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Day

2

SUPPORT

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Dear colleagues,

Behind almost all of our problems with Foot-and-Mouth Disease are four things: the frequency of emergence of new strains, the exceptional virus infectivity and speed of spread, the impact on producers and the lack of security that comes from the limited and uncertain access to suitable vaccines.

Behind almost all our FMD mitigation nightmares is one simple fact: we do not have vaccine security.

Instead, we live with the fear that vaccine will not be available when needed, or if available, will not be effective when used, or achieve the outcomes desired. In FMD free regions, the "standard model" of vaccine banks is being challenged by the potential scale of need and the diversity of circulating FMD strains. In regions not free of FMD, the efforts being made for "risk based vaccination" and optimizing control measures relate to the same problem of lack of vaccine security. The lack of available quality vaccines results in ineffective vaccines being used, with disappointing results for the animal producers as well as nationally.

Without vaccine security, we need elaborate and well-drilled preparedness for an FMD emergency, to contain incursions before they outstrip vaccine supply. In endemic regions, millions of animals - and their owners - cannot access effective vaccines when they need them so lack of supply does matter for food security and livelihoods

Global security of supply of FMD vaccines therefore affects all countries – so what can be done about it? and how do we manage the risks without it? This is a big issue and needs all involved to have an overview of the scale of the problem, and the barriers and constraints to increased security. We must continue to cope with the risks posed by lack of vaccine, or to over-reliance on vaccination.

Dr Keith Sumption
Executive Secretary
European Commission for the Control of Foot-and-Mouth Disease

YOUR AGENDA

DAY 2 Plenary session

5A	VACCINE SELECTION. *WRL session*
08:30	RAPID, ON SITE, DIAGNOSIS OF FMD AND SAFE AND COST-EFFECTIVE SHIPMENT OF SAMPLES USING LATERAL FLOW DEVICES FOR LABORATORY DIAGNOSTICS. *A. Romey*
08:45	THE UTILITY OF POOLED MILK FOR FMD SURVEILLANCE IN NAKURU COUNTY, KENYA. *B. Armson*
09:00	EVALUATION OF ENVIRONMENTAL SAMPLING AS A LOW TECHNOLOGY METHOD FOR SURVEILLANCE OF FMD VIRUS IN AN ENDEMIC AREA **+** ENVIRONMENTAL SAMPLING: A SURVEILLANCE TOOL FOR FMD VIRUS IN MARKETPLACES. *C. Colenutt + E. Brown*
09:15	EFFECTIVE IN SILICO SEQUENCE-BASED PREDICTION OF FMDV VACCINE MATCHING. *E. Ribeca*
09:30	IN-VITRO CORRELATES OF HETEROLOGOUS PROTECTION USING AVIDITY AND IgG-SUB-TYPING ELISAs **+** ASSESSMENT OF EXISTING AND FUTURE VACCINE SELECTION TECH-NIQUES – MOVING FORWARD. *A. Capozzo + R. Reeve*
10:00	*Discussion*

6A	CONVENTIONAL VACCINES. *GFRA session 1*
11:00	**Keynote:** WHAT CAN THEY ACHIEVE, HOW STRAIGHTFORWARD WOULD IT BE TO REPLACE THEM GIVEN AN ALTERNATIVE? *T. Doel*
11:30	**Keynote:** QUALITATIVE ASPECTS OF THE IMMUNE RESPONSES RELATED TO PROTECTION AGAINST FMDV CHALLENGE IN CATTLE. *M. Pérez-Filgueira*
12:00	**Keynote:** SPECIES SPECIFIC FMD VACCINES - WHAT IS THE EVIDENCE? *W. Vosloo*

YOUR AGENDA

7	CHAMPIONING NEW VACCINES. *GFRA session 2*
13:50	INTRODUCTION. *A. Capozzo + F. Maree*
14:00	**Keynote:** VACCINE EFFICACY (VACCINE EFFICACY OF FMD VIRUS-LIKE PARTICLES PRODUCED BY THE BACULOVIRUS EXPRESSION SYSTEM). *B. Charleston + E. Van den Born*
14:30	**Keynote:** THE GMO (ADENOVIRUS) OPTION (A CURRENT PERSPECTIVE ON ADENOVIRUS 5-VECTORED FMD VACCINES). *T. de los Santos*
15:00	**Keynote:** ATTENUATED FMD VACCINES (FMD-LL3B3D VACCINE PLATFORM: SAFE, HIGHLY POTENT, FULLY DIVA COMPATIBLE, INACTIVATED FMD VIRUS VACCINES). *M. Mourino + E. Rieder*

8A	THE FUTURE OF FMD VACCINES
16:00	AN OVERVIEW OF REVERSE GENETIC APPROACHES TO ENHANCED FMD VACCINES IN AFRICA. *F. Maree*
16:15	RATIONAL DESIGN OF ATTENUATED FMDV VACCINES BY ELEVATION OF -CPG- AND -UPA- DINUCLEOTIDE FREQUENCIES. *M. Ryan*
16:30	*Discussion*
8B	VACCINE EFFICACY & EFFECTIVENESS - Improving the use of field studies. *IZS Italy session*
16:45	INTRODUCTION. *G.C. Ferrari + D. Paton*
17:00	FIELD TRIAL TO ESTIMATE THE EFFECTIVENESS OF THE VACCINATION PROGRAM IMPLEMENTED IN THE MAGHREB REGION. *E. Brocchi*
17:15	MODELLING THE IMPACT OF FARMING PRACTICES UPON VACCINE EFFECTIVENESS IN THE ENDEMIC SETTINGS - A CASE STUDY IN KENYA. *M. Tildesley*
from 17:30	POSTER SESSIONS

DAY 2 Parallel session

YOUR AGENDA

MODELLING FREE AND NON-FREE AREAS	5B
REINFORCEMENT LEARNING FOR CONTEXT-DEPENDENT CONTROL OF EMERGENCY OUTBREAKS OF FMD. *W. Probert*	08:30
INVESTIGATING THE BENEFITS OF AN ADAPTIVE MANAGEMENT APPROACH INVOLVING EMERGENCY VACCINATION USING SIMULATED FMD OUTBREAKS IN NEW ZEALAND. *R. Sanson*	08:45
EVALUATING OPTIMAL CONTROL STRATEGIES FOR FMD WITH THE US DISEASE OUTBREAK SIMULATION. *S. Sellman*	09:00
BETWEEN-HERD TRANSMISSION DYNAMICS OF FMD IN KENYA RANGELANDS. *K. Van der Waal*	09:15
USING NETWORKS OF LIVESTOCK MOBILITY TO IMPROVE CONTROL OF ENDEMIC FMD IN NORTHERN TANZANIA. *D. Ekwem*	09:30
LIVESTOCK MOBILITY IN WEST AFRICA: NETWORK ANALYSIS AND APPLICATIONS. *A. Appoloni (Via Adobe)*	09:45
Discussion	10:00

MODELLING BUSINESS SECURITY DURING OUTBREAKS	6B
MODELLING BIOSECURITY. *K. Mintiens*	11:00
SECURE BEEF SUPPLY IN THE U.S. – PLANNING FOR CONTROL AND CONTINUITY OF BUSINESS IN AN FMD OUTBREAK. *M. Sanderson*	11:15
MODELLING MANAGEMENT STRATEGIES FOR VACCINATED ANIMALS AFTER AN OUTBEAK OF FMD AND THE IMPACT ON RETURN TO TRADE. *R. Bradhurst*	11.30
MODELLING THE IMPACT OF REGIONAL MOVEMENT CONTROL POLICIES FOR FMD OUTBREAKS IN DISEASE FREE COUNTRIES. *M. Tildesley*	11.45
Discussion	12.00

