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DOES VIRULENCE DECLINE BY TIME IN WILD BOAR POPULATIONS INFECTED BY CLASSICAL SWINE FEVER VIRUS (CSFV)?

M. LANGE*, S. KRAMER-SCHADT AND H.-H. THULKE

SUMMARY

Classical Swine Fever (CSF) is an endemic viral disease in European wild boar populations causing high economic impact to the pig farming industry. Virulence is a crucial factor determining persistence in local wild boar populations. We considered shift in virulence on the time scale of recent outbreaks using an individual-based spatially-explicit model which represents knowledge on wild boar ecology and CSF virus epidemiology. Two alternative scenarios were supposed as reasonable mechanisms that shift virulence pattern: 1) evolution of pathogen's virulence and 2) selection for host resistance. With both processes we found a possible short term shift to lower virulence. Pathogen evolution, however, resulted in faster decline down to a threshold level, while host selection resulted in slower but continuous decline of virulence. Both mechanisms promoted disease persistence.

INTRODUCTION

Classical Swine Fever (CSF) is a viral disease of *Suidae*, affecting wild boar (*Sus scrofa*) and domestic pigs (Depner et al. 1995; Laddomada 2000; Kaden et al. 2004). The disease is notifiable to the World Organisation of Animal Health (OIE). CSF has serious economic implications for domestic pig farming due to preventive culling and trade restrictions (Meuwissen et al. 1999). Wild boars are assumed to act as reservoir for Classical Swine Fever Virus (CSFV), and 60 % of the primary outbreaks in domestic pig farms are expected to be caused by direct or indirect contact with wild boar (Moenning et al. 1999, Fritzemeier et al. 2000).

Nowadays, CSF occurs worldwide and became endemic in wild boar populations in several European countries. A decrease in virulence during the last decades is assumed to be a crucial reason for disease persistence (Kramer-Schadt et al. 2009). Case mortality, being an expression of virulence, is reported to vary from high to very low, depending on the virus strain (Kaden et al. 2000) and age class of the infected host (Moenning et al. 2003).

Observations from past outbreaks suggested that the case fatality of infected hosts decreases within years or even months of an epidemic in wild boar (Artois 2002; Ruiz-Fons et al. 2008). Virus isolates of recent outbreaks were associated with the moderately virulent genotype subgroup 2.3 (Kaden et al. 2004, Pol et al. 2008). Highly virulent genotypes of group 1 were

· Martin Lange, Helmholtz Centre for Environmental Research – UFZ, Dept. of Ecological Modelling, Permoserstraße 15, 04318 Leipzig, Germany.
Email: martin.lange@ufz.de

restricted to older isolates (Greiser-Wilke et al. 1998, Fritzemeier et al. 2000) which might indicate a pathogen evolution towards reduced virulence. On the other hand, it is discussed whether case mortality is attributed to the condition of the hosts (Depner et al. 1997). Considering those facts, emergence of moderately virulent strains during the time span of a particular outbreak in wild boars could be reasonable.

We tested temporal dynamics of CSF case fatality under two alternative hypotheses: 1) evolution of pathogen's virulence and 2) selection on host resistance. To that end, a spatially-explicit, individual-based wild boar demography model incorporating social behaviour was coupled with a CSFV model attending individual disease courses (Kramer-Schadt et al. 2009). In the model, case mortality and mean infectious period of lethally infected hosts together represent the virulence pattern of a particular CSFV and are subject to mutation (in pathogen) and selection (in host). Results show that both scenarios – host resistance selection as well as pathogen virulence evolution – are able to decrease virulence pattern over the short term of a particular outbreak.

MATERIALS AND METHODS

Model description

The model is based on the approach by Kramer-Schadt et al. (2009). It is described following the ODD protocol (Overview, Design, Details; Grimm et al. 2006, 2010). Sub-models are only partially presented in case they are essential to understand the applied model. For a complete documentation we refer to the online repository (http://ecoepi.eu/CSFWB).

Overview: The CSF wild boar model is a compilation of a spatially explicit, stochastic, individual based demographic model for wild boars (*Sus scrofa*), and an infection and disease course model for CSFV.

Purpose: The model serves for testing the hypothesis of a decreased virulence by either host selection or pathogen short-term evolution in outbreaks.

