FMD Global Situation

December 2011

The World Reference Laboratory for FMD

Dr Jef M. Hammond

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Outline

• Introduction
• WRLFMD
• Current status
  • Disease situation
  • Diagnostics
  • Vaccines
• Future Issues

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FMD

• The most infectious disease known
• A present and continuing severe global threat
FMD

- The most infectious disease known
- A present and continuing severe global threat
- Devastating economic, social and environmental impacts
  - severe productivity losses
  - disruptions in a wide range of agricultural, industrial and social activities
  - major threat to food supply
  - major expense in control and re-eradication
  - high cost of surveillance and emergency preparedness.
FMD

- 7 serotypes and multiple subtypes
- No single vaccine
- No single test
- Each outbreak/situation is different
FMDV Global Issues

- Health
  - Animal welfare – mass slaughter of healthy stock
  - Human welfare – loss of livelihood
FMDV Global Issues

- **Health**
  - Animal welfare – mass slaughter of healthy stock
  - Human welfare – loss of livelihood

- **Global Trade**
  - Excludes many poorer nations from trade
  - Restrictions on many goods (not just meat)
FMDV Global Issues

- Health
  - Animal welfare – mass slaughter of healthy stock
  - Human welfare – loss of livelihood

- Global Trade
  - Excludes many poorer nations from trade
  - Restrictions on many goods (not just meat)

- Cost of Prevention and Outbreaks
  - Surveillance
  - Direct and Indirect (compensation, trade and tourism)
FMDV

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- Highly contagious vesicular disease affecting up to 70 species of cloven-hoofed mammals.
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• 7 different serotypes: O, A, C, Asia1, SAT1, SAT2, and SAT3
FMDV

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- Highly contagious vesicular disease affecting up to 70 species of cloven-hoofed mammals.

- 7 different serotypes: O, A, C, Asia1, SAT1, SAT2, and SAT3

- Large number of subtypes have evolved within each serotype (topotypes).
FMD in cattle
FMD in cattle

UK 2007

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FMDV Infection

• Sheep infected with FMDV may not be diagnosed for a considerable time as signs can be very mild.

• But during this period they will be infectious.
FMDV Infection

• FMD in pigs spreads very rapidly because pigs produce 30 to 100 times as much virus in aerosols as sheep or cattle.

• An infected pig can produce a hundred million infectious doses per day.
FMDV Infection

- Some strains of FMDV affect particular species more than others.
- Transmission, immunity and carrier status all vary between species.
- > 50% infected ruminants become carriers
  - African Buffalo: 5 years
  - Cattle: 3 years
  - Sheep: 9 months
  - Goats: 4 months
- Pigs do not become carriers
Pathogenesis of FMD

**Incubation periods:**
- 2-14 days in individual animals, but dose related
- 4-5 days most common, but may be as short as 24 hours
- 4-14 days for farm incubation period

**Replication sites:**
- Initially in pharynx and/or skin
- Then viraemia and generalisation with high level replication in skin
Transmission

FMDV can be introduced in several ways:

• Direct or indirect contact with infected animals

• Spread of aerosols

• Contact with contaminated objects
  (footwear, clothing, vehicles, vets)

• Milk or meat

• Artificial insemination
FMD Reference Laboratories at Pirbright

International

• European Community Reference Laboratories for FMD & SVD
  – Support and referral diagnosis for NRLs in EU Member States
  – Marginally costed funding from DG-Sanco

• OIE Reference Laboratory for FMD
  – Wide remit in support of safeguarding and promoting international trade
  – No financial support from OIE- charging for services?