YOUR AGENDA

DAY 2 POSTERS

DAY 2 morning / SESSION 5A
EVALUATING THE EFFICENCY OF ENVIRONMENTAL SAMPLING METHODS FOR THE DETECTION AND QUANTIFICATION FMD VIRUS. *E. Brown*
EVALUATION OF ENVIRONMENTAL SAMPLING AS A LOW TECHNOLOGY METHOD FOR SURVEILLANCE OF FMDV IN AN ENDEMIC AREA. *C. Colenutt + E. Brown*
DAY 2 morning / SESSION 6A
DEVELOPMENT OF MASTER VACCINE SEEDS FOR FMD CONTROL IN SUB-SAHARAN AFRICA. *B. Jackson*
STABILIZING FACTORS ASSOCIATED WITH VACCINE ANTIGEN PRODUCTION USING KOREAN LOCAL STRAIN OF FMDV. *K. Ah-Young*
ANTIGENIC PROPERTIES OF STABILIZED VIRUS PARTICLES FOR A FMD DISEASE VACCINE. *J.H. Park*
CHIMERIC SAT2 FMD VIRUS WITH INCREASED CAPSID THERMOSTABILITY FOR IMPROVED VACCINES. *J. Seago*
NEW CAGE-LIKE PARTICLE ADJUVANT INCREASED THE IMMUNOGENICITY AND THE PROTECTION INDUCED BY A VACCINE AGAINST FMD VIRUS A/ARG/2001. *P. Zamorano*
DAY 2 afternoon / SESSION 8B
POST-VACCINATION MONITORING OF TRIVALENT FMD VACCINE CONTAINING O1 MANISA, O 3039, A22 IRAQ TO EVALUATE VACCINE EFFECTIVENESS IN SMALL SCALE FIELD TRIALS. *J.E. Park*
DAY 3 morning / SESSION 9A
FMD OUTBREAK IN LUKULU DISTRICT, EVIDENCE OF VIRAL SPREAD OUTSIDE THE KNOWN ENDEMIC AREAS. *F. Banda*
GENETIC CHARACTERIZATION OF FMD VIRUSES RESPONSIBLE FOR OUTBREAKS IN NIGERIA DURING 2016: RESURGENCE OF THE NOVEL FMD- SAT1 TOPOTYPE. *D. Ehizibolo*
CHARACTERIZATION OF FMDV ISOLATES CANDIDATE STRAINS FOR POLYVALENT VACCINE DEVELOPMENT IN NIGERIA. *H. Ularumu*
DAY 3 morning / SESSION 10A
FMD VIRUS ADSORBED TO GENOTUBE SWABS REMAINS INFECTIOUS AT HIGH TEMPERATURE. *M. Eschbaumer*
COMPARATIVE PERFORMANCE OF MONOCLONAL AND POLYCLONAL-BASED ANTIGEN ELISAS FOR FMDV DETECTION. *L. Henry*
INACTIVATION OF FMDV IN TISSUE SAMPLES TO ENSURE SAFE TRANSPORT FROM INFECTED PREMISES TO DIAGNOSTIC LABORATORIES. *J. Horsington*
DETECTION OF EARLY FMD VIRUS INFECTION IN PIGS USING IgA AND IgM ASAAYS. *S. Parida*
PRODUCTION OF SWINE SEROLOGICAL PANEL FOR THE VALIDATION OF FMD ANTIBODY TEST. *H.M. Pyo*

DAY 2

PARALLEL SESSION		PLENARY SESSION
5B. Modelling free and non-free areas	9:00h	5A. Vaccine selection
6B. Modelling business security during outbreaks	11:00h	6A. GFRA - Conventional vaccines
	14:00h	7. Championing new vaccines
	16:00h	8A. The future of FMD vaccines
	16:45h	8B. Vaccine efficacy & effectiveness. Improving the use of field studies

RAPID, ON SITE, DIAGNOSIS OF FMD AND SAFE AND COST-EFFECTIVE SHIPMENT OF SAMPLES USING LATERAL FLOW DEVICES FOR LABORATORY DIAGNOSTICS

L Bakkali Kassimi[1], G.J. Belsham[2], A.N. Bulut[3], K. Gorna[1], C. Hamers[4], P. Hudelet[4], S. Jamal[5], E. Laloy[1], A. Relmy[1], A. Romey[1], H.G. Ularamu[6], S. Zientara[1] and S. Blaise-Boisseau[1]

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Introduction

Identification of circulating strains is an essential step towards the global eradication of FMD. However, the cost of sending FMD samples is an obstacle to submission of samples to Reference Laboratories due to shipping conditions. A cost-effective and safe method for shipment of samples from FMD-suspected cases, based on the inactivation of FMDV on lateral flow devices (LFDs) has been developed and validated in the laboratory using reference strains and archival samples. This method allows subsequent detection and typing of FMDV by RT-PCR and virus rescue using RNA transfection (Romey et al. 2017). The present study aims to further evaluate this protocol on freshly collected clinical samples through collaboration with field veterinarians in endemic countries in order to test the performance and safety of the entire process directly in the field.

Materials-methods

Epithelium or vesicular fluid samples will be collected from suspect clinical cases of FMD in Nigeria, Turkey and Pakistan and will be tested in the field using LFDs. The selected positive inactivated (or not) LFDs will be analyzed firstly by the national laboratory (Nigeria & Turkey) to ensure that the inactivation process is effective. Then, the duplicated sample will be submitted to European reference laboratories (France, Denmark) for molecular detection and virus rescue by transfection of viral genome.

Results

Sample collection and inactivation on LFDs are in progress. Transfections are currently being optimized to ensure virus rescue from RNA genomes recovered from inactivated LFDs.

Discussion

This study will contribute to demonstrate that using LFDs is a safe way for room-temperature, dry-transport of inactivated FMDV samples from endemic areas. It may substantially decrease the shipping cost thus increasing field sample submission.

THE UTILITY OF POOLED MILK FOR FMD SURVEILLANCE IN NAKURU COUNTY, KENYA

B. Armson[1,2], V.L. Fowler[1], K. Bachanek-Bankowska[1], V. Mioulet[1], P. Kitala[3], D. Machira[3], B. Sanz-Bernado[1], A. Di Nardo[1], E. Chepkwony[4], D.P. King[1], N.A. Lyons[1,5]*

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Introduction

Milk is a non-invasive sample type routinely collected from dairy farms, which could be useful for herd-level foot-and-mouth disease (FMD) surveillance. Using this alternative sample could address some of the potential biases of traditional surveillance methods with under-reporting or sub-clinical infection. Previous studies have demonstrated that FMD virus (FMDV) can be detected in milk samples from experimentally infected cows by real-time reverse transcription polymerase chain reaction (rRT-PCR), before, during and after the development of clinical signs (up to 28 days post contact).

Materials and Methods

This study aimed to investigate the potential of pooled milk as a sample type for FMD surveillance using rRT-PCR, compared with reports of disease incidence in Nakuru County, Kenya. There are typically several FMD outbreaks per year, and many smallholder dairy farmers sell milk to co-operatives who pool milk for onward sales. This study collected weekly, pooled milk samples from six dairy co-operatives alongside periodic cross-sectional surveys of small-holder farmers to gain information on clinical disease, milk production and trends in milk sales.

Results

FMDV RNA was detected in 11/264 milk samples, and SAT 1 serotype was also identified using a type specific rRT-PCR, concurrent with confirmed outbreaks in the study area. FMDV RNA was detected when the FMD incidence in the study area was ≥ 2.5%, i.e. at least one farmer reported having experienced FMD on their farm. This indicates that the pooled milk surveillance system can detect a threshold FMD farm level incidence of 2.5%, when up to 26% of smallholder farmers were contributing milk to pooling facilities.

Discussion

This pilot study identifies potential for using pooled milk for FMD surveillance in endemic regions, although further optimisation is required to maximise the sensitivity of the system, for example through investigating the collection of samples at different levels of the milk supply chain.

EVALUATION OF ENVIRONMENTAL SAMPLING AS A LOW TECHNOLOGY METHOD FOR SURVEILLANCE OF FMDV IN AN ENDEMIC AREA

C. Colenutt[1], E. Brown[1], N. Nelson[2], J. Wadsworth[1], J. Maud[3], B. Adhikari[3,4], S.c. Kafle[5], M. Upadhyaya[6], S.K. Pandey[7], D.J. Paton[1], K. Sumption[3], S. Gubbins[1]

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Introduction

Environmental sampling enables disease surveillance beyond regular investigation of clinical cases, extending data on the circulation of a pathogen in a specific area. Developing straightforward, low technology methods suitable for use in field conditions is key to the inclusion of such approaches alongside traditional surveillance techniques. Environmental contamination by foot-and-mouth disease virus (FMDV) in excretions and secretions from infected individuals promotes transmission, but also presents an opportunity for non-invasive sample collection, facilitating diagnostic and surveillance purposes.

Materials and Methods

Electrostatic dust cloths were used to collect environmental swabs at sites with reported outbreaks of FMDV, in the Kathmandu Valley, Nepal, which is endemic for FMD. A limited number of aerosol samples were also collected. A total of nine sites were visited and sampled between November 2016 and November 2017. Samples were stored in lysis buffer and transported to The Pirbright Institute, where an rRT-PCR assay was used to detect FMDV RNA.

Results

FMDV RNA was detected in environmental samples from premises with animals at all stages of clinical disease, from uninfected, suspected preclinical, clinical and recovering cattle. Categorising lesion ages as fresh (1-5 days), healing (6-10 days) and old (>10 days), there was a significantly higher proportion of positive samples for households with fresh lesions compared with those with old lesions (P=0.02).

Discussion

Development of methods that can reliably detect FMDV RNA in the environment is significant, as this extends the toolbox available for surveillance for this disease.

Development of low technology, straightforward surveillance methods such as this can support a robust response to outbreaks. Pairing these methods with existing and novel diagnostic tests will improve capability for the rapid detection of outbreaks and implementation of timely interventions to control outbreaks. In endemic areas, these methods can be implemented to extend surveillance beyond the investigation of clinical cases, providing additional data to assess virus circulation in specific areas.

