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Preventive Veterinary Medicine 60 (2003) 91–105

PREVENTIVE VETERINARY MEDICINE

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Controlling *Echinococcus multilocularis*—ecological implications of field trials

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Abstract

Two field trials to reduce the prevalence of *Echinococcus multilocularis* in foxes have been conducted in recent years. Although both trials reduced prevalence considerably, they failed to eradicate the parasite in the study region. Following the control trial in northern Germany, prevalence recovered unexpectedly and rapidly, reaching pre-control levels five quarters (15 months) after the end of control. To understand the internal dynamics of the parasite–host system's reaction to control, we developed a spatially explicit simulation model, Echi. The simulation model incorporates the information available concerning fox tapeworm population dynamics.

Using epidemiological parameters to adjust pre-control prevalence, the model predicts the temporal evolution of the prevalence of *E. multilocularis* in controlled foxes without departing from the range of uncertainty of the field data. However, the model does not predict the rapid pre-control recovery observed in the field trial.

The deviation of the model's prediction from field data indicates the involvement of processes not yet taken into account. We modified the model step by step to mimic processes with the potential to cause the rapid post-control recovery of the prevalence of *E. multilocularis* in foxes.

Neither the longevity of tapeworm eggs nor the migratory behaviour of foxes showed any influence on the post-control reaction of the parasite–host system. However, landscape structures leading to a heterogeneous distribution of infected foxes have the potential to alter the system's reaction to control. If infected foxes are concentrated in multiple clusters in the landscape, the model prediction tallied with the range of uncertainty of the field data. Such spatial distribution of infected foxes may be caused by differential abiotic conditions influencing the survival of tapeworm eggs.

The model was found to comply best with field data if the foxes acquire partial immunity by being exposed to the fox tapeworm.

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0167-5877/$ – see front matter
doi:10.1016/S0167-5877(03)00084-9

Both hypotheses explaining the rapid post-control recovery of the prevalence of *E. multilocularis* observed in the fox population were supported by field data.

Both hypotheses have far-reaching consequences for future control trials. The spatial aggregation of infected foxes would enable control efforts to be concentrated on these highly infected areas. However, the acquisition of immunity acts as a buffer to control, necessitating intensified control measures.

Keywords: Echinococcus multilocularis; Simulation model; Wildlife; Parasitic diseases; Management; Control

1. Introduction

The larval form of the small fox tapeworm (*Echinococcus multilocularis*) is considered to be the most dangerous zoonosis in Europe (WHO, 1990). Growing fox populations have increased public awareness of this potential human health risk, increasing pressure on decision-makers (Eckert and Deplazes, 1999; Eckert et al., 2000). In recent years, two field trials in Germany have attempted to control the small fox tapeworm in its natural definitive host, the fox (*Vulpes vulpes*; Romig et al., 2001; Tackmann et al., 2001). Although, both succeeded in considerably diminishing the prevalence of *E. multilocularis* in foxes, it was not completely eradicated. Soon after the end of the trial in northern Germany, the prevalence of *E. multilocularis* in foxes reached the pre-control level (Tackmann, Pers. Commun.). Convincing decision-makers to spend money on tapeworm control will be difficult if intervention only appears to work for as long as the intervention itself lasts. Thus the rapid recovery of *E. multilocularis* prevalence raises the question of whether controlling *E. multilocularis* under field conditions is at all feasible. For improved public health, control strategies are urgently needed that can successfully eradicate the parasite. In order to develop feasible control strategies, understanding the reaction of the parasite–host system to intervention is imperative (Grenfell and Dobson, 1995; Barlow, 1996).

Epidemiological models are often parameterised to fit the equilibrium state of an epidemiological situation. These equilibrium solutions are then extrapolated to estimate the effect of medical interventions such as vaccination, chemotherapy, etc. (e.g. Macdonald, 1957; May and Anderson, 1979; Anderson and May, 1979, 1992; Nokes and Anderson, 1988; Roberts and Aubert, 1995). However, the recent field trials in *Echinococcus* control afford an opportunity to study the small fox tapeworm cycle in a non-equilibrium state. Valuable insights into the temporal dynamics of small fox tapeworm epidemiology can therefore be expected by analysing the field data. A deeper understanding of the underlying dynamics might result in more appropriate estimates of the effectiveness of intervention measures (Thulke, 2000).

If the parasite cannot be locally eradicated, the number of susceptible hosts increases during the control trial owing to previously infected foxes being cured (Mollison, 1995). In this changed epidemiological situation, an increase in the number of infected foxes can be expected until prevalence reaches some epidemic equilibrium determined by epidemiological parameters. However, the indirect life cycle of the small fox tapeworm results in a relatively slow feedback loop between new infections and the transmission of the parasite. Hence, the fast post-control increase indicates the operation of some epidemiological mechanisms not yet taken into account.

