Vaccination in production animals

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Focus on livestock

- AIM of vaccination: Reduce susceptibility
- Many diseases are eradicated
- Many vaccines are forbidden (as they will destroy the surveillance)
- Emergency vaccination is an alternative to eradication
- Vaccination success is measured on the herd level

Different vaccine approaches

Prophylactic vaccination

Standard for humans and companion animals

For livestock: Endemic diseases

Emergency vaccinations (in connection to outbreaks)

Exotic diseases

Vaccinate to kill?!

Post-exposure treatment (vaccination *and* passive antibodies)

Rabies, tuberculosis

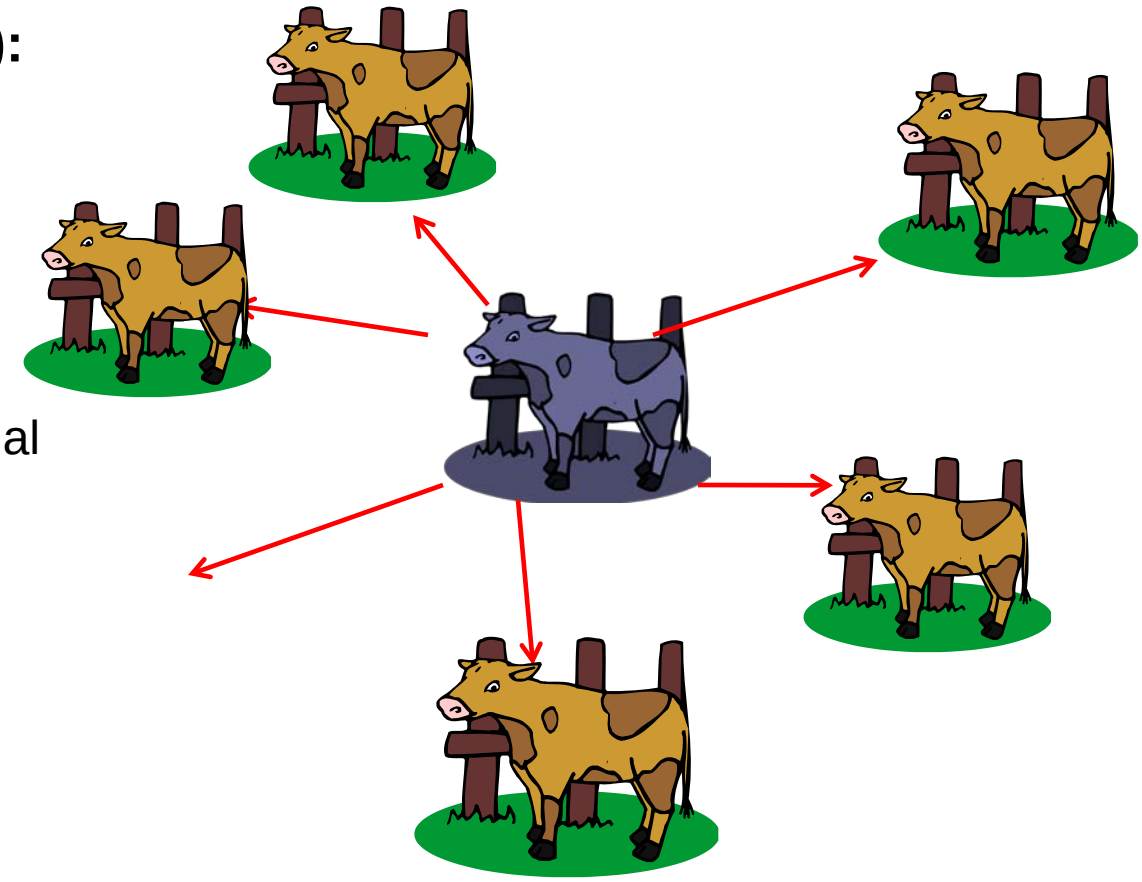
How to measure vaccine efficacy

R(0) index (basic reproduction index):

One sick animal emitting virus:

If a sick animal generates less than one sick animal the disease dies out.

If a sick animal generates more than one new an epidemic is started.

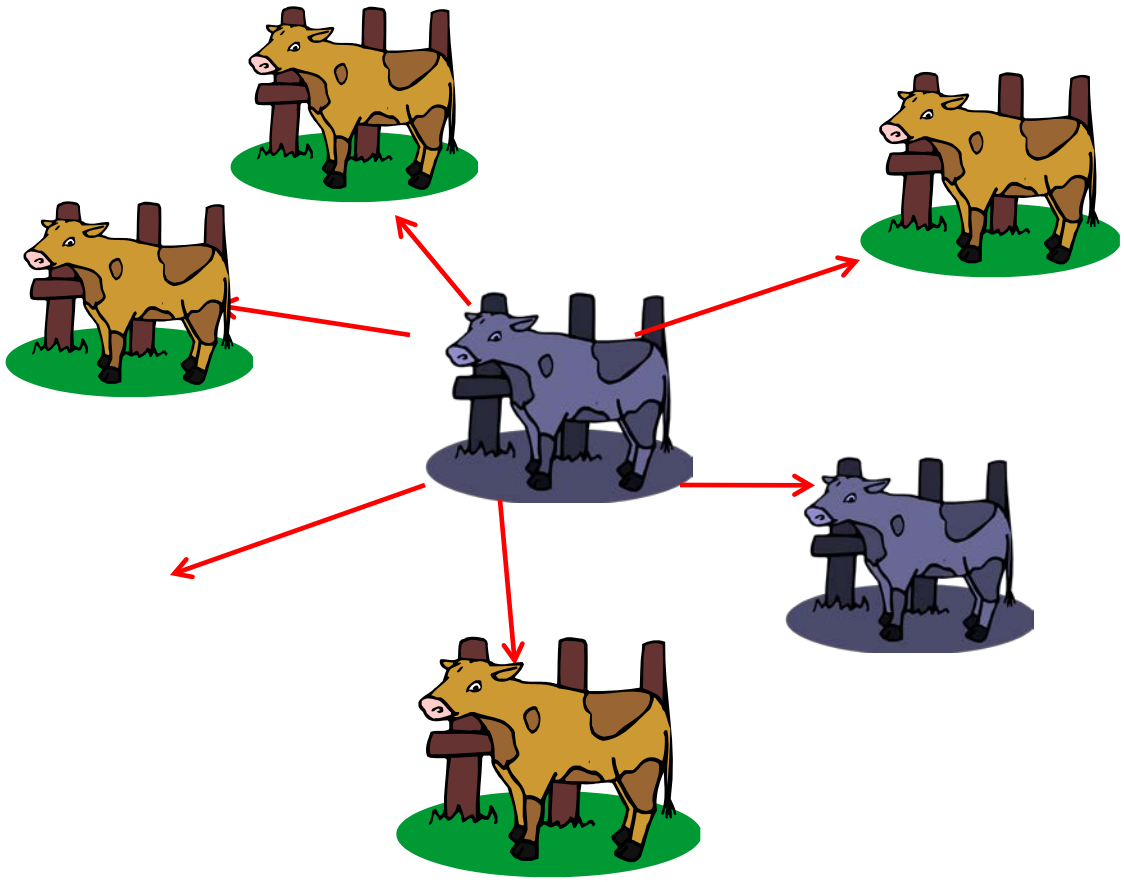


R(O) is 1 when

R(0) index (basic reproduction index):

One sick individual emitting virus result in only one sick animal.

