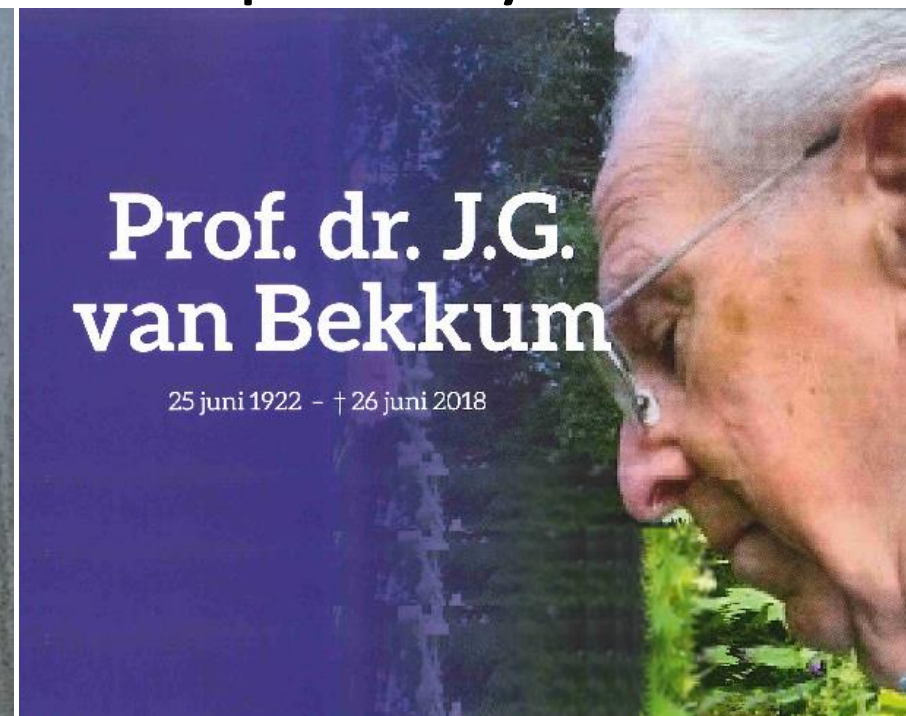




H.S. Frenkel and J.G van Bekkum how they improved vaccine availability and quality





FMDV was a huge challenge



- Before 1950 only Waldman vaccine
- Huge number of cattle needed production
- No containment



Herman Salomon Frenkel (1891 – 1968)

- 1930 appointed director of the state veterinary institute
- Task: "Find the cause and develop methods to control FMD"
- During WWII interned in Theresienstadt



Research on virus culture

- 1930 UK and Germany virus culture in surviving foetal guinea pig skin tissue
- 1935 Frenkel and v. Waveren virus culture in surviving foetal bovine, porcine and ovine skin tissue
- Better supply and no adaptation