Here we use the spatially explicit simulation model "Echi" (Hansen, 2001) to mimic a previously conducted field trial. Starting with the most parsimonious set of assumptions, we compare the model output with field data to explain the unexpected rapid recovery of the prevalence of *E. multilocularis* in the fox population. This paper presents modifications to Echi with the goal of reproducing the fast post-control recovery.

Echi is a spatially explicit, time-discrete simulation model (Hansen, 2001). Each simulation step represents a week. Space is divided into grid cells, each representing the home range of a subpopulation of voles. Foxes are modelled individually. They prey on voles and deposit faeces in randomly selected grid cells within their home ranges. The prevalence of *Echinococcus*-infected voles within a grid cell determines the infection risk for a fox preying in this cell. Capturing an infectious vole leads to the infection of the fox with a random number of worms. Worms perform their ontogenesis in the fox, starting egg production deterministically after a period of time equivalent to the prepatency period of foxes. Likewise, worms die deterministically after reaching the mean lifetime assumed for adult worms in foxes. Eggs shed with the foxes' faeces in randomly chosen grid cells within the foxes' home range are assumed to infect all of the susceptible voles in a grid cell. The vole population dynamics are modelled in the most parsimonious way, assuming a constant mean life expectancy. A proportion of infected voles, equivalent to the inverse duration of the larval development, becomes infectious in each simulation step. In a detailed model description, the set of rules and pseudo-programming code are attached as an appendix to this paper.

Eventually, a set of multiple hypotheses was formulated to explain obvious discrepancies between the model's predictions and empirical data. The four hypotheses represent epidemiological mechanisms that may be responsible for the fast post-control recovery of *E. multilocularis* prevalence. They are deduced from empirical knowledge about the fox tapeworm's ecology.

1.1. Lifecycle of E. multilocularis

Foxes harbour the adult stage of the small fox tapeworm. Adult worms produce eggs at regular intervals (Ishige et al., 1990). Egg packages are shed with the foxes' faeces. Intermediate hosts, mainly small rodents, are infected by the oral uptake of eggs (Eckert, 1996). Foxes, in turn, are infected by preying on infectious intermediate hosts (Eckert, 1996). The infection of both hosts leads to hosts becoming infectious with a time delay (Frank, 1987). Eggs are known to be sensitive to high temperatures and low relative humidity, and lose their infectivity within hours under unfavourable conditions (Veit et al., 1995).

1.2. Field trial

Between April 1996 and June 1997, a control trial was conducted to reduce the prevalence of *E. multilocularis* infection in a focal endemic area of 432 km^2 with a low endemic periphery in Brandenburg, Germany. Foxes were given access to baits each containing 50 mg Praziquantel®. Twenty baits per km^2 were distributed by aircraft during 14 campaigns. The time intervals between consecutive campaigns were 6 weeks in the first year and 12 weeks in the second and third year of the trial. The effects of control measures were monitored

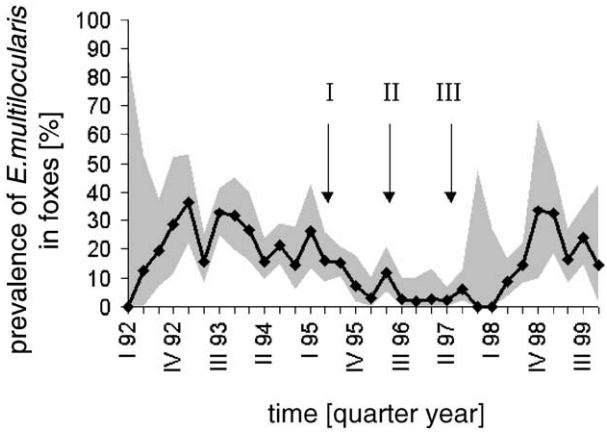

Fig. 1. Prevalence of *E. multilocularis* in foxes. Squares indicate prevalence estimates for quarterly periods, shaded portion indicates 95% confidence interval assuming binomial error distribution. For convenience's sake, quarterly estimates are combined by lines and error ranges are plotted as a continuous variable. With the onset of fox baiting (I) in 6-week intervals, the prevalence of *E. multilocularis* drops rapidly to values close to zero. Raising the baiting interval length to 12 weeks (II) keeps prevalence on a low plateau. Soon after the end of baiting (III), prevalence rises to reach pre-control prevalence five quarters after the end of baiting.

by parasitological examination of more than 2000 foxes shot before, during and after the control trial. Although, the field trial covered a bigger area of 5000 km^2, here our interest is focused on an area with markedly higher prevalence of *E. multilocularis* in foxes in the centre of the study region (Tackmann et al., 1998).

Soon after the onset of the baiting campaigns, the prevalence of *E. multilocularis* in foxes fell rapidly (Fig. 1). Prevalence dropped to values close to 0 during the 6-week baiting intervals. Switching to 12-week intervals resulted in no further decrease in prevalence. Prevalence remained in a low plateau phase (Tackmann et al., 2001). However, soon after the end of the control trial, the prevalence of *E. multilocularis* in foxes rapidly increased, reaching the pre-control level no later than 15 months after the previous campaign.