State variables and scales: The model is composed of two major components, 1) a wild boar demography model considering seasonal reproduction, dispersal and mortality, and 2) a CSF virus model operating on the wild boar population. Wild boar population density and structure are affected by the disease via virus-induced mortality and litter size depression.

All processes take place on a raster map, where each cell represents a functional classification of a landscape into breeding capacity, denoting habitat quality by the number of female boars that are allowed to have offspring. Thereby, density is regulated in the model. The model landscape is represented by a grid of square cells, each representing 4 km² and encompassing a home range of a group of wild boars (Leaper et al. 1999).

The crucial model entity is the individual wild boar, characterised by age in weeks (where one week represents the approximate CSF incubation time; Artois et al. 2002, Moenning et al. 2003), resulting in the age classes piglet (< 8 months ± 6 weeks), yearling (< 2 years ± 6 weeks), and adult. Each host has a location, which denotes its home range cell on the raster grid as well as the individual's family group. Further state variables of the host are the demographic status (disperser or not) and the epidemiological status (susceptible, transiently infected, lethally infected with varying survival times or immune by surviving the infection, vaccination or

maternal antibodies). Each host has a probability of virus-induced death following infection (*M*) and a 'mean' infectious period conditioned on lethal infection ( ).

Process overview and scheduling: The model processes in weekly time steps. Processes of each time step are: infection, wild boar group splitting, reproduction, death and ageing, executed in the given order. In the first week of each year, mortality probabilities are assigned stochastically to represent annual fluctuations in wild boar living conditions, and they are assigned to breed or not, according to the carrying capacity of their home range cell.

Design concepts: Wild boar population dynamics emerge from individual behaviour, defined by age-dependent seasonal reproduction and mortality probabilities, and age- and density-dependent dispersal behaviour, all including stochasticity. The dynamics of the infection emerge from within- and between-group virus transmission, boar dispersal, individual stochastic disease courses, and infectious periods for infected wild boars. The parameter which reflects host mortality induced by infection is subject to alterations according to the simulated scenarios (see below).

Stochasticity is included by representing demographic and behavioural parameters as probabilities and probability distributions, respectively. Annual fluctuations of living conditions are accounted for by varying mortality rates. Course and duration of infection are modelled explicit and stochastic, since the variation in disease outcome between individuals was identified as essential for virus endemicity without reservoirs (Kramer-Schadt et al. 2009).

Initialisation: The model landscape represents 200 km by 50 km of connected wild boar habitat without barriers. The 2,500 grid cells are initialised randomly with uniformly distributed integer breeding capacity values $C_{ij} \in \{1, 2, \ldots, 9\}$. Thus, the mean breeding capacity is 5 females per cell, resulting in approximately 20 boars per cell or a host density of 5 boars per km² (Howells & Edwards-Jones 1997). One wild boar group is released to each habitat cell and group size was three times the local breeding capacity. Initial age distribution is taken from the results of a 100 years model run, conducted by Kramer-Schadt et al. (2009).

Input: The applied model setup does not include any external inputs or driving variables.

Sub-models: In this section we describe sub-models crucial for the simulation experiments. For detailed sub-model documentation we refer to the authors' online repository (http://ecoepi.eu/CSFWB).

Transmission:

Transmission is modelled stochastically. Parameters determine the weekly probability to receive an infection from an infectious group mate $P_{\mathrm{inf}}^{(i)}$ and the probability to receive an infection from an infectious animal in a neighbouring group $P_{\mathrm{inf}}^{(e)}$. For each susceptible animal the probability to become infected accumulates over all infectious animals within the group and in the neighbourhood. Infection might be translocated within the host population during dispersal of sub-adult females.

The transmission parameter was reversely fitted to recorded disease spread velocity of approx. 8 km per quarter (Rossi et al. 2010). The resulting parameter values were assigned constant as $P_{\mathrm{inf}}^{(i)} = 2.08 \cdot 10^{-2}$ within and $P_{\mathrm{inf}}^{(e)} = 2.08 \cdot 10^{-3}$ between groups.