ENVIRONMENTAL SAMPLING: A SURVEILLANCE TOOL FOR FMDV IN MARKETPLACES

E. Brown[1], C. Colenutt[1], J. Maud[2], D. Paton[1], B. Adhikari[3], N. Nelson[4], M. Mahapatra[1], S. Parida[1], S. Chapagain Kafle[5], M. Upadhyaya[6], S. Kafle Pandey[7], K. Sumption[2], S. Gubbins[1]

The Pirbright Institute, Ash Road, Pirbright, Surrey, GU24 0NF. United Kingdom European Commission for the Control of Foot-and-Mouth disease (EuFMD), Food and Agriculture Organisation of the United Nations (FAO), Rome, Italy; Food and Agriculture Organization of the United Nations Representation in Nepal, United Nations Building, Pulchowk, Lalitpur, Kathmandu, Nepal; Met Office, FitzRoy Road, Exeter, Devon, EX1 3PB. United Kingdom; FMD and TADs Laboratory, Department of Livestock Services, Ministry of Livestock Development, Nepal; Veterinary Epidemiology Centre, Department of Livestock Services, Ministry of Livestock Development, Nepal; Directorate of Animal Health, Department of Livestock Services, Ministry of Livestock Development, Nepal

Introduction

Live animal markets bring infected and non-infected animals in close contact providing the potential for direct and indirect transmission, facilitating wide onward spread of disease. Foot-and-mouth disease (FMD) is currently endemic in Nepal where commercialised goat markets are in operation. The Khasibazar market, Kathmandu is a large goat market with an estimated monthly turnover of 30,000 goats. We present data on the use of environmental sampling to detect FMD in this market.

Materials and methods

Four visits were made to the market during 2016/17 (one visit in November 2016, one in April 2017 and two in November 2017). Environmental swabs were taken from the holding pens, from surfaces deemed most likely to have come into contact with secretions and excretions of goats, including; rope ties, mesh fences, floor, walls, feed buckets and weighing scales. The geographical origin of the goats and amount of time spent at the market was recorded for each pen. In total 185 samples were collected and tested for FMD viral RNA by rRT-PCR.

Results

FMDV RNA was detected in five samples from three visits; one from 32 samples during the first visit, one from 43 samples during the second visit and two from 112 samples during the fourth visit. All samples were also screened for peste des petits ruminants virus (PPRV), with four samples positive for PPRV RNA from both the first and fourth visit.

Discussion

Movement of goats through markets has been implicated in the spread of FMDV in Nepal. Detection of FMDV RNA in environmental swabs demonstrates FMDV infected goats have been present at the Khasibazar goat market, although the source of virus cannot be linked to specific animals.

Environmental sampling provides a simple, non-invasive method of detecting FMDV at markets, where clinical signs in animals may not be apparent and where individual sampling is not practical. Environmental sampling data could be used to supplement epidemiological data to identify and predict patterns of spread and highlight potential transmission risks in endemic and FMD- free countries.

EFFECTIVE IN SILICO SEQUENCE-BASED PREDICTION OF FMDV VACCINE MATCHING

M. Mahapatra[1], S. Mahendran[2], L. Ferretti[1], S. Parida[1], P. Ribeca[1]

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Introduction

FMDV has a rich population structure, with a number of strains possibly co-circulating in the same geographic area and new variants rapidly emerging. Available vaccines only offer protection for a limited time, and are prone to the problem of antigenic drift. Hence the importance of serology-based vaccine matching techniques in tackling the virus and informing decision makers. However, those techniques are imprecise and costly; replacing them with in-silico predictions would represent a significant progress in the field.

Materials and methods

A large dataset of titres obtained from neutralisation assays on different FMDV types was used to train machine-learning algorithms. Quantities derived from whole-capsid sequencing information (including biochemical and structural indicators) were used to inform the prediction.

Results

The predictors are able to reproduce observed titres with great accuracy (much greater than methods previously published in the literature). Accuracy appears to be largely independent of the FMDV type and vaccine used.

Discussion

Our novel strategy seems to represent a promising first step towards achieving reliable in silico vaccine matching prediction. Hopefully in the future datasets similar to the one we used will become available for more FMDV types and vaccines, allowing us to extend and explore the scope of our approach.

IN-VITRO CORRELATES OF HETEROLOGOUS PROTECTION USING AVIDITY AND IgG-SUBTYPING ELISAs

A. Capozzo[1], R. Reeve[2], D. Paton[3], A. Ludi[3]

[1]Instituto Nacional de Tecnologia Agropecuaria (INTA). Institute of Virology. Buenos Aires., Argentina; [2]Boyd Orr Centre for Population and Ecosystem Health, Institute of Biodiversity, Animal Health and Comparative Medicine, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK; [3]The Pirbright Institute, Ash Road, Woking, Surrey, GU24 0NF, UK

Introduction

Virus neutralisation tests (VNT) and the liquid phase blocking ELISA (LPBE) are the commonly-used vaccine matching methods, measuring how much an antiserum made against a vaccine strain will cross-react with a field virus. However, the results are often interpreted as how well a vaccine will protect against a given field strain, which is also dependent upon vaccine potency. ELISAs that measure antibody avidity and isotypes appear to provide a better correlation with protection than VNT alone and show good reproducibility. To extend the validation of these methods we have transferred the technology from INTA to WRLFMD, where panels of post-vaccination sera exist from previously conducted challenge studies.

Materials and Methods

Twenty-one day post vaccination serum samples (n=34) from studies which assessed the vaccine viruses A/MAY/97 and A22 IRQ against the field virus A/ASIA/G-VII were tested by VNT, LPBE, avidity and IgG-subtyping ELISAs at The Pirbright Institute with guidance from INTA.

Results

Antisera to the vaccine viruses A22 IRQ and A/MAY/97 have low VNT titres against the A/ASIA/G-VII field strain, giving rise to low r1 vaccine match results; however, the A/MAY/97 appears to protect in-vivo (PD50 > 6). Results will be provided from comparative tests on sera from two heterologous potency studies, analysed as indirect correlates of protection.

Discussion

Future plans include improving the purification method for the required test antigens so that they can be done routinely in diagnostic laboratories. To further validate these assays larger numbers of sera samples from potency tests should be tested. This could be achieved by transferring the methods used and/or sharing the sera with other laboratories that have established the techniques.

ASSESSMENT OF EXISTING AND FUTURE VACCINE SELECTION TECHNIQUES – MOVING FORWARD

R. Reeve[1,], D. Paton[2], A. Ludi[2], A. Capozzo[3]*

[1] Boyd Orr Centre for Population and Ecosystem Health, Institute of Biodiversity, Animal Health and Comparative Medicine, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK; [2] World Reference Laboratory for foot-and-mouth disease, The Pirbright Institute, Ash Road, Pirbright, Woking, GU24 0NF, UK; [3] Instituto Nacional de Tecnologia Agropecuaria (INTA) Institute of Virology. Buenos Aires, Argentina.

Introduction

Since the 1980s the OIE Terrestrial Manual's has promoted r1-values – the ratio of heterologous to homologous antibody titre – as the main in vitro method for vaccine matching. The recommendation is to use virus neutralisation (VN), or failing that liquid phase blocking ELISA (LPBE) or complement fixation (CF) as the test to measure titre. As well as issues with the strength of the correlation between r1 value and vaccine match, there is a secondary problem of a lack of understanding that vaccine efficacy also depends on potency. New assays, especially avidity and IgG isotype ELISAs, have been developed since then that may improve our ability to calculate vaccine match and, more importantly, take account of potency, potentially giving a better insight into vaccine efficacy.

Materials and Methods

Collaborators were identified with data and/or antisera from heterologous and homologous in vivo challenge trials. The resulting data came from ~1000 animals, half of which underwent homologous challenge and half heterologous challenge. VN and LPBE data was available for nearly all of these animals, and avidity and IgG isotype data for ~10%. A Bayesian analysis was carried out to investigate the relationship between all of these assays and protection.

Results and Discussion

Virus neutralisation was found to be better correlated with protection than LPBE, in accordance with earlier studies. The limited data currently available for the new assays is also very promising, but further data is necessary to confirm these conclusions. A variety of antisera have already been identified for further testing, which will take place over the next year, but we would be pleased to broaden our collaboration through data and antisera from other challenge studies (homologous as well as heterologous).

POSTER

EVALUATION OF ENVIRONMENTAL SAMPLING AS A LOW TECHNOLOGY METHOD FOR SURVEILLANCE OF FMDV IN AN ENDEMIC AREA

C. Colenutt[1], E. Brown[1], N. Nelson[2], J. Wadsworth[1], J. Maud[3], B. Adhikari[3,4], S.C. Kafle[5], M. Upadhyaya[6], S.K. Pandey[7], D.J. Paton[1], K. Sumption[3], S. Gubbins[1]

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Discussion

Development of methods that can reliably detect FMDV RNA in the environment is significant, as this extends the toolbox available for surveillance for this disease. Development of low technology, straightforward surveillance methods such as this can support a robust response to outbreaks. Pairing these methods with existing and novel diagnostic tests will improve capability for the rapid detection of outbreaks and implementation of timely interventions to control outbreaks. In endemic areas, these methods can be implemented to extend surveillance beyond the investigation of clinical cases, providing additional data to assess virus circulation in specific areas.

