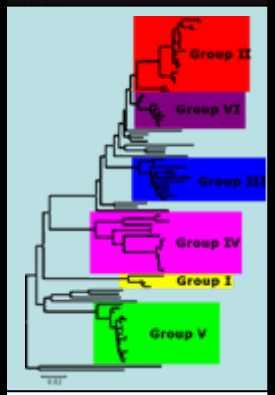
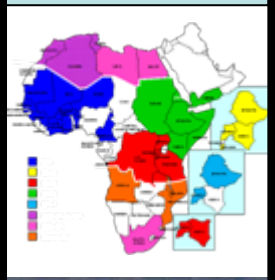
Foot-and-mouth disease diagnostics:

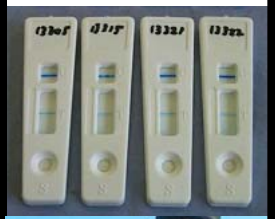
…are we there yet?

Donald King

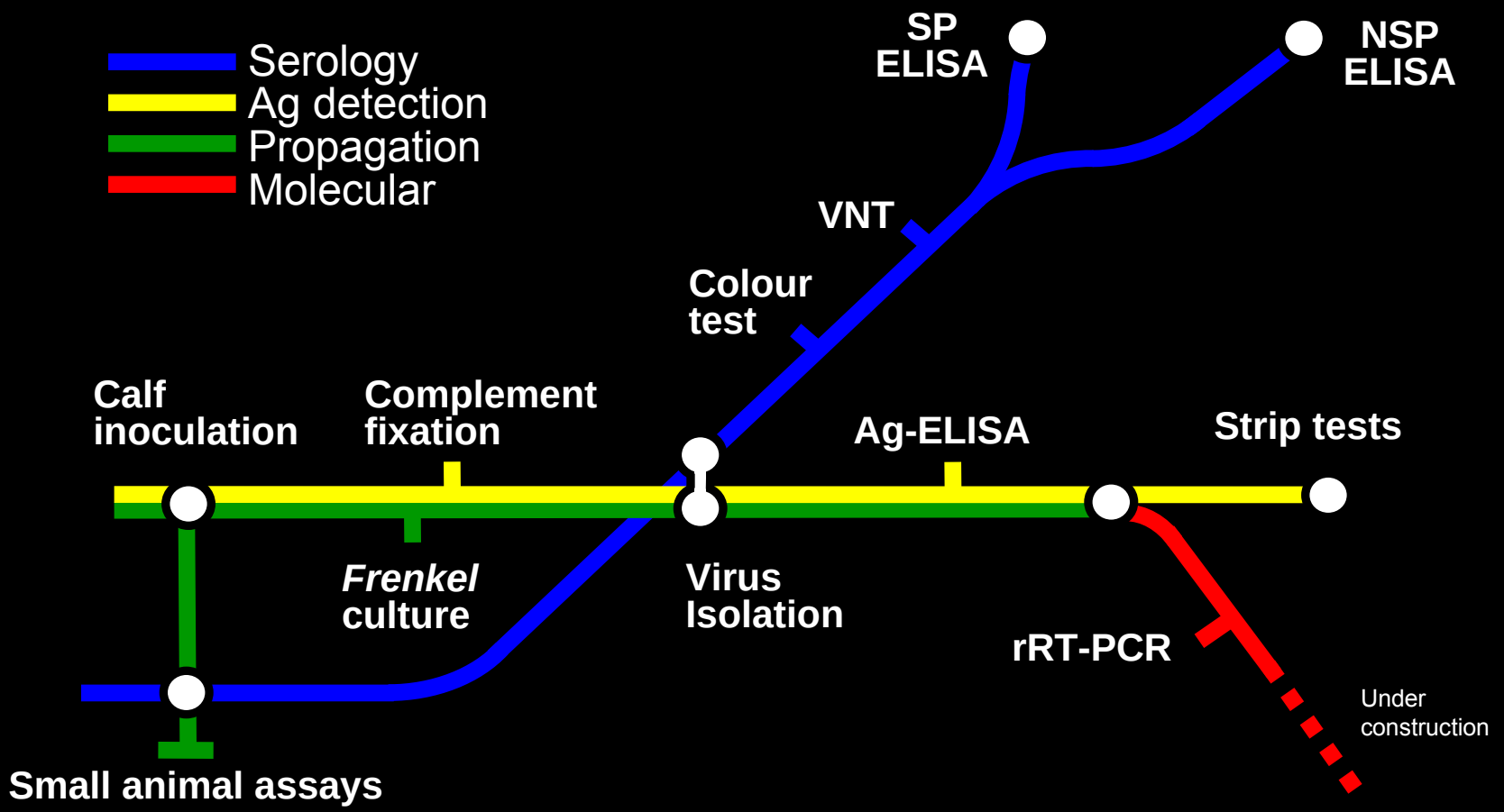
Molecular Characterisation and Diagnostics Group, IAH