1949 Bovine tongue and rumen

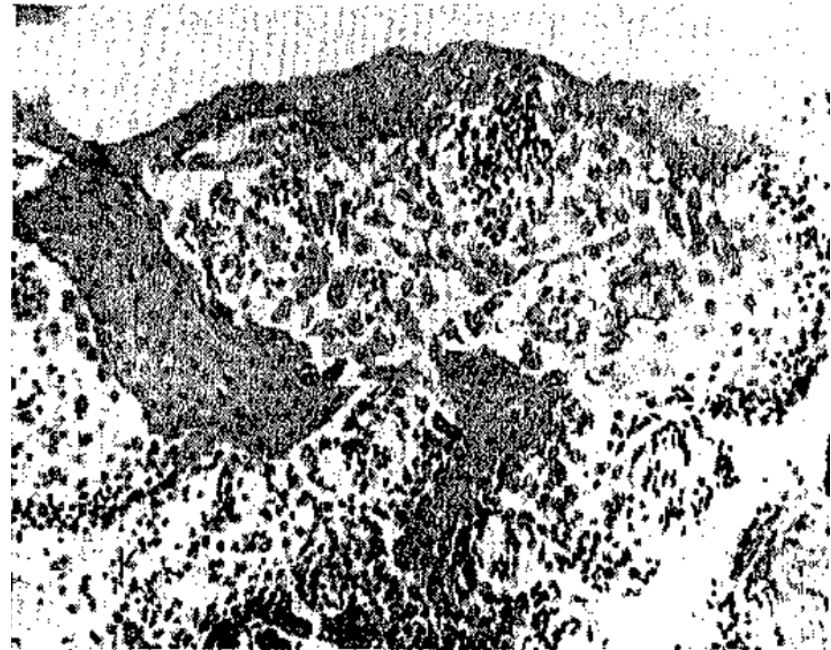
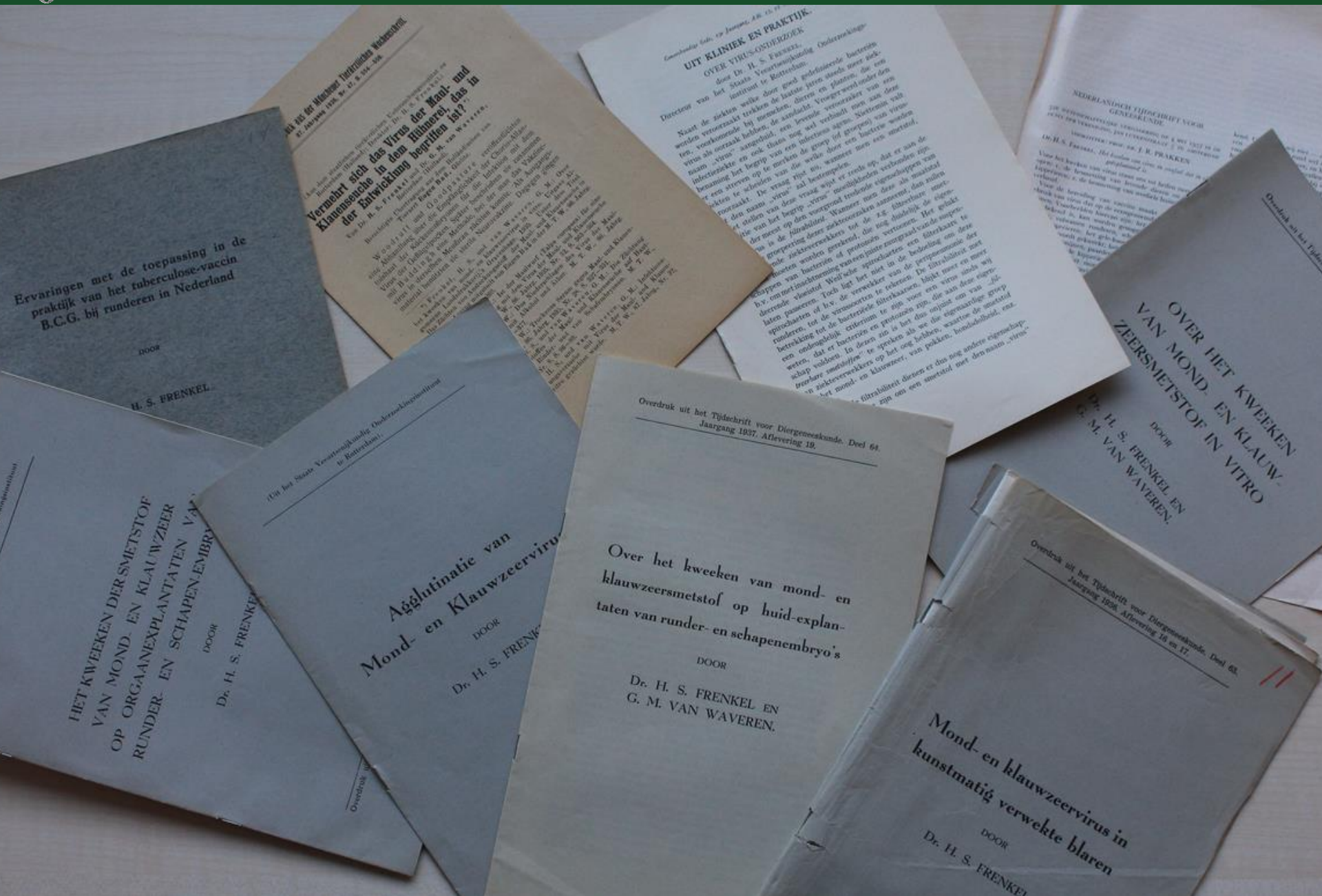


Fig. 2—Vesicle formation in infected explantations of the mucous membrane of the bovine tongue. Parts of the normal skin are still visible. The isolated epithelial cells of the stratum spinosum still adhere by a fine protoplasmic network.