POSTER

EVALUATING THE EFFICENCY OF ENVIRONMENTAL SAMPLING METHODS FOR THE DETECTION AND QUANTIFICATION FMDV

E. Brown[1], N. Nelson[2], S. Gubbins[1], C. Colenutt[1]

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Introduction

Foot-and-mouth disease virus (FMDV) can be found in the breath, secretions and excretions from acutely infected animals and can survive outside of the animal host, implicating the environment as a potential transmission route. The objective of this study was to assess the efficiency of environmental sampling methods for the recovery and quantification of FMDV from the environment.

Materials and methods

Environmental swabs: the surfaces of a range of materials including wood, metal, plastic, glass, brick and rope were spiked with a range of concentrations (101- 106 TCID50) of FMDV O/UKG/34/2001. The virus was left to dry for ~30 minutes, then the surface was swabbed with an electrostatic dust cloth. Swab samples were then tested using qPCR and virus isolation to assess virus recovery from the surfaces.*Aerosol sampling*: stocks of FMDV O/UKG/34/2001,

Environmental swabs: the surfaces of a range of materials including wood, metal, plastic, glass, brick and rope were spiked with a range of concentrations (101- 106 TCID50) of FMDV O/UKG/34/2001. The virus was left to dry for ~30 minutes, then the surface was swabbed with an electrostatic dust cloth. Swab samples were then tested using qPCR and virus isolation to assess virus recovery from the surfaces.Aerosol sampling: stocks of FMDV O/UKG/34/2001, A/TAI/17/2016, and ASIA1/SHAMIR/VV/2001 were aerosolized to validate the collection efficiency of the Coriolis micro air sampler (Bertin Technologies). FMDV was nebulised at concentrations of 102, 104 and 106 TCID50 and at three distances from the sampler: 10cm, 75cm, and 150cm. Sampleswere tested for FMDV RNA and live virus by qPCR and virus isolation, respectively.

Results

Environmental swabs: FMDV RNA was detected from all surfaces at all concentrations, except for brick and wood where 101 was not recovered. Live virus was only recovered from plastic, wood, rope and brick when spiked with higher concentrations of virus (105 and 106 TCID50). Aerosol sampling: all serotypes were detected in respective collected aerosol samples. For each serotype the proportion of virus recovered decreased as the distance between the nebuliser and sampler increased. The higher the starting concentration of virus the more efficient the recovery was from sampled aerosols.

Discussion

This study demonstrates that use of electrostatic dust cloths as swabs and the Coriolis air sampler are efficient methods for environmental sampling where FMDV may be present.

WHAT CAN THEY ACHIEVE, HOW STRAIGHTFORWARD WOULD IT BE TO REPLACE THEM GIVEN AN ALTERNATIVE?

T. Doel

AVAILABLE UPON REQUEST

QUALITATIVE ASPECTS OF THE IMMUNE RESPONSES RELATED TO PROTECTION AGAINST FMDV CHALLENGE IN CATTLE

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Introduction

We have shown that multivalent vaccines, as well as revaccination protocols, could confer complete protection in a well-established vaccine-matching model for cattle using the A24/Cruzeiro and A/Arg/2001 FMDV strains. Experimental groups did not show significant differences among them for a wide range of immunological parameters; however, differences were found between protected and unprotected animals, mainly in the isotype and avidity profiles of the immune sera. In this report, we described some qualitative aspects of the humoral responses found in protected bovines.

Materials and Methods

Serum samples from each vaccination protocol [n=5 each: single dose monovalent 10 µg (1) or 40 µg of A24/Cruzeiro (2); trivalent A24/Cruzeiro-O1/Campos-C3/Indaial (3), or two doses of the 10ug of A24/Cruzeiro vaccine (4)] were assayed using a set of newly developed serological tests. These new ELISA-based protocols were used to quantify avidity according to the isotype of the antibodies against A24/Cruzeiro and A/Arg/2001 FMDV strains as well as the amount of A/Arg/2001-specific antibodies generated by the other three heterologous strains.

Results

Protected animals showed significantly lower IgG1/IgG2 ratios than non-protected ones. Protected cattle also presented higher mean avidity indexes (AI) for antibodies against the A/Arg/2001 but also against the A/24 and O1/Campos strains. Such significant differences were also observed when analyzing IgG1 and IgG2 isotypes separately. Strain-specific analyses also shown that both the C3/Indaial- and O1/Campos-specific antibodies showed cross-reactivity against the A/Arg/2001 strain in a similar manner.

Discussion

Our results would indicate the existence of a higher proportion of cross-reactive IgG2 antibodies, compared to the IgG1 isotype, in the protected individuals. However, higher mean AI against A/Arg/2001 strain found in protected cattle, was not restricted to a specific IgG subclass and it was also detected for other strains (A24/Cruzeiro and O1/Campos). The O1/Campos and C3/Indaial vaccine antigens present in the trivalent formulation effectively generated A/Arg/2001 cross-reactive antibodies observing a similar proportion.

SPECIES SPECIFIC FMD VACCINES - WHAT IS THE EVIDENCE?

W. Vosloo

AVAILABLE UPON REQUEST

POSTER

DEVELOPMENT OF MASTER VACCINE SEEDS FOR FMD CONTROL IN SUB-SAHARAN AFRICA

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Introduction

Many FMDVs, particularly the South African Territories (SAT) serotypes, are thermally unstable and the viral capsid readily dissociates into non-immunogenic pentameric subunits, which can compromise the effectiveness of FMD vaccines. We have carried out stability screens of East African FMDV strains selected from banks of field viruses to identify candidates for new vaccine master seed stocks.

Materials and methods

The respective stability of each virus was determined using ELISA-based and thermofluor assays. Candidate strains for each serotype were cell adapted on BHK cells until clear CPE was observed. Cattle were vaccinated with inactivated virus prepared from candidate seedstock and the sera was used to perform cross neutralisation assays.

Results

The respective stabilities of 40 East African FMDV strains, belonging to the O, A, SAT1 and SAT2 serotypes, were determined. The least and most stable strains within each serotype were further analysed using accelerated stability assays. Differences of up to 7°C in stability were observed between strains belonging to the same serotype, such that the spectrum of stabilities for each serotype overlapped. Long-term storage (> 12 months) of inactivated viruses confirmed SAT1 strains to be the least stable. In neutralisation assays performed to date, O and SAT2 sera have exhibited lower levels of antigenic recognition to strains from

the same serotype in comparison to A and SAT1 sera.

Discussion

This work demonstrates the range of thermal stabilities exhibited by East African FMDV strains belonging to four different serotypes and describes the use of stability analysis as a criterion to include in the selection of candidate FMDV seedstock.

POSTER

STABILIZING FACTORS ASSOCIATED WITH VACCINE ANTIGEN PRODUCTION USING KOREAN LOCAL STRAIN OF FMDV

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Introduction

Outbreak of type O foot-and-mouth disease (FMD) has occurred most frequently all over the world, and there is no exception in South Korea. In the situation of nationwide vaccination in South Korea since 2011, the local isolate, O/SKR/JC/2014, was suggested as a representative strain for domestic vaccine development. Among seven serotypes of foot-and-mouth disease virus (FMDV), types O and SAT2 are notorious for their structural instability. Although it was possible to produce fresh 146S antigens with O/SKR/JC/2014 more than 2*ug/ml*, it was difficult to preserve the intact vaccine antigen for sufficient time. Herein, we aimed to explore several adjustments to produce and maintain intact vaccine antigens using O/SKR/JC/2014.

Materials and methods

Several combinations of media for suspension cell culture and virus propagation were compared in terms of viral titer and the amount of 146S particle. In addition, basal buffers for suspension of concentrated vaccine antigen were also compared. Viral titer was measured by end-point titration to determine the tissue culture infective dose 50 (TCID50) and the amount of 146S particle was calculated by continuous UV spectrophotometry following sucrose gradient centrifugation according to the previous report (Doel et al.1981).

Results

Among combinations of media that resulted in high titers more than $5x10^7$ $TCID_{50}$*/ml*, three combinations exhibited high stability when the O/SKR/JC/2014 seed viruses were stored at -70^{0}C. In particular, purified 146S particles was the least degraded when they were suspended in potassium-based solution not only for 4^{0}C maintenance, but also for -70^{0}C storage,

which should expose vaccine antigen to the degradation due to freeze-thaw cycle.

Discussion

Those exquisite adjustments could be usefully applied to other FMD vaccine strains in case the vaccine antigens are subject to fragility in the process of vaccine production or during storage in experimental temperature.