Where we've been



Laboratory diagnosis of FMD

Approaches:

- Detection of FMD virus
- Detection of FMDV-specific antibody (SP/NSP)

- Samples collected:
  - Tissue (vesicular epithelium)
  - Blood (sera or whole blood)

  - “probang” samples
  - Milk
  - Swabs from mucosal surfaces
  - Environmental samples (air samples etc..)

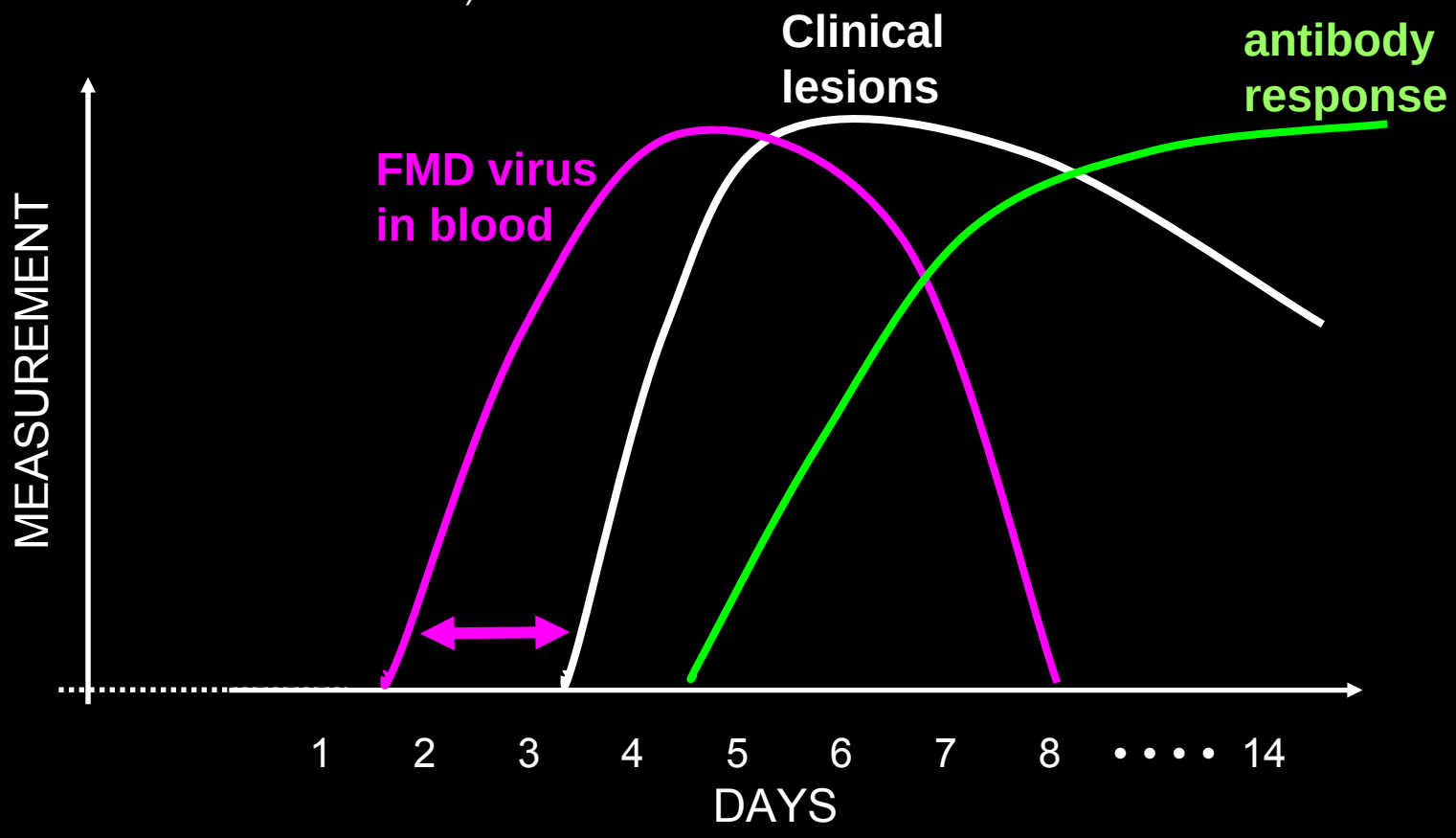
Diagnostic windows

What are we trying to do?

2 Active surveillance for infected animals (including pre-clinical cases)

1 Rapid confirmation of clinical signs

3 sero-surveillence for FMDV exposed animals



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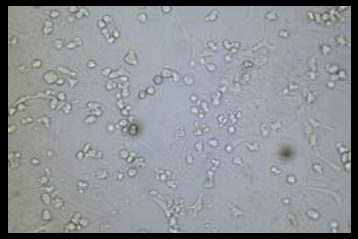
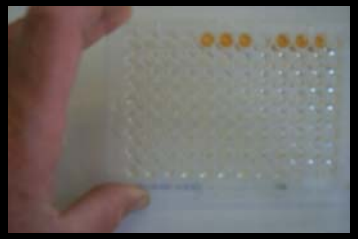
Representative “in contact” cattle data from Alexandersen et al., 2003 and unpublished data from IAH

Current assays for FMDV detection



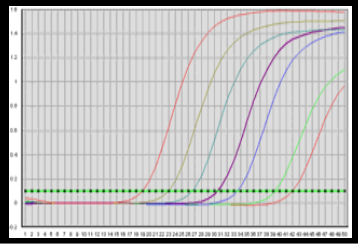
Virus isolation (CTY or IBRS2)