R(0) = 1 the disease is maintained

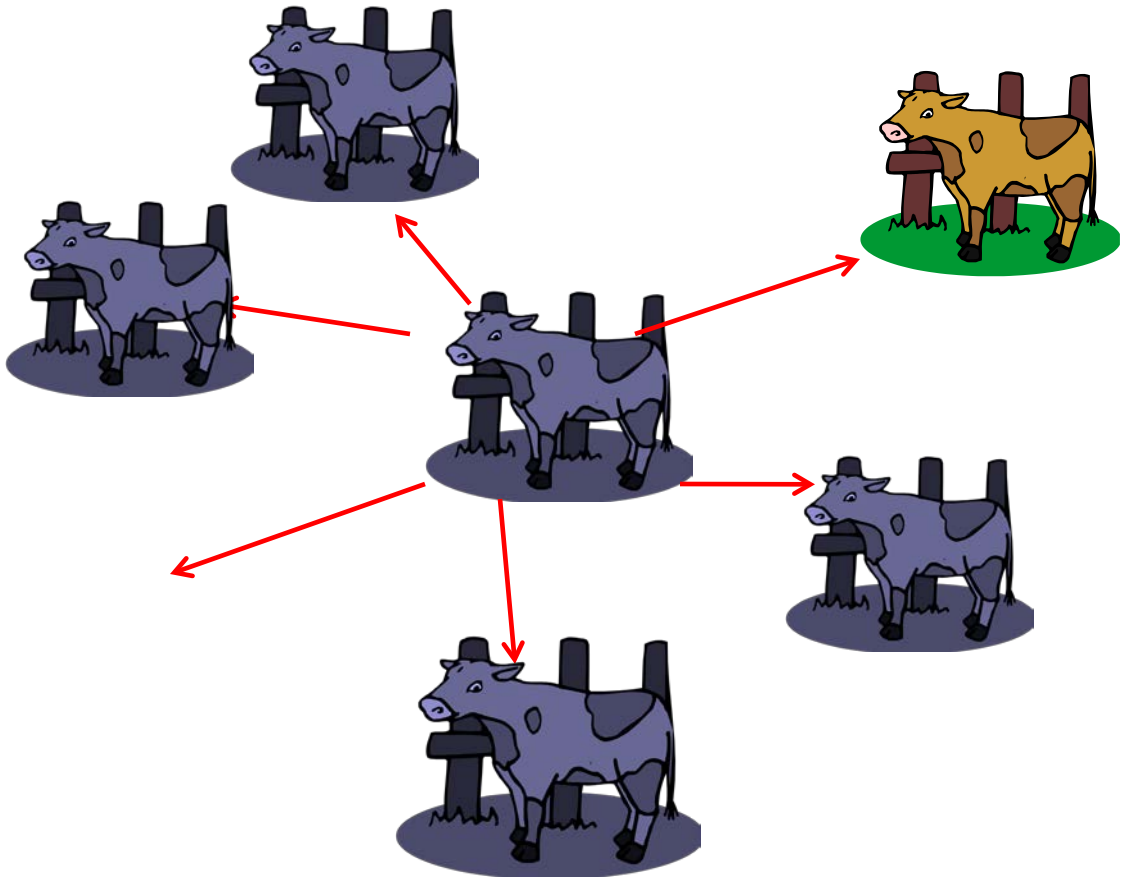


If R(0) > 1 disease is spreading

R(0) index (basic reproduction index):

One sick individual emitting virus result in several sick animals.

Knowing the R(0) for a disease is important (why vaccinate for a disease that does not spread)



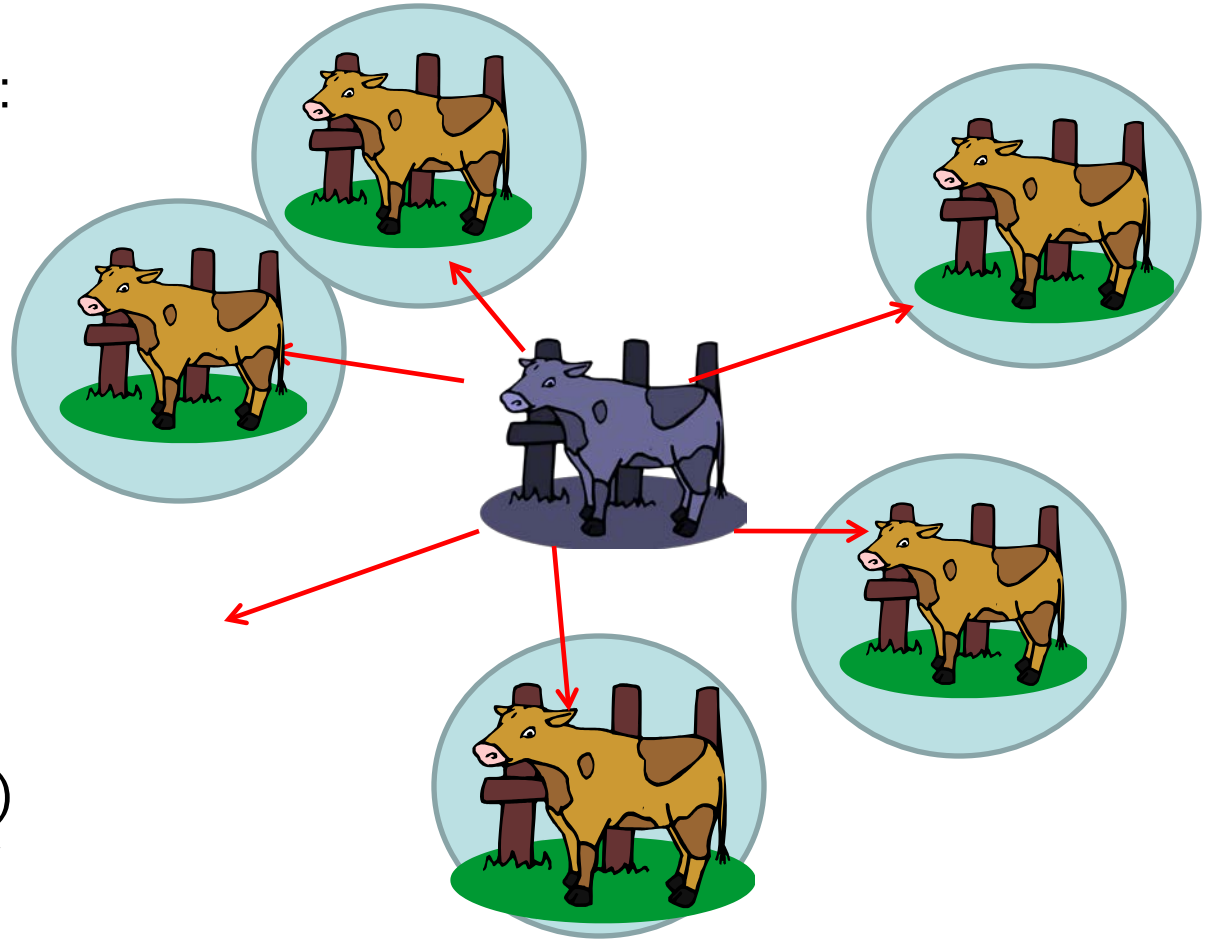
Vaccination must reduce R(O)