Disease course:

The disease course sub model is described by two parameters: individual case mortality M and , the mean infectious period of lethally infected hosts. On infection, the host is stochastically assigned either as lethally infected (with probability *M*) or as transiently infected (1-*M*). *M* applies unchanged for yearlings $M^{(y)}$, is decreased for adults to $M^{(a)} = M^2$ and increased for piglets to $M^{(p)} = \sqrt{M}$ to represent age-dependent disease outcomes (Dahle & Liess 1992). Transiently infected wild boars are infectious for one week and turn immune three weeks later (Artois et al. 2002; Moenning et al. 2003). Differing from the approach of Kramer-Schadt et al. (2009), the infectious period (in weeks) of lethally infected hosts is drawn from an exponential distribution with mean . Lethally infected hosts remain infectious until death.

Highly-lethal CSFV outbreaks are expected to coincide with short mean infectious period of lethally-infected hosts while longer mean infectious period of lethally-infected hosts should coincide with moderate case-fatality (Day 2003). In the model this qualitative correspondence is represented ad hoc according to:

$$\mu = (1 - M)^x \cdot s + 1. \qquad (1)$$

In these *M* – – relations exponent *x* and scaling factor *s* are chosen to represent linear or quadratic relations (Fig. 1 a) (see section 'Simulation experiments'). In the simulation scenarios, i.e. pathogen's virulence evolution and host resistance selection, case fatality *M* is modulated directly and the mean infectious period indirectly via Equation (1).

Host selection:

Each individual host inherits its case mortality value $M_{offspring}$ from the mother (M_{sow}). In case of lethal infection, the individual's infectious period is drawn from the exponential distribution with mean according to Equation (1), inserting $M_{offspring}$. At beginning of a simulation run, individuals' case mortality *M* is drawn individually from an inverse beta distribution 1–*Beta*(,), i.e. the probability of transient infection is distributed as *Beta*(,). Parameters and were selected to achieve mean case mortality of all yearlings of $M^{(y)} = 0.8$. Case mortality of adults $M^{(a)}$ and piglets $M^{(p)}$ is determined according to section 'Disease course'. The resulting average case mortality over the entire population and one simulated year was 0.76.

Pathogen evolution:

At infection, each individual host inherits case mortality $M_{inherited}$ from the infecting host ($M_{transmitted}$). Mutation is introduced by a randomised shift of case mortality:

$$M_{inherited} = M_{transmitted} + r(b_{virus}) - \frac{b_{virus}}{2} \qquad (2)$$

where b_{virus} is twice the maximum shift and $r(b_{virus})$ is a uniformly distributed random number drawn from $U(0, b_{virus})$. In case of lethal infection the corresponding mean infectious period is derived from eq. (1) using $M_{inherited}$.

Case mortality of the initially released virus is $M = M^{(y)} = 0.8$. Case mortality of adults $M^{(a)}$ and piglets $M^{(p)}$ is determined according to section 'Disease course'. The resulting average case mortality over the entire population and one simulated year was again 0.76.

Parameters, simulation experiments, analysis

Independent variables: The primary independent variables of the study are the virulence evolution scenarios (i.e. host selection versus pathogen evolution), the M – – relation, the mutation strength of the virus b_{virus} for pathogen evolution, and the initial distribution of the expected case mortality (i.e. parameters and of the beta distribution) for host selection.

Dependent variables: The average case mortality over the entire population of hosts and over each simulated year was measured. Moreover, the time point of each virus extinction event was recorded.

Simulation experiments: Evolution scenarios were either host selection or virus evolution. Both scenarios were simulated for linear and quadratic M – – relations (Fig. 1 a). Parameters of Equation (1) are:

- Linear relation: $x = 1$, $s = 10$
- Quadratic relation: $x = 2$, $s = 16.875$

where s was chosen to achieve for both scenarios equal maxima of the effective mean infectious periods $T_{inf} = 3.5$ weeks over all infected hosts (Fig. 1 b).