1-4 days



Ag ELISA

~4 hours



Automated TaqMan® RT-PCR

~5 hours

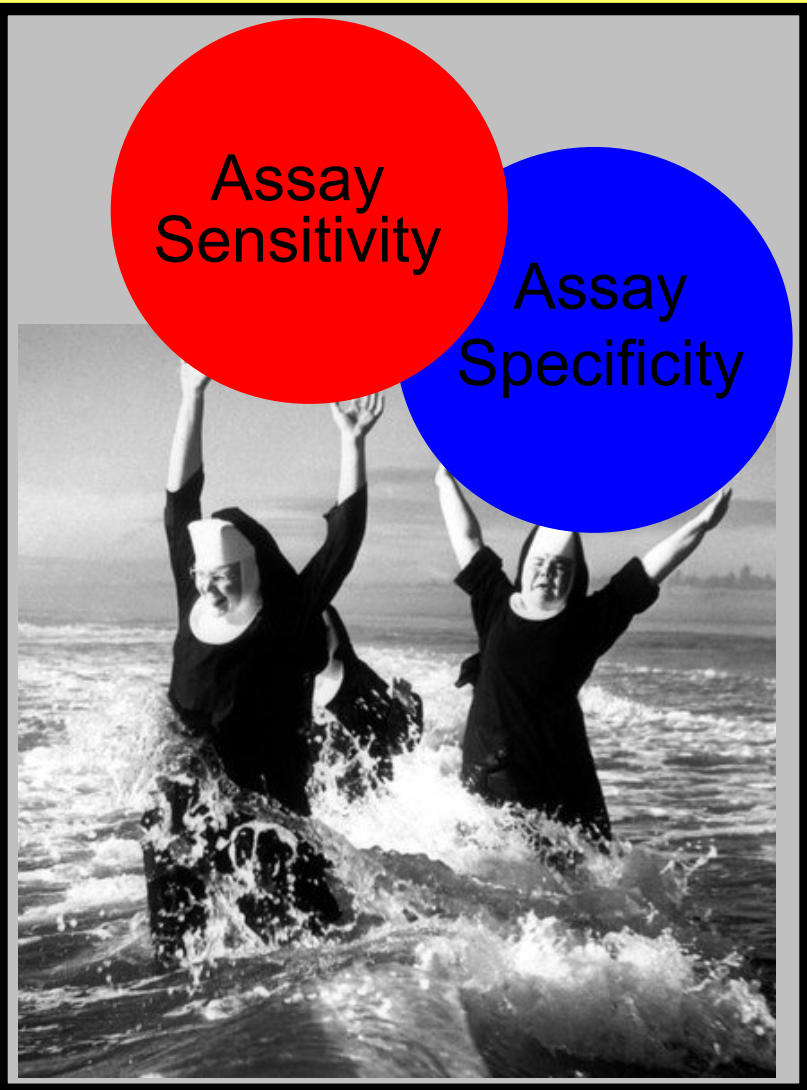
1

10

100

Time to report result (hrs)

New assay formats: considerations



Routine use in WRL

- Reliability
- Performance
  - Limit of detection
  - Ability to correctly identify infected animals with diverse FMDV strains
- Speed
- Scalability
- Cost ?

The road ahead.....

Foresight
Making the future work for you

OFFICE OF SCIENCE AND INNOVATION
Infectious Diseases:
preparing for the future
http://www.foresight.gov.uk/

What can we expect?

Technologies

Improvements in:

- Computer power
- Communications
- Detector chemistries
- Sequencing capability

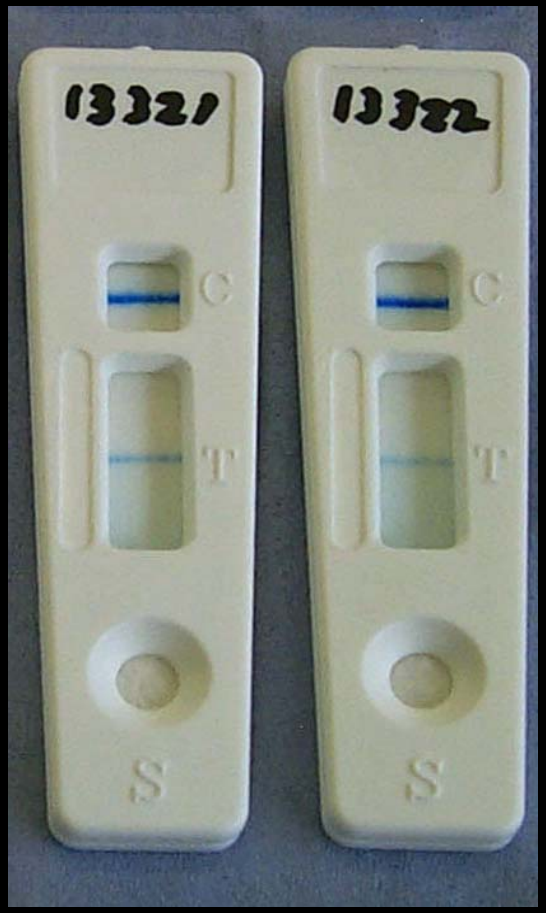
Drivers for Change

- Tools to support rapid decision making
  - "Point-of-care diagnostics"
  - Highly parallel assay formats for:

    [i] differential diagnosis
    [ii] strain characterisation

Lateral-flow devices FMDV Antigen detection

- Developed by IAH in collaboration with international partners
- Quick and simple to perform
- Pan-serotypic
- During 2007: used for rapid (<10 mins) confirmation of FMD in the field (IP7)
- Also useful in the Lab
- LFD marketed by Svanova Veterinary Diagnostics



Validation data for pan-reactive LFD

- Sensitivity data generated for archived clinical samples

	ELISA		1F10 (gold-particle)	
Virus serotype	**Fraction**	**%**	**Fraction**	**%**
FMDV type O	121/126	96	119/129	92.2
FMDV type A	32/41	78	36/41	87.8
FMDV type C	14/24	58.3	15/24	62.5
FMDV type SAT 1	13/24	54.2	16/24	66.7
FMDV type SAT 2	28/32	87.5	18/32	56.3
FMDV type SAT 3	9/10	90	7/10	70
FMDV type Asia 1	36/40	90	39/40	97.5
Total	253/297	85.2	250/300	83.3

Data from Nigel Ferris (IAH)

Rapid detection of FMDV in the field: Portable PCR platform

- Non-specialist user
  - Nucleic acid extraction
  - PCR set-up
  - Analysis
- 5 independent modules
- Battery operated
- Decontaminate by immersion
- Field trial (Turkey) later in 2008
- Platform for other livestock diseases

Smiths Bio-Seeq™

Molecular Characterisation & Diagnostics Group

Rapid communication of results

Slide from Carmelo Volpe (Smiths)

Non-invasive sampling

BioCapture 650

BioBadge 100

- Air-samplers (MesoSystems)
- Hand held
- Simple-to-use

	BioCapture	BioBadge
Cattle 3 dpi	10.24	11.23

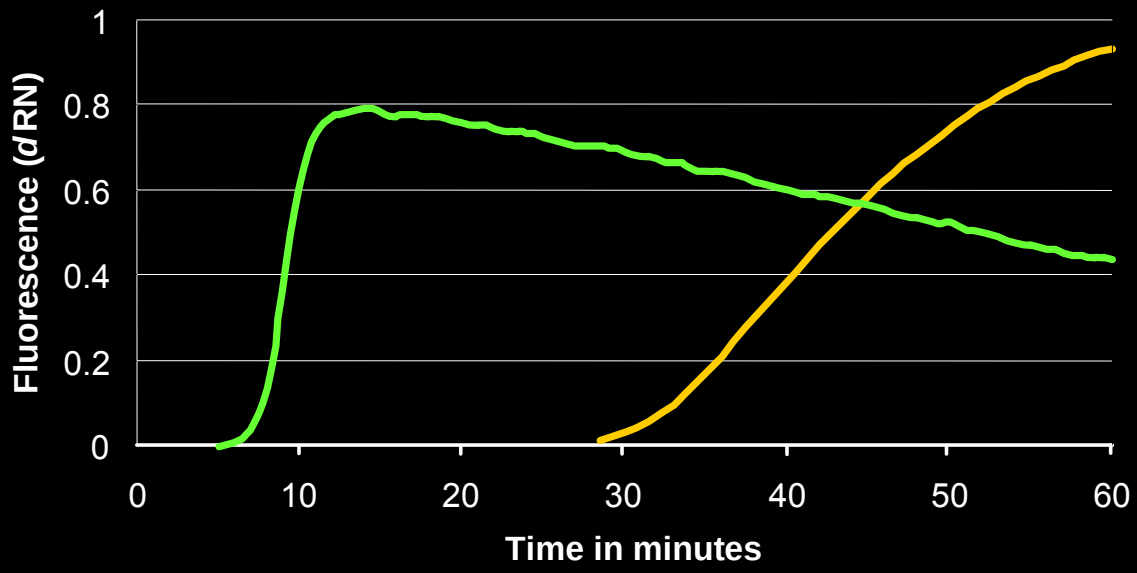
Log10 FMDV copies detected by rRT-PCR after 5 minute collection near animals infected with FMDV (serotype Asia-1) (Ryan et al., 2007)

- Integrated with FMDV detector?
- located in high-risk areas?