R(0) index (basic reproduction index):

One sick animal emitting virus result in less than only one sick animal.

RESULT:

The virus needs susceptible individuals and R(0) decreases to below 1.. Hurray!



Vaccination will reduce

- The number of susceptible animals thereby reducing R(0)

- This could be measured by:
  - Mortality (number of dying individuals)
  - Morbidity (number of sick individuals)
  - Presence of virus in animals (or antibody correlate)

- Sterilizing immunity is optimal but rare

To end a vaccination campaign

Stop vaccination!

Measure status by

- introduction of non-vaccinated sentinel animals (to be followed closely)
- Test young stock
- Remove vaccinated animals test the other

DIVA diagnostics if DIVA vaccinated

- Genetic DIVA or discriminating antibody test

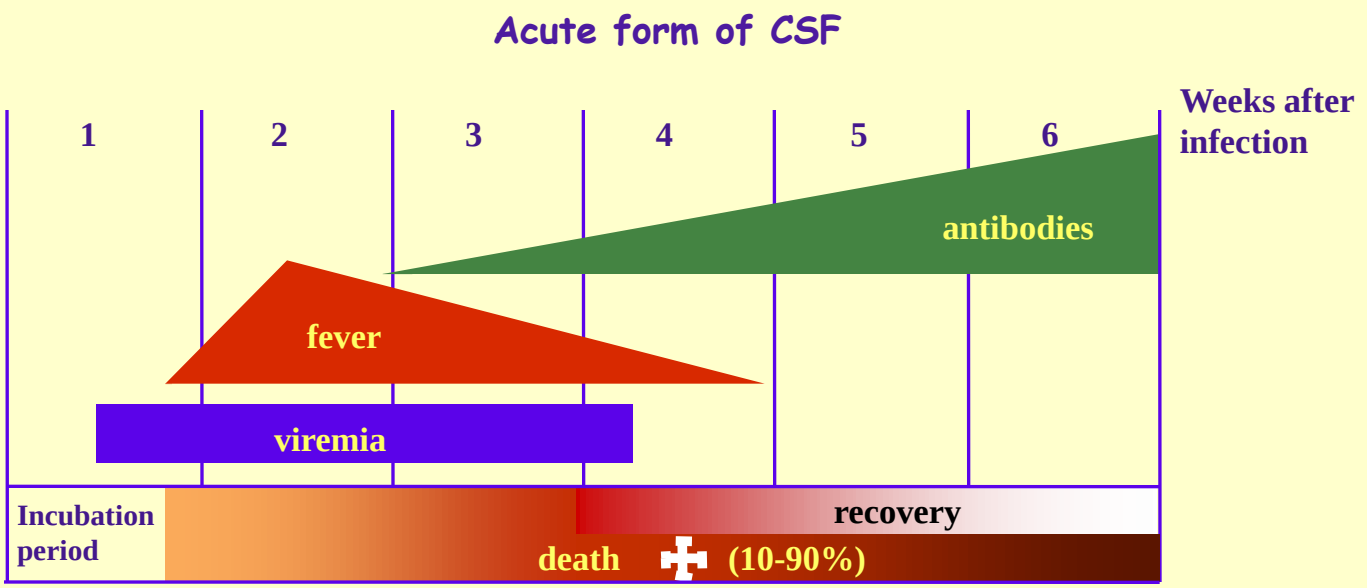
Surveillance & Vaccination

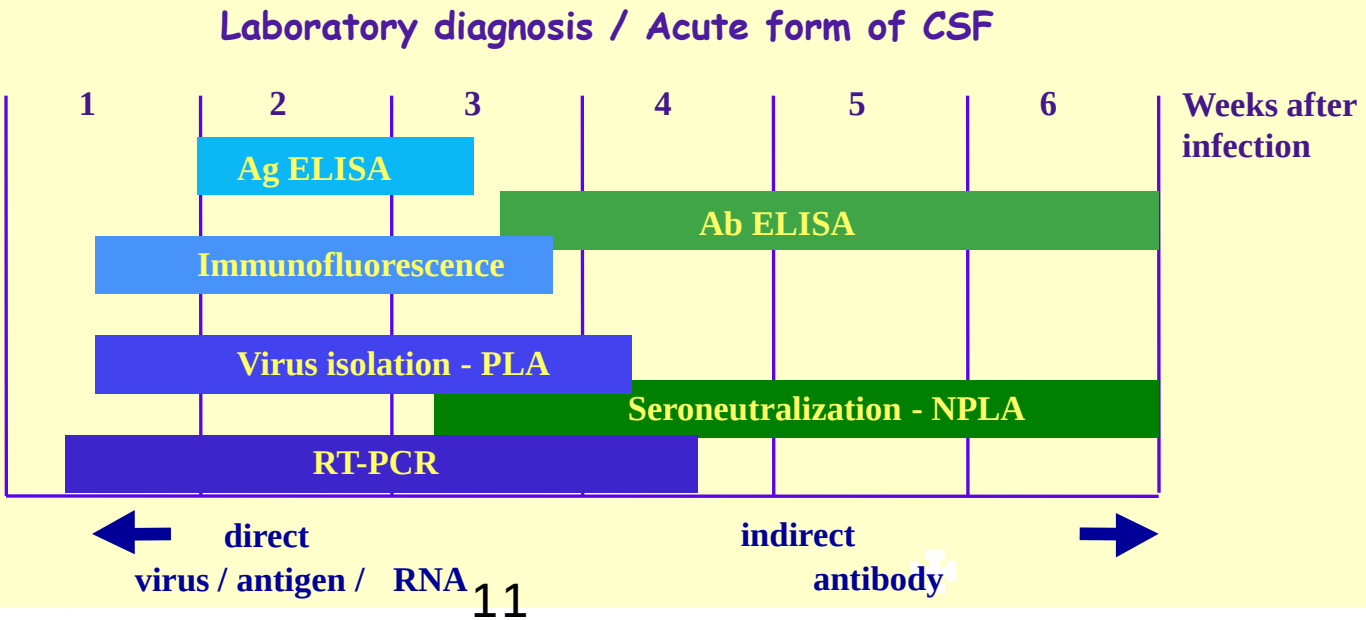
With imperfect vaccines we have to monitor the disease