• World Reference Laboratory for FMD designated by FAO
  – WRLFMD
  – Global surveillance and threat recognition
  – Reference Laboratory Network of OIE/FAO FMD Labs
  – Small financial contribution from FAO
World Reference Laboratory for FMD - WRLFMD

- 24/7 Diagnostic Service
- Global surveillance
- Strain characterisation
- Vaccine matching (Bulgaria, South Korea)
- Extensive library of isolates
- Test improvement & Development, validation,
- Quality assurance
- Reagent supply
- Training
- Advice & Reports
The WRLFMD website contains quarterly and annual reference laboratory reports. 
http://www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm
Institute for Animal Health (IAH)
Reference Laboratories

Providing Global Support for Global Disease Control

Background
The Institute for Animal Health (IAH) is a world-leading centre of excellence for research and diagnosis of major diseases of farm animals sponsored by the Biotechnology and Biological Sciences Research Council (BBSRC). Our mission is to deliver high quality fundamental, strategic and applied science focussed on infectious animal diseases. The institute is currently situated on two sites located at Compton in Berkshire and at Priston in Somerset. A Government decision to build a new, state-of-the-art, high containment virology laboratory on the Priston site by 2013 will result in the closure of the Compton laboratory. The Priston Laboratory has both unique specialist high-containment laboratory and large animal facilities providing outputs that advance veterinary and medical science and places it firmly within the ‘One Health’ area. The ability to study existing and emerging infectious diseases in the natural animal hosts is key to the institute’s strategy, and training scientists, technicians and veterinarians is an important part of our remit.

Reference Laboratories
The IAH hosts both National and International ISO accredited Reference Laboratories including the FAO World Reference Laboratories for FMD, BP and PPR, and European Community OIE and Defra National Reference Laboratories for Foot-and-mouth disease, Bluetongue, African swine fever, Hendra virus and Peste des petits ruminants.

Reference Laboratories at the Institute for Animal Health
- African horse sickness
- Swine vesicular disease
- Vascular stomatitis
- Sheep and goat pox
- Lumpy skin Disease
- Marek’s disease

“Global Disease Information for Global Disease Control”

These Reference Laboratories underpin IAH strategies with a unique presence and an enabling capability making available the best possible disease information as near to real time as possible. We maintain the capacity to provide rapid diagnosis and emergency response and carry out specific tests in support of National and international disease surveillance. We are able to: Characterise novel pathogens in vitro and in vivo, produce comprehensive reports, offer vaccine evaluation and recommendations, give expert advice on control strategies, undertake statutory testing in support of animal trade, maintain unique reference collections and sequence databases, influence OIE/WHO regulations for livestock trade, improve international laboratory capacity and capability through extensive networks, training projects and highly successful proficiency testing schemes and supply of diagnostic reagents and kits.

“Institutional Global Network providing Early Warning”

The European Community Reference Laboratories support and provide referral diagnoses for National Reference Laboratories in EU Member States. The OIE Reference Laboratories have a wide remit in support of safeguarding and promoting international trade and the World Reference Laboratories designated by FAO provide global disease surveillance and threat awareness, with the

Institute for Animal Health (IAH)
Reference Laboratories

The Reference Laboratories maintain a number of specific websites detailing much of the information generated by our activities. As well as recent results and epidemiological information we also make our reports available from these sites.

Training and Knowledge Exchange
The Reference Laboratory staff carry out official and ad hoc laboratory training courses for:

- FMD and Other Vascular Diseases
  Dr. Iain Aitken
  iain.aitken@bbsrc.ac.uk
- ST, PPR, ASF and other Non-Vascular Diseases
  Dr. Chris Dara
  chris.dara@bbsrc.ac.uk
- Marek’s Disease
  Dr. Vesna Goluca
  vesna.goluca@bbsrc.ac.uk

BBSRC
bioscience for the future
FMD Distribution

• FMD is endemic in most of Southern Asia, Africa and parts of South America.