2. Materials and methods

2.1. Parameters

Table 1 summarises the parameters used in the model. The number of voles each fox consumes per time step (infection probability of foxes I_{fox}), the number of defecations per fox (infection probability voles I_{vole}) and the proportion of grid cells offering suitable conditions for the survival of tapeworm eggs were used to adjust the pre-control prevalence of *E. multilocularis* in foxes (i.e. any given epidemiological situation). These parameters were specified for each scenario. Below a threshold of 1% of the equilibrium prevalence of *E. multilocularis* in voles, residual prevalence in the respective cell was neglected. This numerical threshold is also given in the scenarios.

Table 1
Parameters for Echi

Parameter	Value	Reference
Fox population density	2 individuals/km^2	Trewhella and Harris (1991)
Fox home range size	1.6 km^2	Trewhella and Harris (1991), Wandeler and Lüps (1993)
Life expectancy of fox	83.9 weeks	Roberts and Aubert (1995)
Prepatency period of fox	4 weeks	Eckert (1996)
Life expectancy adult worm	9 weeks	Ishige et al. (1990)
Egg release interval of worms	1 week	Heath and Osborn (1991)
Maximum number of protoscolices per vole	1000	
Life expectancy of vole	26 weeks	Roberts and Aubert (1995)
Duration of development of larvae in vole	12 weeks	Roberts and Aubert (1995)
Threshold	1% of equilibrium prevalence of *E. multilocularis* in voles	
Life expectancy egg	1 week[a]	

[a] The value for life expectancy of eggs is a model simplification that represents the most optimistic situation. The effect of longer egg survival is investigated in scenario 1 and systematically in Hansen (2001). Below a threshold of 1% of the equilibrium prevalence of *E. multilocularis* in voles, residual prevalence in the respective cell is neglected. The value for the number of protoscolices per vole is chosen to be high enough that higher values that might occur in nature have no significant impact on the dynamics of transmission. All other values are taken from the literature and transformed to fit the model time step of 1 week.

2.2. Modelling control

The time intervals between consecutive campaigns were chosen to resemble those used in the field study as closely as possible. Assuming 20 baits per km^2 are enough to assure each fox has access to at least one bait, we modelled each campaign by randomly curing 70% of all foxes (Trewhella and Harris, 1991).

2.3. Analysis

Field data are given in the form of prevalence estimation for each quarter (Tackmann et al., 2001). Consequently, model prevalence was measured as the mean of 12 simulation weeks. Model runs were repeated 30 times; mean and 95% confidence intervals were calculated.

To validate the uncertainty of the model prediction (U), the relative error was calculated as follows:

$$U_{\text{subset}} = \frac{\sum_t (P_{t,\text{S}} - F_t)^2}{\sum_t (P_{t,\text{R}} - F_t)^2}$$

where U_{subset} is the model uncertainty in the subset of the data (sum of all data points t in subset), $P_{t,\text{S}}$ the predicted data point at time t in scenario S, $P_{t,\text{R}}$ the predicted data point at time t in reference scenario R, F_t the data point from field trial at time t.

Errors were calculated for the whole duration of the field study (32 values), pre-control interval (13 values), initial control phase with baiting every 6 weeks (5 values), second control phase with baiting every 12 weeks (9 values), and post-control phase (10 values).

2.4. Simulation experiments

Four hypotheses for the rapid post-control recovery of the prevalence of *E. multilocularis* in the fox population were converted into different model scenarios. In each scenario, model parameters were used to adjust the pre-control prevalence of *E. multilocularis* in foxes to field data. The parameters used are shown in the graphs. For each scenario the same simulation experiment was conducted and the effect on prevalence monitored.

Below, each of these possible explanations is derived from known facts about the fox tapeworm cycle. All the hypotheses argue that a particular ecological mechanism partially hampers the control effort. The hypotheses were translated into model scenarios, changes to the model structure or parameters that mimic the given hypothesis.