- Serological surveillance
- Virological surveillance
- Import surveillance (animal products)
- Clinical surveillance
- Pen side tests in different formats

Laboratory diagnosis of CSF

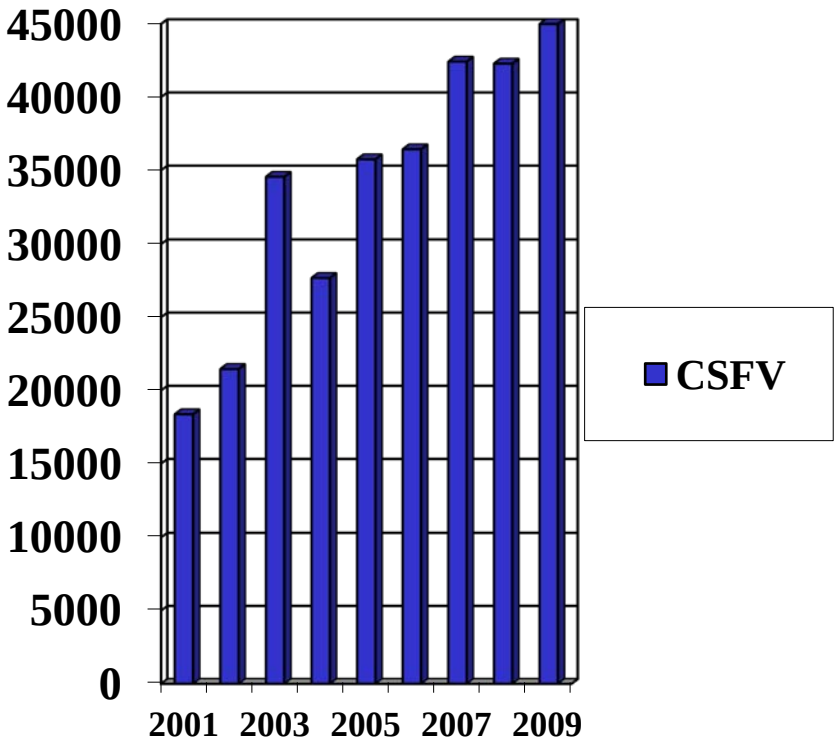
(Meindl-Boehmer, 2004)





Serosurveillance

- In Denmark our CSFV free status is verified by serological surveillance
- 20-45.000 blood samples are analysed every year for CSFV
- Prophylactic vaccination would cause antibodies



So what happens after CSF?

- Immediate stand-still; pig transport banned
- All live and killed export would be stopped
- All pigs herds would be visited by a vet; samples would be analysed
- Pig herds with infected pigs would be slaughtered
- DK would be divided into ”infected” and ”clean” areas
- Lots of work; lots of losses

DIVA vaccines, marker vaccines

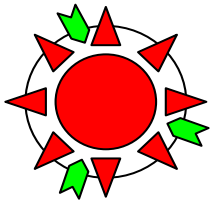
Differentiating **I**nfected from **V**accinated **A**nimals

Diagnosing **I**nfection in **V**accinated **A**nimals

Vaccinated?	**Infected?**	TEST RESULTS	
		ANTIBODY	MARKER ELISA
Not vaccinated	Not infected	-	-
	Infected	+	+
DIVA vaccinated	Not infected	+	-
	Infected	+	+

