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Compiled by the Disease Preparedness Section Office of the Chief Veterinary Officer

Exotic Animal Diseases Bulletin

Foot and Mouth Disease vaccine

Foot-and-mouth disease (FMD) is the most infectious terrestrial animal disease known. It is a highly contagious vesicular disease affecting a wide range of domesticated and wild cloven-hoofed mammals including cattle, sheep, goats, swine and wild ruminants.[1] Infected animals exhibit blisters and ulcers in the mouth, feet and udder, lose weight and stop producing milk. Although the disease is rarely fatal in adult animals, high mortality can result in the young. On recovery ruminants can become 'carriers' with persistent sub-clinical infection.

Australia is the world's largest exporter of beef and wool, the second largest exporter of sheep meat and a major exporter of dairy products, with total export trade in livestock commodities in excess of $15 billion. As FMD is a significant issue in international trade, an outbreak in a country like Australia would have a severe economic impact.[2]

Accordingly, Australia invests considerable resources in FMD prevention and preparedness. Australia's planned response to an FMD incursion is detailed in our national emergency animal disease plan, AUSVETPLAN.[3] It relies upon early detection, rapid diagnosis and rapid response. The preferred policy remains one of 'stamping out' of all infected and in-contact or exposed susceptible animals. However it is important that Australia makes best use of new vaccine and diagnostic technologies to optimise FMD preparedness and response plans, as highlighted in the recent 'FMD New Technologies Report'.[4]

The FMD risk to Australia's livestock industries is significant, with all of Australia's domestic cattle, sheep and pigs along with a very large feral animal population totally susceptible. There is no natural resistance and animals have not been vaccinated. Of primary importance to Australia is that the immune responses of Australian cattle, sheep and pigs to the available FMD vaccines are largely unknown.

FMD vaccination

The Department for Environment Food and Rural Affairs in the UK has recently announced a new vaccination preparedness plan for FMD. Whilst the basic disease control policy in the event of a future outbreak in the UK would be the culling of infected and exposed animals, the use of vaccination would be considered if additional control measures were required.

Similarly, Australia has been evaluating the tools for controlling FMD since 2001. Government and industry agreed that Australia should maintain an FMD vaccine bank to allow access to vaccine in an emergency. Vaccination may be considered as an adjunct to directly control disease spread, or as a complementary tool to buy time to implement the traditional stamping-out control methods. The bank is maintained as a commercial arrangement by the Australian Government and industry with Merial Animal Health Ltd., and is managed by Animal Health Australia. This replaces Australia's former membership of the International Vaccine Bank, hosted by the UK.

Vaccination in the face of an outbreak does raise a number of issues. There will be a delay in formulating and transporting the vaccine, and after administration there is a period before protective levels of antibody are reached when vaccinated animals are still susceptible. Differentiating vaccinated animals from infected animals is difficult, and also vaccination could give rise to the 'carrier state'. After the outbreak is controlled and a country wishes to resume trade, vaccinated animals will need to be removed before freedom from FMD can be proven, unless a reliable diagnostic test that differentiates between vaccinated and infected animals is available and acceptable to trading partners.

Diagnostic tests that differentiate infected from vaccinated animals (DIVA) have been relatively widely tested in cattle, but there is a lack of knowledge as to their reliability in sheep and pigs.[5,6] Given that sheep are likely to be of great epidemiological significance in any FMD outbreak in Australia, the lack of a reliable DIVA testing system for sheep and other species may impact on any control strategy involving mass vaccination. The status of many of the more recent advances in diagnostics is described further in a report on new technologies for FMD commissioned by DAFF.4

What do we know about the effectiveness of FMD vaccines?

Currently, FMD vaccines are potency tested in cattle and generally give good levels of protection.[7] Most diagnostic tests for either FMD virus or antigen detection, and the detection of antibodies in serum, have been developed for cattle. However, protection is short-lived and serotype-specific, with a number of different antigen strains often required to provide a complete protective spectrum within a serotype.

FMD vaccination in sheep is less well

understood. There is little published information describing the immune responses of sheep to the FMD vaccines and no information relating to sheep breeds specifically adapted to Australian conditions. Current opinion is that if the vaccines work in cattle they will work in sheep, although the dose-related protective immune response and the longevity of the immune responses generated are poorly understood.

The development of protective levels of serum antibodies in pigs vaccinated with FMD vaccine is also poorly understood. Vaccination can prevent clinical disease but does not stop excretion and spread of virus to susceptible pigs and it is has been suggested that significant numbers of animals fail to develop protective immune responses following vaccination.

