FMD diagnostics: current developments and application in the context of FMD control in endemic countries

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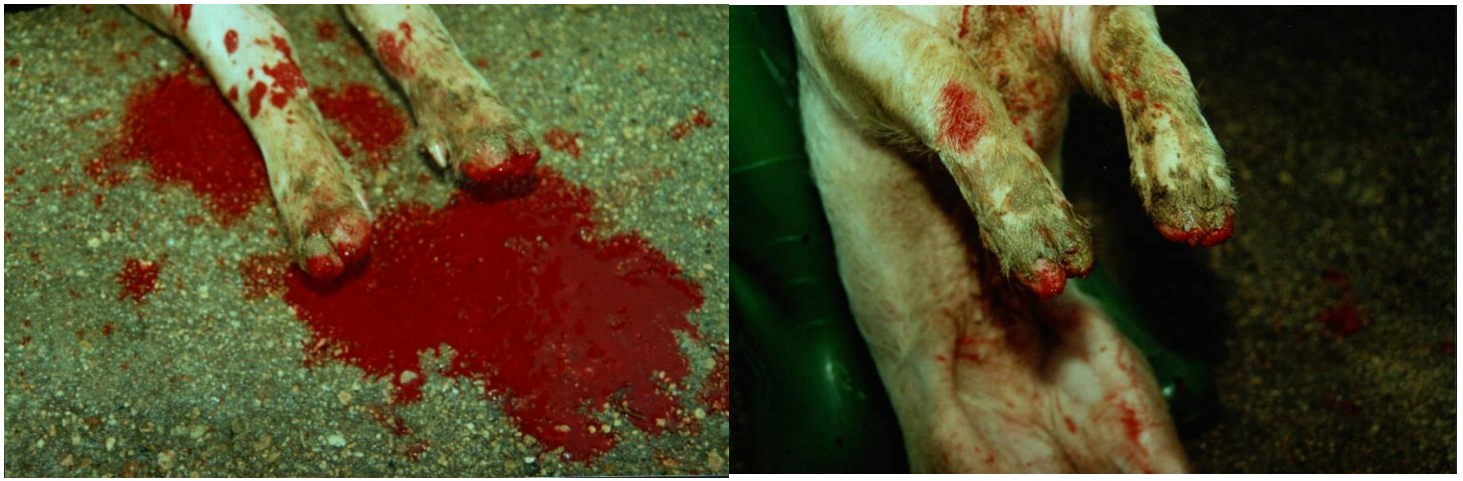
Introduction