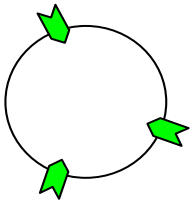
A: CSF marker vaccine

B: Pig antibody response

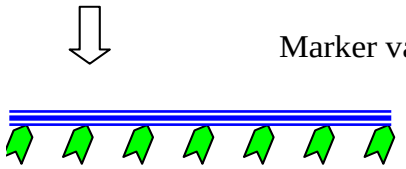


Infection

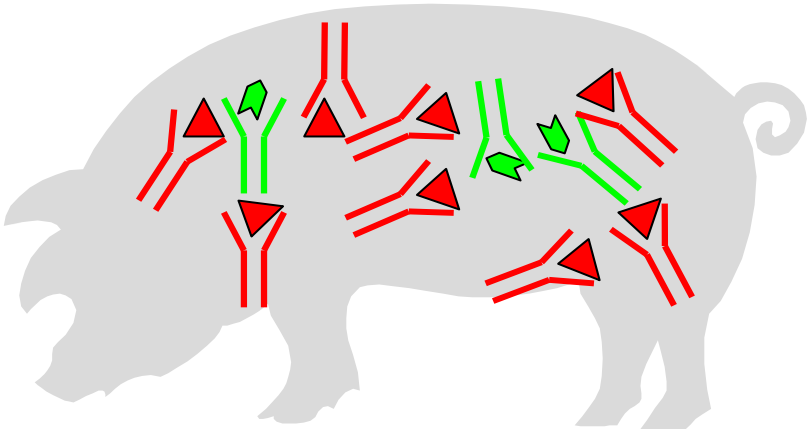
Wildtype virus

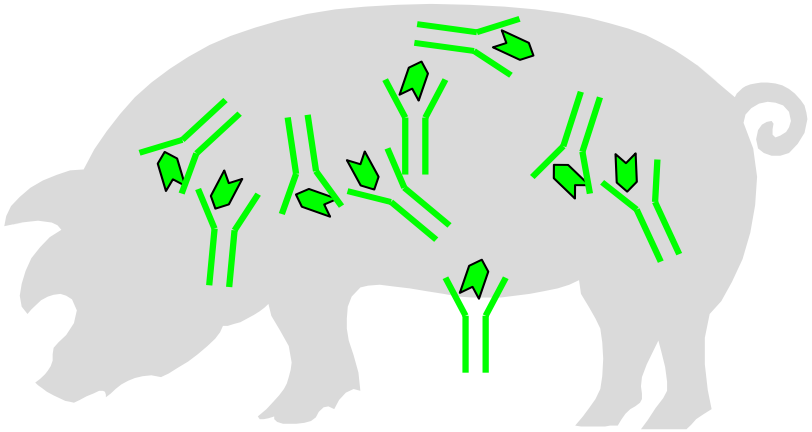


Vaccine only with protective virus and adjuvants

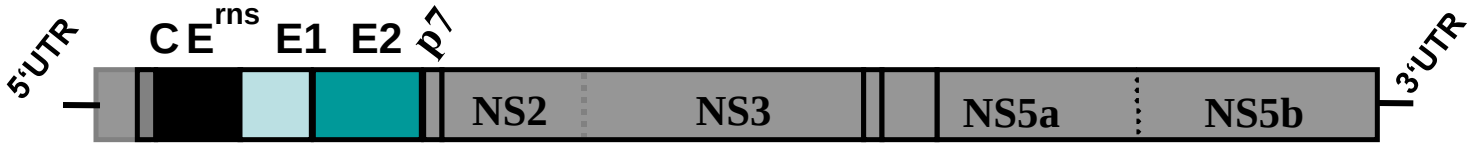


Marker vaccination



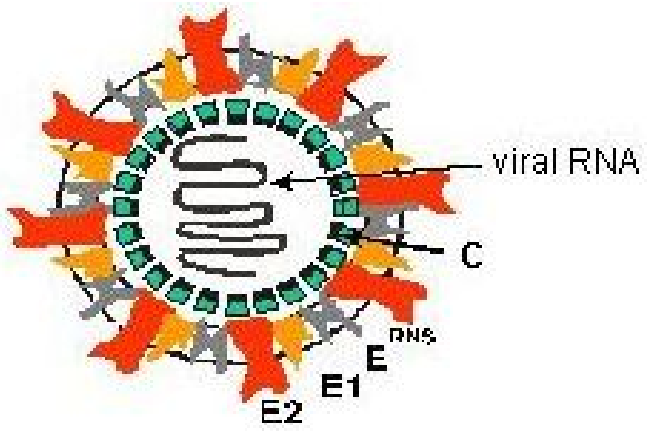


DIVA diagnostic - principles



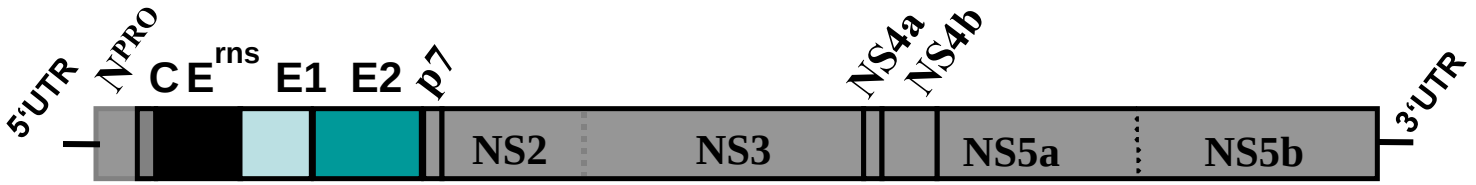
Major epitope for protection.
Species specific

Ab are produced, pan pestivirus. Usefull for bac produced E2

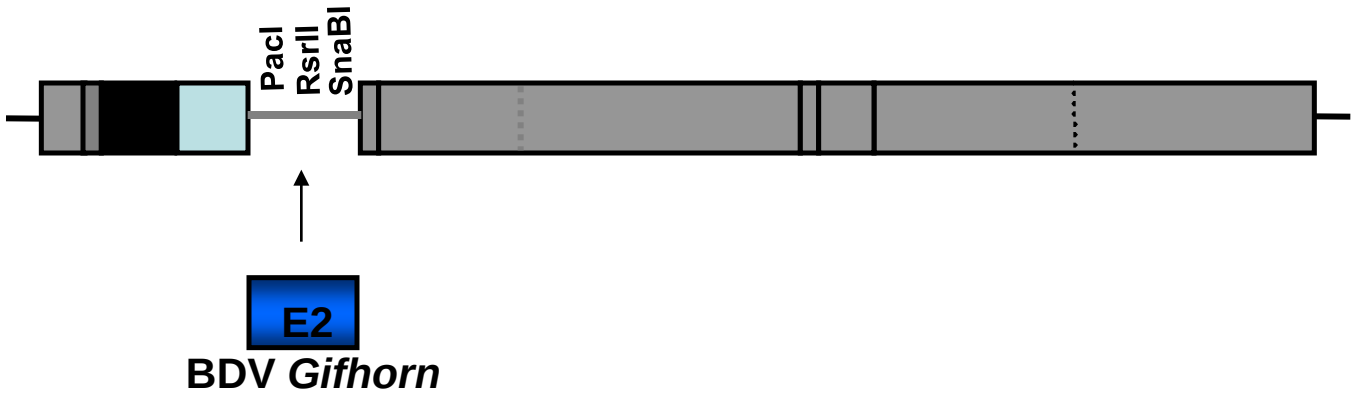


Construction of chimeric pestivirus, tailormade DIVA vaccines

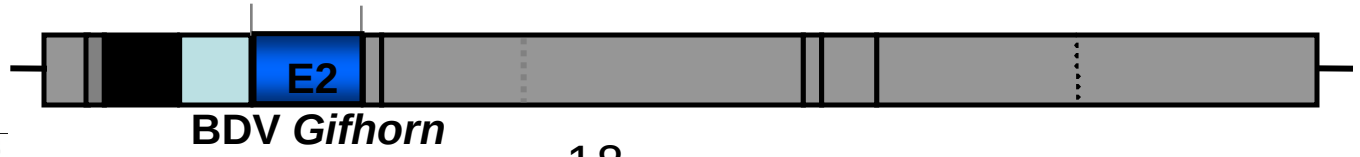
Infectious clone of BVDV *cp7* [Meyers et al. 1996]



Deletion mutant: cp7ΔE2 [Reimann et al. 2004]



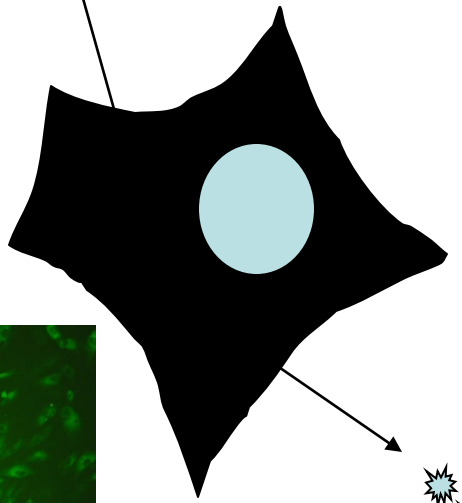
BVDV with E2 from BDV: cp7_E2gif [Rasmussen et al. 2007]

