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 direct of the state veterinary institute
• Task: "Find the cause and develop methods to control FMD"
• During WOII 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
- 1949: Bovine tongue and rumen

Better supply and no adaptation
Machinery in the 50-ties

- Brushing tongues
- Harvesting epithelium
- Virus culture in "open" incubators with oxygen and CO$_2$ 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
Jaap van Bekkum 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 geëente runderen"

FMD persistent infection (Carriers)

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

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

\[ V_t / V_o = [Q_t / Q_o]^n, \]

where \( Q_o = V_o \cdot n \); \( V_o \) is the concentration of virus particles in the body, which is the serum-virus concentration at time \( t = 0 \) and \( Q_t \) is the concentration of antigen receptors at time \( t \). For the quotient \( Q_t / Q_o \) and for different daarmee samenhangende grootheden kunnen formules worden afgeleid.

<table>
<thead>
<tr>
<th>Nummer van het rund</th>
<th>Aantal dagen verlopen sinds laatste eetling</th>
<th>Serumliter tegen type</th>
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<td>334</td>
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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
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 Bekkum developed)
  - Vaccination campaign
    - Check immune response in the field (like van Bekkum did)