POSTER

ANTIGENIC PROPERTIES OF STABILIZED VIRUS PARTICLES FOR A FMD VACCINE

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Introduction

Foot-and-mouth disease (FMD) virus is easily inactivated at high temperatures and destroyed in acidic conditions. Hence, it is necessary to increase the stability of FMD virus (FMDV) for its use as an antigen to produce more stable vaccines. This study evaluated whether the single or combined substitution of a single amino acid in VP1 (N17D) or VP2 (H145Y) increases virus stability in seven FMDV serotypes.

Materials and methods

The used an infectious clone carrying the full genome of the O1 Manisa strain, which is the representative vaccine strain of FMD. It is also conducted experiments under acidic conditions to assess the stability of FMDVs carrying seven different P1 genes and the same NSP gene.

Results

The stabilities of the viruses of serotypes O, Asia1 and C, but not A, SAT1, SAT2, or SAT3, were enhanced compared with the parental virus. In the case of serotypes A, SAT1, SAT2, and SAT3, we found that substitution of 2–3 amino acids in the P1 region improves stability under stimulation that induces resistance and cell passage, revealing a novel resistance-related sequence. We injected an experimental vaccine that contained the antigen that persists under acidic conditions into mice, and we confirmed the protective capability of this antigen against challenge infection.

Discussion

To increase the acid resistance of FMDV, replacing specific amino acids may generally improve

virus stability.

POSTER

CHIMERIC SAT2 FMDV WITH INCREASED CAPSID THERMOSTABILITY FOR IMPROVED VACCINES

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Introduction

Many FMDVs, particularly the South African Territories (SAT) serotypes, are thermally unstable and the viral capsid readily dissociates into non-immunogenic pentameric subunits, which can compromise the effectiveness of FMD vaccines. Here we report the construction of a chimeric clone between the SAT2 and O serotypes, designed to have SAT2 antigenicity, but improved stability.

Materials and methods

An established reverse genetics workflow was used to produce recombinant chimeric SAT2 FMDVs. The respective stability of each virus was determined using ELISA-based and thermofluor assays. Cryo-EM analysis of inactivated recombinant FMDVs was performed to investigate capsid structures. Cattle were vaccinated with wild type and stabilised viruses following exposure to an elevated temperature and subsequent VNT assays were performed to determine the levels of neutralising antibodies generated.

Results

Characterisation of the chimeric virus showed growth kinetics equal to that of the wild type SAT2 virus with better thermostability, attributable to changes in the VP4 structural protein. Sequence and structural analyses confirmed that no changes from SAT2 were present elsewhere in the capsid. We show such thermostable SAT2 viruses can induce improved neutralizing-antibody responses following the exposure of vaccine to an elevated temperature.

Discussion

This work highlights the potential benefit of vaccines with improved thermal stability and gives an insight into the viral components that influence stability.

POSTER

NEW CAGE-LIKE PARTICLE ADJUVANT INCREASED THE IMMUNOGENICITY AND THE PROTECTION INDUCED BY A VACCINE AGAINST FMDV A/ARG/2001.

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Introduction

Foot and Mouth Disease is an acute disease caused by Foot and Mouth Disease Virus (FMDV) which causes important economy losses, this is why it is necessary to obtain a vaccine with new and economic adjuvant that stimulates protective immune response. The murine model used predicts the FMD-vaccines' quality in cattle.
New cage-like particle or Immunostimulant Particle Adjuvant (ISPA) are lipid boxes formulated with dipalmitoyl-phosphatidylcholine, cholesterol, steralamine and QuilA.

Materials and Methods

BALB/c mice were immunized and at 21 dpv challenged with FMDV; cattle were immunized S.C. The methods used were: ELISA; seroneutralizing assay; lymphoproliferation and CD4+/ CD8+ stained.

Results

Mice (n=5) were immunized subcutaneous with: inactivated FMDV (iFMDV); iFMDV-ISPA; Commercial vaccine; ISPA or PBS, at 21 dpv animals were challenged with infective FMDV. 100% of mice vaccinated with iFMDV-ISPA or commercial vaccine were protected and only 40% in iFMDV group. At this time, iFMDV-ISPA group presented FMDV-Ab titers: 5.06±0.07 higher than iFMDV (3.8±0.3) ($p<0.05$) and similar than commercial vaccine (4.62±0.02) group A significant increase in the levels of Ab α-FMDV IgG1, IgG2a, IgG2b and IgG3 was detected in iFMDV-ISPA group with respect to FMDV group.
At 21 dpv, when splenocytes were stimulated with inactivated virus, iFMDV-ISPA group showed higher proliferation than iFMDV, ISPA or PBS groups ($p <0.05$), and similar than commercial vaccine group. A slight increase was observed in CD4+/IFNα+ population in iFMDV-ISPA and commercial vaccine groups compared to iFMDV.
Calves (n=4) were vaccinated with iFMDV or iFMDV-ISPA, at 30 dpv there was an increase in total Ab α-FMDV (3.7±0.6) in iFMDV-ISPA calves, in comparison with iFMDV group ($p<0.05$). SNT were 1.8± 0.3 (correlated with Percentage Expectation of Protection (PEP), higher than 80%) and 1.02±0.02 in iFMDV-ISPA calves and iFMDV respectively ($p<0.05$).

When Bovine-DCs were incubated with ISPA, an increase of CD40 and IL6 expression was detected (preliminary results).

Discussion

In mice, the inclusion of ISPA in an FMD-vaccine induced an increase in humoral and cellular immunity., and a better protection against viral challenge. In cattle, the antibodies against FMDV are linked to PEP higher than 80%.

REINFORCEMENT LEARNING FOR CONTEXT-DEPENDENT CONTROL OF EMERGENCY OUTBREAKS OF FMD

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Introduction

Emergency disease control interventions can, do, and should adapt to reflect the progression of an outbreak. Reinforcement learning (RL) is a methodology that can be used in combination with epidemiological simulation models to search for, and test, control policies that are context-dependent, thereby recommending different actions as an outbreak progresses. Rather than testing the performance of a pre-determined set of control actions RL allows for the discovery of control policies. The resultant RL policies provide an upper bound on management performance against which simpler policies can be evaluated.

Materials and Methods

We apply RL to the control of a hypothetical FMD outbreak. The decision problem is to determine the extent of culling or vaccination around currently confirmed infected premises so as to stop the spread as quickly as possible. Management performance of the RL policy is compared against policies that do not adapt through time.

Results

In all simulated outbreaks, the policies generated by the RL algorithm were adaptive. That is, it was optimal to change control interventions through time. Most striking was how the optimal action changed as the area of the outbreak changed – for small outbreaks it was optimal to vaccinate in a large radius around infected premises but for larger outbreaks it was optimal to cull at a medium radius. All policies were heavily dependent upon carcass disposal capacity.

Discussion

We illustrate methodology for generating control policies that are tailored to each future outbreak scenario. Such methods can capitalise upon the wealth of stochastic epidemiological models currently available.

INVESTIGATING THE BENEFITS OF AN ADAPTIVE MANAGEMENT APPROACH INVOLVING EMERGENCY VACCINATION USING SIMULATED FMD OUTBREAKS IN NEW ZEALAND

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Introduction

This study investigated personnel resource requirements and the performance of an early decision indicator (EDI) to trigger emergency vaccination.

Materials and methods

InterSpread Plus was used to simulate 5000 FMD outbreaks in New Zealand. Four response strategies were evaluated: Stamping-out only (SO) and SO plus vaccination initiated by three mechanisms: randomly started between days 11-35 of the response (VAC); started on day 21 (VACf); or deployed if the number of infected premises (IPs) or the estimated dissemination rates exceeded certain threshold values between days 11-35 (TRV).

Parameters that were varied randomly included the number of personnel, whether airborne spread occurred, farm classes vaccinated and surveillance visits per person per day. Outputs,

including time to first detection, total IPs, outbreak duration, total man-days, vaccine doses used and if and when the EDI trigger was fired, were collected for each iteration. Data were analysed using contingency table analyses, univariable tests and multivariable analyses.

Simulations were stopped if 90 days had elapsed without IPs or when the outbreak reached 365 days.

Results

IPs were highly right skewed (median = 10, interquartile range (IQR) = 3 – 34, range = 0 – 50,582); as was duration (median = 20 days, IQR = 7 – 39, range = 0 – 360). Logistic regression showed that the number of veterinarians available, the response strategy and the EDI trigger firing were associated with large or long epidemics.

Vaccination reduced the number of IPs and duration compared to SO, and the TRV strategy performed the best in terms of the fewest IPs and the shortest duration.

Discussion

This study showed the benefits of an adaptive management response to FMD outbreaks. Compared with previous studies it provided more information to support vaccination decision-making and insights into resourcing requirements when responding to FMD outbreaks in New Zealand.