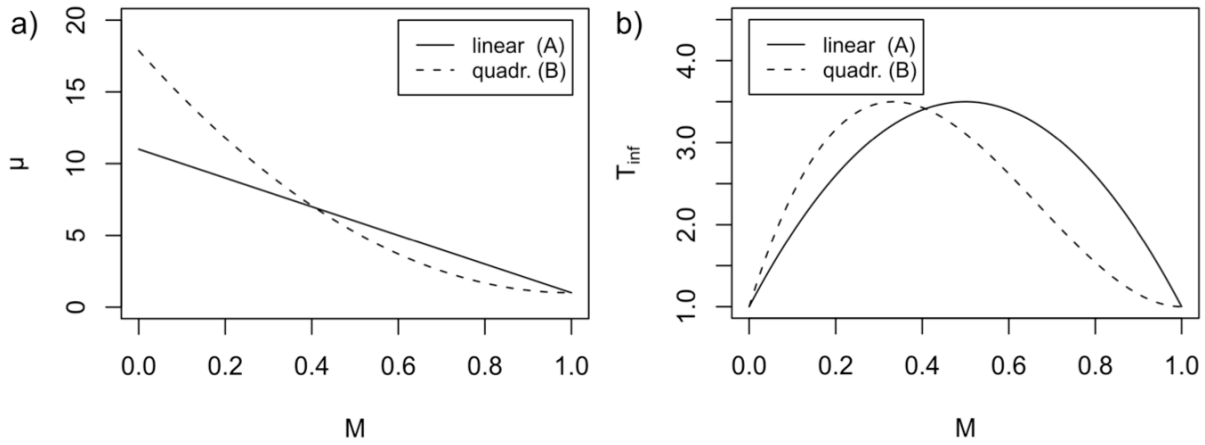

Fig. 1 a) Mean infectious period μ of lethally infected hosts, and b) effective mean infectious period T_{inf} over all hosts, as function of average case mortality M for different M – – relations $\mu = (1 - M)^x \cdot s + 1$. Solid: $x = 1$, $s = 10$ (linear), dashed: $x = 2$, $s = 16.875$ (quadratic).

For reference, simulations were performed with linear and quadratic M – – relation but without evolution or selection.

For pathogen evolution, different realisations of the mutation strength parameter were simulated: $b_{virus} \in \{0.0, 0.01, 0.05, 0.1\}$.

For host selection, two alternative beta distributions were used for initialisation of individual host's case mortality values: $1 - Beta(0.5, 2)$ (solid in Fig. 2) and $1 - Beta(2, 8)$ (dashed in Fig. 2). For both scenarios, however, average case mortality over the entire initial population was kept as 0.76.

All simulations were performed for 40 years or until host or virus went extinct. The virus was released to the boar population in a random week of the sixth year by infection of one randomly selected boar individual.

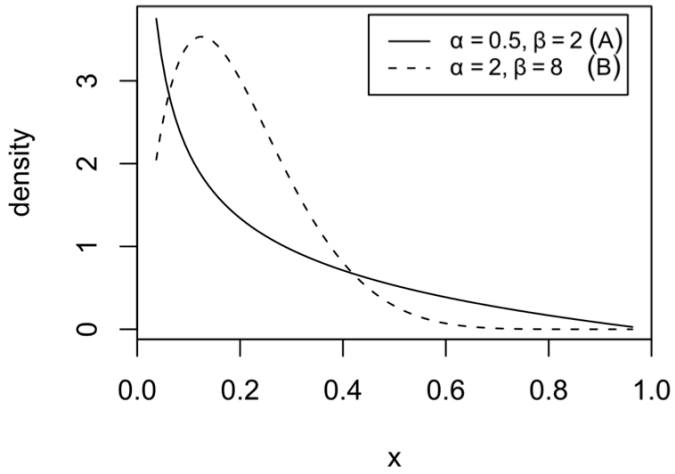

Fig. 2 Probability density functions of beta distribution as used for initialisation of individual's case mortality parameter in the host selection scenario.

For each scenario, 500 model runs were conducted to achieve minimum precision of $\pm 5\%$ with 95% confidence for proportions.

Analysis: Aggregated case mortality values, $\overline{M}$, were calculated over 500 repetitions over the 52 weeks of each year, weighted by the number of hosts receiving an infection in the particular week. The mean infectious period after lethal infection and the effective mean infectious period T_{inf} over all hosts infected in a particular week were calculated from aggregated case mortalities $\overline{M}$ (Fig. 1).

Survival curves of the virus in the host population were determined by calculating the proportion of runs in which the virus was not yet extinct until the particular time step.

Analysis was performed using GNU R 2.9.2 (R Core Development Team), plots were created with SigmaPlot® 10.0 (Systat Software Inc.).

