

be responsible for preserving intact viruses capable of infecting susceptible cells as they come into contact with germinal centres.

African buffalo (*Syncerus caffer*) are typically infected with all three South African Territories types of FMDV by 2 years of age and these viruses can be transmitted to farmed livestock. Buffalo harbour persistent virus in greater amounts and for longer periods than cattle and thus provided us with further opportunities to define the sites of viral localisation.

FOOT-AND-MOUTH DISEASE VIRUS EARLY PATHOGENESIS: NOVEL FINDINGS TO AN OLD PROBLEM

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Foot and mouth disease (FMD) is a devastating disease of cloven hoofed animals (ruminants, pigs) that continues to limit trade and cause economic hardship in many parts of the world. Understanding the basic mechanisms of viral pathogenesis, including the viral and host determinants of virulence is pivotal to developing effective control and eradication tools. We have combined veterinary pathology with molecular biology and bioinformatics approaches in order to better understand the virus – host interaction under conditions that mimic natural infection. Using a novel cattle aerosol inoculation method we histologically characterized the primary replication site of FMDV infection and the early events leading to viraemia, generalization and disease. Two approaches were used to explore virulence determinants in the viral genome; we introduced either random mutations or targeted mutations in regions predicted to influence pathogenesis in a FMD infectious virus cDNA clone. Viable viruses were recovered with mutations in coding and non-coding regions that were characterized in a relevant aerosol exposure model in cattle. A mutant virus containing a 19 amino-acid insertion between the two polyprotein initiation codons in the 5' end of the viral genome was attenuated in cattle after aerosol exposure. Furthermore, replication of this mutant virus was restricted to the primary replication sites in the pharynx. The application of functional genomics to the understanding of the FMD virus – host interaction in a relevant animal inoculation model uncovered novel pathogenesis mechanisms and deepened our understanding of this relevant animal disease.

A STOCHASTIC PROBABILITY MODEL TO QUANTIFY THE RISK OF TRANSMISSION OF FOOT AND MOUTH DISEASE VIRUS AT THE WILDLIFE/LIVESTOCK INTERFACE OF KRUGER NATIONAL PARK, SOUTH AFRICA.

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In Southern Africa, the African buffalo (*Syncerus cafer*) is a natural reservoir of foot and mouth disease virus (FMDV) and outbreaks of FMD with SAT 1, 2 and 3 strains from buffalo origin are common among cattle grazing outside protected areas.

Therefore, there is a need for epidemiological tools that allow analyzing and understanding host/pathogen interactions susceptible to occur during the process of disease transmission at the wildlife/livestock interface.

Based on data obtained in South Africa, a stochastic model to quantify the yearly risk of transmission of FMDV from buffalo to cattle grazing in adjacent areas of KNP has been developed. Data were gathered from literature sources, available data collected by South African State Veterinarians in Kruger National Park (KNP) and its buffer zone, and from semi-structured questionnaires implemented in cattle farming areas.

We used the yearly total population of buffalo in KNP at different stages of life, the prevalence of FMDV in buffalo according to age, the yearly number and age of buffalo escaping from KNP, the probability of excreting FMDV according to age, the estimated time and frequency of contact with cattle in the buffer zone, the rate of FMDV excretion according to infectious status and the number of cattle in the buffer zone and their vaccination coverage. The model is based on a stochastic Monte Carlo simulation process and has been constructed with the use of an Excel spreadsheet combined with @Risk 5.0 software application (Palissade Corporation, Inc).

The output of the model is the probability of at least one cattle in the buffer zone becoming infected with FMDV by buffalo in the buffer zone. The model simulations show that it is 250 fold more likely for a carrier buffalo to cross the KNP fence than it is for an acutely excreting buffalo to do so. Moreover, the probability for an adult carrier buffalo to contact cattle is almost 300 times bigger than for a young excreting buffalo to do so.

Nevertheless, the mean probability for an excreting young buffalo to transmit FMDV to cattle per year is almost 70.2 fold higher than for a carrier buffalo to do so.

The final risk estimation for a buffalo to cross the fence and infect unvaccinated cattle is a mean probability of 0.06 with a 90% confidence interval ranging between 0.013 and 0.305.

Sensitivity analysis showed that the main inputs having an influence in our risk estimation were the time of contact between wildlife and cattle ($R^2=0,5$), the number of buffalo that escape from the park (particularly young animals) ($R^2=0,39$), the time of viraemia ($R^2=0,29$) and the vaccination coverage in cattle herds ($R^2=0,21$).

The model is sensitive to different event scenarios such as a massive escape of buffaloes and a drop in vaccination coverage. A massive escape of 1000 buffalo/year increased the mean risk of transmission to 0.482, CI 90% [0.07- 0.93], almost 8 times higher than with the average scenario.

Equally, a drop to different levels of vaccination coverage (75%, 50% and 25%), increased the mean probability of risk of transmission to cattle from 0.1 to 0.3, respectively, with 90% confidence intervals progressively approaching 0.9.

Despite the model relies on important assumptions in terms contact and transmission rates between buffalo and cattle and does not consider vaccination efficiency or contacts of cattle entering the park, it is a useful tool to improve our understanding of host pathogen interactions during FMD transmission at the wildlife livestock interface. It is also useful to assess the impacts of different control strategies in the transmission process (e.g. removal or erection of fences, variations in vaccination coverage). It is not spatially explicit, but can be run on specific areas of the KNP Western boundary if information is available.

