Comparison of transmission of FMDV in groups of vaccinated and non-vaccinated calves

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Abstract
To quantify the effect of a single vaccination on FMDV transmission in cattle, we performed two experiments with 26 calves each. In 12 groups of 4 calves each, two calves were inoculated intranasally with O/NET FMDV and two calves were contact exposed to the inoculated calves. And 2 groups of 2 calves were only vaccinated to serve as vaccine control group.

With the results of clinical inspection, virus isolation and RT-PCR in heparinised blood and mouth swab and sputum samples and the results from the NS ELISA, we determined whether contact-infections occurred. With the final size of the infection we estimated the maximum likelihood estimator MLE for the reproduction ratio R. We found that a single vaccination led to a Rv < 1. This was a significant reduction of virus transmission when compared to the Rc in non-vaccinated groups of calves.

Introduction
An outbreak of foot-and-mouth disease occurred in The Netherlands in 2001 (Bouma et al., 2001). The capacity for pre-emptive culling and destruction appeared to be insufficient and therefore emergency vaccination was applied. Although in cattle it is known that vaccination prevents clinical signs of FMD, little is known about the effect on transmission (Donaldson et al., 1989). Experiments with pigs showed that emergency vaccination reduces transmission of FMD virus (Salt et al., 1998). Extrapolation of results from pigs to cattle may not be valid, because difference in susceptibility and clinical appearance are known (Kitching, 2002; Kitching and Alexandersen, 2002; Kitching and Hughes, 2002). Therefore the important question remains, whether single vaccination can reduce FMDV transmission sufficiently in cattle to stop an epidemic (R < 1).

The objective of the study was to quantify the effect of vaccination on the virus transmission within groups of calves.

Materials, methods and animals
For our experiments we used 12 groups of 4 calves each; of which 6 groups were vaccinated. In each group of 4 calves, 2 calves were intranasally inoculated (days post challenge = DPC 0) with 1500 CID50 (cow infectious dose 50%) of the first cattle passage of the FMD field isolate O/NET2001. Transmission of FMDV to contact exposed calves was observed by recording the clinical signs and by virus isolation and RT-PCR on OPF (oropharyngeal fluid from mouth swabs) and plasma (from heparinised blood samples). Antibody response to the FMDV infection was detected by a virus neutralization assay on serum samples. At the end of the experiment (DPC 29-30-31), probang sputum samples and white blood cells were collected for virus isolation and RT-PCR.

Virus isolation on secondary ovine kidney cells was performed to measure virus titres in plasma, OPF and sputum samples Terpstra et al., 1990). The sera were tested in virus neutralisation assay and NS-ELISA (Dekker and Terpstra, 1996).

The calves were classified as S (=susceptible), I (= infectious) and R (= recovered) at the beginning and the end of the experiment. In both groups, a contact-exposed calf was classified as infectious at the end of the experiment when it showed clinical signs or when virus isolation or RT-PCR was positive for FMDV. The inoculated calves were all classified infectious by definition.

Transmission was quantified with the maximum likelihood estimator (MLE) for the reproduction ratio (R) in the S-I-R model.

Results
Clinical signs
In the vaccinated groups one inoculated calf had a small lesion in its mouth. Neither the other inoculated nor the contact-exposed vaccinated calves showed clinical signs.

In the non-vaccinated groups, vesicles in the mouth, on the coronary band or in the interdigital spaces were observed in 10 out of 12 inoculated calves, where 7 out of 12 contact-exposed calves showed clinical signs. The signs were very mild and did not have effect on behaviour or feed intake.
**Virus Isolation and RT-PCR in OPF and plasma**

In both the vaccinated and non-vaccinated groups 11 out of 12 inoculated calves tested positive in the OPF. In the vaccinated groups no positive samples were found in the OPF of contact-exposed calves. In the non-vaccinated groups 8 out of 12 tested positive. RT-PCR showed the same results, but in the vaccinated 2 and in the non-vaccinated 3 contact exposed calves also tested positive. No VI or PCR positive samples were found in the plasma of the vaccinated calves. But VI in the non-vaccinated calves tested 2 out of 12 contact exposed and 6 out of 12 inoculated calves positive. RT-PCR tested 10 out of 12 inoculated and also 2 out 12 contact exposed calves positive.

In the probang sputum samples with virus isolation and RT-PCR 11 animals tested positive. Of these, 3 animals were inoculated vaccinated calves, 5 were inoculated non-vaccinated calves. These calves are carriers because they were tested 28 DPC. Three contact-exposed non-vaccinated calves tested positive. All WBC samples at 28 DPC were tested negative.

**Antibody tests**

All vaccinated calves, except one, showed a rise in neutralizing antibodies in the virus neutralization test 14 days after vaccination. No fourfold increase in antibody titre was observed after inoculation. All inoculated non-vaccinated calves developed a VN titre higher than 0.3 \(10^{\log_{10}}\) TCID \(_{50}\). Out of 12 contact-exposed calves 8 showed a positive antibody titre after contact with inoculated calves.

When testing in the NS ELISA in the vaccinated groups we found 6 out of 12 inoculated and 1 out of 12 contact exposed calves positive. In the control groups 10 out of 12 inoculated and 5 out of 12 contact exposed calves tested positive.

The animals that served as vaccine controls tested negative for all tests with exception of the virus neutralization assay. Neutralizing antibodies were found as a result of the vaccination, because they were not inoculated or contact exposed to FMDV, which was proved by negative test results in the NS-ELISA.

The test results were applied in the S-I-R model, and this resulted in a Maximum Likelihood Estimator for R in the vaccinated groups \(R_v = 0.17\) \((p=0.04)\). The MLE for R in the non-vaccinated groups was \(R_0 = 3.30\) \((0.032)\). When testing \(H_0: R_0 <= R_v, p = 0.004\).

**Discussion and conclusion**

From the estimators for \(R_0\) and \(R_v\) we conclude that vaccination significantly reduced virus transmission in free-roaming calves. The reproduction ratio in our experiment is estimated within the herd, but R can be estimated at different levels. The \(R_v\) within the study is <1, it implicates that major outbreaks within the herd are not likely to occur (De Jong and Bouma, 2001). This also means that the probability of the infection being transmitted to other herds is very small, because an infected animal will probably infect fewer animals in other herds than in the same herd (Van Nes et al., 1996).

Also less indirect contacts are likely between herds when compared to indirect contacts within herds. In the control groups a significant \(R_0\) above 1 is estimated which implies a chance of a major outbreak within a herd. With increased numbers of infected animals and increased virus load a chance of a major outbreak between herds increases as well.

Single vaccination may therefore be an important tool in reducing virus transmission during an epidemic of FMD.

**References**


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<td>Not infectious</td>
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Table 1: Results of transmission in vaccinated, non-vaccinated and control groups of calves