RESULTS

Fig. 3 shows the simulation output in terms of the evolving $\overline{M}$, i.e. aggregated case mortality, during simulation for the two scenarios, being pathogen evolution and host selection, and the two M – – relations (linear and quadratic). According to Fig. 1 b the maximum effective infectious period T_{inf} (i.e. 3.5 weeks) was expected to be achieved with $\overline{M} \approx 0.5$ for the linear M – – relation and $\overline{M} \approx 0.33$ with quadratic M – – relation. Next we explore the simulated dynamics of $\overline{M}$ values over the time course of 35 years and the two evolution scenarios.

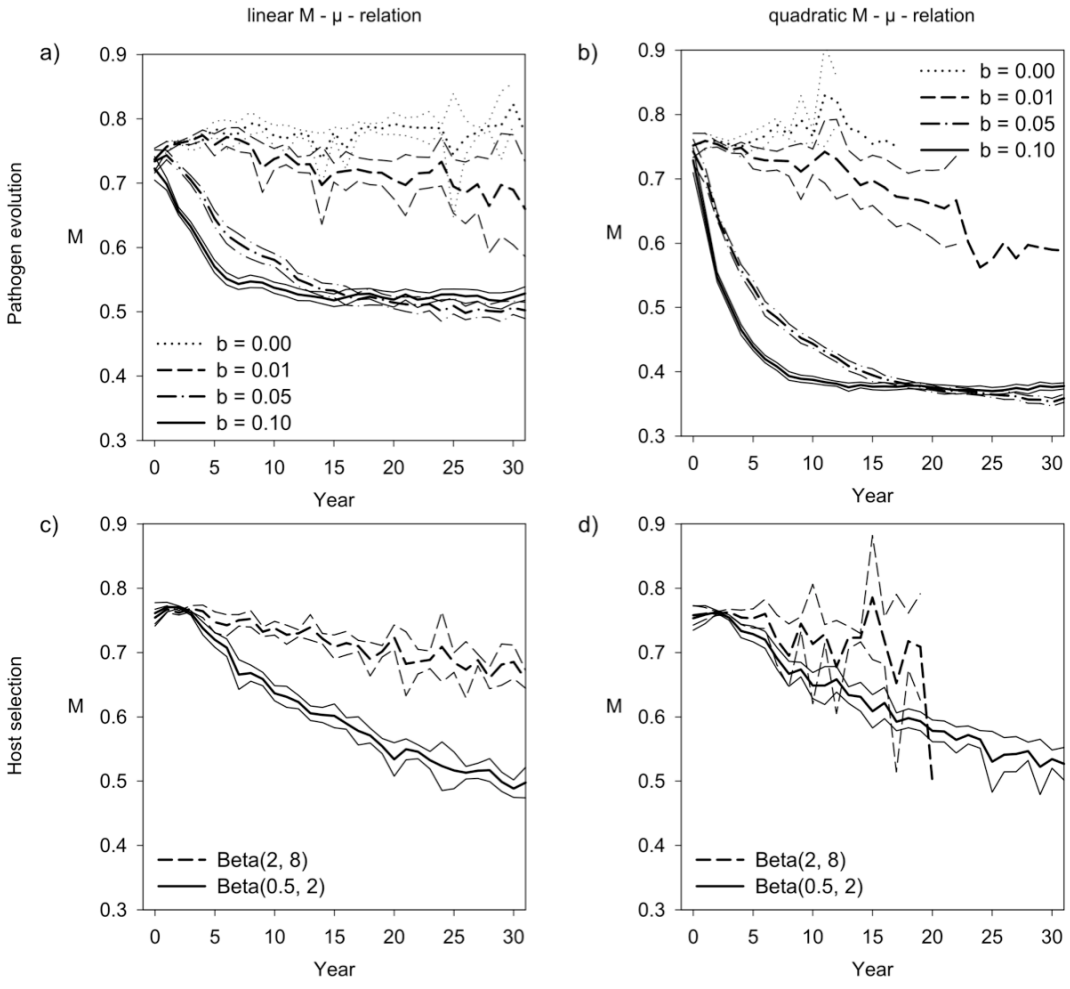

Fig. 3 Mean (thick) and 95 % confidence intervals (thin) of aggregated case mortality $\overline{M}$ for a), b) pathogen evolution, c), d) host evolution with a), c) linear, b), d) quadratic M – – relation.