• Most of Europe, North and Central America, Australia, New Zealand and Japan are free of FMD.
Diagnosis Laboratory diagnosis of FMD

Approaches:
- Detection of FMD virus, antigen or nucleic acid
  - Virus Isolation
  - Antigen Elisa
  - Lateral Flow Device
  - Automated TaqMan® RT-PCR
- Detection of FMDV-specific antibody (SP/NSP)
  - Virus Neutralization Test
  - Liquid Phase Blocking Elisa
  - Solid Phase Competition Elisa
  - 3ABC Elisa (Non structural protein NSP)
Current assays for FMDV detection

- Virus isolation (CTY or IBRS2): 1-4 days
- Ag ELISA: ~4 hours
- Automated TaqMan® RT-PCR: ~5 hours

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New technologies / new opportunities

1. Lateral-flow devices for FMDV antigen
2. Mobile PCR
3. Isothermal assays

- Faster (more rapid detection)
- Ability to support diagnosis based on clinical signs

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Future challenges

- Many technologies
  - picking the “winning” assay format
- Key role of commercial partners
  - Is the market viable?
  - IP – freedom to operate
- Who uses the tests?
  - expectation of stakeholders
  - Freely available vs control of local diagnosis/reporting
- Use in FMD-endemic countries
New Vaccines

New Generation FMD Vaccines

• Longer duration of protection;

• Faster onset of protection;

• Broader spectrum of protection

• More potent immunity to prevent viral replication and development of viral carriers

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New Vaccines

New Generation FMD Vaccines

• Better discrimination of vaccinated animals that go on to become infected;

• Thermostable- no/reduced cold chain

• Safer to make and easier to administer.
Enhanced Surveillance: OIE/FAO Lab network

- **WRLFMD**: Pirbright, UK
- **RRLSEA**: Pakchong, Thailand
- **LVRI**: Lanzhou, China
- **FGI ARRIAH**: Vladimir, Russia
- **PDFMD**: Mukteswar, India
- **RRLSSA**: Gabarone, Botswana
- **FMD-Laboratory**: Embakasi, Kenya
- **PANAFTOSA**: Rio de Janeiro, Brazil
- **LFADLCT**: Argentina
- **ARC-OVI**: Onderstepoort, RSA
- **PIADC**: Plum Island, USA
- **CODA-CERVA-VAR**: Ukkel, Belgium

Approximately ~2300 samples tested during 2010
Outputs

Current
• Highly detailed analysis of virus
  • Origin
  • Serotype
  • Genotype/strain
  • Possible source
  • Vaccine matching by lab assay
  • Animal experiments
• Detailed reports

Progress
• Complete genome analysis
• Epitope mapping
• Antigenic cartography

• Combine data from all inputs to provide a more comprehensive analysis
• Use of high potency vaccines

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Conjectured Status of FMD

- **Endemic**
- **Intermediate, sporadic**
- **Free with vaccination**
- **Countries with multiples zones:**
  - FMD-free, free with vaccination or not free
  - Free. Virus present in game parks
- **Free**

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Visualization of Regional Virus Pools as an Aid to Global Control

Divides the Globe into 7 pools each with

- Multiple serotypes but topotypes mainly confined to that pool
- Each pool may need tailored vaccines and strategies
Conjectured Status of FMD

Pool positions are approximate and colours indicate that there are three principal pools, two of which can be subdivided into overlapping areas.

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The network laboratories received more than 2,300 samples in 2010 from 38 countries. 80% of the samples characterised in 2010 were of the O serotype.

*Note that serotypes C and SAT 3 were not detected.*

Asia 1 only in India
Samples and virus isolates made by region in 2010.

In total 38 different countries submitted 2,338 samples to OIE/FAO FMD Network Laboratories
- 53% to WRLFMD

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*samples
isolates

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VP1 sequence analysis in 2010.