- Hypothesis 0: The model as described in the appendix was able to predict the temporal dynamics of the prevalence of *E. multilocularis* in the fox population.
  - Scenario 0 (reference scenario): The model was not altered in any way from that described in Appendix A.
- Hypothesis 1 (longevity of eggs): Long-lived tapeworm eggs represent constant infection pressure on the intermediate host. This might result in the unchanged prevalence of *E. multilocularis* in the intermediate host and consequently in high infection pressure on the definite host despite the control measure. Thus we can expect a rapid post-control recovery of prevalence due to the delayed dying-off of infectious eggs in the habitat of intermediate hosts.
  - Scenario 1 (longevity of eggs): In the reference scenario, tapeworm eggs only survived for a week. To test hypothesis 1, in this scenario eggs survived for 3 months.
- Hypothesis 2 (dispersion from residual infections): Baits are usually assumed to be distributed heterogeneously on the home range level (Breitenmoser and Müller, 1997). Thus, during control, the fox tapeworm might be eradicated in some home ranges while in others the cycle still runs. Migrating foxes can bridge large distances and thus overcome local saturation effects (Trewhella et al., 1988). The home ranges in which eradication was not achieved, then form a source for the reinfection of the whole area, particularly in autumn, when fox cubs disperse (Labhardt, 1990).
  - Scenario 2 (dispersion from residual infections): In the reference scenario foxes did not disperse. In the dispersion scenario, each fox randomly chose a new home range every autumn.
- Hypothesis 3 (landscape features lead to the local concentration of the infection): The eggs of *E. multilocularis* lose their infectivity within hours if abiotic conditions are unfavourable (Veit et al., 1995). Thus, varying small scale conditions (e.g. low temperature and high relative humidity) will lead to a clumped distribution of infectious *E. multilocularis* eggs in the landscape. Moreover, such small-scale changes in humidity, etc. are likely to follow specific landscape structures (e.g. humidity will be higher in the vicinity of a creek (Staubach et al., 2001)). Assuming an immobile population of intermediate hosts (i.e. voles remain where they were infected), only in areas with favourable conditions for the survival of eggs can first intermediate hosts and then foxes be infected. Hence, *E. multilocularis* reduction measures will perform well in unfavourable areas but worse in patches favourable to *E. multilocularis*. Eventually,

these selected areas might be responsible for the swift post-control recovery of prevalence.

- Scenario 3 (landscape features lead to the local concentration of the infection): In the reference scenario areas favouring the survival of tapeworms, eggs were distributed randomly on the grid. These favoured areas were now aggregated in two ways to mimic different landscape features: swamps and creeks.
  - Scenario 3.1 (swamp): The swamp was modelled by a vertical strip of cells covering 7/18 of the area (i.e. 7 km out of the total 18 km length of simulated area). In the selected strip 15% of the grid cells supported egg survival. In the excluded area, only 2% of the grid cells supported egg survival. A total of 8% of grid cells supported egg survival (as in the reference scenario).
  - Scenario 3.2 (creeks): Creeks were modelled by five vertical strips each 80 m wide. In these strips 60% of the grid cells supported egg survival. The strips were evenly spaced on the grid. No grid cells between the strips supported egg survival. A total of 13% of all grid cells supported egg survival in the creek scenario.

- Hypothesis 4 (acquired immunity): In summer adult foxes tend to be infected with the small fox tapeworm less often than juveniles if overall regional prevalence is high. One possible explanation for this phenomenon is that foxes acquire partial immunity against new infections after they have first been infected with the small fox tapeworm. Assuming this acquired immunity, the epidemiology of the small fox tapeworm includes a proportion of foxes that are partially immune against infection. During the control trial this proportion will diminish because immune foxes will die while newborn foxes will face a lower infection risk and thus will either acquire no immunity at all or will mature before they do (Mutapi et al., 1999; Selhorst et al., 2001).

  At the end of the control trial, the fox population has a bigger proportion of susceptible individuals. Any residual infection pressure will increase the prevalence of *E. multilocularis* in foxes rapidly when control is stopped.
  - Scenario 4 (acquired immunity): In the reference scenario a previously infected fox could again be infected immediately after recovery. In the immunity scenario a fox cannot be infected for 25 weeks after recovery.

3. Results

Using the reference scenario, the model Echi predicted the effect of control measures on the prevalence of *E. multilocularis* in foxes, both in the temporal dynamics and in the absolute values (Fig. 2, top left). Using model parameters to adjust pre-control prevalence, the model reacted to the control strategy used in the field trial such that model predictions remained well within the range of uncertainty of the field data. However, as soon as fox baiting had ceased, the field trial reported a rapid increase in tapeworm prevalence. Although the model's reference scenario also exhibited rising prevalence, the slope of increase was much gentler than that found in the field trial.

Neither an increase in the longevity of tapeworm eggs (Fig. 2, top right) nor the inclusion of migratory behaviour of foxes (Fig. 2, centre left) altered the response of the prevalence of *E. multilocularis* in foxes to control measures.