Once validated, it can be improved by integrating new information such as vaccine efficiency and has the potential to be adapted to other contexts in Southern Africa if good quality data become available.

GETTING TO THE HEART OF FMDV PATHOGENESIS.

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Background: The pathogenesis of FMDV in the natural host has been investigated primarily in domesticated animals, namely cattle, sheep and pigs. Epithelial involvement in FMDV infection is at the forefront of investigators minds, and thus is examined most frequently.

It has been noted that non epithelial infection in susceptible animals may occur, namely that of the heart, with neonatal animals presenting with signs of this pattern of infection. The presenting sign is almost exclusively death, with a subsequent gross histopathological observation of a "myocarditis". Cellular localisation of FMDV replication, kinetics of infection, and prevalence of FMDV induced cardiac damage in any animal has not been assessed previously

Aims: To investigate in detail, the cardiac pathology caused by infection of neonatal lambs with FMDV.

Methods: 8 neonatal lambs were infected with serotype O FMDV UKG/2001 via direct inoculation, and 4 were infected via direct contact. These lambs were sequentially euthanized at time points up to 10 days post infection. Serum samples were collected daily, with heart tissues being collected at each post mortem time point.

Using immunofluorescence microscopy and monoclonal antibodies to both viral structural and non-structural proteins, the presence of FMDV replication in the heart tissue was investigated. Subsequent inflammatory cell infiltrates were also characterised using immunofluorescence and leukocyte specific markers.

Cardiac troponin T levels were measured in all serum taken in the experiment as a non invasive way of assessing cardiac damage.

Results/Conclusion: The presence of FMDV replication in the heart, and subsequent cellular localisation of this replication have been investigated. Immunofluorescent microscopy of the cardiac inflammatory cell infiltrate using leukocyte specific markers has allowed a much more sensitive recognition of myocarditis to be achieved when compared to traditional H&E staining of tissues.

Analysis of serum samples taken, using a cardiac troponin T based assay, has allowed the daily progression of cardiac disease to be assessed, revealing a high prevalence of subclinical cardiac damage during FMDV infection.

The serum markers of cardiac damage, combined with the FMDV localisation/tissue damage, and inflammatory cell infiltrate characterisation have allowed a complete picture of FMDV heart infection to be drawn.

In addition, correlations between immune responses and progression of cardiac disease in FMDV have also been noted, seemingly more beneficial than detrimental to survival of the animal.

This is the first study to demonstrate replication of FMDV in the heart of a natural host, and to demonstrate the prevalence of cardiac damage in infected animals using a serum based test. This study may be the basis upon which the prevalence of cardiac damage in field outbreaks may be assessed, which is currently unknown.

THE DAIRY INDUSTRY'S ROLE IN MANAGING FMD OUTBREAKS

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The Australian dairy industry will be a major partner with the Commonwealth and State/Territory governments in the control and eradication of a Foot-and-mouth disease (FMD) outbreak in this country. An outbreak of FMD would have a severe impact on the dairy industry. The Australian dairy industry is highly efficient and operates to international standards. The industry is a major player in the world dairy trade with around 50% of production nationally being exported, with Victoria (66%) and Tasmania (62%) particularly aligned with FMD-sensitive export markets.

This presentation will discuss the impacts and the arrangements that the Australian dairy industry has to meet its partnership obligations in the event of an FMD outbreak.

Australian Dairy Farmers, the peak dairy farmer organisation, is a signatory of the governments-industries Emergency Animal Disease Response Agreement (EADRA). The dairy industry operates in a collaborative partnership involving farmers, manufacturers and service organisations. The location and nature of the dairy industry is likely to favour the persistence and spread of FMD. As milk is a perishable product, the industry needs a rapid response. The cooperation across the supply chain enhances effective implementation of a FMD response. The dairy industry therefore has a major interest in preparing to implement a collaborative response and acts in partnership with the Australian Government and the State and Territory governments. The industry provides scientifically sound inputs to the development of contingency plans, particularly AUSVETPLAN, in relation to issues that impact on the industry. The industry will fulfil all the responsibilities arising from the EADRA but will insist that its interests are recognised in policy development and operational decision making.

Dairy Australia, on behalf of the industry, has developed and maintains the *Critical Incident Management and Recovery Plans for the Australian Dairy Industry (CMR Plan)*. The CMR Plan provides a national coordinating mechanism for the whole industry. The industry also has representatives prepared to perform the representational roles required by the EADRA and AUSVETPLAN.

Issues for the Australian dairy industry arising from an FMD outbreak, include

- The impact an outbreak and associated response would have on the industry
- Arrangements the industry has for delivering its obligations under the EADRA and AUSVETPLAN, including
 - The CMR Plan
 - Implementation of a livestock standstill
 - Arrangements for enhanced biosecurity of dairy farms
 - Measures to minimise the risk from milk tankers collecting milk from farms within the designated areas
- The importance of a scientifically sound and rational response in Australia and internationally to an FMD outbreak in accordance with international protocols to minimize the impact on the industry
- Under commercial conditions, milk and dairy products derived from milk pasteurised in accordance with the World Organisation for Animal Health (OIE) Terrestrial Animal Health Code (consistent with the EU Directive and FSANZ standards) are negligible risk since the virus is eliminated through the manufacturing process.