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



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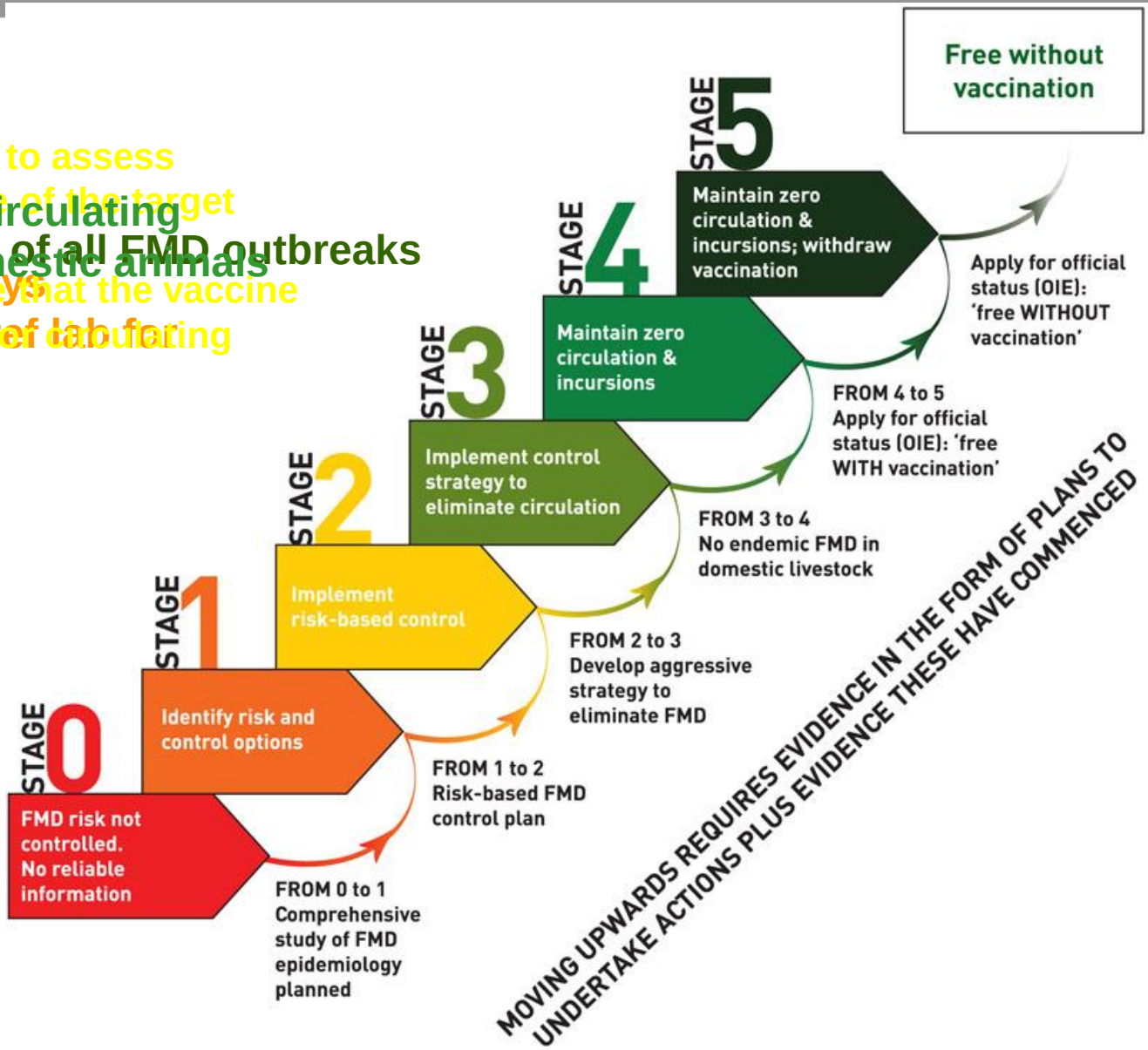
Introduction

- 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

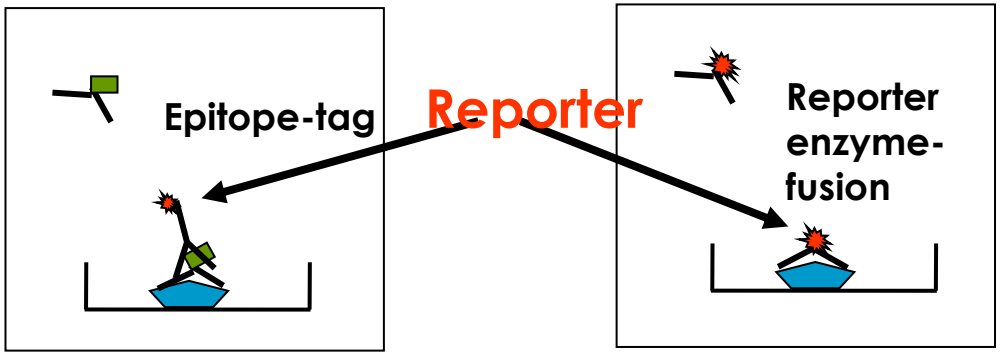
Diagnostics and the PCP

Stage 2
Serological surveys to assess
Stage 4
Stage 3
•FMD virus is not circulating
endemically in domestic animals
•Rapid detection of all FMD outbreaks
Stage 1
•Laboratory evidence that the vaccine
used is appropriate for obtaining
•Serological surveys
•Sample capacity of laboratory
characterisation