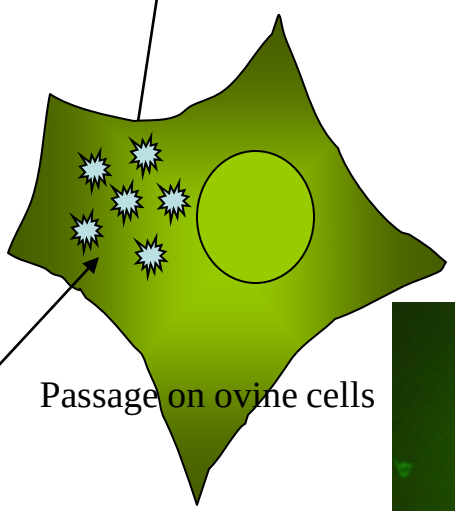


From clone to chimeric virus

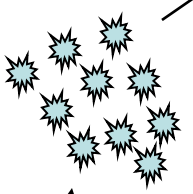
transcription

Transfection in bovine cells

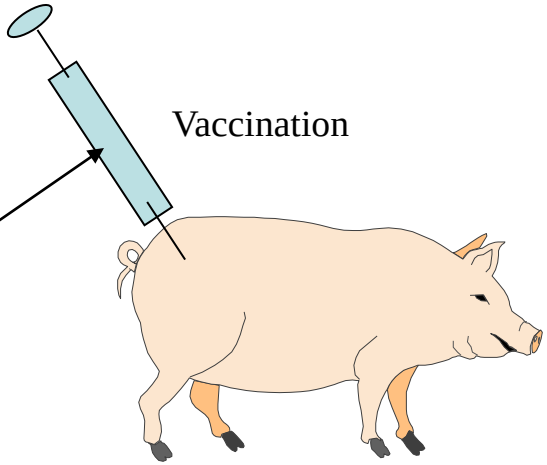




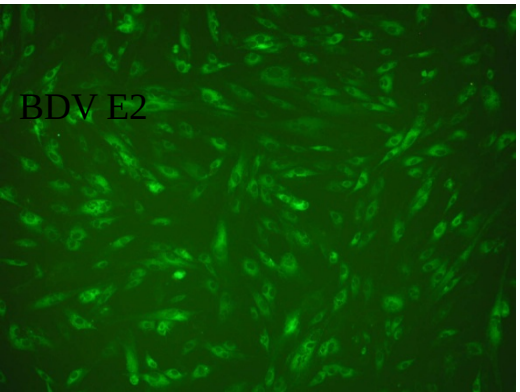
Passage on ovine cells



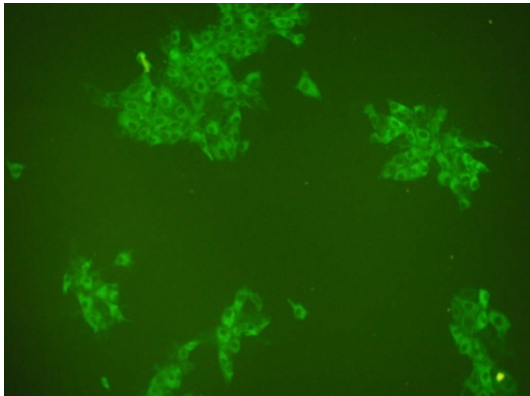
Chimeric virus



Vaccination



BDV E2



DIVA Vaccine - principles

The DIVA vaccine must be protective

There must be accompanying DIVA diagnostic tests

The optimal specificity and sensitivity is crucial

High throughput methods needed.. 10 000 analyses per day is nothing

Additional confirmatory tests for positive reacting animals

Vaccines against parasites

The anti-**parasite** vaccine successes

– *Rhipicephalus microplus* (tick)

- Target a tick gut membrane-bound protein, Bm86, using a recombinant protein in a potent adjuvant. These antibodies bind to the tick's gut surface when taking a blood meal, causing the rupture of gut wall and tick death.
- Not naturally exposed during infection and needs boosting

– *Dictyocaulus viviparous* (cattle lungworm)

- Irradiated larvae providing immunity similar to natural infections

– *Theileria parva* (East Coast Fever)

- *The MUGUGA cocktail:* Live protozoa administered with simultaneous oxytetracycline treatment

Immunity in *Ascaris suum* ?

Ascaris suum	Lung larvae 7 days post challenge (30,000 eggs 10 weeks post last inoculation)		Small intestine larvae 14 days post challenge	
	Mean larvae ± SD	% reduction	Mean larvae ± SD	% reduction
Control	1,888 ± 1,120	-	11,100 ± 1,921	-
3 x Immunized (5,000 eggs)	551 ± 371	66.5 ± 20.5 *	830 ± 1,171	92.6 ± 10.4 ***

- **The paradox of *Ascaris immunity*:**

Pigs may take up ~5,000 eggs/day, but rarely more than 100 worms are found in a pig (0.05% of uptake over 6 week period). Too many worms may kill the host and stop transmission.

The pigs AND *Ascaris* need to reduce the number of larvae to survive!!!

Pigs do not develop immunity against small numbers of adult worms

Ascaridia galli vaccine?– Food for thought!

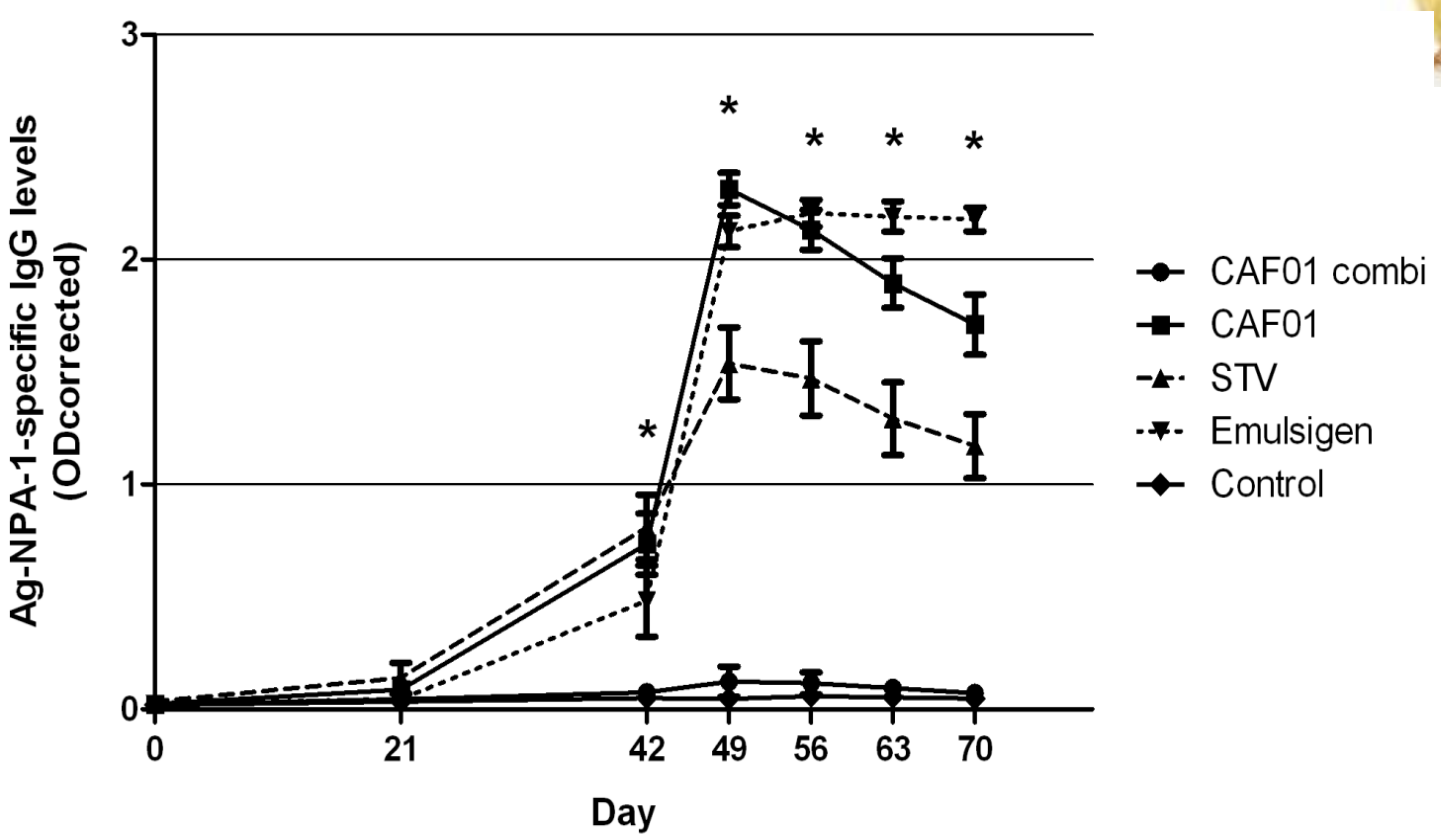
- Natural immunity is questionable:
  - No immune response to imitate
  - Vaccine induced immune response MUST be different from the natural response!