EVALUATING OPTIMAL CONTROL STRATEGIES FOR FMD WITH THE US DISEASE OUTBREAK SIMULATION

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Introduction

Spatially explicit simulation models can aid policy decisions and identify efficient control strategies for different scenarios. In two theoretical studies we analyzed (1) the effects of spatial clustering of premises on the course of Foot and Mouth Disease (FMD) outbreaks, and (2) the efficacy of different control strategies for controlling such outbreaks. In the U.S., the premises' locations are largely unknown below the county scale, necessitating assumptions about their spatial distribution. A better understanding of how such assumptions affect simulations, in combination with detailed analysis of control strategies would help develop more efficient preparedness plans.

Materials and Methods

The US Disease Outbreak Simulation (USDOS) is a data-driven, spatially explicit disease spread model simulating continental scale outbreaks. It was developed for the U.S. livestock demographic in a collaborative effort between Colorado State, Warwick, and Linköping Universities with support from the U.S. Department of Homeland Security Science and Technology Directorate.
Using USDOS, the effect of spatial clustering of premises on FMD outbreaks was analyzed analytically and through stochastic simulations in two sets of different spatial distributions of the U.S. cattle population—one random and one where the premises' locations were simulated to provide more realistic distributions.
Control strategies based on combinations of movement bans, culling and vaccination strategies were evaluated for simulated FMD outbreaks. The outbreaks were initiated in all parts of the U.S. and included realistic constraints on amount of time and resources that could be allocated regionally.

Results

Study one showed how realistic spatial distributions of premises can have a pronounced effect on epidemiological predictions, indicating unrealistic estimates of premises locations should be avoided. Study two revealed that control strategies are most efficient when applied rapidly with maximum resource allocation, but resource constraints may cause mitigation efforts to be outpaced for larger outbreaks. Substantial regional differences were identified, both in terms of the effect of clustering and choice of control strategy.

BETWEEN-HERD TRANSMISSION DYNAMICS OF FMD IN KENYA RANGELANDS

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Introduction

Transmission of foot-and-mouth disease virus (FMDV) is driven by patterns of contact across multiple scales. Between-herd contact can be challenging to quantify, but can sometimes be directly measured through questionnaires or observation and/or indirectly inferred through phylogenetic data. Here, we present an overview of results from several studies related to transmission dynamics of FMD in Laikipia County and the Masai Mara Ecosystem (MME) in

Kenya, both of which are characterized by pastoral cattle production and abundant wildlife.

Materials and Methods

We performed VP1 sequencing (Sanger and next-generation) on oropharyngeal fluid samples collected from cattle and wild buffalo in Laikipia. Maximum likelihood and Bayesian phylodynamic methods were applied to assess genetic clustering of FMDV within buffalo herds and wildlife-livestock transmission. In addition, data on between-herd contacts were collected from a combination of GPS-tracking of cattle and buffalo herds and questionnaires administered to herders in Laikipia and MME.

Results and Discussion

Molecular epidemiology: We recovered 75 SAT1 and SAT2 sequences from buffalo. For SAT1, separate phylogenetic clusters were found in different buffalo herds despite being sampled from a relatively small area, suggesting strong spatial and social mechanisms determining between-herd transmission. No SAT1 or SAT2 viruses were found in sympatric cattle that mix with buffalo, indicating that cross-species transmission is rare. However, at a broader spatial scale, SAT1 and SAT2 viruses found in buffalo were phylogenetically related to sequences associated with several cattle outbreaks elsewhere in central Kenya.
Dynamics of between-herd contact: Daily foraging contacts among cattle herds increased during the dry season driven by aggregations around water sources. This increases the vulnerability of contact networks to pathogen spread. In MME, GPS-tracking data on buffalo, impala, and cattle were analyzed to identify hotspots of between-herd and between-species interaction.

Results of these studies advance current knowledge of between-herd contact dynamics in buffalo and cattle populations in East Africa, thus contributing to the broader epidemiological understanding needed for more effective control measures in the region.

USING NETWORKS OF LIVESTOCK MOBILITY TO IMPROVE CONTROL OF ENDEMIC FMD IN NORTHERN TANZANIA

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Introduction

Foot-and-mouth disease (FMD) remains endemic in East Africa, causing significant reductions in livestock production. Traditional livestock management systems relying on sharing of communal resource areas are predominant in this part of Africa. Unrestricted movements are widespread and are considered important drivers of FMD outbreaks in cattle. Yet they remain poorly understood. Unravelling livestock mobility patterns, particularly herd connectivity at resource areas and markets, is essential in order to determine disease dynamics and devise appropriate control strategies.

Materials and Methods

Focusing on areas of high-prevalence disease in northern Tanzania, our study mapped communal shared resources areas and investigated livestock herd movements around these areas across seasons. Information on livestock movements was collected in two districts representative of agro-pastoral and pastoral production systems – Serengeti and Ngorongoro – respectively. Data was generated through community-level participatory mapping, collection of livestock movement permits, and tracking of selected cattle herds using Global Positioning System (GPS) collars.

Results

For each village (n=140) in the two study districts, we identified the position of livestock resource areas (e.g. grazing and watering), markets, areas of livestock mixing, the volume of livestock traffic and frequency of interactions at specific points. Network analyses have revealed the influence of seasonality on livestock connectivity through shared resource areas and identified villages that act as key linkages across networks.

Discussion

Community structure matrices of connected villages have enabled us to uncover differences in the contact patterns of livestock movement networks that provide some understanding on how endemic FMD might spread in agro-pastoral and pastoral management systems. We are now using network vulnerability and resilience measures as proxies to demonstrate the effectiveness of interventions (e.g. targeted vaccination) at key transmission nodes (villages, communal grazing areas, etc.). Building on the network analyses, we will parameterise FMD virus transmission models that will allow us to assess the risk of transmission at shared resource areas in both settings.

5B
SESSION

LIVESTOCK MOBILITY IN WEST AFRICA: NETWORK ANALYSIS AND APPLICATIONS

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Introduction

In West Africa, livestock mobility is a complex phenomenon involving different types of movement (commercial and transhumance), different spatial scales (from local/village level to international) and different time scales (a day for commercial movements till several month for transhumant). In this work we present some analysis on livestock mobility network data in Senegal and Mauritania for 2014.

Materials and Methods

Data have been collected by the CNERV in Mauritania and by the DSV in Senegal. In both countries, a system of movement certification has been put in place: every time a herd is moved a certificate should be issued indicating Origin and Destination of the movements as well as the herd's size, the convoy type and other information.

Results

The analysis has shown the existence of two mobility patterns throughout the year: the first related to routine movements from January to August; the second strictly connected to the religious festivity of Tabaski. These mobility patterns are different in terms of animals involved, the means of transportation and destinations. Results from these analyses were used to estimate the rate of transmission of infection from one node to the other and to identify the nodes playing a pivotal node in the diffusion of diseases.

Discussion

These results can be used by Veterinarian offices and public health officers to inform control policies (prioritization of vaccination, market's closure etc) and surveillance network according to the period of the year, the species involved and the diseases considered.

6B
SESSION

MODELLING BIOSECURITY

K. Mintiens

AVAILABLE UPON REQUEST

SECURE BEEF SUPPLY IN THE U.S. PLANNING FOR CONTROL AND CONTINUITY OF BUSINESS IN AN FMD OUTBREAK

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Introduction

Response to an FMD introduction in the U.S. would include movement controls, enhanced biosecurity and surveillance, depopulation and potentially vaccination. Control efforts would be disruptive to livestock industries and could cause long term economic damage. Contrasting short term goals of disease control and business continuity must be balanced to reach the long term goals of disease eradication and livestock industry survival.

Materials and Methods

USDA APHIS Cattle Health Programs funded the "Secure Beef Supply plan". University personnel identified working groups of academic, industry and regulatory representatives to develop guidance for Managed Movement, Biosecurity, Surveillance, and Contingency Planning. Plans focus on: 1.) controlling disease transmission risk through managed movement and enhanced biosecurity; and 2.) early detection through active observational surveillance of cattle. The goal is to identify procedures and provide training materials to decrease transmission risk while supporting substantial industry business continuity.

Results

Guidance documents and training materials were produced for beef producers, packers, regulatory officials and veterinarians on Managed Movement, Biosecurity, Surveillance and Contingency Planning. Training materials focus on recognition of FMD signs and implementation of biosecurity and surveillance principles to decrease disease transmission risk. Documents and materials support criteria to allow movement permits for low risk movements in order to support continuity of business. Documents and materials are available at www.securebeef.org.

Discussion

The response to an FMD introduction in the U.S. would be disruptive and risk severely damaging a large portion of the livestock industries. A well planned response that balances the needs for disease control and business continuity in the livestock industries is necessary. This will require stakeholder training to minimize disease transmission risk during essential business practices while control measures are implemented. The Secure Beef Supply plan is an attempt to provide guidance to all stakeholders and optimize disease response and control.