Vaccine trials at AAHL

Vaccine studies are being undertaken at the CSIRO Australian Animal Health Laboratory (AAHL) to address these gaps in our knowledge by answering the following questions:

1. How soon after vaccination can we detect antibody?
2. What antibody titres are generated and do these correlate with expected protective levels?
3. Are there different responses between species?

These trials will also generate a vital pool of reagents to enable the testing of diagnostic assays to assist Australia's FMD preparedness and allow evaluation of the DIVA tests in cattle, sheep and pigs.

Using enzyme linked immuno-sorbent assays (ELISAs), we can measure the presence of antibodies to FMD virus (FMDV), structural proteins that are produced following infection or vaccination, and non-structural proteins that are only produced following infection. This strategy enables us to investigate the feasibility of using DIVA strategies in all target species. Our data can then be compared with virus neutralisation test (VNT) results provided by Merial Animal Health Ltd. The VNT is used as the gold standard for demonstration of FMD type specific antibody.8. However, the VNT procedure requires mixing test serum with live FMDV and measuring free FMDV in cell culture and as there is no access to live FMD virus in Australia, this work must be carried out overseas.

Progress to date

Sheep and cattle housed in the high security large animal facility at AAHL have been vaccinated with three of the FMD vaccines from Australia's vaccine bank. Blood samples collected at regular intervals have been tested for the presence of anti-FMDV antibodies using the ELISA at AAHL and the VNT at Merial Animal Health Ltd.

Substantial progress has been made on identifying the interval between vaccination and the appearance of antibody, the level of antibody titres achieved and the differences between the species in their response to vaccination.

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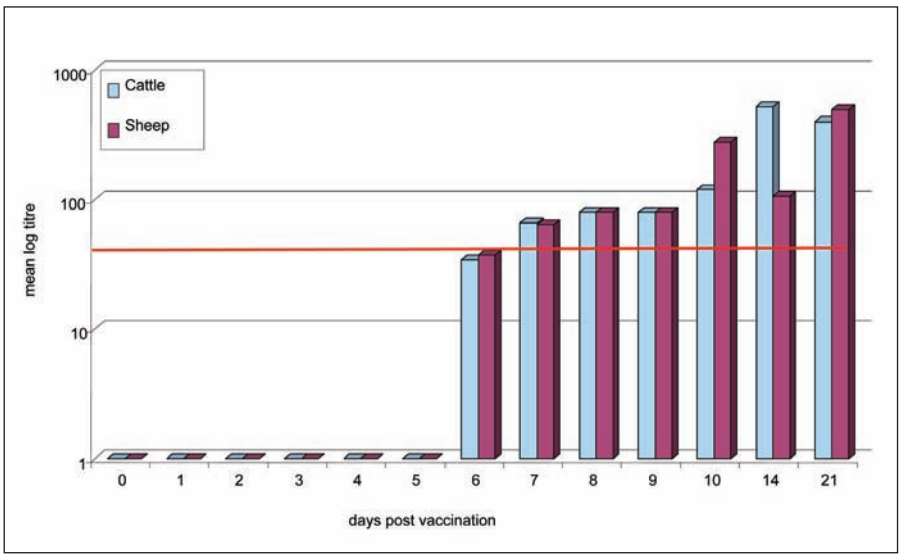

Figure 1. Mean Liquid Phase Blocking ELISA titres for sheep and cattle vaccinated with FMD vaccine 1. 1/40 cut-off titre represented by red line.

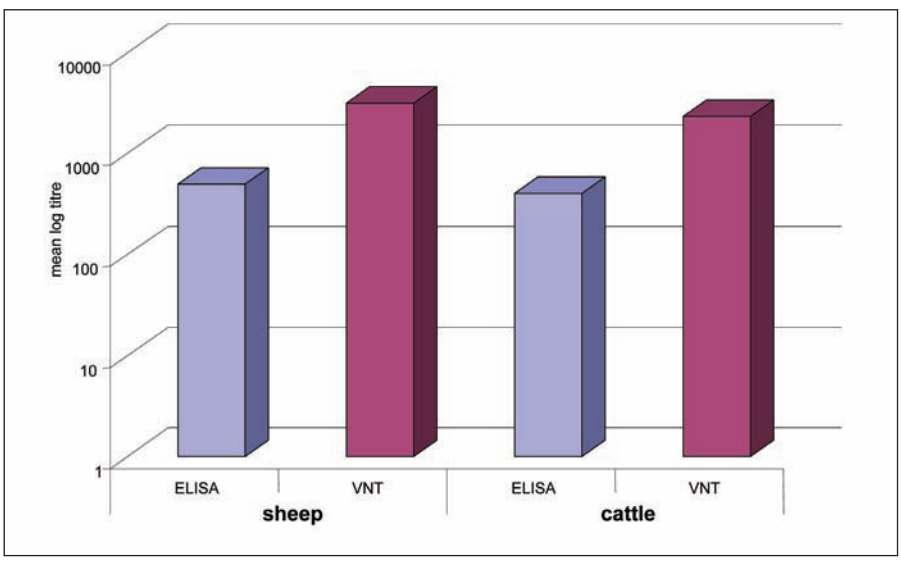

Figure 2. Comparison between mean Liquid Phase Blocking ELISA titres and mean VNT titres in final bleed sera from sheep and cattle vaccinated with FMD vaccine 1.