- Life cycle in 2 locations:
  - Larvae in tissues
  - Adults are ”ectoparasites”!
  - Vaccine can only target one stage

- Epidemiology:
  - Numbers of eggs and larvae are much higher than desired for survival of *Ascaridia*
  - 100% anti-larval immunity necessary for protection
  - Immunity against adult stages can be against reproduction

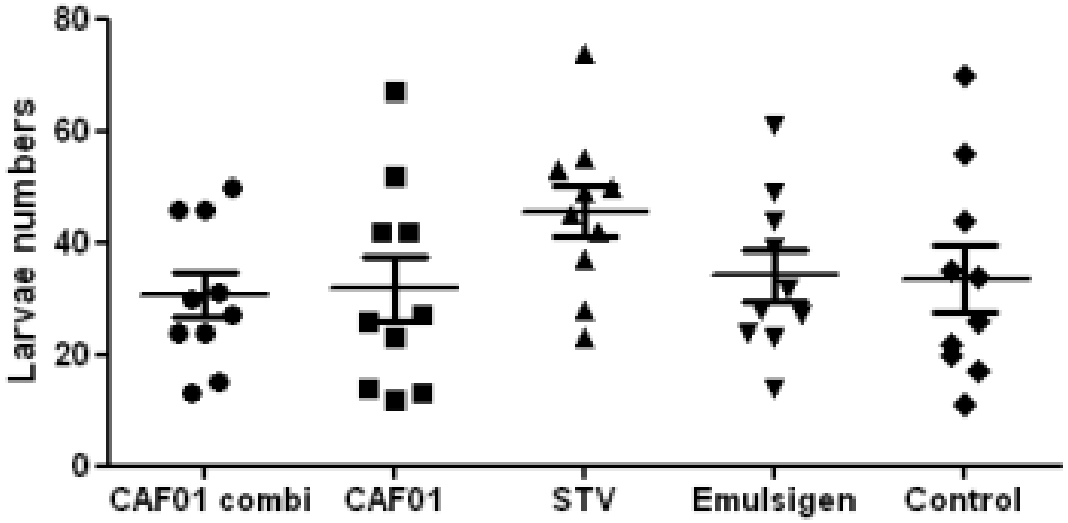
Development of a vaccine against *Ascaridia galli*

Ag-NPA-1 specific IgG in serum



Dorte Vadekær

A. galli larval counts at day 8/9 post infection



No protection!

Dorte Vadekær

Parasites may influence vaccines

Steenhard et al. 2009. *Ascaris suum* infection negatively affects the response to a *Mycoplasma hyopneumoniae* vaccination and subsequent challenge infection in pigs. Vaccine 27: 5161–5169

Four groups of pigs:

Ascaris suum trickle infected + M. hyop vaccine (w3) + M hyop challenge (w7)

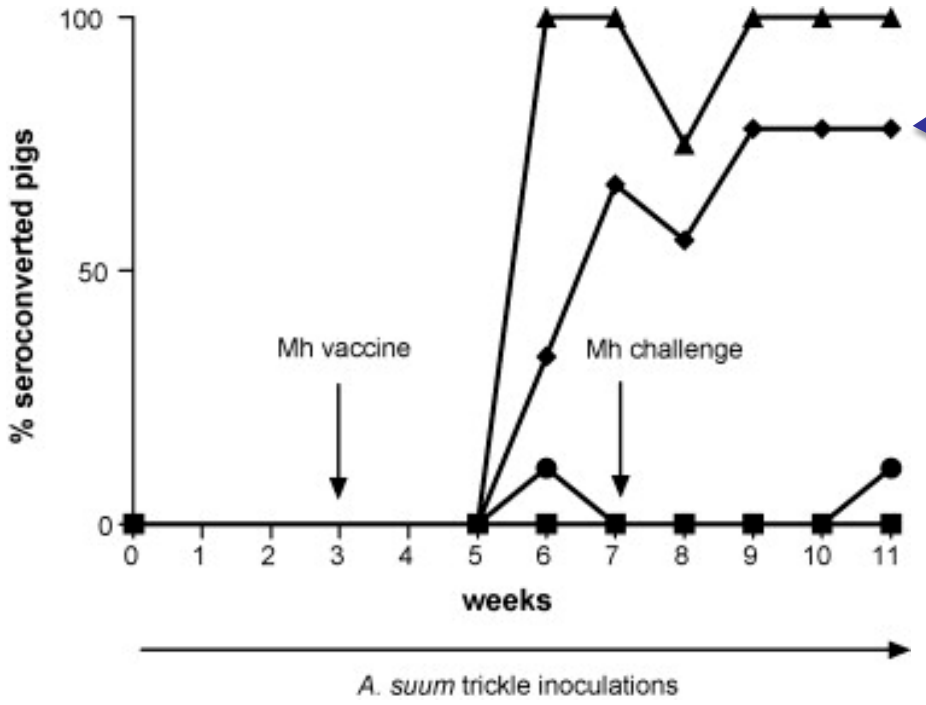
Ascaris suum trickle infected + M hyop challenge (w7)