MODELLING MANAGEMENT STRATEGIES FOR VACCINATED ANIMALS AFTER AN OUTBEAK OF FMD AND THE IMPACT ON RETURN TO TRADE

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Introduction

An incursion of foot-and-mouth disease (FMD) in a previously FMD-free country can cause significant economic damage from the immediate and prolonged closure of FMD-sensitive markets. Whilst emergency vaccination may help with disease containment, the presence of vaccinated animals complicates post-outbreak surveillance and the recovery of FMD-free status.

We present enhancements to the Australian Animal Disease Spread Model (AADIS) that allow comparisons of post-outbreak management strategies for securing proof-of-freedom from FMD and return to trade. These include:

surveillance of previously infected areas (according to configurable sampling regimes), in order to obtain statistical confidence of freedom from FMD, and

economic assessment of retaining vaccinated animals in the population compared to removing them to waste or for salvage.

Materials and methods

A case study is presented that compares vaccinate-and-retain, vaccinate-and-remove-to-waste and vaccinate-and-remove-for-salvage strategies, and their impact on the recovery of FMDsensitive markets (per OIE guidelines).

Results

Removing vaccinated animals resulted in higher post-outbreak management costs but lower overall costs (due to reduced trade losses), than retaining them.

Under the assumptions of the study there were no cost benefits of salvaging vaccinated animals. The potential salvage revenue was offset by trade losses associated with the increased time required for removal, and the delay in regaining markets.

Discussion

The new modelling capability will support the development and refinement of post-outbreak management policies that facilitate the earliest possible recovery of FMD-free status and return to trade.

MODELLING THE IMPACT OF REGIONAL MOVEMENT CONTROL POLICIES FOR FMD OUTBREAKS IN DISEASE FREE COUNTRIES

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Introduction

The revenue of livestock farms in disease free countries is largely based on the movement of animals, either through selling animals to other farms or moving animals to slaughter. Therefore, adopting any form of movement restrictions has substantive economic consequences for the livestock industry. In this paper, we use state of the art mathematical models to investigate the cost-effectiveness of local and regional movement control upon outbreaks of FMD in the UK. Such policies, if implemented effectively, could balance the need of the containing and controlling the spread of infection with the economic incentive of maximising business continuity for a large number of unaffected farms.

Methods and Results

We use a sophisticated spatial stochastic model of foot-and-mouth disease (FMD) that has been extensively previously utilized previously to investigate optimal interventions for FMD outbreaks. In this paper, upon notification of an infected farm, we introduce livestock movement bans within a given radius of the notified farm. We then determine the radius that minimizes the overall cost of the outbreak. When determining cost, we take a national perspective, considering direct costs to the farms, as well as the agricultural sector, exports and the tourist industry. We show that for FMD, in contrast with past policy, the economically optimal strategy is to ban movements in a relatively short radius around infected farms; the precise balance between disease control and maintaining 'business as usual' varies between different regions of the country.

Discussion

Our model predictions demonstrate that movement restrictions have a dramatic impact on the cost of livestock diseases such as FMD, implying that large-scale movement bans are generally prohibitively expensive. This work suggests that movement controls need to be carefully matched to the epidemiological and economic consequences of the disease, and optimal bans can have substantial financial benefits.

VACCINE EFFICACY OF FMD VIRUS-LIKE PARTICLES PRODUCED BY THE BACULOVIRUS EXPRESSION SYSTEM

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Introduction

Vaccine production is currently carried out in high containment manufacturing facilities, resulting in very high production costs and lack of production capacity. There is also room for improving the stability of conventional killed foot-and-mouth disease virus (FMDV) vaccine, and the time to market should be improved in case of new outbreaks. To address these issues, a system to express FMDV virus like particles (VLPs) was developed. The possibility of producing VLP-based FMD vaccines in conventional facilities greatly increases the flexibility and significantly lowers costs of commercial manufacturing. The utility of VLPs can be further enhanced by improving their thermostability and stability at low pH by introducing structure-guided amino acid changes in the VLPs.

Materials and Methods

VLPs were expressed in insect cells using the baculovirus expression system and used to formulate vaccines with an appropriate adjuvant. Cattle were vaccinated with these vaccines and the virus neutralising antibody titres (VNT) were measured. Vaccine efficacy was also determined in vaccination-challenge experiments.

Results

Mutations that have been predicted to enhance VLP stability were cloned into baculovirus expression constructs and stabilized VLPs could be expressed for A, O, Asia1, and SAT2 strains at satisfying yields. VLP-based vaccines induced neutralising antibodies in cattle consistent with protection. This was confirmed by high containment cattle challenge experiments in several cases.

Discussion

Virus-like particles have now the potential to be a commercially viable alternative to conventional killed vaccines.

A CURRENT PERSPECTIVE ON ADENOVIRUS 5-VECTORED FMD VACCINES

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Over the years, viral vectors have been used to deliver FMDV structural proteins, with the aim of synthesizing virus-like particles (VLPs) in infected cells, potentially inducing both, humoral and cell-mediated immunity. Numerous groups have focused on using different viral vectors, including vaccinia virus, fowlpox virus, attenuated pseudorabies virus (PRV) or "single cycle" Semliki forest virus (SFV). Most of these FMD vaccines were tested in a limited number of livestock species, usually requiring vaccination boosts and offering partial protection in swine and/or cattle.

To date, the most successful strategy to induce protection against FMD in livestock, as an alternative to the inactivated whole FMDV vaccine, is the use of a recombinant-replication-defective human adenovirus type 5 coding for FMDV capsid proteins and also the 3Cpro that allows for the in vivo assembly of VLPs (Ad5-FMD). These vaccines protect swine and cattle from clinical disease as early as 5 days post vaccination. In fact, an Ad5-FMD serotype A24 vaccine has been recently granted licensure for emergency use in cattle in USA. The main advantages of this vaccine platform are: i) it does not require a high containment facility for production; ii) it has intrinsic DIVA capabilities; iii) it does not require the adaptation of field strains to vaccine production in cell culture; and iv) it is genetically stable. However, the Ad5-FMD technology requires further industrial development for large scale production and broad use internationally, especially in developing countries. In this section we will discuss recent developments aimed at improving vaccine potency, vector stability, route of delivery, all strategies focused on achieving fast protection with one vaccine dose, at the lowest cost possible and with not significant side effects. Furthermore, we will discuss current challenges and possible solutions aimed at improving Ad5-FMD vaccine performance.

FMD-LL3B3D VACCINE PLATFORM: SAFE, HIGHLY POTENT, FULLY DIVA COMPATIBLE, INACTIVATED FMDV VACCINES

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Introduction

Traditional chemically-inactivated foot-and-mouth disease virus (FMDV) vaccines are used to control FMD around the world in spite of drawbacks - (1) large quantities of virulent FMDV are used, with the risk of virus escaping from manufacturing facilities or incomplete inactivation during the vaccine formulation process; (2) traditional vaccines produced from wild type FMDV are not fully compatible with a DIVA approach, since small amounts of nonstructural proteins (NSPs) may still be present; and (3) they do not fully protect animals from persistent infection.

Materials and methods

A novel, marked FMD-LL3B3D vaccine platform under development by Zoetis Inc. and The United States Department of Agriculture - Agricultural Research Service, consists of an attenuated virus platform containing negative markers in the NSPs 3B and 3Dpol. This vaccine platform allows for the easy exchange of capsid coding sequences. In contrast to wild-type FMD vaccine viruses, the FMD-LL3B3D vaccine platform viruses induce no clinical signs of FMD and no shedding of virus in cattle or pigs when inoculated as a live virus. This vaccine platform uses existing FMD vaccine manufacturing technology without the biosafety risk associated with FMD vaccine production.

Results

Cattle immunized with a variety of inactivated FMD-LL3B3D vaccine constructs formulated with a proprietary adjuvant system were protected from challenge with parental virus. Two negative markers allow the FMD-LL3B3D vaccines to be fully DIVA compatible.

Discussion

This vaccine platform, currently undergoing development, provides opportunities for safer and higher potency FMD vaccines in support of global disease control and eradication programs.

AN OVERVIEW OF REVERSE GENETIC APPROACHES TO ENHANCED FMD VACCINES IN AFRICA

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Introduction

The control of FMD in Africa is complicated by several factors, including the unique epidemiological situation where five of the seven serotypes are present on the African continent; the antigenic diversity of each serotype; maintenance of the virus by persistently infected African buffalo, instability of SAT type vaccines; and the socio-economic conditions in Africa. The most successful way to manage the disease in Africa is via regular livestock vaccination programmes and physical separation of wildlife and livestock. Here we discuss the progress that has been achieved in the development of improved vaccine seed viruses, tailored for the conditions in Africa, using structural design and reverse genetics.

Materials and methods

We compared vaccines based on genetically modified or structurally stabilised vaccine and wild type antigens in eliciting protective immunity against live virus challenge. Epitope-replaced mutant viruses were also assessed in terms of antigenic distance using virus neutralisation assays and reactivities to SAT2-specific monoclonal antibodies (mAbs).