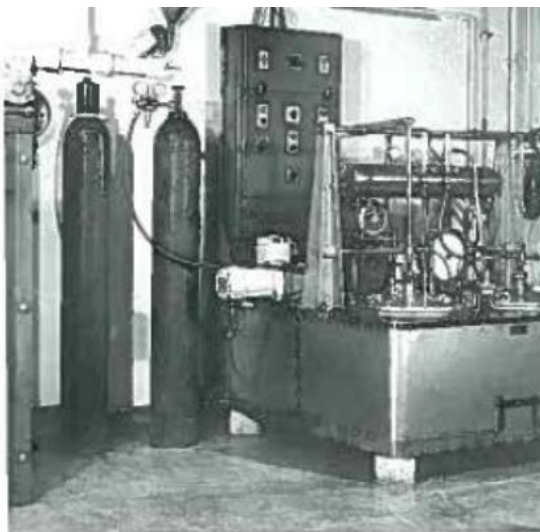


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Machinery in the 50-ties



- Brushing tongues
- Harvesting epithelium
- Virus culture in "open" incubators with oxygen and CO₂ and antibiotics
- Storage of formulated vaccine

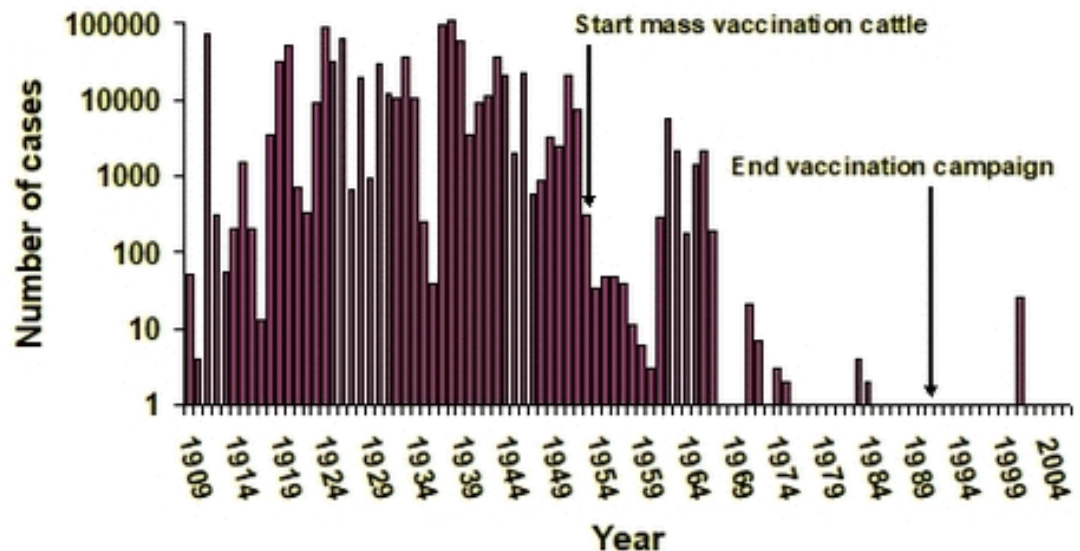




In-vitro culture enabled control

- NL first country with nation-wide prophylactic and emergency vaccination
- Followed by other European countries

Number of FMD cases in the Netherlands





Jaap van Bakkum 1922 - 2018

- DVM 1951
- 1956 Deputy director "SVOI"
- 1959 Member of the RG of the STC
- 1960 Director "SVOI"
- 1972 Professor virology
- 1982 Research director "CVI"
- 1986 Retirement, also as chairman of STC



Research on FMDV 2 main topics

Antibody response and protection

- Thesis 1959 "Neutraliserende antistoffen in sera van tegen mond- en klauwzeer geënte runderen"

