Diagnostic tools and their role in the global control of foot-and-mouth disease

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Introduction

• Accurate diagnosis is important
  – Prevalence of infection
  – Serotypes and topotypes
  – Immune profile (post outbreak or post vaccination)
  – Sub-clinical infection and carriers
Introduction

• Diagnostic tests provide epidemiological information vital for countries embarking on the progressive control pathway

• Success as measured by surveillance acts as incentive to progress along the pathway towards improved disease control and ultimately eradication

• The specific need for diagnostic assays will change as countries move along the pathway
Diagnostics and the PCP

Stage 1
• Serological surveys to assess prevalence in different husbandry systems
• Circulating strains known
  • Samples sent to ref lab for characterisation or locally done

Stage 2
• Implement risk-based control

Stage 3
• Implement control strategy to eliminate circulation

Stage 4
• Maintain zero circulation & incursions; withdraw vaccination

Stage 5
• Maintain zero circulation & incursions

Free without vaccination

Additional information:
- From 0 to 1: Comprehensive study of FMD epidemiology planned
- From 1 to 2: Develop aggressive strategy to eliminate FMD
- From 2 to 3: No endemic FMD in domestic livestock
- From 3 to 4: Apply for official status (OIE): ‘free WITHOUT vaccination’
- From 4 to 5: Apply for official status (OIE): ‘free WITHOUT vaccination’
Diagnostics and the PCP

Stage 2
- Ongoing monitoring of circulating strains
- Targeted serological surveys to determine prevalence
- Serological surveys to assess vaccination coverage of the target population(s)
- Laboratory evidence that the vaccine used is appropriate for circulating strains of virus
Diagnostics and the PCP

**Stage 3**
- Rapid detection of all FMD outbreaks with detailed analysis of outbreak virus
- Credible epidemiological evidence of control
- Monitoring of vaccination and population immunity
Diagnostics and the PCP

Stage 4
- FMD virus is not circulating endemically in domestic animals
  - Serological surveys
- Detailed investigation into incursions
Fitness for purpose

- Tests needed for different PCP stages
  - Stage 1 – determine level of virus circulation
    - Serological assays and especially NSP
    - Typing of circulating viruses
  - Stages 2 – 4: control measures with improvement of labs
    - Serological assays and titres determined
    - RT-PCR, VI
    - Further characterisation of circulating viruses
Need for appropriate reagents

Vaccine matching \(\rightarrow\) reagent matching!

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

- Heterologous reactions give low titres
  - Incorrect interpretation of vaccine reactions
  - Misinterpretation of circulating viruses
- Cross reactions make it difficult to determine serotype
  - Sera react to more than one serotype
- May be more problematic when exposed to more than one serotype
  - Virus or antigen needed for serotyping

Fig. 5. A comparison of homologous and heterologous saturation curves: (a) O1 BFS 1860 vs. O Jersey 1/81; (b) O1 BFS 1860 vs. O1 Lausanne 65. Replicate titrations of O1 BFS 1860 serum against the homologous and heterologous viruses were performed as matched pairs using the same dose of homologous and heterologous antigen.

Ouldridge et al., 1984
Point of care devices

- **Lateral flow devices**
  - Good sensitivity and specificity
  - Quick and easy to use
  - Expensive

- **PCR/LAMP**
  - Lack of interest by commercial companies
  - Small units for lab use

- **Expensive commercial tests encourage local development**
  - Validation
  - Quality control
The future of POC devices

• Policies needed for notifiable diseases
• Control over sales and distribution
  • Prevent sales without governmental approval
• Used by competent persons
  • Training needed for operators
• Fit for purpose
  • Ensure the correct test is used for the available samples
The future of POC devices

• Regulations on notification for pos and neg results
  – Protocols when a result is negative

• Regulations on submission of samples to labs
  – When should samples also be taken and send to a lab?

• Record keeping
  – species, age, epidemiological info, etc.

• Validation in different countries/regions
Role of laboratories

• Confirmation of the index case in QA environment
• POC devices may become more prevalent
  – Labs confirm negative/inconclusive results
  – Developing and validating devices and making recommendations on their use
• Surveillance – high throughput (post outbreak and vaccine monitoring)
• Responsible for reagent stockpiles
• Participate in proficiency testing/organise PT
• Responsible for validation, determining uncertainty of measurement and precision
Role of laboratories

- **Characterisation of disease agents**
  - Sequencing and phylogenetic analysis
  - Mapping epitopes
  - Forensic tracing

- **Vaccine matching**
  - r-values
  - Antigenic cartography

- **Research**
  - Develop and validate new diagnostic assays
  - Improved/novel vaccines
  - Correlates of protection
Quality control and validation

• OIE terrestrial manual: Principles of validation of diagnostic assays for infectious diseases
  – Assay validation criteria
    • 1. Fitness for intended purpose(s)
    • 2. Optimisation
    • 3. Standardisation
    • 4. Robustness
    • 5. Repeatability
    • 6. Analytical sensitivity
    • 7. Analytical specificity
    • 8. Thresholds (cut-offs)
    • 9. Diagnostic sensitivity
    • 10. Diagnostic specificity
    • 11. Reproducibility
    • 12. Ruggedness
Conclusions

- Diagnostic requirements change as countries move through the PCP
- Region specific reagents are essential
- Most commercial assays are too expensive for widespread use in resource poor countries
- In house tests need to be validated
- Collaboration needed between the different labs developing assays – choose the best test for the region

- Good laboratory diagnostics will only be meaningful when there are sufficient resources - submission of samples and to act upon results
Thank you!

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