Vaccination: overcoming the constraints to achieving effective immunity rates

A. Dekker
Vaccine does not work

- To many animals without sufficient immunity
  - No vaccination
  - Poor vaccine (quality control in session 2D)
  - Short duration of immunity
  - No vaccine response due to maternally derived Ab's
  - Poor vaccine match (session 2B)
- Insufficient data
No control with vaccine alone

- 1961 – 1967 outbreaks in non-vaccinated pigs due to introduction from neighbouring countries
- Control successful after European co-ordination of control

Number of FMD cases in the Netherlands

Start mass vaccination cattle
End vaccination campaign

Year
Number of cases


100000 10000 1000 100 10 1
In field studies often short lived Ab response

Fig. 2. The decay of antibody titre. Data from a trial of commercial FMDV vaccine in 30 cattle in Saudi Arabia.

Frenkel vaccine could induce long lasting immunity after repeated (3) vaccination


FIG 1: Persistence of neutralising antibodies against homologous FMD virus type A (●●●), type O (□□□□) and type C (○○○○) in 30 cattle after three consecutive annual vaccinations.
Good duration of immunity in experiments

Type O Cedivac vaccine DOI studies in 1991 and 2007
Comparison of titres found in field and experiments for vaccine release (Netherlands 2001)

• In the field 24% ≤ 1.05
• median titre ≈ 1.50 similar in both populations
• Agreement between both results

In the field only cattle was sampled
Experimental sera from pigs
What is the difference between various studies?

- **Vaccine quality**
  - Amount of antigen
  - Quality of the antigen (146S vs 12S)
  - Quality of the adjuvant

- **Dutch 2001 results** show experiments can be a predictor for the result in the field
Vaccine trial when buying vaccine

- Vaccinate at least 5 cattle
- Collect serum samples (sufficient amounts)
  - 0, 1, 2, 3, 4, 6 and 8 weeks after vaccination
- Repeat test at least at half the shelf life
- Use sera as standards when repeating tests
- Antibody concentration not always correlated with protection
Interference of maternally derived Ab's

Immune response in presence high Ab titre

Recent studies in calves (see poster)

A2 Iraq VNT titre

A Turkey 14/98 VNT titre

Weeks post-vaccination

Weeks post-vaccination
Recent studies in pigs (see poster Chenard et al.)

Mean VNT titre 1.73 in piglets after colostrum uptake

Piglets vaccinated at age of:
- 2 weeks
- 4 weeks
- 6 weeks
- 8 weeks
- not vaccinated
- 2 weeks no MDA

VNT titre 1.50 in adult pigs 4 weeks post-vaccination with a 6 PD50 vaccine
Conclusion

- In emergency vaccinate also young animals
- Study best time for vaccination in young animals every time vaccine is changed
  - Higher Ab's in dams might prevent response if offspring
  - Better adjuvant might induce Ab response earlier
- Insufficient data from field studies with good quality vaccine (with quantified quality)
Epidemiological needs for vaccine

- 1972 OIE sets standard of 70% protection
  - If $R_0$ is 3.3 then with 30% susceptibles $R_v \approx 1$
    - Fraction to be removed $1 - 1/R_0$
  - Within herd $R_0$ is higher (6 in cattle 40 in pigs)
  - Between herd transmission in UK $R_0=3.6$ (Ferrari, M. J., Bjørnstad, O. N. & Dobson, A. P., 2005, Estimation and inference of R0 of an infectious pathogen by a removal method, Mathematical Biosciences 198(1):14-26.)

- Current vaccines (3 PD$_{50}$/dose, 70% protection) work only with concurrent movement control
Experimental "within pen" transmission studies in the Netherlands

- **Pigs**
  - O Taiwan vaccination – O Taiwan challenge
  - O Manisa vaccination – O Taiwan challenge
  - O Manisa vaccination – O Netherlands 2001 challenge

- **Calves**
  - O Manisa vaccination – O Netherlands 2001 challenge

- **Dairy cattle**
  - O Manisa vaccination – O Netherlands 2001 challenge

- **Sheep**
  - O Manisa vaccination – O Netherlands 2001 challenge
  - Asia- Shamir vaccination – Asia-1 Turkey challenge
Experimental design

- Non-vaccinated and vaccinated groups
- Half the animals *infected* other half *exposed* by contact
- Calculate
  - Average number of new infections per infectious individual (R)
  - Average number of new infections per day
  - Infectious period
Pig experiments with O Taiwan challenge

- Vaccination O Manisa or O Taiwan 14 days before infection
  - No infection of inoculated pigs (intradermal in the bulb of the hoof)
  - $R_v$ cannot be estimated (no infectious pigs)
- Vaccination O Taiwan 7 days before infection

<table>
<thead>
<tr>
<th></th>
<th>$\beta$</th>
<th>$T$</th>
<th>$R_v$</th>
</tr>
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<tbody>
<tr>
<td>No vaccine</td>
<td>6.1</td>
<td>6.5</td>
<td>40</td>
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<tr>
<td>Single dose</td>
<td>2.0</td>
<td>5.3</td>
<td>11</td>
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<td>4-fold dose</td>
<td>0.4</td>
<td>2.3</td>
<td>1</td>
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$\beta$ = number of new infections per infectious individual per day
Pig experiments with O Netherlands challenge

- Vaccination O Manisa 14 days before infection
  - Infection by direct contact to non-vaccinated inoculated pigs

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<th>$R_v$</th>
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<tbody>
<tr>
<td>No vaccine</td>
<td>6.8</td>
<td>6.6</td>
<td>44</td>
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<tr>
<td>Single dose</td>
<td>0.7</td>
<td>4.7</td>
<td>3.3</td>
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$\beta = \text{number of new infections per infectious individual per day}$
Reproduction ratio $R$ in calves, dairy cattle and sheep (O manisa vaccine and O NET challenge)

<table>
<thead>
<tr>
<th>Category</th>
<th>Non-vaccinated</th>
<th>Vaccinated 2 weeks before challenge</th>
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<tbody>
<tr>
<td>Calves</td>
<td>2.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Dairy cattle</td>
<td>∞</td>
<td>0</td>
</tr>
<tr>
<td>Sheep</td>
<td>1.14</td>
<td>0.2</td>
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Conclusion

- Emergency vaccination with potent vaccines is a very good tool to control FMD outbreaks
- Vaccination significantly reduces "within pen" transmission
  - Most data obtained 2 weeks after vaccination
  - $R<1 \Rightarrow$ only small outbreaks
- Good quality vaccines should be sufficient for eradication in endemic areas
- Based on published data from field trials there is still much room for improvement