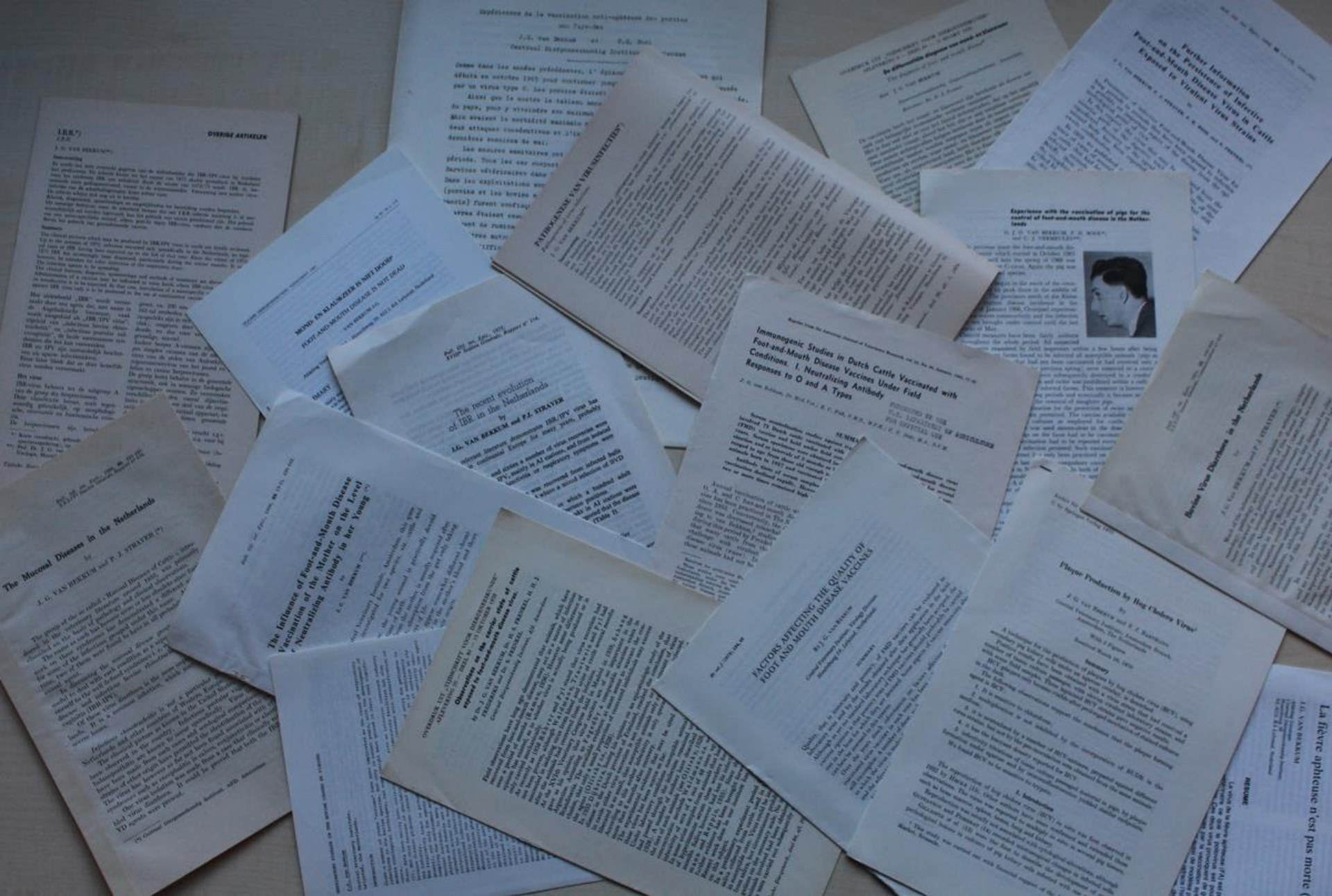
FMD persistent infection (Carriers)

- "Observation on the carrier state of cattle exposed to FMDV." Tijdschrift Voor Diergeneeskunde 84: 1159-1164.



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Quantification of Ab response

Kinetisch wordt de verdwijning van de actieve virusdeeltjes gegeven door de formule

$$V_t / V_o = [Q_t / Q_o]^n, \quad (6)$$

waarin $Q_o = V_o \cdot n$; V_o = de concentratie van virusdeeltjes in de buis welke het serum-virusmengsel bevat, ten tijde $t=0$ en Q_t = concentratie niet-bezette receptoren op tijd t . Voor het quotient Q_t / Q_o en voor verschillende daarmee samenhangende grootheden kunnen formules worden afgeleid,

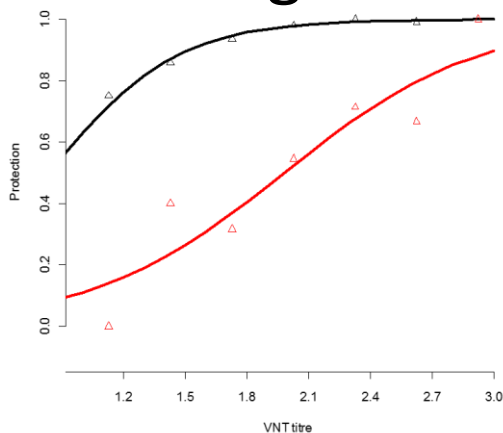
- Mathematics
- Probit analysis
- Previously implemented by Brooksby
- Good titre for 1 year