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Antibodies to FMDV structural proteins could be detected in both sheep and cattle at day 6 post vaccination by ELISA. Antibody levels continued to rise throughout the course of the trials (Figure 1). The data from Merial have demonstrated these animals have very high levels of serotype specific FMDV neutralizing antibodies, and these results are enabling a preliminary comparison to be made between the levels of antibody detected by ELISA at AAHL and the VNT (Figure 2). When further vaccination data is obtained, it may be possible to identify an ELISA value that correlates with a protective VNT titre and thus confidently allow prediction of protection for any animal following vaccination with any of the vaccines in the vaccine bank.

The trials also show promising results for DIVA strategy development. Following a single vaccination, no antibodies to a particular FMDV non-structural protein have been detected in any vaccinated animals. Combined with the ability of the structural protein antibody ELISA's to specifically detect antibodies to FMDV structural proteins in a time dependent manner, this provides a mechanism to differentiate between vaccinated and unvaccinated sheep and cattle. It also strongly suggests that differentiation between infected and uninfected vaccinated animals will also be possible at least at the herd level. However, further studies are necessary to confirm this.

So far, the focus of the work has been on cattle and sheep. Future work is planned to enable the testing of all the vaccine bank vaccines in pigs as well as cattle and sheep.

These studies have also provided a pool of catalogued and tested FMD serological reagents. With continued testing of the vaccines in the vaccine bank, it will be possible to develop a comprehensive Australian serum pool allowing Australia to contribute to the worldwide development and standardization of current and future FMD diagnostic assays. This will give vital confidence in Australia's FMD diagnostic capability and in turn will improve Australia's overall FMD preparedness.

Further information is available from Dr Jef Hammond (email: jef.hammond@csiro.au).

References

1. Samuel AR and Knowles NJ. Foot-and-mouth disease virus: cause of the recent crisis for the UK livestock industry. Trends Genet 2001;17:421-4.
2. Productivity Commission 2002. Impact of a Foot and Mouth Disease Outbreak on Australia. Research Report, AusInfo, Canberra.
3. Animal Health Australia. AUSVETPLAN. Edition 3, AHA, Deakin. http://www.animalhealthaustralia.com.au/aahc/index.cfm?E9711767-B85D-D391-45FC-CDBC07BD1CD4. Accessed 6 July 2007.
4. AusVet Animal Health Services Pty Ltd, and CSIRO Livestock Industries, Australian Animal Health Laboratory. Review of the potential impacts of new technologies on Australia's Foot-and-mouth disease (FMD) planning and policies — report to Australian Government Department of Agriculture, Fisheries and Forestry. 2005.
5. Kitching RP. Future research on foot and mouth disease. Rev sci tech Off int Epiz 2002;21:885-889.
6. Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-mouth Disease (EUFMD). Food and Agriculture Organization of the United Nations, Rome, 2004.
7. Doel TR. Natural and vaccine induced immunity to FMD. Curr Top Microbiol Immunol 2005;288:103-31.
8. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals. Office International des Epizooties, Paris, 2006.

Medical and veterinary cooperation in the US

The American Medical Association (AMA) and the American Veterinary Medical Association (AVMA) have pledged cooperation in efforts to address threats from zoonoses.

The AMA House of Delegates resolved unanimously in June to work together with the veterinary profession in cases involving diseases such as rabies, West Nile virus and avian influenza.

It was noted that cooperation between medical and veterinary experts had provided early warning of disease outbreaks in the past. Examples cited included the North American outbreak of West Nile virus, Ebola outbreaks, sick cats as a warning of high mercury content in fish, and lead poisoning in dogs as a warning of dangers to children from lead based paints.

President of the AVMA, Dr Roger Mahr, was cited as referring to the concept of 'one world, one health, one medicine' as demonstrating the need for close cooperation between those involved in veterinary medicine, human medicine, public health and environmental science.

The AMA resolution includes references to disease transmission across species and joint development and evaluation of new diagnostic methods, medicines and vaccines.

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