

# Intranasal vaccination of calves from birth onwards: duration of nasal vaccine virus shedding

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## INTRODUCTION

The intranasal use of attenuated vaccines can interfere with diagnostics used during clinical outbreaks, especially when such outbreaks occur shortly after vaccination. Demonstration of the presence of pathogens in nasopharyngeal swabs and/or broncho-alveolar lavages shortly after intranasal vaccination with attenuated vaccines often raises the question whether the recovered agent is originating from the vaccination or whether it consists of a wildtype infection.

## OBJECTIVE

The aim of the study was to provide information on the duration of nasal shedding of vaccine virus after intranasal application of two live attenuated viral vaccines, and whether concurrent use of both vaccines could be of influence.

## MATERIALS AND METHODS

Controlled longitudinal multicenter field trial on three large dairy farms located in The Netherlands and Belgium. Evaluation of different vaccination protocols in new-born calves.

- ▶ **Experimental calves**  
Total of 58 calves randomly allocated to four groups
  - ▶ Group RSP (n=17) vaccinated intranasally with vaccine A [Bovilis<sup>®</sup> Intranasal RSP™ Live], first week of life.
  - ▶ Group NASC (n=17) vaccinated intranasally with vaccine B [Bovilis<sup>®</sup> Nasalgen<sup>®</sup>-C], first week of life.
  - ▶ Group RSP+NASC (n=17) vaccinated concurrently with both intranasal vaccines in a different nostril, first week of life.
  - ▶ Group Control (n=7) non vaccinated controls.
- ▶ **Sampling of the calves**
  - ▶ On inclusion + weekly for 4 consecutive weeks: serum, nasopharyngeal swab (NPS)
- ▶ **Laboratory testing**
  - ▶ Last sampling point (week 4): non-endoscopic broncho-alveolar lavage (nBAL)
- ▶ **Serum**
  - ▶ On inclusion IgG titer: ELISA (BioX).
  - ▶ Bovine respiratory syncytial virus (BRSV) antibody: ELISA (In-house).
  - ▶ Bovine corona virus (BCoV) antibody: ELISA (BioX).
  - ▶ Bovine para-influenza 3 virus (PI3) antibody: ELISA (IDEXX).
- ▶ **NPS and nBAL**
  - ▶ RT-qPCR for BRSV, PI3 and BCoV.

Intranasal vaccination resulted in PI3 vaccine strain excretion in nasopharyngeal secretions for maximum 2 weeks.

BRSV and BCoV vaccine strains were not detected in nasopharyngeal secretions from one week after intranasal vaccination onwards.

One month after intranasal vaccination no vaccine strains were detected in BAL samples



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## RESULTS

### Passive transfer of immunity (PTI)

- ▶ The calves were categorized using their serum IgG concentration at the age of 2-7 days (Table 1).
- ▶ Overall, the division of the calves into PTI groups corresponded well with the recommendations by Lombard et. al. (2020). However, a marked difference in PTI between farms was recognized.

TABLE 1. Categorization of the experimental calves (2-7 days old) according to the IgG serum titer grouped by farm.

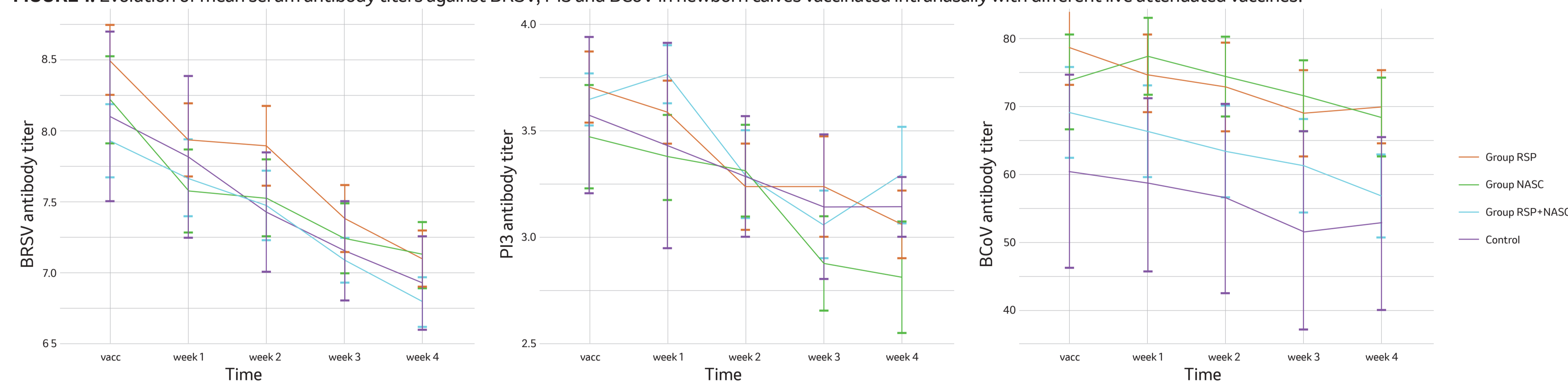
Serum IgG (Recommended percentage)	< 10 g/l (<10%)	≥10 - <18 g/l (20%)	≥18 - < 25 g/l (30%)	≥ 25 g/l (40%)
Farm A	-	6 (37.5%)	7 (43.8%)	3 (18.8%)
Farm B	3 (14.3%)	11 (52.4%)	6 (28.6%)	1 (4.8%)
Farm C	-	1 (4.8%)	4 (19%)	16 (76%)
All calves	3 (5.2%)	18 (31.0%)	17 (29.3%)	20 (34.5%)

## RESULTS

### Serum antibody titers

- ▶ The serum antibody titers in newborn calves against BRSV, PI3 and BCoV showed a typical decline from birth onwards.
- ▶ As expected, the typical pattern of declining maternal antibodies was not influenced by the applied intranasal vaccination protocols (Fig 1).
- ▶ No significant difference between the vaccination groups at any time point could be detected by repeated measures ANOVA.