Alternative detector technologies

Isothermal amplification (RT-LAMP)

- Nucleic acid amplification at a single temperature
- No need for fragile precision instrumentation
- Basis of disposable device / cost effective
- More suitable for use in the field
- Very rapid, similar sensitivity to RT-PCR



Dukes et al., 2006

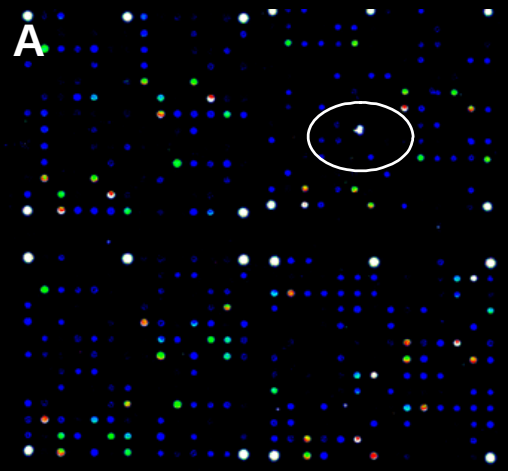
Detection and characterisation?

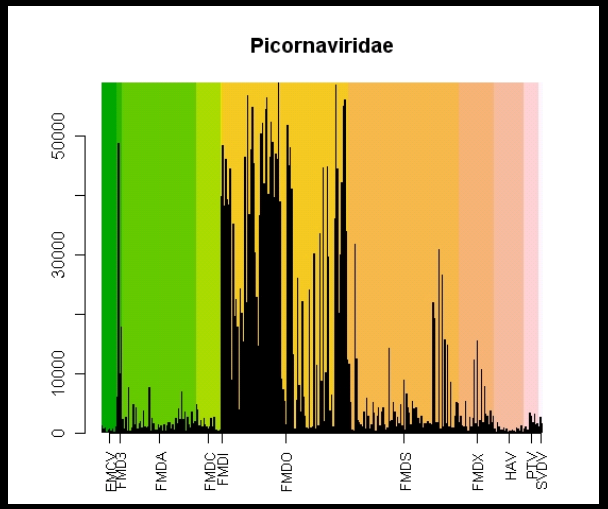
Viral MicroArray

Potential Benefits:

- Thousands of experiments in parallel
- Differential diagnosis
- Viral Typing of FMDV isolates
- Clarification of mixed infections
- Portable formats emerging

O UKG 12/2001





DEFRA funded Biochip project (April 06-09)

http://www.bio-chip.co.uk/

Potential scenario for field diagnosis of FMD

Veterinary visit → **Clinical diagnosis**

Lateral-flow devices (LFDs)
Sensitivity ~80%
→
- Rapid confirmation of positives?

"Rapid" Molecular assays
Sensitivity>95%
→
- Ability to confirm negatives
- Additional surveillance use
- Strain characterisation?

Future challenges

- Rapid development of technologies
- Key role of commercial partners
  - Is the market viable?
- Use in FMD-endemic countries
- Availability of technology
  - Provide freely vs control of local diagnosis/ reporting for notifiable diseases

Summary and Prospects:

1. FMDV-specific assays have been developed to address wide range of clinical circumstances
   - Role of WRL for assay validation
2. Likely to be increased demand for testing in future
   - Active surveillance for disease in high risk animals
   - Pre-clinical testing
   - Integration of different assay formats (virol/sero)
3. Devolved and POC formats offer potential to significantly decrease assay time
   - Support of diagnosis based on clinical signs
   - Involvement of end-users and stakeholders is vital

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