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

Aldo Dekker

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

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

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

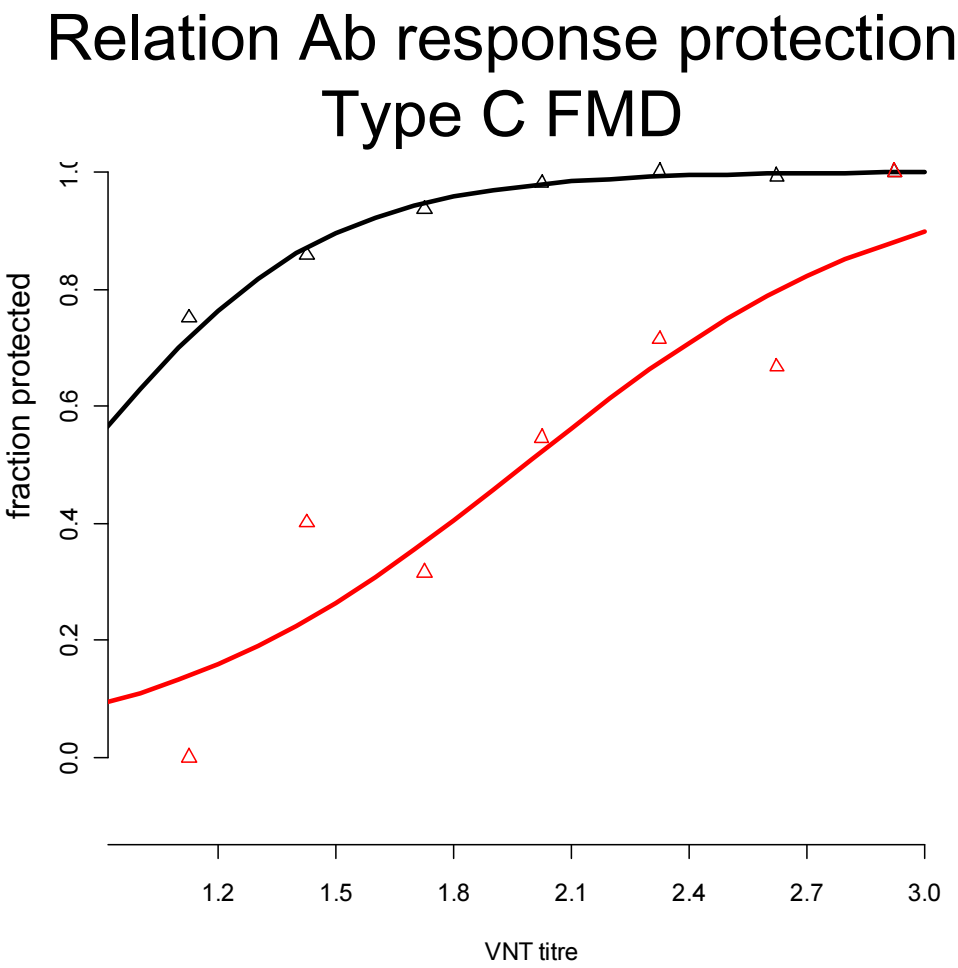
Historical analysis Ab response protection

