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Impact of myxomatosis in relation to local persistence in wild rabbit populations: The role of waning immunity and the reproductive period

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Abstract

Many diseases are less severe when they are contracted in early life. For highly lethal diseases, such as myxomatosis in rabbits, getting infected early in life can represent the best chance for an individual to survive the disease. For myxomatosis, early infections are attenuated by maternal antibodies. This may lead to the immunisation of the host, preventing the subsequent development of the lethal form of the disease. But early infection of young individuals requires specific demographic and epidemiological contexts, such as a high transmission rate of the pathogen agent. To investigate other factors involved in the impact of such diseases, we have built a stochastic model of a rabbit metapopulation infected by myxomatosis. We show that the impact of the pathogen agent can be reduced by early infections only when the agent has a long local persistence time and/or when the host subpopulations are highly connected. The length of the reproductive period and the duration of acquired immunity are also important factors influencing the persistence of the pathogen and thus, the impact of the disease. Besides confirming the role of classical factors in the persistence of a pathogen agent, such as the size of the subpopulation or the degree of connectivity, our results highlight novel factors that can modulate the impact of diseases whose severity increase with age.

Keywords: Maternal immunity; Infectious diseases; Stochastic model; Metapopulation; Critical community size

1. Introduction

Sooner or later all parasites become extinct from their host population. How long this takes is a fundamental question of modern epidemiology. Many theoretical studies (Anderson and Britton, 2000; Nasell, 1995) have focussed on this question, giving rise to the concept of critical community size (CCS, Bartlett, 1956).

The CCS of a host population infected by a given parasite defines a point where the two time scales of extinction are very different between populations below or above the CCS. Above the CCS, the pathogen can maintain itself almost indefinitely and individuals are regularly exposed to the disease agent. Below the CCS, the agent will rapidly die out after its introduction. If reintroduction of the pathogen does not occur rapidly, the susceptible pool of the host population will be replaced, e.g. through births or waning immunity. The next reintroduction of the agent then results in a large epidemic since most individuals are susceptible.

As revealed by recent studies, this dichotomy in pathogen circulation may have important implications. Rapid extinction from a host population may have an evolutionary cost for the pathogen. In host populations made up of small and isolated subpopulations, persistent strains tend to replace invasive but non-persistent ones (Keeling, 2000). Another interesting example is the case of bubonic plague. The transmission of the bacteria *Yersinia pestis* to humans often occurs when the rat population is below the CCS (Keeling and Gilligan, 2000a, b). This is

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because large epidemics in rats generate a demographic crash in the host population causing fleas to transfer to an alternative host species, such as humans, transmitting the bacteria to them. These examples illustrate the fact that the CCS may significantly alter the entire relationship between the host and the parasite, whether the host population is above or below the CCS.

Recently, Fouchet et al. (2006) suspected a central role for pathogen persistence time in host–parasite interactions for which maternal antibodies can attenuate the disease. In such interactions, an early infection of the host is crucial since it permits active immunisation of the host without the cost of developing the normal and, typically, more severe form of the disease (Zinkernagel, 2001, 2003). Non-exposure at a young age could be detrimental because the young then becomes susceptible to developing the most severe form of the disease as soon as maternal protection has disappeared. Using a mathematical model, Fouchet et al. (2006) showed that the impact of such a disease ultimately decreases with its transmission rate and tends to be negligible for very high transmission rates. The model also revealed a lower impact of the disease for longer reproductive periods of the host and for waning (compared to lifelong) acquired immunity. The correlation found between the impact of the disease and factors that could influence the persistence of the parasite led Fouchet et al. (2006) to hypothesize that the impact of the disease could decrease with its persistence. The deterministic model employed in that study could not address this question.

In a more recent paper, Fouchet et al. (2007) have presented results that support this theory. They studied the impact of a disease potentially attenuated by maternal antibodies during the course of fragmentation of the host population. This study showed that the reduction in the average size of each host subpopulation, and thus of the local persistence time of the pathogen agent, initially led to an increase in the impact of the disease.

Here we chose the example of the rabbit (*Oryctolagus cuniculus*)–myxomatosis interaction to analyse the general case of infectious diseases that may have less impact on a population when young individuals can experience the infection during the time they are still protected by maternal immunity. We develop a stochastic model to understand how the impact of the disease is affected by extinction and reintroduction events. First, we quantify the extinction time by considering a simple homogeneous mixing model. This allows us to determine the key factors for virus persistence. Second, we connect a set of subpopulations with homogeneous mixing to form a metapopulation. To explore alternative possibilities to those tested by Fouchet et al. (2007), we analyse the case where persistence times are varied without altering the subpopulation size. We show that the suggestion intuited from the deterministic model provided by Fouchet et al. (2006), i.e. that waning immunity and the length of the reproductive period affects the impact of myxomatosis, was correct when a more relevant model was considered. We conclude that extinction and reintroduction events are crucial factors in the impact of the disease. This study allows us to isolate factors that can be important for disease management.

2. Material and methods

2.1. The rabbit–myxomatosis interaction

Rabbit populations are socially and spatially structured. Within a social group, conflicts occur between males for access to females, whereas females generally compete for access to reproductive sites. Fights between individuals of different social groups are less frequent, and are mainly due to defence of the group territory (Cowan, 1987). Dispersal of juveniles of less than four months of age is common. Males typically disperse more than females (Richardson et al., 2002).

In France, mean rabbit density varies between populations, ranging from less than 1 rabbit/ha to more than 20 rabbits/ha (Marchandeau et al., 2006). Rabbits are seasonal breeders, commencing around February and finishing between July and November, depending on food availability (Cooke, 1981, 1982; Myers and Poole, 1962; Poole, 1960; Wheeler and King, 1985; Wood, 1980). Mean annual mortality is approximately 50% (Cowan, 1987; Parer, 1977; Rogers et al., 1994).

Myxoma virus is a leporipoxvirus that induces myxomatosis in the European rabbit. When released in Australia (1950) and in Europe (1952) the virus spread extensively, causing significant damage to rabbit populations (Giban, 1956). During subsequent years the impact of the virus remained high, but was significantly lower than during the initial epidemics. Several factors may explain this decrease in virus impact. First, intermediate virulent strains, which are less virulent than the introduced strains, have selective advantage over these more virulent strains because more virulent strains have a smaller reproductive ratio (Dwyer et al., 1990; Fenner, 1983; Fenner and Fantini, 1999; Fenner and Ross, 1994). Second, rabbits have developed a genetic resistance against the virus (Sobey, 1969). Finally, rabbits that have survived myxomatosis become immune (Fenner and Ratcliffe, 1965; Saurat et al., 1980). Waning of acquired immunity has been observed in laboratory conditions (Saurat et al., 1980) and suspected in the field (Marchandeau and Boucraut-Baralon, 1999), but the capacity of adults to transmit the disease following re-infection is not yet established. Part of the immunity of the dam is transferred to offspring via maternal antibodies, which are protective for around one month (Fenner and Marshall, 1954; Kerr, 1997; Sobey and Conolly, 1975).

The virus can be transmitted through three routes. Mechanical transmission by arthropod vectors, such as fleas and mosquitoes biting the host, is the most efficient (Fenner and Chapple, 1965). Mosquitoes are able to travel long distances and keep the virus active for long periods