Relation between antibody response and protection in FMD vaccine depends on vaccination-challenge interval, route of injection and vaccine quality

Aldo Dekker
Outline

- Correlation between antibody response and protection
  - Purpose
  - History of research
- Current study
  - 447 cattle sera
  - Forward logistic regression analysis
  - Relation between antibody response and protection in FMD vaccine depends on antigen and vaccine dose
- Best vaccine is the vaccine that induces the highest antibody response
Correlation between antibody response and protection

- Use for vaccine release
  - Producers develop own criteria
  - Standard interval vaccination and measuring antibody response

- Use for post vaccination monitoring
  - Variation between producers
  - Different intervals vaccination and sampling
Historical analysis Ab response protection

- Loeffler and Frosch, 1897
  - Passive antibodies can protect against infection
- Van Bekkum et al. 1969
  - 566 cattle
  - 2 weeks post vaccination type C (n=424)
  - 9-49 months post vaccination 3 serotypes (n=142)
- Pay and Hingley, 1987
  - 360 vaccinated and challenged cattle
  - 3 weeks post vaccination
  - 3 serotypes
- Eblé et al. 2009
  - Intradermal vaccination better protection at lower Ab dose
Historical analysis Ab response protection

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Results van Bekkum et al. 1969

Relation Ab response protection
Type C FMD

- Relation between Ab and protection
  - Protection 2 weeks after vaccination at a lower Ab titre compared to 9 – 49 months after vaccination
- Cattle sampled at 9 – 49 months after last vaccination had been vaccinated 2 – 10 times

2 weeks post vaccination
9 to 49 months post vaccination
Results van Bekkum et al. 1969

Frequency distribution Ab titres

- Titres 2 weeks higher then 9 to 49 months post-vaccination

2 weeks post vaccination
9 to 49 months post vaccination
Intradermal versus intramuscular vaccination

- Pigs
- Difference in relation between Ab titre and protection against virus shedding (mouth swabs)
- Intradermal vaccination (in red) better protection at lower Ab dose
Shelf life: Indication for degradation of 146S

Goris et al. 2008 (Vaccine 26: 3432-3437)
Clear decrease in vaccine efficiency in 10 months
Experimental vaccine
No data available from commercial producers
**Little decrease in Ab titre**

<table>
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<tr>
<th>Trial</th>
<th>Protection</th>
<th>LPB ELISA</th>
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<tbody>
<tr>
<td></td>
<td>%</td>
<td>mean titre</td>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
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<tr>
<td>6</td>
<td>75</td>
<td>2.49</td>
</tr>
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</table>

Confidence in indirect assessment of foot-and-mouth disease vaccine potency and vaccine matching carried out by liquid phase ELISA and virus neutralization tests.

Robiolo, B., La Torre, J., Maradei, E., Perez Beascochea, C., Perez, A., Seki, C., Smitsaart, E., Fondevila, N., Palma, E., Goris, N., De Clercq, K., Mattion, N.
Lelystad vaccine registration dossier

- 447 cattle used in challenge experiments
- 240 cattle used in potency tests (3 times 5 cattle vaccinated with 1, ¼ and 1/16th dose, challenged 4 weeks after vaccination
- 9 different strains
  - A Iran 87, A TUR/14/98, A_{10}Holland, A_{22}Iraq, A_{24}Cruziero, Asia-1 Shamir, O Algeria, O_{1}BFS, O_{1}Manisa
- VNT titre obtained using primary porcine kidney cells
- Forward logistic regression analysis
  - Titre, log(dose), µg Ag, µg Ag in full dose, strain
Forward logistic regression analysis

- Protection as result variable
- Various explanatory variables
  - Titre, \( \log(\text{dose}) \), \( \mu g \text{ Ag} \), \( \mu g \text{ Ag in full dose} \), strain
- Selection based on AIC

Univariate analysis

- Antibody titre best predictor of protection
- Logarithm of the dose second best predictor
- Higher dose induces a higher antibody response
Forward logistic regression analysis

- Multivariate model

\[
\text{Logit(protect)} \sim \text{Antibody titre + strain + } \mu g \text{ per full dose + log(dose) + strain:titre}
\]

- For each \( \mu g \) of extra antigen in the vaccine the antibody titre that protected 50\% of the cattle was reduced 0.04 \( (10^{\log}) \)

- Cattle vaccinated with a 4 fold higher dose need a 0.08 \( (10^{\log}) \) less antibody titre for 50\% protection

- When analysing 240 results from potency tests interaction is absent and each batch has a different result
O Manisa antibody titre response curve

Red full dose
Blue 1/4 dose
Green 1/16 dose
Conclusion

- Complete replacement of standard potency tests is not possible
  - Each vaccine producers should establish their own criteria based on protection experiments and use serology for batch release

- Monitoring antibody response is a good method for post vaccination monitoring
  - Higher antibody titre correlate with higher level of protection

- Better vaccine induces higher antibody titres and protects already at a lower antibody titre