modelling of survival and recapture. Interactions between month and cowpox prevalence are shown. No other models with interactions had lower QAICc values than the simple additive model. np = number of parameters. The most parsimonious are given in bold

<table>
<thead>
<tr>
<th>Survival</th>
<th>Recapture</th>
<th>QAICc</th>
<th>np</th>
<th>Deviance</th>
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<tr>
<td>(A) Bank voles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Base model</td>
<td>a + mo</td>
<td>m + (st* year) + (seas* year) + n + tm + e</td>
<td>4107.1</td>
<td>34</td>
</tr>
<tr>
<td>(2) Investigating effect of cowpox on survival at individual level</td>
<td>a + mo + psc</td>
<td>m + (st* year) + (seas* year) + n + tm + e</td>
<td>4098.9</td>
<td>35</td>
</tr>
<tr>
<td>(3) Investigating effect of cowpox on survival at population level</td>
<td>a + mo + cp</td>
<td>m + (st* year) + (seas* year) + n + tm + e</td>
<td>4089.5</td>
<td>35</td>
</tr>
<tr>
<td>(4) Investigating effect of cowpox on recapture at population level</td>
<td>a + (mo*cp)</td>
<td>m + (st* year) + (seas* year) + n + tm + e + cp</td>
<td>4109.0</td>
<td>35</td>
</tr>
<tr>
<td>(B) Wood mice</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Base model</td>
<td>a*sx + st + mo</td>
<td>m + (st* year) + (seas* year) + n + e</td>
<td>5786.3</td>
<td>36</td>
</tr>
<tr>
<td>(2) Investigating effect of cowpox on survival at individual level</td>
<td>a*sx + st + mo + psc</td>
<td>m + (st* year) + seas* year + n + e</td>
<td>5785.4</td>
<td>37</td>
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<td>(3) Investigating effect of cowpox on survival at population level</td>
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<td>(4) Investigating effect of cowpox on recapture at population level</td>
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<td>5785.68</td>
<td>37</td>
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</table>
Effect of cowpox virus on rodent survival

Although the best model for bank voles did not include an interaction between month and cowpox, for the following reasons we believe there is good evidence that the effect of cowpox on survival varied through the year in bank voles as well as wood mice. As we had no a priori reasons to predict which of the interactions were biologically meaningful, 11 additional parameters had to be included in the month × cowpox model. Consequently, although there is a substantial drop in deviance when the interaction is included (Table 4), the model is highly penalized in terms of QAICc. When the effect of cowpox is allowed to vary with season (i.e. only two additional parameters needed) there is a drop > 2 in the QAICc of the model (QAICc = 4086, np = 37). Thus, there is some evidence that the effect of cowpox on bank vole survival does vary over time. When the parameter estimates for the month × cowpox model are examined, cowpox appears to have a similar effect on bank voles as on wood mice, with little or a negative effect on survival from December to July, but a strong positive effect in August–November (Fig. 4b).

In neither species was there evidence of interaction between cowpox prevalence and sex, site or age.

Recapture rates did not vary with the prevalence of cowpox in bank voles or wood mice (Table 4).

Discussion

In both species, survival exhibited more within-year (monthly) than between-year variation. Consistent with other studies (e.g. Flowerdew 1985) both bank voles and wood mice had high survival rates during winter months and low survival in spring. Low apparent survival in spring may be related to increased dispersal prior to breeding (Gliwicz 1988). In addition, cowpox infection influenced survival, and the effect of cowpox appeared to depend on the time of year.

EFFECT OF COWPOX ON SURVIVAL

While there was no evidence of an effect of infection on survival in wood mice when the analysis was conducted at the individual level, at the population level summer survival rates increased and winter survival rates decreased with increased cowpox prevalence. In bank voles, examination of the effect at both the individual and population level indicated that, on average, infection increased survival. At the population level there was evidence that the effect of cowpox on bank voles changed through the year. The pattern observed was similar to that observed in wood mice, with the strongest positive effect in late summer and autumn and no effect or a slight negative effect in winter.

SPECIES DIFFERENCES: STATISTICAL ARTEFACT?