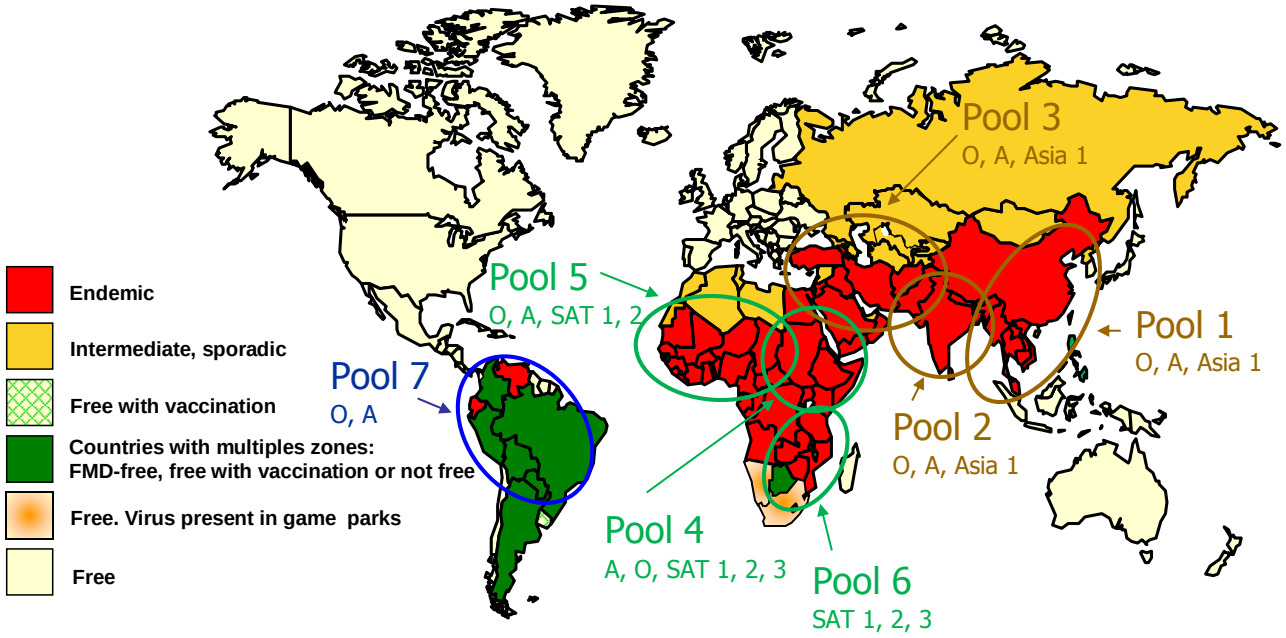
Fitness for purpose

- **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 ⟶ 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

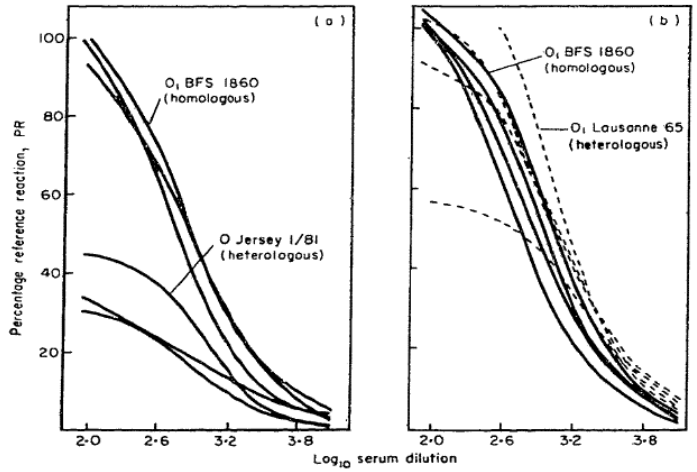


Fig. 5. A comparison of homologous and heterologous saturation curves: (a) O_1BFS 1860 vs. O Jersey 1/81; (b) O_1BFS 1860 vs. O_1 Lausanne 65. Replicate titrations of O_1BFS 1860 serum against the homologous and heterologous viruses were performed as matched pairs using the same dose of homologous and 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

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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)**
- **Characterisation of disease agents**
- **Responsible for reagent stockpiles**
- **Participate in PT rounds**
- **Responsible for validation, determining uncertainty of measurement and precision**

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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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