Pathogen evolution

For pathogen evolution, aggregated case mortality $\overline{M}$ decreased immediately after virus release. The speed of decline depended on mutation frequency, i.e. parameter b_{virus} (Fig. 3 a or b). With high mutation force, $b_{virus} = 0.1$, aggregated case mortality $\overline{M}$ rapidly converges to the threshold value, i.e. 0.5 for the linear and 0.33 for the quadratic relation, which results in a maximum mean infectious period $T_{inf} = 3.5$ weeks. With the linear M – – relation $\overline{M}$ became

less than 0.55 after 7 years of virus perpetuation (solid in Fig. 3 a), and falls below 0.4 after 8 years of virus perpetuation with the quadratic relation (solid in Fig. 3 b).

For an intermediate mutation force b_{virus} = 0.05, virulence shift was slowed down, but the case mortality corresponding to the maximum effective infectious period was still reached within the simulated 35 years after virus release (dash-dotted in Fig. 3 a and b; $\overline{M} < 0.55$ after 11 years with the linear M – – relation, and $\overline{M} < 0.4$ after 15 years with the quadratic relation). For even lower mutation force b_{virus} = 0.01, shift in $\overline{M}$ values was very slow and the maximum effective infectious period was not achieved within the simulated time span (dashed in Fig. 3 a and b).

Host selection

Under the host selection scenario, a 3 to 4 years phase of unchanged aggregated case mortality $\overline{M}$ with decreasing variation between runs was followed by continued decrease of aggregated case mortality values ($\overline{M}$) (see Fig. 3 c and d) independent of the applied M – – relation.

The temporal dynamics of $\overline{M}$ were strongly influenced by the distribution of M in the initial population (see Fig. 2):

When initial case mortalities were drawn from the beta distribution *Beta*(2, 8), the fraction of "resistant hosts", i.e. hosts with low case mortality value, was very small which resulted in a very slow decrease of $\overline{M}$ (dashed in Fig. 3 c and d).

When initial values of M were drawn from the beta distribution *Beta*(0.5, 2), the larger fraction of hosts with a low value of M allowed for faster decline of $\overline{M}$ (solid in Fig. 3 c and d). The value of $\overline{M}$ that corresponds to the maximum effective infectious period T_{inf} = 3.5 weeks (i.e. $\overline{M}$ = 0.5, see Fig. 1 b) was achieved by year 29, assuming the linear M – – relation (solid in Fig. 3 c), and not approached ($\overline{M}$ = 0.33) for the quadratic relation (solid in Fig. 3 d).

Persistence

The survival curves of the simulated combinations of scenarios and M – – relations showed a similar extinction pattern (Fig. 4, selected scenarios). Within the first year after virus release, the virus extincted in a noticeable proportion of simulations (30 – 40 % for linear M – – relation, about 50% for all scenarios with quadratic relation). The initial phase was followed by about 3 years of stability, i.e. very few virus extinctions, designating the epidemic phase of the outbreak (EFSA 2008). From year 4 to year 8, extinction probability was high again, denoting the transition between the epidemic and endemic phase. In the model the virus had achieved the edges of the simulation area and could no longer conquer unaffected regions. If the transition to the endemic phase had happened, only stochastic extinction events determine the progress of the survival curves (May 1976).

Both evolution scenarios increased the probability of long-term persistence of the virus in the simulated population compared to the reference scenarios (dotted lines in Fig. 4). Only pathogen evolution reduced the case mortality sufficiently fast to efficiently increase disease persistence beyond year 4 (dashed in Fig. 4). Especially in the transition between epidemic and endemic phase (approx. 4^{th} – 8^{th} year in Fig. 4), where the disease fades out with high

probability (solid and dotted lines in Fig. 4), pathogen evolution strongly increased virus survival, since case lethality already had decreased and hence the effective mean infectious period had been maximised during the preceding phase.

