Interpretation of results of foot and mouth disease surveillance to distinguish between vaccinated and infected cattle.

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DIVA
Differentiating Infected Vaccinated Animals

VIAA : Virus Infection Associated Antigen

NSP : Non-Structural Proteins
ELISAs : recombinant proteins
3A, 3B, 3ABC, 3D, 2B, 2C
EITB : Enzyme-linked
ImmunoelectroTransfer Blot
NSP - Tests
fit for purpose for surveillance programmes:
- detecting circulation of virus
- prevalence survey
- outbreak management (especially recovery
- substantiating freedom of infection
Surveillance programmes:
- 95% confidence
- design prevalence: 2% among herds
  5% within herds
- sample design
- test performance characteristics (Se/Sp)
Interpretation Results DIVA

Test performance characteristics:
- Diagnostic Se/Sp
- Never 100/100%
- Missing real pos / having false pos

Cannot rely on serosurveillance alone!
Combine with:
- clinical surveillance
- virological survey
- cluster analysis
- profiling
Validation NSP Tests

- Index test / In-house tests / Commercial tests
- Validation scheme OIE / Independent validation
- Se/Sp cattle / pigs / sheep / (buffalo)
- Sub-populations: naive / vaccinated / vac-inf
- NSP Ref sera cattle / pigs / sheep
- Secondary standards / working standards
  (sera vac animals <> infected animals)
- Serum panels (Test development <> batch test)
Interpretation of results
Subclinical circulation of virus?

(Endemic) Regions with vaccination
After emergency vaccination
- Sheep / Vaccinated cattle / pigs
- Non-observed animals (meat / hobby)
- Wild-life: African buffalo, impala, kudu, ?
  Israel: gazelle / wild boar
- Asian buffalo: draft power
  milk (Pakistan, Italy)
Surveillance: circulation of virus?

Profiling

- Individual level: SVD SR<>RP
  result profile different tests
titer VNT, MAC-ELISA, IgM ELISA, IgG ELISA

- Population level: FMD / BT
  frequency distribution of results
  reactivity categories

- <> dichotomised classification of positive and negative results
Serological Profiling

+ Cluster Analysis: time/space
+ SP tests: VNT/SPCE/LPBE
+ Titer / Ratio (T/C)
+ Purified Vaccines
+ Cluster Analysis: time/space
+ SP tests: VNT/SPCE/LPBE  +  Virus Isolation
+ Titer / Ratio (T/C)
Outbreak Profile

Time

Space

Bergmann et al., 2003
Freedom of infection

1) Endemic region
   Systematic vaccination
   Free with vaccination

2) Free region with outbreak
   Emergency vaccination
   Free without vaccination
Freedom of infection

Circulation of virus?

- Clinical surveillance
- Movement control
- Regional collaboration among countries
- etc, all in place
- Serosurveillance for subclinical circulation
- Profiling, SP-test, VI, Cluster analysis
Freedom of infection

Serosurveillance:

95 Confidence, 5% within herd (risk approach)
NSP test Sp 98%
Positive: follow-up to rule out indicator of +s

Some positives!

- Vaccine not well purified
- False positives
- Carriers
Vaccine not well purified

- OIE Code:
  Regaining FMD free status
  Recognising FMD free with vaccination
  Test vaccinated animals for NSP-Ab

- OIE Manual:
  Double dose of maximum amount Ag
  Calves vaccinated 3 X period of 3–6 m
  Tested 30–60 days after last vaccination
False Positives

Lab: Confirmation test (EITB)
Retest + Test-2 (non-covariant Sp)
Sp↑, Se ↓

Probang (Se 50%)
Profile: SP sero / Paired serology
Epidemiology (risk based), Cluster analysis
Future: IgA (saliva) / IgM serum
False Positives

Serosurveillance:
NSP test Sp 98%
Herd cut-point
= maximum number of positive seroreactors

Not fully compatible with OIE rules (?)
Carriers

Prevalence: 0.1-0.2% of herds
only 1 per herd (Arnold et al., 2008)

Serosurveillance:
95 Confidence, 2% herds, 5% within herd
Sp 98%, Se carriers 90%

Detecting all carriers = impossible
Principal that carriers are missed is more important than the actual number

Se↑: test all animals and only cull positive
Epidemiology (target), SP sero, IgA, IgM
Vaccine coverage

All schemes of serosurveillance should be seen as providing one element in the overall synthesis of evidence for freedom from infection (Martin et al. 2007).
If a highly effective vaccine is applied rapidly and comprehensively and (clinical) surveillance is thorough, then the extent of subclinical infection (carriers) is likely to be very low.
Vaccine coverage

Providing evidence that these requirements have been met and that vaccine coverage is guaranteed is therefore at least, if not more, important than post-outbreak serosurveillance. (Paton et al, 2006; Arnold et al, 2008)
Thank you!