CODA-CERVA-VAR
Centrum voor Onderzoek in Diergeneeskunde en Agrochemie

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

DIVA

NSP - Tests

fit for purpose for surveillance programmes:

- detecting circulation of virus
- prevalence survey
- outbreak management (especially recovery
- substantiating freedom of infection

DIVA

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

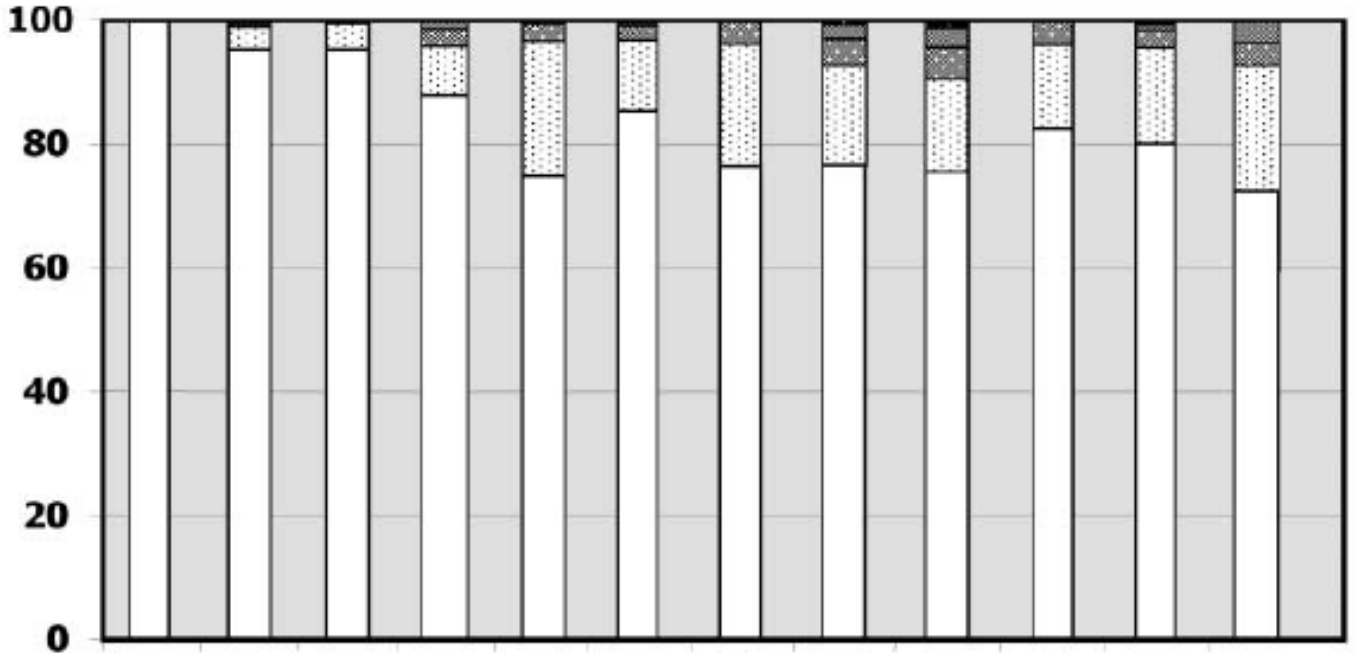
  milk (Pakistan, Italy)