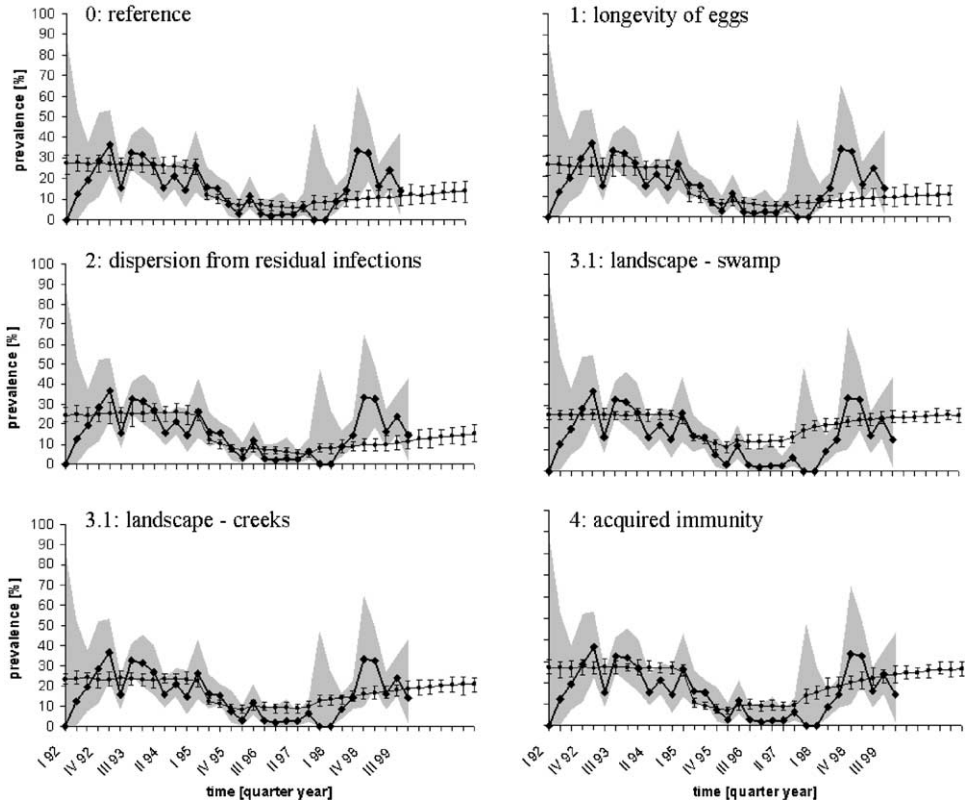

Fig. 2. Top left: predicting field data with the simplest model. $I_{vole} = I_{fox} = 12$, favourable grid cells: 8%, threshold: 0.0022. The quantitative and qualitative dynamics of the prevalence of *E. multilocularis* in foxes from field data (thick line) is reproduced by the model prediction (thin line with 95% confidence interval) for the duration of the control trial. The fast increase in prevalence in foxes however is shown only in a mitigated way. Top right: longevity of eggs. $I_{vole} = I_{fox} = 10$, favourable grid cells: 8%, threshold: 0.0022. The dynamics of the prevalence of *E. multilocularis* in foxes does not deviate from the reference scenario if tapeworm eggs live for 12 weeks instead of 1 week. Centre left: dispersion from residual infections. $I_{vole} = I_{fox} = 12$, favourable grid cells: 8%, threshold: 0.0022. The dynamics of the prevalence of *E. multilocularis* in foxes do not deviate from the reference scenario when foxes migrate once a year into a random new home range. In the reference scenario there is no migration. Centre right: landscape features lead to local concentration of the infection: swamp. $I_{vole} = I_{fox} = 12$, threshold: 0.0028, favourable grid cells concentrated in the centre of the grid (s. scenario description). Prevalence of *E. multilocularis* in foxes is higher at the end of the control trial if infected foxes are concentrated in the centre of the landscape. However, the plateau phase is much higher than in field trials. Bottom left: landscape features lead to local concentration of the infection: creeks. $I_{vole} = I_{fox} = 13$, threshold: 0.0028, favourable grid cells concentrated in strips (s. scenario description). In the creek scenario infected foxes are distributed along strips with good conditions for the survival of tapeworm eggs. This small-scale heterogeneity causes the model prediction to fit field data without leaving the area of uncertainty of the latter. Bottom right: acquired immunity. $I_{vole} = I_{fox} = 13$, threshold: 0.0043, favourable grid cells 15%. The model provides the best prediction of field data when foxes are protected against reinfection for a fixed time.