These results may reflect interesting differences in the way infection affects survival of the two host species. However, the power to detect the effects of cowpox infection on survival depended on the species and on the level at which the analysis was conducted. The power of the analysis at the individual level depended on the number of individuals that became infected and was therefore higher in bank voles than wood mice. Thus the lack of an effect at the individual level in the wood mice may be a result of lack of power. In contrast, in the analysis at the population level, the power to detect an interaction between month and cowpox prevalence depends on the number of recapture and is therefore higher in wood mice than in bank voles. In addition, the timescale of cowpox infection means that any negative effect on survival will be underestimated (see below). This, compounded with low power, may have prevented us detecting an interaction between prevalence and month in the bank voles. In particular it could explain the lack of a negative effect on survival in winter in bank voles.

A further statistical issue to consider is the use of overdispersion factors to account for lack of fit in the global models. In both species we suspect part of the lack of fit may have been due to non-random heterogeneity in recapture rates and such structural failure in models can result in biased survival rates (Lebreton et al. 1992). Unfortunately there is no accepted method of dealing with such problems. As we found similar effects of cowpox infection at both the individual and population levels, we are confident this did not influence our main conclusions.
For the above reasons, we believe it is appropriate to assume that infection affects both species similarly. In what follows, we discuss why any negative effect on survival is likely to be underestimated. We then address why cowpox infection may increase survival, at least in some months, and discuss why the effect may change through the year.

UNDERESTIMATING PATHogen INDUCED MORTALITY FROM LONgITudINAL DATA

Data from any longitudinal study inevitably come in the form of a sequence of point samples, rather than as a continuous monitoring of individuals’ infection status. At best, therefore, one can deduce only that an individual must have become infected at some (unknown) time between two sampling-points. The fundamental difficulty with analysing these types of data is that the capture history of hosts that die soon after becoming infected terminates in an ‘uninfected’ state. Any negative effect of infection on survival is therefore unavoidably underestimated.

Underestimation of the effect of infection is likely to be most severe for acute infections, such as cowpox, that typically only persist for a period shorter than that between sampling points (Fig. 1). A further challenge arises when infections are detected on the basis of antibody as the host is inevitably seronegative in the early stages of infection and their infection status therefore remains undetected. When, as in cowpox, both these features are present, a potentially large proportion of those dying from the infection may not be detected as having done so. Thus, observed seroconverters may consist of individuals that have survived the infection, while other less fit individuals that become infected may die prior to seroconverting. This alone could lead to infected individuals that have survived to seroconversion appearing to survive better than ‘negative’ individuals.

In such cases, looking for correlations between pathogen prevalence and survival rates at the population level may prove more informative. If a large number of infected individuals are dying before seroconversion, average survival rates should be lower when cowpox prevalence is high. However, in the present study cowpox appeared again to increase summer survival at the population level. We can therefore conclude, at least in summer, that there are not large numbers of infected animals dying before seroconversion, and this undermines the suggestion that the positive effect of cowpox on survival is artefactual.

WHY DOES COWPOX INCREASE HOST SURVIVAL?

An increase in survival of infected hosts has previously been shown in an experimental study of an insect–microparasite association (Hurd, Warr & Polwart 2001). However, to our knowledge this is the first demonstration of such an effect in a field study of a vertebrate–microparasite relationship.

One possibility is that the observed association between cowpox virus infection and increased survival in the summer occurs, not because infected individuals survive better, but because individuals that enjoy higher survival are more likely to become infected. We tested this by examining whether individuals that were infected with cowpox also survived better in the time period immediately after recovering from the infection. There was no evidence of this, and therefore we are confident the increase in survival is a consequence of cowpox infection.

There are (at least) three alternative explanations that could produce a positive effect, all involving an effect of infection on life history strategy or behaviour. Changes in the behaviour of parasitized animals are widespread (e.g. Poulin 1995), and may arise as a result of the pathogenesis of the infection, selection on the host to minimize fitness costs, or selection on the parasite to maximize its own fitness (Poulin 1995).