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

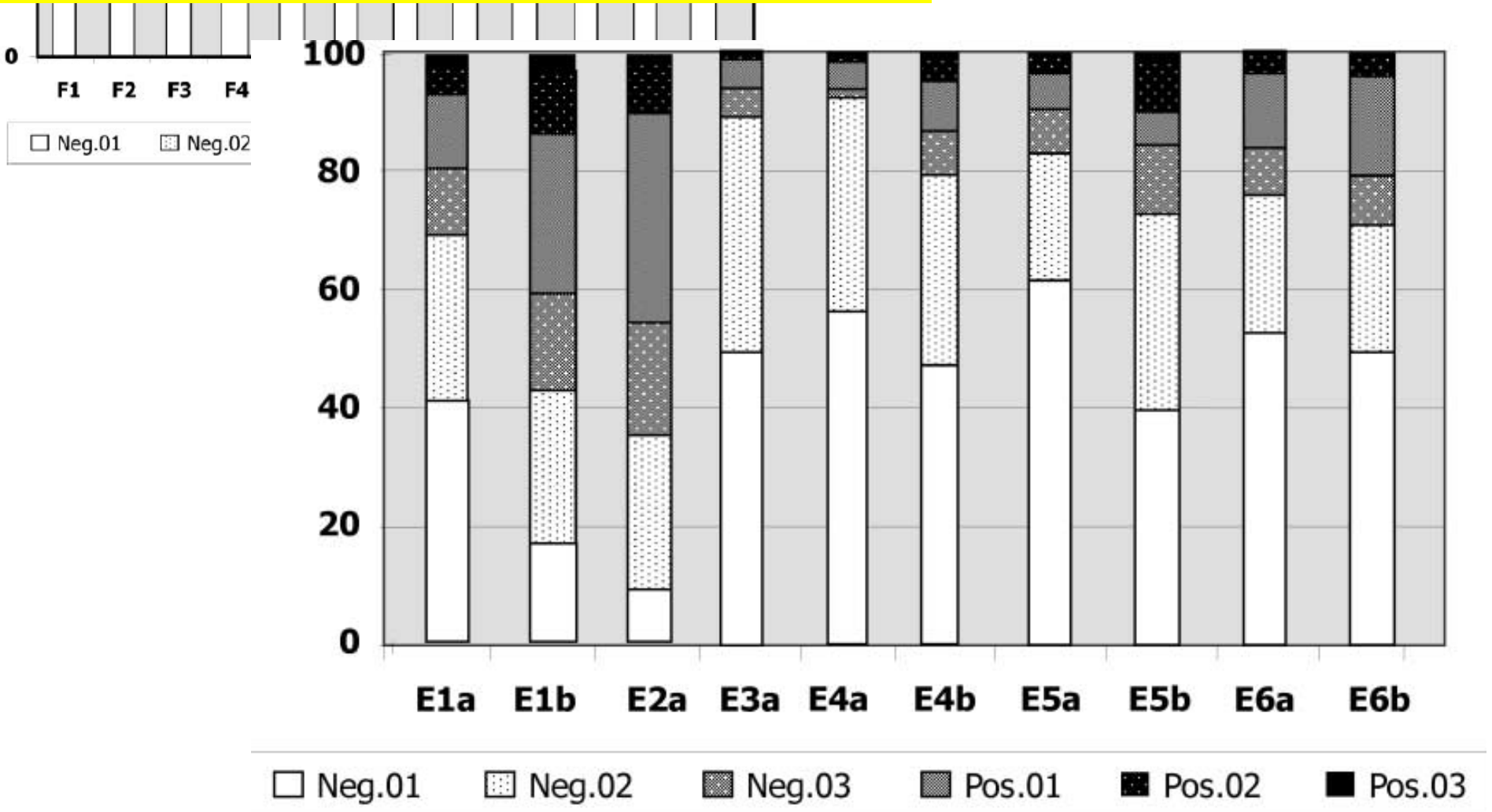
+ Cluster Analysis: time/space

+ SP tests: VNT/SPCE/LPBE

+ Titer / Ratio (T/C)

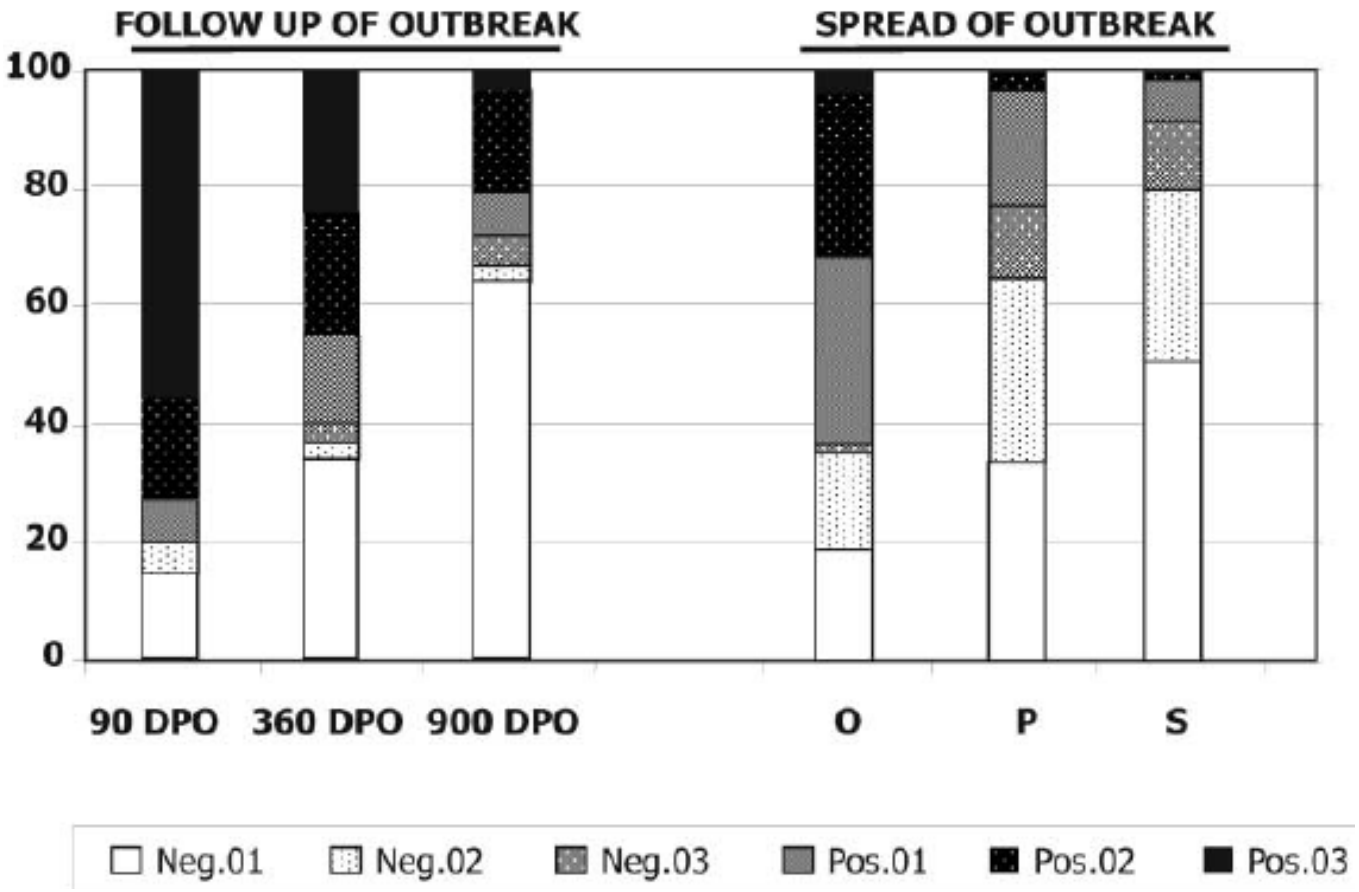
+ Virus Isolation

Probang



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

- Serosurveillence 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).

Vaccine coverage

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 postoutbreak serosurveillance. (Paton et al, 2006; Arnold et al, 2008)

Thank you !