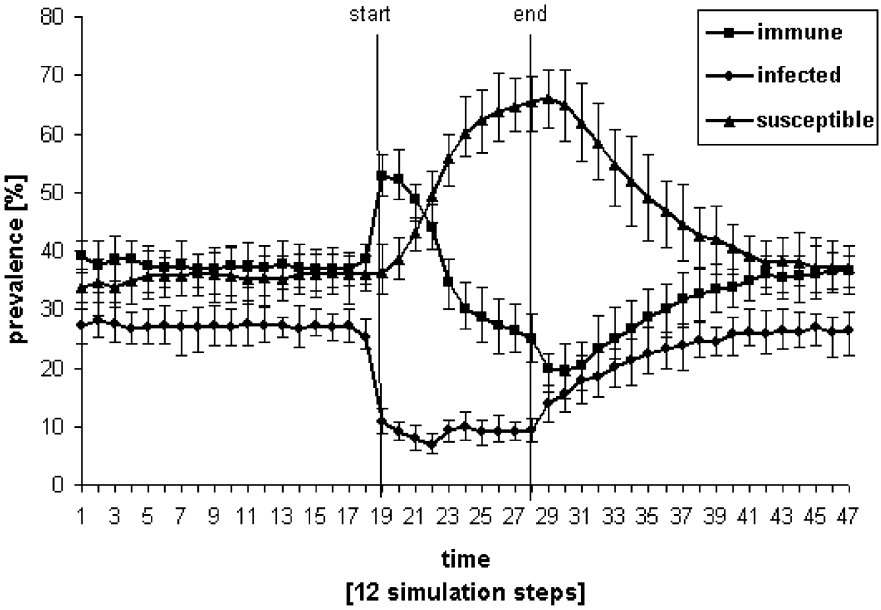

Fig. 3. Dynamics of infected, immune and susceptible proportion of foxes. In the endemic equilibrium state 40% of foxes are protected against infection. With the start of the control measure this value rises to over 50% due to many foxes losing their parasites owing to the control. At the end of the control only 20% of foxes are immune. Simultaneously, the prevalence of susceptible foxes rises from around 30% to above 60%. In this highly susceptible population the end of the control causes a steep increase in infections with *E. multilocularis* (mean and 95% CI each).

The model reacted to landscape structures (Fig. 2, centre right and bottom left). In the swamp scenario, prevalence under control dropped to only about 15%, thus deviating from the uncertainty range of the field data (Fig. 2, centre right). In the creek scenario, the model showed no deviation from field results (Fig. 2, bottom left).

The closest agreement between field data and model predictions was achieved when assuming that foxes acquired immunity against infections (Fig. 2, bottom right).

Table 2
Relative error of scenarios for different temporal windows using the Echi model[a]

	Total	Pre-control	6 weeks phase	12 weeks phase	Post-control
Reference	1.00	1.00	1.00	1.00	1.00
Eggs	1.00	0.88	1.13	0.80	1.13
Migration	0.93	0.84	1.09	0.86	1.03
Swamp	1.09	0.90	1.53	6.84	0.99
Creeks	**0.80**	0.81	0.98	2.55	**0.70**
Immunity	**0.90**	1.00	1.31	2.56	**0.68**

[a] Values smaller than 1 indicate a better fit to field data than the reference scenario, values greater than 1, a worse fit. The scenarios creeks and immunity exhibit the best reproduction of field data in total and in the post-control time window are shown in bold.

Assuming that foxes acquired immunity against infections with the fox tapeworm, for the chosen parameter about 40% of the population was protected against infection (Fig. 3). Because some 30% of foxes were infected, only 30% of the fox population was vulnerable to infection. With the onset of control, the proportion of immune foxes dropped, and consequently, the proportion of susceptible foxes rose. At the end of the control trial only 20% of foxes were immune. With 10% still infected, 70% of the fox population was susceptible. This led to a sharp increase in the prevalence of infected foxes.

The deviation of model predictions from field results for the six scenarios are summarised in Table 2. The creek and the immunity scenarios showed the best overall prediction.

4. Discussion

A field trial to reduce *E. multilocularis* in its natural definite host, the red fox, pushed the ratio of infected foxes to values close to zero. Nevertheless, *E. multilocularis* was not completely eradicated, and soon after the end of the control attempt prevalence quickly rose to reach the pre-control level five quarter years after the end of baiting (Fig. 1, Tackmann et al., 2001). We developed the simulation model Echi to investigate the underlying processes determining the temporal dynamics of the prevalence of *E. multilocularis* and its reaction to intervention. The process model incorporates all the processes assumed to influence the epidemiology of the small fox tapeworm (Grimm et al., 1996).

The reference scenario reflects the prevailing ideas about the epidemiology of the small fox tapeworm. A homogeneous fox population interacts with a spatially structured vole population. The system has no 'memory' as the individual infection history of a fox does not alter its future fate (Roberts and Aubert, 1995). The model predicted the reaction of the parasitic cycle reasonably well (Fig. 2, top left). However, unlike the natural system, the model system did not return to the initial state. This shows that the internal dynamics of the modelled system must be different. The reference scenario was a representation of the prevailing ideas about the fox tapeworm cycle. Thus, the discrepancy between the temporal dynamics of the reference scenario and the field data indicates the involvement of processes not yet taken into account. To identify these processes we included additional ideas into the model step by step.

Neither the longevity of tapeworm eggs (Fig. 2, top right) nor dispersion from residual infections (Fig. 2, centre left) altered the reaction of the parasite system to control measures. This does not mean that these processes are not important for the epidemiology of the fox tapeworm; it merely means they do not explain the observed rapid recovery of tapeworm prevalence. Scenario 2 mimics the maximum possible dispersion, because this does not alter the overall dynamics, it is very unlikely that other processes with the potential to overcome local saturation effects will have a significant impact on the temporal dynamics of the system.

The two landscape scenarios are based on our previous findings that the fox tapeworm cycle is more robust against small variations in epidemiological parameters if it performs on a heterogeneous landscape (Hansen, 2001). The known sensitivity of tapeworm eggs to high temperature and low humidity motivates the modelling of the heterogeneous landscape by assuming that only part of the landscape offers abiotic conditions suitable for the survival

of tapeworm eggs. In the reference scenario these areas are distributed randomly over the whole region modelled. However, in a natural landscape, abiotic conditions are likely to vary in their reaction to landscape structures. Humidity conditions for instance will certainly follow the availability of surface water.

