Quantification of foot and mouth disease virus excretion and transmission within groups of sheep with and without vaccination

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Abstract:
The aim of this study is to quantify FMDV O/NET2001 virus excretion and transmission in groups of sheep with and without vaccination.

Material and Methods: Transmission of FMDV was studied in experiments with 6 groups of 4 non-vaccinated, and in 6 groups of 4 single-vaccinated lambs. Two lambs per group were inoculated with FMDV and the other two were exposed by direct contact to the inoculated sheep. We estimated the transmission rate $\beta$ using a generalized linear mixed effect model, the reproduction ratio $R$ using the final size method, and the duration of the infectious period using parametric (exponential) survival analysis.

Results: Clinical signs were mild and rare. Virus was excreted in oropharyngeal fluid before and after clinical signs were observed and also in subclinically infected sheep. In the non-vaccinated groups, the transmission rate $\beta$ was 0.105 (0.044;0.253) per day, and the reproduction ratio $R_n$ 1.14 (0.3;3.3). The duration of the infectious period was estimated to be 21.11 (10.6;42.1) days. In the vaccinated group, $\beta$ and duration could not be determined due to limited observations of virus excretion in oropharyngeal fluid. The reproduction ratio $R_v$ was 0.22 (0.01;1.78). The non-vaccinated lambs had a significantly higher mean daily virus excretion and number of days virus was excreted compared to the vaccinated groups.

Conclusion: Virus transmission did not differ significantly between vaccinated and unvaccinated groups, although the $R_v$ tends to be lower than $R_n$. Since in this experiment within-pen transmission was studied, it seems reasonable to assume that the between-herd transmission will be lower because of the lower contact rate between farms. Vaccination has a significant effect on mean daily virus excretion and number of days virus is excreted. Therefore vaccination of sheep should be considered in FMD contingency plans, especially since clinical diagnosis in sheep is difficult.

Introduction:
An outbreak of foot-and-mouth disease occurred in The Netherlands in 2001(Bouma et al., 2003). The capacity for pre-emptive culling and destruction appeared to be insufficient and therefore emergency vaccination was applied. In cattle it is known that vaccination prevents clinical signs of FMD, and single vaccination reduces virus transmission (Donaldson & Kitching, 1989, Orsel et al., 2005, Orsel et al., 2006). Experiments with pigs showed that emergency vaccination reduces transmission of FMD virus (Eble et al., 2004, Salt et al., 1998). Extrapolation of results from pigs and cattle to sheep may not be valid, because difference in susceptibility, infectivity and clinical appearance are known (Kitching, 2002, Kitching & Alexandersen, 2002, Kitching & Hughes, 2002). Therefore the important question remains whether FMDV can sustain in a susceptible sheep population and, if so, whether single vaccination can reduce FMDV transmission sufficiently to stop an epidemic ($R < 1$). The objective of the study was to quantify virus transmission within groups of lambs and in addition to determine the effect of vaccination thereon.
Materials and Methods:

We used 12 groups of 4 lambs each; lambs in 6 groups were vaccinated 14 days prior to inoculation with a DOE O-Manisa vaccine. In each group of 4 lambs, 2 lambs were intranasally inoculated with approximately 1500 CID<sub>50</sub> (cow infectious dose 50%) of the first cattle passage of the FMD field isolate O/NET2001. This dose is equal to 10<sup>4.6</sup> plaque forming units on secondary lamb kidney cells. Transmission of FMDV to contact exposed lambs was observed by recording the clinical signs and by virus titration and RT-PCR on OPF (oro-pharyngeal fluid from swabs) and plasma (from heparinised blood samples) (Terpstra et al., 1990). Antibody response to the FMDV infection was detected by a virus neutralization assay (Dekker & Terpstra, 1996) and NS ELISA on serum samples. At the end of the experiment (Day 29-30-31), probang sputum samples were collected for virus isolation.

The mean daily virus excretion (MDV) was calculated per lamb for each day that virus was detected in the oro-pharyngeal fluid (OPF) samples to compare the virus excretion in the different groups. The transmission rate parameter \( \beta \) in the non-vaccinated groups of lambs was calculated using a generalised linear model (GLM) described by Klinkenberg et al (Klinkenberg et al., 2002). The estimation of \( \beta \) was based on the numbers of newly infected (C), susceptible (S) and infectious (I) lambs per day. The duration of the infectious period, \( T \), was based on the presence of virus in the OPF samples. \( T \) was estimated with a parametric survival analysis with an exponential distribution (S-PLUS 7.0). Finally we quantified the virus transmission with a S-I-R model in which the lambs were classified as S (=susceptible), I (= infectious) and R (= recovered) at the beginning and the end of the experiment. Lambs were classified as infectious when they showed clinical signs or when one of the laboratory tests gave a positive result. Transmission was quantified with the maximum likelihood estimator (MLE) for the reproduction ratio (R) in the S-I-R model.

Results:

Clinical signs were mild and rare. Virus was excreted in oropharyngeal fluid before and after clinical signs were observed. Virus was also isolated from sheep without clinical signs. The MDV excretion between vaccinated and non-vaccinated lambs differed significantly (p=0.001). Within the vaccinated or the non-vaccinated groups no difference was observed between the inoculated and contact-exposed lambs, which is an indication for the validity of our inoculation method with respect to the excretion of infectious virus of lambs. In the non-vaccinated groups, the transmission rate \( \beta \) was 0.105 (0.044;0.253) per day, and the reproduction ratio \( R_{nv} \) 1.14 (0.3;3.3). The duration of the infectious period was estimated to be 21.11 (10.6;42.1) days. In the vaccinated group, \( \beta \) and duration could not be determined due to limited observations of virus excretion in oro-pharyngeal fluid. The reproduction ratio \( R_v \) was 0.22 (0.01;1.78). When testing the hypothesis as to whether transmission in groups with and without vaccination is the same, no significant difference was found (p=0.11). Final size of infection is shown in figure 1.

Discussion:

Transmission expressed as reproduction ratio \( R \) did not differ significantly between vaccinated and unvaccinated groups, although the \( R_v \) tends to be lower than \( R_{nv} \). However, this experiment studied within-pen transmission, and it seems reasonable to assume that the between-herd transmission will be lower because of the lower contact rate between farms. Vaccination has a significant effect on mean daily virus excretion and number of days virus is excreted. Therefore vaccination of sheep should be considered in FMD contingency plans, especially since clinical diagnosis in sheep is difficult, and virus is excreted before, after and without clinical signs.

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References:


Figure 1  Final size of infection in twelve groups of four lambs

Non-vaccinated groups

Vaccinated groups

Infectious lamb

Susceptible lamb