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SIMULATION BASED INVESTIGATIONS ON THE CONSEQUENCES OF CHANGED RABIES SPREADING WITHIN IMMUNISED FOX POPULATIONS

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L'immunisation à large échelle des populations européennes de renards contre la rage fait l'objet de beaucoup d'attention. Au cœur du débat, il y a la possibilité de réduire considérablement les fonds publics destinés à la lutte contre la rage sans menacer la santé publique. Les connaissances actuelles sont encore insuffisantes pour apprécier le succès final de la campagne et pour interpréter les derniers cas sporadiques. Les nouvelles conclusions de notre modèle impliquent que la rage peut persister malgré un taux de vaccination supposé correct. Ceci dit, l'éradication arrive après 6 ans de vaccination à large échelle. Le modèle associe une échelle population hôte et une approche individuelle des renards. Il est possible pour la première fois d'étudier le comportement du système virus-hôte à la bonne échelle spatiale et temporelle, sans négliger les petits événements aléatoires de la diffusion de la rage.

INTRODUCTION

Rabies is one of the most hazardous zoonoses in the world. Although in Europe rabies occurs mainly in a sylvatic cycle, it causes numerous human infections as well (WHO 1980). For 15 years the current epidemic has been controlled by oral immunisation of the reservoirs, especially of red foxes (Vulpes vulpes). The red fox lives in almost all habitats, including urban regions, and moreover, has a reproduction rate that is enormous. These particular circumstances require extensive immunisation programmes. Different vaccination strategies have been used to solve the resulting trade off between the considerable expenditure of public funds necessary to combat rabies (Curk 1991) and the remaining risk for public health.

Measures taken in Germany towards rabies control aim at the eradication of the disease rather than a short-term reduction of incidence. Economic studies and empirical evidence favour large-scale and long-term vaccination of all foxes, as has been applied in Eastern Germany for at least five years. With 108.000 km² of territory, Eastern Germany currently represents the largest coherent vaccination area in Europe (Stöhr&Meslin 1996).

The vaccination campaign in Eastern Germany causes drastic decrease of rabies incidence *(fig. 1)* and some regions are currently assumed to be free of the disease. Consequently, politicians have been encouraged to terminate the vaccination programme in view of the cost of such measures.

Unfortunately, single cases occur sporadically over space and time despite of continuous vaccination *(fig. 1)*. From this observation, one can expect the potential risk of a new outbreak after termination of the vaccination programme. It was, therefore, the main goal of our study, to gain insight into the epidemiological background of last sporadic rabies cases in a continuously vaccinated host population.

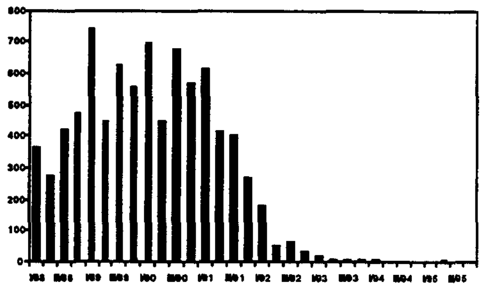

Figure 1 : Detected rabies cases from Eastern Germany 1989-1996 ; three monthly (WHO Collaborating Centre)

We find low-level persistence of rabies to be a reason for the sporadically detected cases *(fig. 4)*. This form of the disease is a local phenomenon which is triggered by the small stochastic occurrences of rabies spread within immunised fox populations.

As is well known, an estimate of the detection rate for rabies is only 10% (Schlüter&Müller 1995), and some authors assume that only 2% of the underlying cases will be detected (Braunschweig 1980). On the other hand, this estimate is based on a homogeneous distribution of prevalence over space and time. Finally, as our study shows, low-level persistence of rabies occurs via small clusters which move over space and time. In summary, a low-level persistence of the disease would match with such rare sporadic cases as observed in Eastern Germany during the past several years.

Our investigations focus on the most crucial questions concerning rabies control by oral vaccination. These include the effect on prevalence in percentage, the chance of eradication of the disease, the risk of low-level persistence of rabies and implications for further strategies and emergency measurements after termination of the vaccination campaign. Thus, we introduced the disease-related approach in our model, avoiding entanglement with sparse empirical knowledge, such as controversial assumptions about home-range sizes, and without neglecting the transparency necessary to explain the basic spreading mechanisms. This approach provides the potential to handle simulations on a wide range of spatial and temporal scales, which has not been possible within any other existing model.