- 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

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

Results van Bekkum et al. 1969



- 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

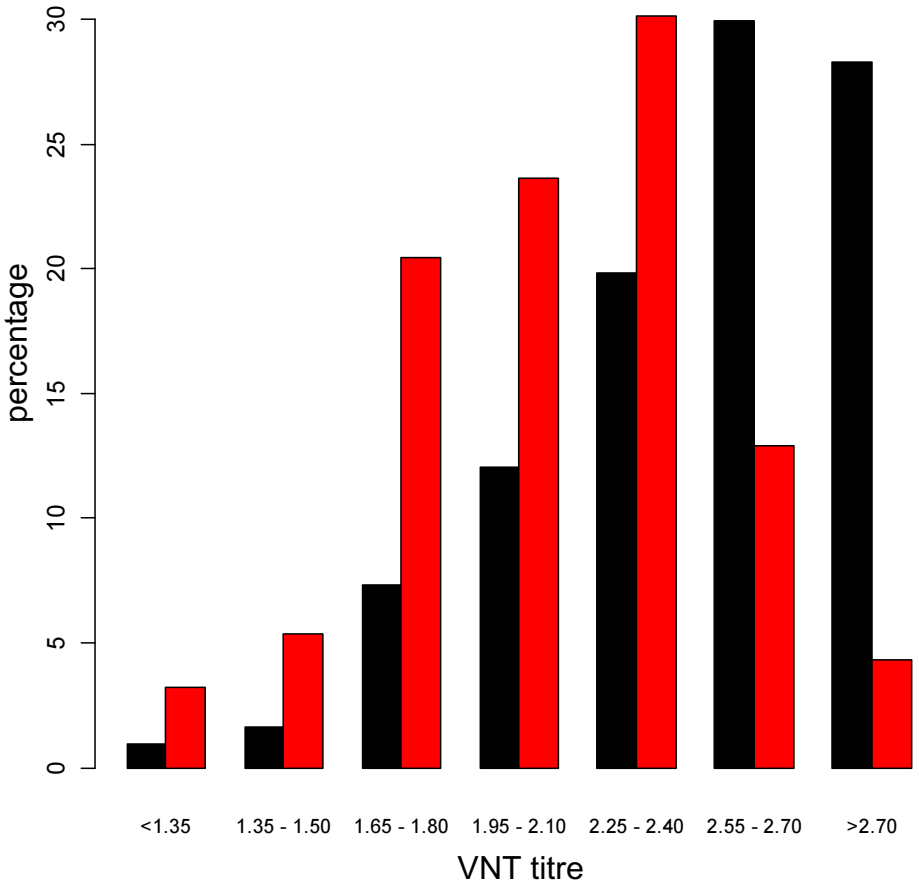
2 weeks post vaccination

9 to 49 months post vaccination

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

Results van Bekkum et al. 1969



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

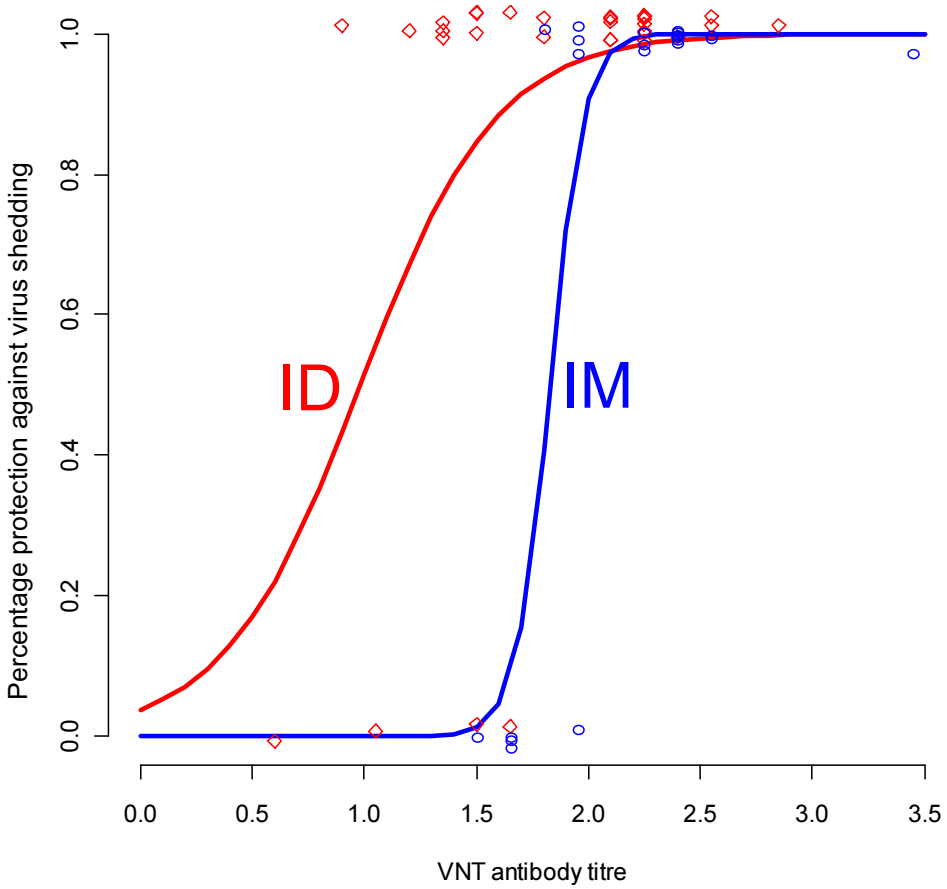
2 weeks post vaccination

9 to 49 months post vaccination

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

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

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

Shelf life: Indication for degradation of 146S

Summary of six identical, replicate FMDV A_{24} Cruzeiro vaccine potency tests using homologous FMDV A_{24} Cruzeiro challenge

Trial	Date of vaccination	Date of challenge	Vaccinated animals		PPG (%) [95% confidence interval]
			Protected	Total	
1	18 January 2006	17 February 2006	16	16	100.0 [80.6–100.0]
2	18 January 2006	17 February 2006	15	16	93.8 [71.8–98.6]
3	10 October 2006	9 November 2006	15	16	93.8 [71.1–98.5]
4	10 October 2006	9 November 2006	13	16	81.3 [56.2–93.0]
5	7 November 2006	7 December 2006	14	16	87.5 [64.2–96.3]
6	7 November 2006	7 December 2006	12	16	75.0 [50.2–89.4]

