The Effect of Vaccination on Undetected Persistence of Foot-and-Mouth Disease Virus in Cattle Herds and Sheep Flocks

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ABSTRACT
The importance of foot-and-mouth disease virus carrier animals - those in whom virus persists after recovery from disease or acute infection - and their potential role in the spread of disease remains unclear. We attempt to quantify the effect of emergency vaccination – and especially the time of application - on the likely number of such animals, using simple probabilistic models and data from challenge experiments on both cattle and sheep. The number of persistently infected animals in a group is predominantly determined by the number of animals initially infected and the level of vaccination, although in cattle herds the number of carriers may potentially increase if challenge occurs shortly after vaccination. We conclude that the quality of inspection is the principal factor influencing whether or not carrier herds occur and present results on the requisite test sensitivity for successful sero-surveillance.

KEYWORDS Epidemiology, Modelling, Foot-and-Mouth Disease, Persistence, Vaccination.

INTRODUCTION
Foot-and-mouth disease (FMD) is a highly contagious disease of cloven hoofed animals endemic in many parts of the world. It is of global social and economic importance although it can be successfully controlled with vaccination and has been eradicated in a number of countries.

The application of emergency vaccination for control purposes induces immunity and reduces both disease and viral transmission, although protection is not immediate and depends on the time, strength and strain of subsequent challenges. The virus has been found to persist in ruminants, at low levels, beyond the period of acute infection or disease. Transmission by such carriers has been recorded in buffalo (Dawes et al., 1994), but not in domestic species, and the epidemiological significance of such animals remains unclear.

We consider the potential for carrier cattle and sheep to remain undetected in herds or flocks in a normally disease-free context (where the response to disease is eradicating through culling etc.). For this to occur we first require animal to become infected, for the infection not to be noticed (more likely if there is little disease), and for some of the recovered animals to go on to become carriers. We assume that if infection is detected anywhere in a herd then all animals are removed.

METHOD
We consider a simple model without within-herd spread, deemed appropriate for vaccinated herds (Orsel et al., 2007), applying results from transmission experiments on cattle (Cox et al., 2007) and sheep (Parida et al., 2008). These provide estimates at different times (0, 10 and 21 days post vaccination for cattle; 0, 4 and 10 days post vaccination for sheep) of the following probabilities: \( p \), the probability of challenged animal becoming infected; \( q \), the probability of an infected animal developing the disease; \( r \), the probability of a diseased animal becoming a carrier; and \( s \), the probability of a sub-clinically infected animal becoming a carrier; to which we fit appropriate continuous functions (Schley et al., 2009).

The probability of an individual animal becoming a carrier given that it has been challenged is therefore given by

\[
t = pqr + p(1-q)s
\]

where \( t \) is the time of challenge post vaccination, \( d = 0 \) for unvaccinated animals.

We assume that animals change state independently, and so probabilities are binomial (henceforth, define \( P_x(a|b) \) as the binomial probability mass function of \( a \) successes out of \( b \) trials with individual success probability \( x \)). To calculate the probability of \( m \) carriers remaining undetected in a group of \( h \) challenged animals, the probability of animals developing detectable clinical signs is important. For simplicity we assume that disease is detected within the herd (and the group therefore removed) if \( J \) or more animals develop the disease, so that:

\[
P_{h \text{ challenged}}^m = \sum_{i=0}^J P_i(h|i) \left( \sum_{j=0}^{J-1} P_j(m-j) \left( \sum_{k=0}^{m-k} P_k(m-k|i-j) \right) \right).
\]

To calculate the probability of \( m \) undetected carriers in a group of \( n \) animals, we need to define the probability that \( h \) out of \( n \) animals will be challenged. From the 2001 UK outbreak this is approximated using
a negative binomial distribution with mean $\mu = 4.21 + 3.86 \times 10^3 n$ and dispersion $k = 1.12$ (Schley et al., 2009). The probability of such herd being subsequently found through sero-surveillance using a test with sensitivity of S% and specificity of 100% (on the assumption that positive results will be intensively followed up) is given by:

$$P(\text{detection|present in herd}) = \sum_{m=1}^{n} \left[ (1 - (1 - S)^n)^{m} \right] \frac{P(m \text{ carriers out of } n \text{ animals})}{1 - P(0 \text{ carriers out of } n \text{ animals})}$$

RESULTS

For cattle challenged with O UKG 2001 the probability of an individual animal becoming a carrier is approximated by

$$t = e^{-6.01 \times 10^{-7} d} (3.55 \times 10^{-2} e^{-1.56 \times 10^{-6} e} + (1 - e^{-1.56 \times 10^{-6} e}) e^{-3.99 \times 10^{-6} d})$$

this is 36% for an unvaccinated cow. This drops to 20% if animals have been vaccinated 30 days in advance, but in between rises to 49% for challenge at 6 days post vaccination. This is because vaccination offers quicker protection against disease than it does against infection, and subclinical animals are more likely to become persistently infected. This is particularly important when the control of disease through the removal of infected herds if detection relies upon clinical signs. It is almost certain that a herd with a reasonable number of animals initially challenged will contain at least one carrier, with prevention relying on good detection rather than vaccination.

For sheep challenged with O UKG 2001 the probability of an individual animal becoming a carrier is approximated by

$$t = 8.21 \times 10^{-1} (2.00 \times 10^{-3} - 6.25 \times 10^{-1} e^{-2.00 \times 10^{-3} d})$$

this is 31% for an unvaccinated sheep. This quickly drops to near zero, although amongst a large number of challenged animals the probability of at least one carrier remains high. Vaccination has a significant impact on the probability of disease $q$, but not any other parameter in the model, so that detection is usually possible except in unvaccinated or very recently vaccinated animals. Since it is often difficult to spot clinical signs in sheep anyway, however, the benefits of vaccination are less ambiguous.

For a randomly selected UK farm (sizes based upon the 2006 Agricultural survey, initial number of infections based upon records of the 2001 outbreak) the expected number of carrier cattle is less than three, meaning that any sero-surveillance test would need a sensitivity of at least 89% in order to detect infection with 95% confidence – more if there is prior detection by clinical signs.

CONCLUSIONS

The persistence infection remains an important issue in FDM epidemiology until the transmission of disease by carrier animals can be ruled out. The number of persistently infected animals in a group is predominantly determined by the number of animals initially infected and the quality of disease detection. As a result the benefits of vaccination with regard to this are not straightforward, although it should be remembered that, on an epidemic scale, vaccination decreases transmission (both through increased protect and reduced virus excretion) which is usually the greater priority.

REFERENCES


ACKNOWLEDGEMENTS

This work was supported by the UK Biotechnology and Biological Sciences Research Council (IAH 1320); the UK Department for the Environment, Food and Rural Affairs (SE2812, SE1122) and the FMD Imrocon project of the EU 6th Framework Programme (SSPECT- 2003-503603).