Results

Inter- and intra-serotype chimeric vaccines conferred protective immunity. However, capsid swapping, during the production of chimeric vaccine seed viruses, may transfer other undesirable traits such as capsid instability and poor cell culture adaptation, which are limitations that were overcame by site-directed mutagenesis of the amino acid(s) associated with improved performance. Recently, we compared SAT2 viruses, containing mutations adjacent to the inter-pentameric interfaces to improve the conformational stability of the capsid, as vaccine antigen and found it to elicit superior protective immune responses in cattle. Using charge-dampened mutants the reactivity of anti-FMDV antibodies in the sera from structurally stabilized SAT2 FMD vaccinated animals against dominant antigenic sites on the structurally-exposed protein targets were assessed.

Discussion

Chimeric viruses, enhanced epitopes, cell-culture adapted viruses and stabilised are important improvements to African FMD vaccines. Any applied research into the development of novel FMD vaccines and disease control strategies for Africa need to enable a fit-for-purpose approach to FMD control in Africa.

RATIONAL DESIGN OF ATTENUATED FMDV VACCINES BY ELEVATION OF –CPG- AND –UPA- DINUCLEOTIDE FREQUENCIES

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Introduction

Live, attenuated, vaccines have classically been developed by serial passage of virus in tissue-cultured cells: progeny viruses are analysed for attenuation throughout this process. Often, attenuation is based upon a small number of key mutations which may back-mutate during vaccine production, or, following administration: reversion to virulence. Modern molecular biology, in combination with reverse genetics, has facilitated FMDV attenuation by deletion/mutation of virus proteins, or, by transposition of RNA secondary structures. An alternative method - Synthetic Attenuated Virus Engineering (SAVE) - produces attenuated viruses by the rational design of genomes to include high numbers of synonymous mutations. Initially attributed to alteration of codon-pair bias, it has been shown that attenuation is due to elevation of –CpG-/–UpA- dinucleotide frequencies.

Materials and methods

Using synthetic biology we have produced FMDV 'replicon' systems which allow us to quantify RNA replication in real-time, in live cells. Our replicons allow the rapid determination of replicative fitness and, constructed as 'cassette' systems, allows genomic regions to easily be replaced. In this manner the various strategies of FMDV attenuation have been compared.

Results

Data will be presented comparing the replicative fitness of a wide range of published modified FMDV genomes, together with our SAVE genomes, in a range of cell-types. Replicons have been converted into infectious copies and virus rescued.

Discussion

Attempts in the 1960s to produce live, attenuated, FMDV vaccines via the 'classical' method were unsuccessful – most probably through a lack of genetic stability. Attenuation by SAVE, however, involves high numbers (many 100s) of such mutations providing a very much higher degree of stability. Our attenuation strategy is the introduction of synonymous mutations into the replication proteins (alone) producing a 'pre-attenuated' genomic 'backbone' into which capsid proteins from any sub-type can be inserted to produce a vaccine: a rapis response to new outbreak strains.

FIELD TRIAL TO ESTIMATE THE EFFECTIVENESS OF THE VACCINATION PROGRAM IMPLEMENTED IN THE MAGHREB REGION

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Introduction

Routine or emergency vaccination are strategic tools to control FMD. Preliminary estimates of vaccine effectiveness can be obtained by confined field studies, contributing to optimizing control programs.

Field trials to evaluate effectiveness of FMD vaccines currently used in the Maghreb region have been designed; here we report the results obtained from the trial conducted in Morocco.

Materials and Methods

A bivalent vaccine (A/Eritrea-98 6PD50 and O-Manisa/O-3039 3PD50) was administered to 20 naïve calves and 20 previously vaccinated cattle. Sera were checked before and 30 days post vaccination (DPV), with an intermediate sampling 5 or 10 DPV for vaccinated and naïve cattle respectively. The level of virus neutralizing (VN) antibodies against the vaccine strains and the field viruses was determined; in addition, sera were titrated using IZSLER ELISA kits.

Results

In previously vaccinated cattle, vaccination elicited a strong and fast increase (up to 10X, 5 DPV) of neutralizing antibodies, suggestive of protective immunity, with overlapping titres against the two type O vaccine strains and the field virus O-ALG/1/2014 (lineage O-Ind2001); antibodies had further increased at 30 DPV, reaching average titres of ≥ 3 Log10. Analogous trend was observed for type A, though titres to the vaccine strain were 3-fold higher than those against the field virus A/Algeria/1/2017 (despite both belong to the same lineage A/Africa/G-IV).

All naïve calves seroconverted from negative to positive after vaccination, but the level of VN antibodies remained lower than in the boost-vaccinated group. The best immune response was observed against the vaccine strain A/Eritrea-98, with 95% animals overcoming the presumed protective threshold, whilst only about 50% achieved sufficient immunity against the other FMDV strains tested.

ELISA provided results consistent with VNT for boost-vaccinated cattle, whilst it was less sensitive to detect antibodies in prime-vaccinated calves.

Discussion

A booster vaccination is necessary to elicit a strong and fast increase of antibodies, cross-neu-

tralizing field circulating viruses.Simple and feasible field trials enable producing relevant information for improving FMD control and preparedness against reoccurrence of outbreaks.

MODELLING THE IMPACT OF FARMING PRACTICES UPON VACCINE EFFECTIVENESS IN ENDEMIC SETTINGS – A CASE STUDY IN KENYA

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Introduction

In many lower and middle-income countries in Africa, the Middle East and Southern Asia, livestock owners bear a significant impact as a result of regular FMD epidemics. However, lack of information on localized risks and appropriate prevention measures affects their ability to effect control. Additionally, the inherent uncertainty in disease reporting, inconsistent implementation of interventions and the use of imperfect vaccines means that there are significant challenges for policy makers and local farmers in managing the disease. It is therefore crucial to develop bespoke modelling tools that can appropriately capture farming practices in endemic regions and to establish appropriate controls accordingly.

Methods

In this work, we use epidemiological, demographic and behavioural transect study data gathered through a series of EuFMD training workshops to develop a cross scale mathematical model to predict the spread of FMD in Nakuru County, Kenya. The model is then utilized to investigate the potential for reactive vaccination to reduce the incidence of FMD in the future.

Results

Analysis of the transect study data indicates that farmers that use common grazing and water sources are at increased risk of infection with FMD. The mathematical model results show that the use of high efficacy vaccines is crucial to decrease the incidence of FMD in Nakuru, even when vaccine coverage is relatively low. In addition, in the presence of limited resources, targeting control towards those farms that are at increased risk through shared resources can have beneficial effects when controlling future outbreaks.

Discussion

Our work highlights the fact that traditional proximity-based models are inappropriate to capture FMD transmission in countries such as Kenya, where local farming practices can have a significant effect upon infection risk. We have also highlighted the urgent need for procurement and deployment of high efficacy vaccines to ultimately assist in progression towards disease freedom.

POSTER

POST-VACCINATION MONITORING OF TRIVALENT FMD VACCINE CONTAINING O1 MANISA, O 3039, A22 IRAQ TO EVALUATE VACCINE EFFECTIVENESS IN SMALL SCALE FIELD TRIALS

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Introduction

In 2018, Foot-and-Mouth disease viruses of the A/ASIA/SEA-97 lineage emerged in pigs in South Korea. A factor which has contributed to outbreak of this virus in pigs was unvaccinated with serotype A. Because of outbreaks of FMDV, mostly of serotype O , type-O vaccination of pigs is obligatory. Therefore, emergency vaccine containing A22-IRAQ was administered in pigs during and around the time of an outbreak in March, 2018. The aim of this study was to evaluate the immune response of emergency vaccination in field farm against vaccine strains as well as a field strain from A/SKR/5/2018 which was isolated from Gimpo in South Korea to assess vaccine effectiveness in field trials.

Materials and methods

In general, it is useful to test using ELISA Kit for assessing large-scale serological immune response, however the sensitivity of commercial ELISA kit was found to be limited by species. Therefore, small-scale farm (National Institute of Animal Science, NIAS) was purposely selected that had accurate individual vaccine history information to assess vaccine-induced virus neutralization (VN) titres to the vaccine and field strains. 25 pigs vaccinated twice 4 weeks interval bleed every week after prime vaccination up to 8 weeks.

Results

The VN-titres of all pigs from NIAS achieved a sufficiently high level against vaccine virus, A22-IRAQ and field virus, A/SKR/5/2018 respectively in 2 weeks and 4 weeks after prime vaccination, and remained high up to 8 weeks.

Discussion

Previously, vaccine matching studies carried out by the World Reference Laboratory, Pirbright indicated that the r1 value was 0.43 based on VNT. In this study, we showed that emergency vaccination using inactivated vaccine with high r1(>0.3) value with the field strain provided high VN-titers, which may be justifiable as protection in pigs. In addition, monitoring post-vaccination serology is an important component of evaluation for FMD vaccination programs.

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