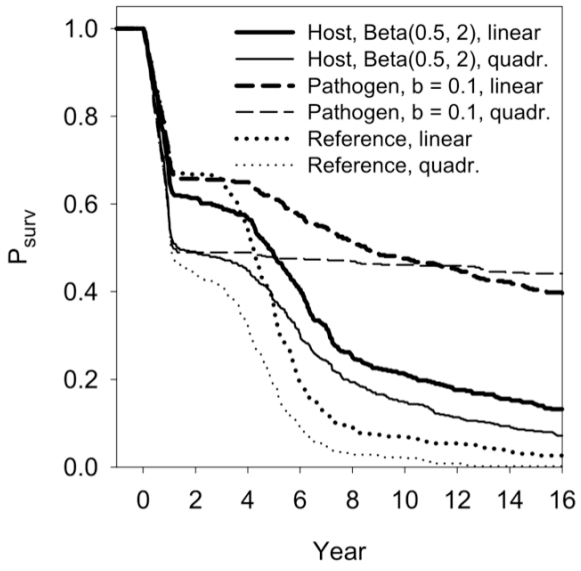

Fig. 4 Virus extinction curves.

DISCUSSION

The perception of decrease in severity of CSF outbreaks in wild boar was investigated. Such an alteration of severity is usually associated with fewer animals that are dying due to a CSFV infection. Decrease in severity may either be related to one outbreak, i.e. a very rapid dynamic (Artois et al. 2002; Ruiz-Fons et al. 2008); or over many outbreaks, i.e. a slow dynamic continued over several populations (Greiser-Wilke et al. 1998). Rapid decrease in severity may be associated with reducing virulence of the virus (Leifer et al. 2010) or with increasing host resistance (Depner et al. 1997). How far these changes could contribute to a perceived decrease in case mortality and a dramatically prolonged persistence of virus in natural populations as observed in the last decades in Europe (Rossi et al. 2005; EFSA 2008; von Rüden 2008) remains an important issue.

Severity or virulence evolution via host selection or pathogen evolution was investigated using an established epidemiological model (Kramer-Schadt et al. 2009). The analysis focussed on the evolution of virulence in terms of case mortality *M*, the dependent mean infectious period of lethally infected hosts (Day 2003), and the impact of virulence evolution on possible long-term disease persistence. The stochastic, individual-based, spatially-explicit modelling approach was chosen to cope with individual variability, stochasticity, and space as these were foreseen to influence disease dynamics. The model is able to reflect individual disease courses, ecological traits of the host and density dependent disease and population dynamics based on existing knowledge, e.g. Artois et al. (2002), EFSA (2008) or Kramer-Schadt et al. (2007).

The infection of individual wild boar with CSFV is well known to vary with regard to the disease outcome (EFSA 2008). Transient infections with subsequent recovery after short infectious periods are reported as well as lethal infections that results in animal dying quickly

within 4 weeks, or chronic which allowing long infectious periods of up to 120 days (Kramer-Schadt et al. 2007). The feature is represented in the model by stochastic case mortality (parameter *M*) and stochastic life-expectancy of lethally infected hosts (parameter as mean). In the field the actual case mortality will be the only pattern to be recorded and, hence, the pattern that determines perceived severity of an outbreak. In order to mimic the perception of reduced disease severity, we incorporated mechanisms that modulated case mortality *M* in the model version. The modulation was driven by two processes that reflect either pathogen evolution (i.e. selection on *M* due to the dependent infectious period) or host selection (i.e. selection on *M* due to survival of the infected hosts). To underpin the temporal dynamic of the two processes, alternative mutation forces and initial distributions of the characteristic *M* in the host population were considered without being exhaustive.

The approach to model and parameterise selection or adaptation was considered as plausible but ad hoc and served as a pathway to understand the quantitative effect on case mortality and persistence in a qualitative relationship. The model does not consider the relationship between virulence and infectiousness, which could slow down virulence shifts in an advanced stage of an outbreak.

Evolutionary scenarios

Assuming appropriate parameters, host selection and pathogen evolution show an efficient decline in virulence over the period of a particular outbreak. Evolution of the pathogen occurs much faster than host selection due to shorter "generation times". The generation time of the pathogen which is decisive for evolution equals the time span from infection of the host till infection caused by this particular host. The mean generation time is thus even shorter than the mean infectious period T_{inf}. For host selection, the evolutionary decisive generation time equals the generation time of the host, i.e. at least 6 months.

Starting with high virulence, i.e. high case mortality and a short infectious period after lethal infection, host selection as well as pathogen evolution could decrease virulence with both *M* – – relations. Pathogen evolution with strong mutation forces b_{virus} caused a rapid virulence decrease already in the epidemic phase (1^{st} – 4^{th} year in Fig. 3 a and b). Host evolution, on the other hand, caused a slower virulence shift which starts with the endemic phase (Fig. 3 c and d) as during the epidemic phase only parts of the population were affected where no selection took place yet.