The limited activity zone of foxes will accordingly lead to foxes finding themselves in areas with an abundant source of infected voles while others are relatively safe from infection. Thus, the spatial distribution of infected foxes will secondarily follow the same landscape structures. This line of argument is supported by a GIS-based study that found a link between the infection status of hunted foxes and the proximity of moist soils (Staubach et al., 2001). In order to assess the impact of this heterogeneous spatial distribution of infected foxes on the temporal dynamics of the prevalence of *E. multilocularis* in foxes under control, we analysed two virtual landscapes.

The swamp scenario mimics an area with moist soils in the centre of the region. The dynamics of prevalence of *E. multilocularis* in foxes differs from the reference scenario (Fig. 2, centre right), thus providing evidence that the small-scale distribution of infected foxes can significantly alter the reaction of the system to control measures. However, under the given spatial structure, the model predictions do not fall within the range of uncertainty of field data.

The landscape in north Germany is often characterised by a number of creeks originally used to drain the soil and to render formerly wet meadows suitable for agricultural land use. The creek scenario mimics this more typical landscape. Under this spatial structure the model prognosis fits field observations without exceeding the error bars (Fig. 2, bottom left).

The landscape scenarios represent examples of virtual landscapes. They prove that the landscape structure is an important factor influencing the temporal dynamics of the fox tapeworm cycle. They are not meant to be a complete analysis of all possible landscapes. The examples given stress the need to consider spatial aspects on different scales to predict the outcome of control measures (Lloyd and May, 2001). The most convenient way to do this is to use spatially explicit models such as the Echi model presented here. This type of model can be adjusted to represent real landscapes and thus provide reliable predictions for control planning.

It is known from other parasites—such as the closely related dog tapeworm *Echinococcus granulosus* (Gemmell et al., 1986; Hertzberg et al., 1995; Torgerson, 2001)—that hosts exhibit an immune response against intestinal parasites. A Swiss study supports the age-dependent prevalence of *E. multilocularis* in other areas (Gottstein, 1992). The authors also assume an immune response by foxes against infection with *E. multilocularis*.

In the immunity scenario we assume that adult foxes acquire partial immunity against reinfection. Within 25 weeks after recovery from an infection, the fox cannot be infected again. Under this assumption, the basic epidemiology of the fox tapeworm changes from a classical susceptible–infected system to one with a proportion of foxes being immune to infection (susceptible–infected–immune). The model predictions do not deviate from the uncertainty of the field results (Fig. 2, bottom left). Hence, the assumption of acquired immunity is an intuitive possible explanation for the rapid recovery observed of the prevalence of *E. multilocularis* in foxes.

In the simulated situation, 40% of foxes were immune to infection (Fig. 3). Under control, this proportion initially rose to a level of over 50%. This might be a model artefact because in

the model every single fox became immune after an infection even if the end of the infection was caused by chemotherapy. Whether this happens under field conditions is currently unknown. It is possible that treatment with Praziquantel alters the immune competence of foxes (Mutapi et al., 1998).

The proportion of immune foxes dropped during control because foxes lose their immunity either by dying and being replaced by new, susceptible ones or by reaching the end of the interval for which they are immune. Simultaneously, fewer foxes became infected because the fox prevalence was reduced and secondarily the prevalence in the intermediate host was reduced as well. Therefore, at the end of the control trial, only 20% of foxes are immune. The proportion of susceptible foxes rose from about 35% to above 60%. When the control measure ended, the unhampered reproductive potential of the fox tapeworm led to a rapid increase in the prevalence of *E. multilocularis* in foxes (Fig. 2, bottom left).

Immunity here was modelled as an all-or-nothing response. Under natural conditions the response might be less extreme, meaning foxes may need a higher infection dose for a reinfection. This would change the quantitative but not the qualitative behaviour of the system because the qualitative reaction was based on the fact that a proportion of foxes are not infected, be it due to total protection or insufficient infection dose. Equivalently, the overall dynamics would not change if the assumed immunity was for life instead of short-term.

Both the creek and the immunity scenarios showed a higher residual prevalence in the time window where control was repeated at 12-week intervals (Table 2). This might be an indication that the 70% bait uptake rate assumed in the model was too pessimistic and more foxes are reached in the field. However, as we are addressing post-control recovery, this can be disregarded as insignificant.

Two reasonable assumptions explain the rapid post-control recovery of the prevalence of *E. multilocularis* in foxes: the assumption that infected foxes are distributed inhomogeneously and the assumption that previously infected foxes acquire increased protection against reinfections. These findings supplement the image we have of the infection dynamics of the fox tapeworm. Both hypotheses highlight the need for a higher resolution in empirical research. The importance of the location of infected foxes in the creek scenario demonstrates the potential for interactions between the fox tapeworm cycle and landscape structure, which calls for a higher spatial resolution in empirical research. On the other hand, the susceptibility of individual foxes might be determined by their individual infection history if the assumption of acquired immunity finds empirical support. This in turn calls for a higher temporal resolution of empirical research.