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METHODS

Keeping in mind the uncertainties of former rabies models concerning the social or territorial behaviour of red foxes, such as the basic reproduction rate of the disease, the estimation of contact rates or the individual differences in incubation periods (Anderson et al. 1981, Voigt et al. 1985, Murray et al. 1986, Smith&Harris 1991), we develop a new way of modelling the host population within the concept of **Infection Communities**. The concept of an Infection Community (IFC) is based on the characteristics of rabies and the known establishment of temporal social fox communities of small size in which contact rates can be assumed high enough to spread a potential infection throughout the whole group immediately. With this concept, we introduce a way to examine the spread of rabies disease related and to avoid intricate theoretical problems concerning unknown social and epidemiological factors. Moreover, because the definition of IFC is not area-dependent, our model output is robust against varying population densities.

We implemented a two-dimensional grid-based cellular automata to arrange the IFCs in space. Any cell represents one IFC. Each IFC can hold precisely one of the following states: **SUSCEPTIBLE** for IFCs in which all members are susceptible for an infection, **INFECTED** for IFCs in which at least one animal is infected and **EMPTY** for extinct IFCs as a result of an infection. The spatial arrangement of IFCs was exposed to whole area vaccination twice a year. This was accomplished by introducing three new states representing IFCs a proportion of which is immunised. The actual proportion in such 'partially immunised' IFCs depends on the assumed mean immunisation rate *(fig. 2)*.

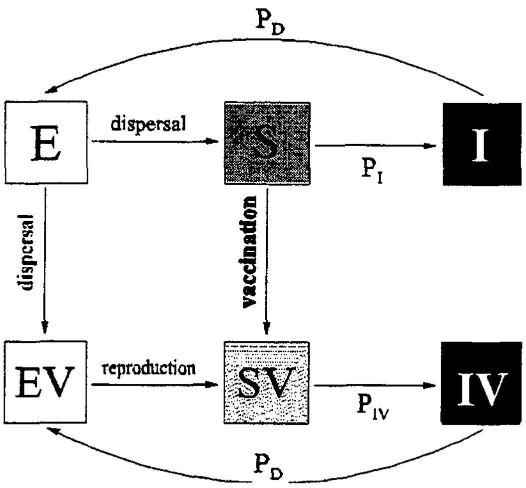

Figure 2 : The six staes of IFCs. E = empty; S = sus-ceptible; I=infected; V=under Vaccination. The arrows sign the possible stae transitions with the responsible rea-sons. P_I = probability of infection; P_D = probability of dead after infection.

Rabies can spread by the following three probabilistic mechanisms: neighbourhood infection, mating period and dispersal. Most local spread of rabies by neighbourhood infection is caused by interactions and conflicts between adjacent IFCs. With a changeable probability, a susceptible IFC will be infected if there is an infected neighbour. For the first time in such a study, we considered the spatial effect of the increased dispersal activity of itinerant adults during the mating period in our model, taking three rings of neighbouring IFCs into account. Introducing the stochastic effects of the annual dispersal of fox cubs, the movement of and occurrences of infection among single foxes are described on an individual basis. Both the number of dispersing cubs and the distribution of dispersal distances follow most recent field data of red foxes (Goretzki et al. 1997). Because immunisation reduces the susceptible part of the host population, the onset of vaccination in turn reduces the infection probabilities within the three spreading mechanisms in an appropriate manner.

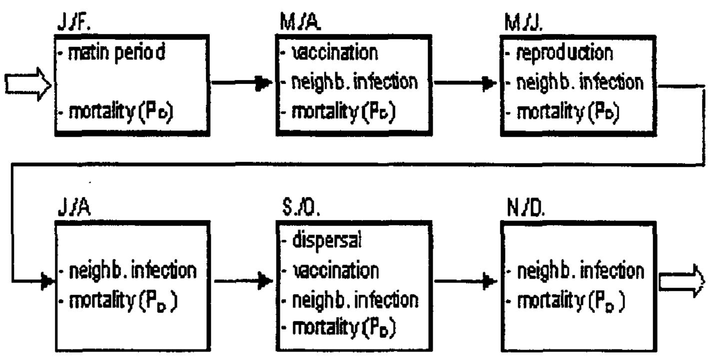

Figure 3 : The sequence of single processes during one year. Reproduc-tion is scheduled just in May because of the delayed effect of an offspring infection for the whole IFC.