M. hyop vaccine (w3) + M hyop challenge (w7)

M hyop challenge (w7)

Thorovax Vet (Schering Plough AH) (inactivated Mh mixed with an aluminium hydroxide as adjuvant)

Seroconversion after vaccination is reduced in *A. suum* pigs

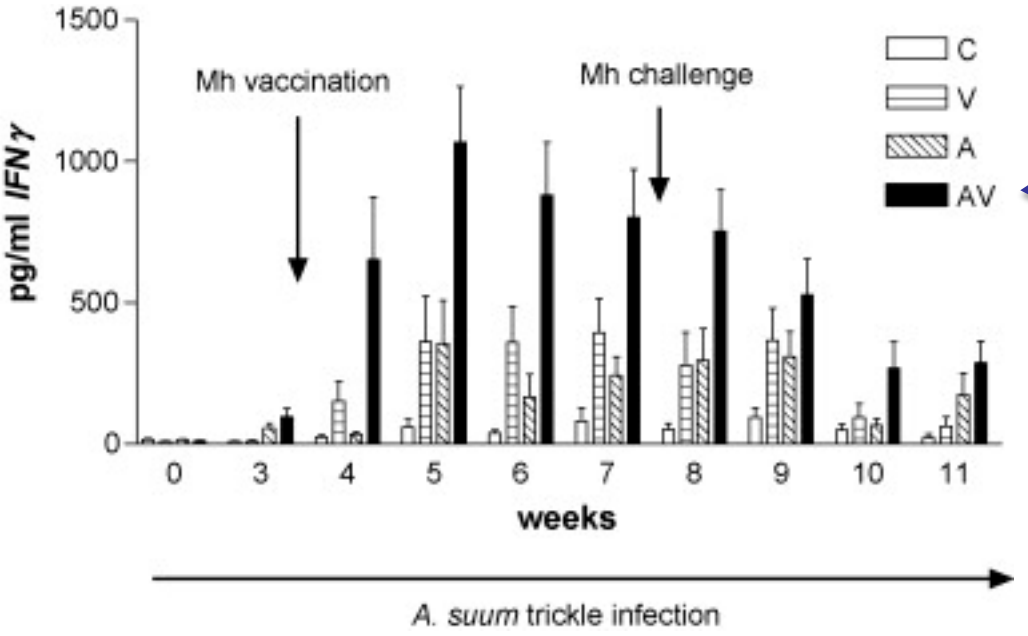


A. suum trickle infected pigs

Sero-conversion to Mycoplasma hyopneumoniae (Mh) vaccine or Mh challenge in four treatment groups measured by an ISO/IEC17025 accredited monoclonal blocking ELISA. (■) Untreated control pigs (C) (n = 9–6), (▲) pigs vaccinated at week 3 with *M. hyopneumoniae* (Mh) vaccine (V) (*n* = 9–8), (●) pigs repeatedly inoculated with *A. suum* (A) (*n* = 9), and (♦) pigs repeatedly inoculated with *A. suum* and vaccinated at week 3 with Mh vaccine (AV) (*n* = 9). All pigs were inoculated with Mh at week 7.

Steenhard et al. *Vaccine* 2009

Mycoplasma-specific IFN-γ is increased in *A. suum* pigs

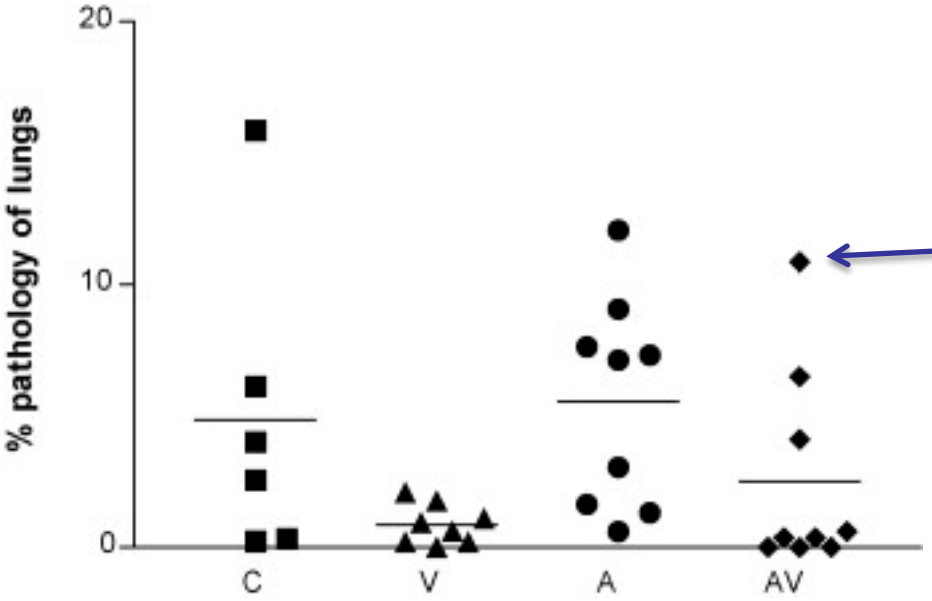


A. suum trickle infected pigs

Mean IFNγ (±SEM) secreted into supernatants from PBMCs stimulated with M. hyopneumoniae membrane antigen (MhmAg). Untreated control pigs (C) (n = 9–6), pigs vaccinated at week 3 with M. hyopneumoniae (Mh) vaccine (V) (n = 9–8), pigs repeatedly inoculated with *A. suum* (A) (*n* = 9), and pigs repeatedly inoculated with *A. suum* and vaccinated at week 3 with Mh vaccine (AV) (*n* = 9). All pigs were inoculated with Mh at week 7.

Steenhard et al. *Vaccine* 2009

Mycoplasma-specific IFN-γ is increased in *A. suum* pigs
Mycoplasma-protection at challenge is reduced in *A. suum* pigs



A. suum trickle infected pigs

Mean percentage of lung affected by pneumonic lesions. (■) Untreated control pigs (C) (n = 9–6), (▲) pigs vaccinated at week 3 with M. hyopneumoniae (Mh) vaccine (V) (n = 9–8), (●) pigs repeatedly inoculated with A. suum (A) (n = 9), and (♦) pigs repeatedly inoculated with *A. suum* and vaccinated at week 3 with Mh vaccine (AV) (*n* = 9). All pigs were inoculated with Mh vaccine at week 7 and euthanized week 11

Steenhard et al. *Vaccine* 2009

Spørgsmål ?


The Cow-Pock — or — the Wonderful Effects of the New Inoculation! — Vide the Publications of ye Anti-Vaccine Society.