Nummer van het rund	Aantal dagen verlopen sedert laatste enting	Serumtiter tegen type		
		O	A	C
Jan. 4	334	2,9	4,2	2,3
Jan. 6	288	4,5	4,3	niet ingezet not done
Jan. 8	285	3,5	2,7	3,1
Jan. 9	285	4,2	3,4	3,5
Jan. 17	301	4,0	3,8	3,3
Jan. 23	287	4,8	3,5	4,3
Jan. 24	302	3,9	4,3	niet ingezet not done
Jan. 25	278	3,5	2,5	2,0
Jan. 26	324	4,5	3,4	niet ingezet not done
Jan. 37	314	4,3	3,7	niet ingezet not done
Jan. 242	315	4,7	4,3	niet ingezet not done
Jan. 252	293	3,0	niet ingezet — not done	3,2
Number of the animal	Number of days elapsed since last vaccination	O	A	C
Serum titer against type				

TABLE 49. Serum titers against different virus types in Dutch cattle immunized with trivalent vaccines under field conditions

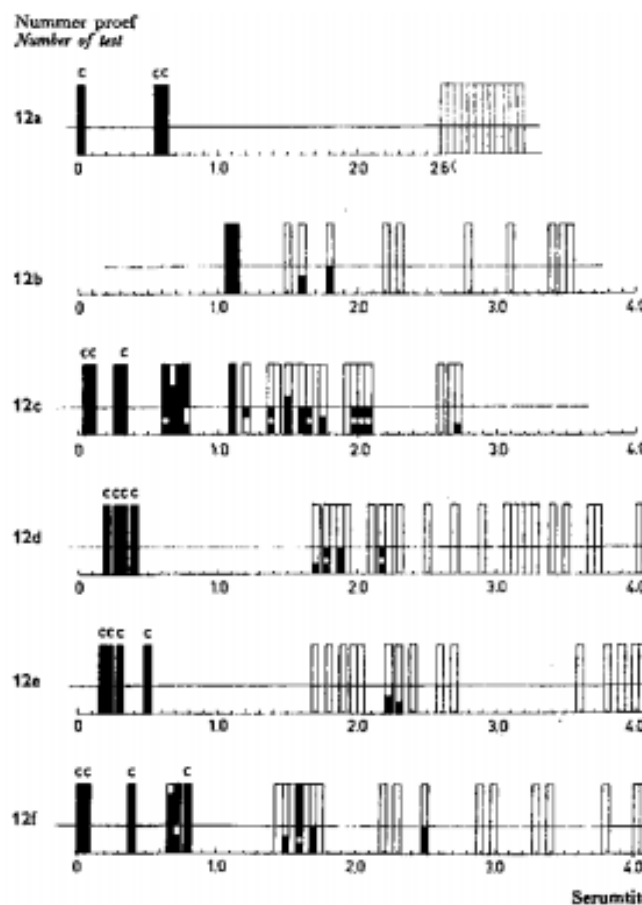
Relation Ab response and protection

- High antibody titres are correlated with protection
- Relation depends on interval vaccination challenge



2 weeks post vaccination

9 to 49 months post vaccination



Elk zuiltje stelt een proefrund voor. De uitbreiding van de mond- en klauwzeerafwijkingen is aangegeven door voor elk aangetast weefsel of lichaamsdeel een blokje zwart te maken. Hiervoor is het volgende schema gebruikt:

7	1	Bepaalde afwijking op de tong.
6	2	Uitgebreide tonglaesie.
5	3	Defecten aan verhemelte, lippen en/of pens.
4	4	Afwijkingen aan extremiteten.
3	5	
2	6	
1	7	

c = ongeënt rund.

One column is used for each animal. The degree of involvement is recorded by blackening squares for the affected tissues according to the following arrangement.

1	Local lesion on the tongue.
2	Extensive tongue lesions.
3	Vesicles formed on palate, lips, dental pad and/or rumen.
4	Foot lesions.
5	
6	
7	

c = Non-vaccinated control.

FIG. 30. Resistance against challenge by swabbing the mouth with a towel drenched in a virus suspension, in cattle with different levels of neutralizing antibody



Current challenges FMD vaccine

- Cheap production
 - Simple production systems (like surviving tongue epithelium)
 - High yields of antigen
 - Stable antigen or alternatives for stabilisation
- Good quality control
 - Vaccine
 - 146 S content
 - Potency tests by serology (like van Bakkum developed)
 - Vaccination campaign
 - Check immune response in the field (like van Bakkum did)