- 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

Trial	Protection	LPB ELISA	
	%	mean titre	Expected protection
1	100	2.50	89.9
2	93.8	2.66	91
3	93.8	2.15	80.4
4	81.3	2.21	83
5	87.5	2.38	87.3
6	75	2.49	88.9

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 Beascoechea, 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_1BFS, O_1Manisa
- 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(dose), µg Ag, µg 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

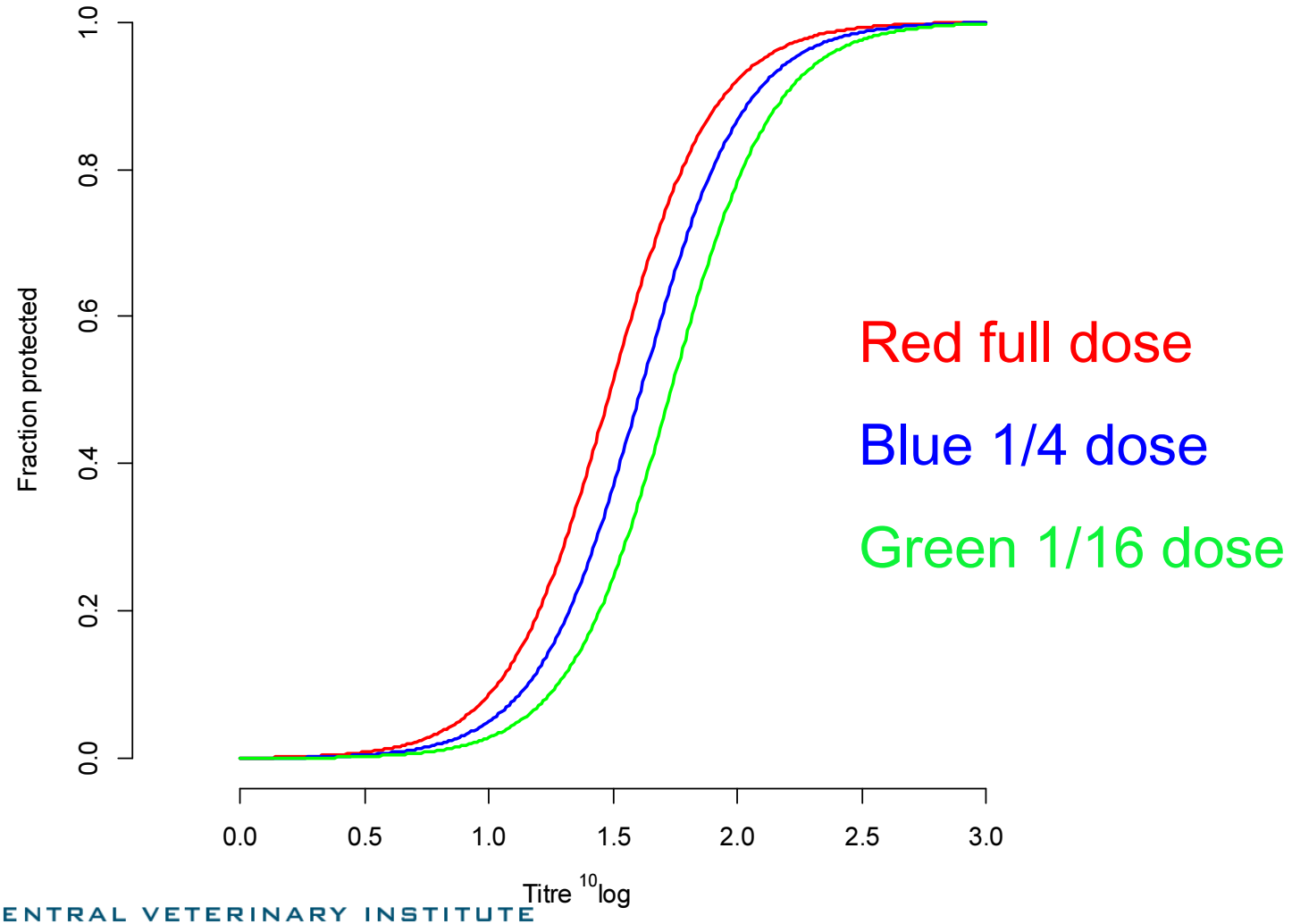
Forward logistic regression analysis

- Multivariate model

Logit(protection) ~ Antibody titre + strain + µg per full dose + log(dose) + strain:titre

- For each µg 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



CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

GFRA
Global Foot-and-Mouth Disease Research Alliance

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