As the analysis looks at the effect of cowpox on apparent survival, a positive effect could result from infection reducing an individuals’ probability of emigrating. Dispersal is often assumed to be costly and dispersers may suffer higher mortality than philopatric individuals (Byrom & Krebs 1999). Consequently, individuals experiencing stress as a result of infection may decide not to disperse. Few studies have investigated whether parasites affect host dispersal decisions. All studies to date involve macroparasites (see Boulainier, McCoy & Sorci 2001 for review) and show either no effect (Jaenike, Benway & Stevens 1995) or an increase in dispersal rates (e.g. Sorci, Massot & Clobert 1994). Cowpox infection appeared to increase survival predominantly in late summer. If cowpox infection did decrease the probability of dispersing one might expect the effect to be most pronounced in April and May, when most dispersal occurs (Gliwicz 1988). However, at least in bank voles, dispersal can also occur in autumn (Gliwicz 1988) and this explanation deserves more detailed investigation.

A second explanation is that cowpox infection changes host behaviour such that exposure to other sources of mortality (e.g. predation) is reduced. Such a change in behaviour may have manifested itself in changes in recapture rates. We found no effect of cowpox prevalence on recapture rates. However, this does not rule out more subtle changes in behaviour. For example, in striped skunks (Mephitis mephitis Schreber) infected with rabies, both the mean rate and distance of travel in a night decreased between the preclinical and clinical periods of infection (Greenwood et al. 1997).

Lastly, infection may trigger a change in reproductive strategy that increases survival. Life history theory predicts that greater reproductive effort may result in reduced life expectancy (Stearns 1992). Consequently, a potential explanation for the observed result is a diversion of resources away from reproduction, perhaps
towards mounting an immune response, and a consequent reduction in reproductive costs. There is mounting empirical evidence of host life-history responses to parasitism (e.g. Hurd et al. 2001). Some parasites may themselves benefit from reductions in reproductive effort, either because the resources available to them may increase (Obreski 1975), or because increased lifespan in the host may increase transmission (Hurd et al. 2001).

Adaptive changes in reproductive effort appear particularly feasible in small mammals, as such species tend to have flexible reproductive strategies and reproduction is known to be costly (Lambin & Yoccoz 2001). Several lines of evidence lend some support to this hypothesis. First, in a previous experimental study, we showed that the infection of young bank voles and wood mice with cowpox virus delayed reproduction by approximately 1 month (Feore et al. 1997). Secondly, at the population level cowpox only has a positive effect on survival in summer when reproduction is occurring. Lastly, excluding individuals first caught as seropositive adults, the average minimum age of individuals at the time of seroconversion is 18 weeks for bank voles and 19 weeks for wood mice, and therefore most individuals will be reproductively active when infected.

As the potential value of current and future reproductive success may differ between the sexes, one might predict a sex-difference in the effect of infection. Some studies have shown such differences (e.g. Hurd et al. 2001). Although to date we have found no sex-differences in the effect of cowpox on demographic parameters, this may be a consequence of lack of power and further work is needed.

**SEASONAL DIFFERENCES IN THE EFFECT OF COWPOX**

If increases in the survival of infected individuals during the summer occur because infected individuals stop reproducing, then the effect of cowpox on winter survival rates may be negative simply because neither infected nor uninfected animals are reproducing. Thus, the patterns observed may be the result of cowpox reducing survival in its own right (the only effect in winter), but also suppressing reproductive effort, and hence increasing survival to an extent that outweighs the negative effect of infection during the reproductive season. Note that, on this interpretation, cowpox virus infection has a negative effect on fitness (reproductive output, combining survival and reproduction) throughout the year.

Alternatively, the effect of a parasite may be contingent on extrinsic factors such as food availability or competition (Minchella & Scott 1991). Nutritional deficiencies are known to alter immunocompetence and increase the risk of infection (Chandra 1997). Individuals infected with cowpox during the summer may be able to compensate for any energetic costs. In winter, mortality of woodland rodents depends on food availability (e.g. Pueck et al. 1993) and nutritional stress may make a compensatory response to infection impossible. Consequently, survival may decrease in winters with high cowpox prevalence. In bumble-bees (Bombus terrestris L.) kept under favourable conditions, infection with trypanosomes caused no mortality. However, when the hosts were starved the infection increased the host mortality rate by 50%, suggestive of condition-dependent virulence on the part of the trypanosome (Brown, Loosli & Schmid-Hempel 2000).

On either interpretation, we have demonstrated an effect of an endemic microparasite infection on survival rates in natural populations of vertebrates. We have also demonstrated that the pattern of the effect is not simple, and is likely to be the result of subtle and changing interactions with other processes—a conclusion that is, we believe, almost certain to apply more generally.

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**References**