It cannot be ruled out that, as new insights emerge, additional hypotheses may be formulated to explain the observation. Moreover, a combination of different processes currently known or unknown may have a similar effect. The aim of this study was to reveal theoretically possible explanations for the field observations and thus to direct further empirical research towards these areas.

Irrespective of which hypothesis turns out to be supported by empirical data, both possibilities are inconsistent with the common notion of interacting populations (Roberts and Aubert, 1995). Instead, the infection cycle of the small fox tapeworm appears to be highly dynamic in both time and space. An increased awareness and understanding of the ecological processes that affect these dynamics will lead to more reliable predictions of control success. Eventually, cost-efficient control strategies will be available.

Both scenarios that showed no deviations of the model prognosis from field data have far-reaching consequences for control planning. In the first case, where infected foxes followed landscape structure such as creeks, the control effort can be concentrated on these core areas, which are easily recognized by the pilots distributing baits. Thus, control costs could be significantly reduced, which in turn would allow longer baiting periods at the same costs.

The second scenario, where foxes are immune to reinfection, is less optimistic. In this case, the fox population becomes increasingly vulnerable to infection the more the prevalence of *E. multilocularis* drops during control. This buffer mechanism (Jeltsch et al., 2000) explains why the prevalence of *E. multilocularis* in foxes usually remains on an intermediate level, but also means that a further reduction of low prevalence becomes more and more difficult.

Appendix A. Set of rules for the simulation model Echi

The model is best described by a set of rules. We use a set of basic rules (B1–B4) which determine the structure of the model, and a set of simulation rules (S1–S4) which determine transitions between time steps. Simulation rules are performed every time step:

- B1 (the grid): The space is represented by a set of 901 × 450 grid cells. Each grid cell stands for the home range of a subpopulation of voles. Grid cells are defined to measure 20 m × 20 m adding up to a simulated area of 162 km^2.
- B2 (voles): Voles are represented by an infective but not yet infectious and an infectious proportion of the total subpopulation of a grid cell.
- B3 (foxes): Foxes are modelled individually, 325 foxes populate the grid of 162 km^2. Foxes have home ranges. They prey and deposit faeces exclusively within their home range. Each home range is populated by 0–3 foxes.
- B4 (worms): Tapeworms have three stages, each is represented differently in the model.
  - B4.1: Adult worms in the definite host are represented by numbers of individuals in individual foxes. The time since infection determines the age of the individual worms and hence the start and duration of egg production.
  - B4.2: Proportions of the subpopulation of voles in the different infective stages represent larvae in the intermediate hosts. Voles can be either infected but not yet infectious or infected and infectious.
  - B4.3: Eggs shed with the foxes' faeces are represented solely by their position in a grid cell.
- S1 (time step): The model performs in discrete time steps, one simulation step is 1 week.
- S2 (foxes): Foxes prey on voles, deposit faeces and suffer mortality.
  - S2.1 (foxes prey on voles): Foxes consume a fixed number of voles in each time step. Whether a fox captures an infectious vole or not depends on the prevalence of infectious voles in the chosen grid cell. If a fox consumes an infectious vole, he is infected with 1–1000 tapeworm larvae. Infected foxes cannot be infected again.
  - S2.2 (foxes deposit faeces): Foxes deposit a fixed number of faecal packages in each time step. In general all faecal packages from an infectious fox contain tapeworm eggs. In the rare case that a fox harbours fewer adult worms than he defecates, the number of contaminated faecal packages equals the number of adult worms.

- S2.3 (foxes suffer mortality): Foxes have a fixed probability of dying. A dead fox is replaced by a new one that is assigned to a random home range.

- S3: Let S_n, V_n, and W_n be the proportion of susceptible, infected but not yet infectious, and infectious voles at time n respectively, then $S_n + V_n + W_n = 1$, the population is constant in time.

  If infective eggs are positioned in the grid cell, then $V_{n+1} = V_n + S_n$. Proportions change such that

$$W_{n+1} = W_n + \frac{V_n}{d} - \frac{W_n}{l} \quad \text{and} \quad V_{n+1} = V_n - \frac{V_n}{d} - \frac{V_n}{l}$$

  where d denotes the mean duration of the larval development until the first protoscolices appear and l denotes the mean life expectancy of voles.

- S4 (worms): Worms in foxes age, produce eggs and die, tapeworm larvae in voles mature and eggs lose their infectivity.
  - S4.1 (worms in foxes age, produce eggs and die): After (time to maturation of larvae in foxes) time steps worms in foxes age are considered to be adult and begin egg production. After (mean life expectancy of worms in foxes) time steps, the worms die.
  - S4.2 (tapeworm larvae in voles mature): If the prevalence drops below a numerical threshold, they are set to zero (see S3).
  - S4.3 (eggs lose their infectivity): After one time step, eggs lose their infectivity.

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