Evolution of the pathogen is driven by the mean infectious period T_{inf}. The 'virus strain' with the longest mean infectious period has the highest rate of secondary infection, i.e. the highest basic reproduction number R_0, and can thus reproduce most successfully. Simulations start with one 'defined virus', so the rate of virulence shift over time is determined by the mutation force parameter b_{virus}. A higher b_{virus}, results in a faster virulence shift. Pathogen evolution works towards the case mortality value where the infectious period achieves its maximum of T_{inf} = 3.5 weeks. The quadratic *M* – – relation thus causes convergence to a lower mortality level (*M* = 0.33), compared to the linear relation (*M* = 0.5) (see Fig. 1 b)).

Host selection is driven by the survival probability of infected hosts. Hosts that are more resistant have a higher probability to survive infection, thus have a greater reproductive success. The rate of virulence shift over time is determined by the distribution of potential case mortality in the initial host population. A higher fraction of hosts with a low potential case mortality, i.e. the more "resistant" hosts, results in a faster shift in virulence. Host resistance selection favours

hosts with a low probability of virus-induced death. It thus works towards continuously lowering case mortality.

Persistence

Virus survival curves revealed the characteristic pattern of invasion, epidemic, and endemic phase (EFSA 2008; Kramer-Schadt 2009). After virus release a high proportion of simulated outbreaks faded out within the first year. For the quadratic M – – relation, the probability of early virus extinction was much higher (50%) compared to the linear relation (30 – 40%). The difference is caused by a higher mean infectious period T_{inf} in the linear case, causing a higher probability of secondary infections. Obviously this dynamic is mainly independent of the assumed evolutionary scenario as the selection processes were not functioning while the outbreak had already faded out.

From years 1 to 4 after virus release when, in the epidemic phase, the infection wave progresses through the naïve population, rather few extinctions occur. This time, which is basically defined by the spatial extent of the wild boar population (not varied in our simulation), is available for the selection mechanisms, i.e. towards host resistance or low virulence (less lethal).

During the transition to the endemic phase that followed, extinction probability rose again. As Kramer-Schadt et al. (2009) have shown, only outbreak simulations with moderate virulence could survive the transition towards the endemic phase, hence getting long-term persistent as observed in France and Germany. Virus persistence in our simulations was thus determined by the successful evolution towards reduced virulence features, i.e. lower case fatality. Persistence was increased by host selection as well as pathogen evolution where suitable parameters (= 0.5, = 2 and $b_{virus} \geq 0.05$, respectively) allowed a fast decrease of virulence. Pathogen evolution exhibits a faster decline in mortality towards maximum effective mean infectious period T_{inf} (Fig. 1 b), resulting in higher virus persistence probability in the endemic phase.

When comparing linear versus quadratic M – – relations, the probability of virus presence with the quadratic relation exceeded the one for the linear relation after 12 years, although showing a lower value at the start of the endemic phase. This phenomenon can not be explained by the effective mean infectious period T_{inf}, since its maximum value, as the target of pathogen evolution, is equal for both scenarios. Instead the further reduction of case mortality, M and the resulting higher population densities for the quadratic M – – relation decreased the extinction probability in the endemic phase.

The evolutionary gain driving a virulence decrease in the short term of a particular outbreak induces an advantage for the virus in the long term too. Prolonging the mean infectious period of affected hosts, the decline in virulence promotes maintenance of the infection chain and thus facilitates disease persistence. A virus strain persisting in a local population has an increased chance to cause further outbreaks in neighbouring or remote areas.

Conclusions

The perception of declining case fatality in the course of an outbreak would have been possible with both mechanistic scenarios, although the smooth dynamics with host selection might be less apparent in the field. Both host mediated and pathogen mediated mechanisms producing lower case fatality result in an increased probability of persistence. However, the shorter generation time of pathogen mediated selection enables a rapid dynamic that might be

sufficient to reach an endemic situation within reasonable time of a CSFV outbreak in wild boar, e.g. about 8 months in the French Vosges mountains or German Pomerania. Future research is required to investigate the implication of both assumptions with regard to the apparent picture if the virus had invaded new, naïve populations in the past, and how long highly virulent situations were actually observed.

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