We use a temporal scale of two months, which is supported by the cycle of rabies infection and is consistent with the annual rhythm of red foxes *(fig. 3)*. The model output fits known wave patterns in the spatial spread of rabies, as well as long or short cycles in time series of rabies incidence without vaccination (Jeltsch et al. 1997). In the same manner, the model reproduces a drastic decrease in rabies occurrence within the first two years of vaccination as observed in field data *(fig. 1)* and assumed by other authors (Anderson et al. 1981, Schenzle 1995). If the host population has been relaxed and the assumed efficacy of vaccination is low, say less than 60%, the epidemic clearly recovers and can exceed the incidence level of the equilibrium state before vaccination. These aspects, together with more theoretical improvements, guarantee a reliable tool for simulation based investigations of rabies spread in immunised populations.

Our results are produced by simulating 10 years after the onset of vaccination on a square lattice of 20,000 cells, which corresponds to an area of about 20-40 thousand km². For each epidemiological meaningful parameter configuration, 100 simulation runs were performed to balance the stochastic effects of the model. Varying all parameters of the model over their meaningful range gives a set of probabilistic results, which reflect the general behaviour of the system in a whole set of different biological situations. We can discuss our results in terms of the proportion of the chosen parameter space that leads to a certain result, avoiding the need to declare one single parameter configuration to be the most suitable (see also Spear&Hornberger 1983). This simulation experiment was carried out for immunisation rates between 64 and 74 percent.

RESULTS

The immunised fox-rabies-system can produce a low-level persistence of the disease, the detection of which is at least uncertain with practicable surveillance measures. Studying this phenomenon systematically, we defined a low-level persistence of rabies to be when the actual prevalence in the host population is never zero and always less than 0.2% *(fig. 4)*. Low-level persistence of rabies can occur within 11% of the entire parameter space we examined. The final occurrence is a stochastic event and afterwards the disease can persist within the defined range of prevalence for more than ten years despite continuous vaccination. Low-level persistence of the disease produces typical patterns of small local clusters which move over space and time.

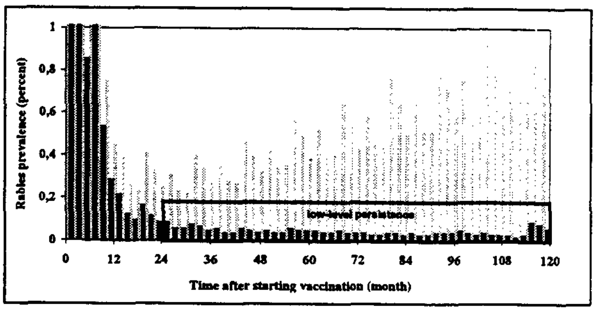

figure 4: Definition of low-level persistence of rabies. two years after the onset of vaccination the actual is steadily under 0.2%. To the contrary the simulation background clearly

The chance of eradicating the disease increases together with the increased assumed immunisation rate, as anticipated. For every immunisation rate we examined the probability of eradication over time. We found that eradicating rabies is generally impossible before three years of continuous vaccination. Within 3-6 years of vaccination, the probability of eradication shows a steady increase and after six years eradication of the disease becomes almost certain. The remaining risk is mainly caused by potential low-level persistence of rabies and could be reduced by the time of vaccination at best asymptotically. Only increasing the immunisation rates up to 80% could help. However, this would require further financial outlay combined with decreasing cost-benefit efficiency.

CONCLUSIONS

In summary, a long-term and large-scale oral vaccination campaign of red foxes for at least 3 and at most 5-6 years seems to be a effective measure in rabies control. A further continuation of the vaccination programme is less efficient and therefore not recommended for practical and economic reasons. Vaccination should be terminated. However, because of the possibility of covered low-level persistence of rabies, we advise preparation of financial and logistical means to deal rapidly with a potential new local outbreak. Consequently, our investigations actually involve the examination of the spatio-temporal dynamics of such new outbreaks and the derivation of efficient emergency programmes.

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