In total 750 VP1 sequences were characterised in 2010:

648 (86%) from WRLFMD

The remaining 102 (14%) came from other laboratories.
Vaccine matching by VNT 2011

O Manisa vs O PanAsia 2

A22 vs A Iran 05

Asia 1 Shamir
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<th>No Asia 1 in 2010</th>
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Afghanistan, Pakistan, Iran, Bahrain & Turkey have all reported outbreaks of Asia 1.
Serotypes Identified 2011

- O: 38%
- A: 10%
- SAT1: <1%
- SAT2: 1%
- NVD: 42%
- Asia 1: 9%

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FMD Outbreaks 2011

>900 Samples from 23 Countries

23 countries
~900 samples
>600 positive
FMD Outbreaks 2011
>900 Samples from 23 Countries
Vaccine Selection

- OiE/FAO FMD Reference Laboratory Network
- FMD Vaccine Bank Holders Network
**Current FMD Threat Analysis**

Serotype O - widespread circulation
- FMDV type O – ME-SA topotype – PanAsia-2 lineage
- FMDV type O – SEA topotype – Mya-98 lineage

Serotype A - widespread circulation
- FMDV type A – ASIA topotype – Iran-05 lineage
- FMDV type A – ASIA topotype – other

Serotype Asia 1 – limited circulation - risk of further spread
- Several reports in 2011 associated with poor laboratory vaccine matching
  - this is being closely monitored by OIE FMD reference laboratory at Pirbright

Serotypes SAT – restricted circulation
- Have not established outside of Africa

Serotype C
- No reports of serotype C since 2004

Institute for Animal Health
Vaccine Recommendations
(National & European antigen banks)

**HIGH PRIORITY**
- O Manisa
- O BFS or Campos
- A-Iran-05
- A24 Cruzeiro
- A22 Iraq
- Asia 1 Shamir
- SAT 2 Saudi Arabia (or equivalent)

**MEDIUM PRIORITY**
- A Argentina 01
- A Iran 96
- A Iran 99
- A Eritrea
- A Iran 87 or A Saudi Arabia 23/86 (or equivalent)
- A Malaysia 97 (or Thai equivalent such as A/NPT/TAI/86)
- A Taiwan 97 (pig-adapted strain or Philippine equivalent)
- SAT 1 South Africa
- SAT 2 Zimbabwe

**LOW PRIORITY**
- A15 Bangkok related strain
- A Kenya
- A87 Argentina related strain
- SAT 1 Kenya
- SAT 2 Kenya
- SAT 3 Zimbabwe
- C Noville

Within category: not in order of importance
Vaccine Recommendations
(National & European antigen banks)

HIGH PRIORITY
- O Manisa
- O BFS or Campos
- A-Iran-05
- A24 Cruzeiro
- A22 Iraq
- Asia 1 Shamir
- SAT 2 Saudi Arabia (or equivalent)

MEDIUM PRIORITY
- A Argentina 01
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- A Iran 87 or A Saudi Arabia 23/86 (or equivalent)
- A Malaysia 97 (or Thai equivalent such as A/NPT/TAI/86)
- O Taiwan 97 (pig-adapted strain or Philippine equivalent)
- SAT 1 South Africa
- SAT 2 Zimbabwe

LOW PRIORITY
- A15 Bangkok related strain
- A Kenya
- A87 Argentina related strain
- SAT 1 Kenya
- SAT 2 Kenya
- SAT 3 Zimbabwe
- C Noville

Within category: not in order of importance
Global Activities

• OIE/FAO FMD Reference Laboratory Network - developing relationships

• Increased workload - samples

• Increased demand for
  • Training
  • Proficiency testing
  • Accreditation

• Ref Labs need dedicated funding from this initiative
WRLFMD Summary

- FMD present in many regions/ Significant impact on livelihoods
- Major risk of spread through movement of animals and products
- Vaccination alone is not enough- Education and bio-security
- What can we do together within the networks?
- Twinning projects – diagnostics training/ epidemiology/QA
- Improve surveillance- not all about NSP testing!
- Obtain clinical samples: characterise serotypes/sequence/ vaccine match
- Decreased funding will affect all reference laboratories and control plan

Institute for Animal Health
The Network Provides a global ‘real time virus map’ for the implementation of better informed control measures for FMD

A major combined effort both National and Global is needed for control

Meeting in Bangkok 2012

Preparation of a Global Strategy to Control FMD