FIGURE 1. Evolution of mean serum antibody titers against BRSV, PI3 and BCoV in newborn calves vaccinated intranasally with different live attenuated vaccines.

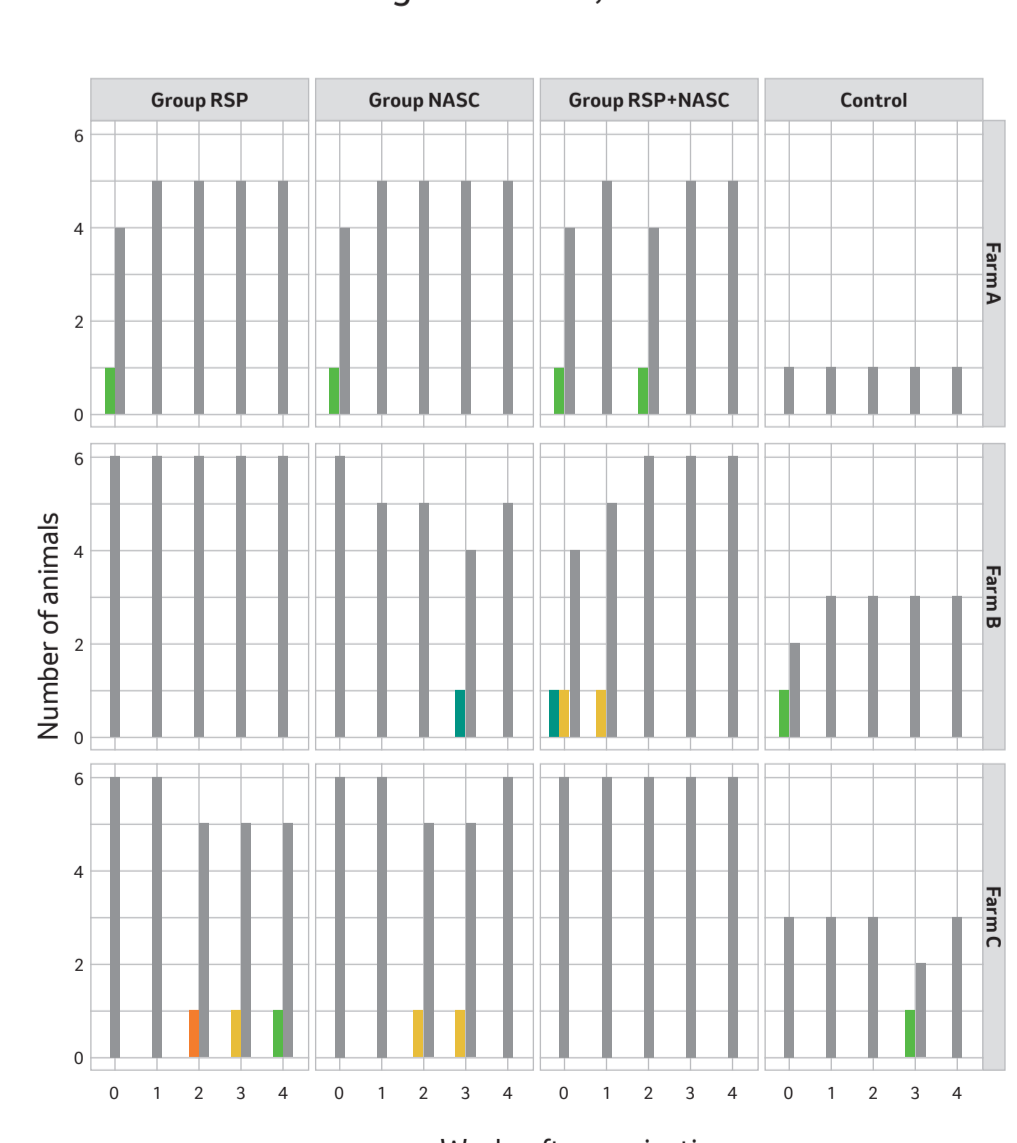


## RESULTS

### BRSV vaccine and wild-type virus

- ▶ On two farms, A and B, BRSV was already detected in nasopharyngeal secretions of newborn calves aged less than one week old before the intranasal vaccinations were done. On those farms, this wild virus circulation seemed to persist at a low level for two to three weeks. Differentiation of the BRSV strain detected one, two and three weeks after intranasal vaccination on those farms is on-going.
- ▶ On Farm C, BRSV was detected two, three and four weeks after the intranasal vaccinations and this in non-BRSV vaccinated as well as in BRSV vaccinated calves. This consisted of wild BRSV: vaccine strain specific RT-qPCR on nBAL samples were negative (Fig 2).

FIGURE 2. RT-qPCR values for BRSV in nasal swabs from newborn calves vaccinated intranasally with different live attenuated vaccines against BRSV, PI3 and BCoV.

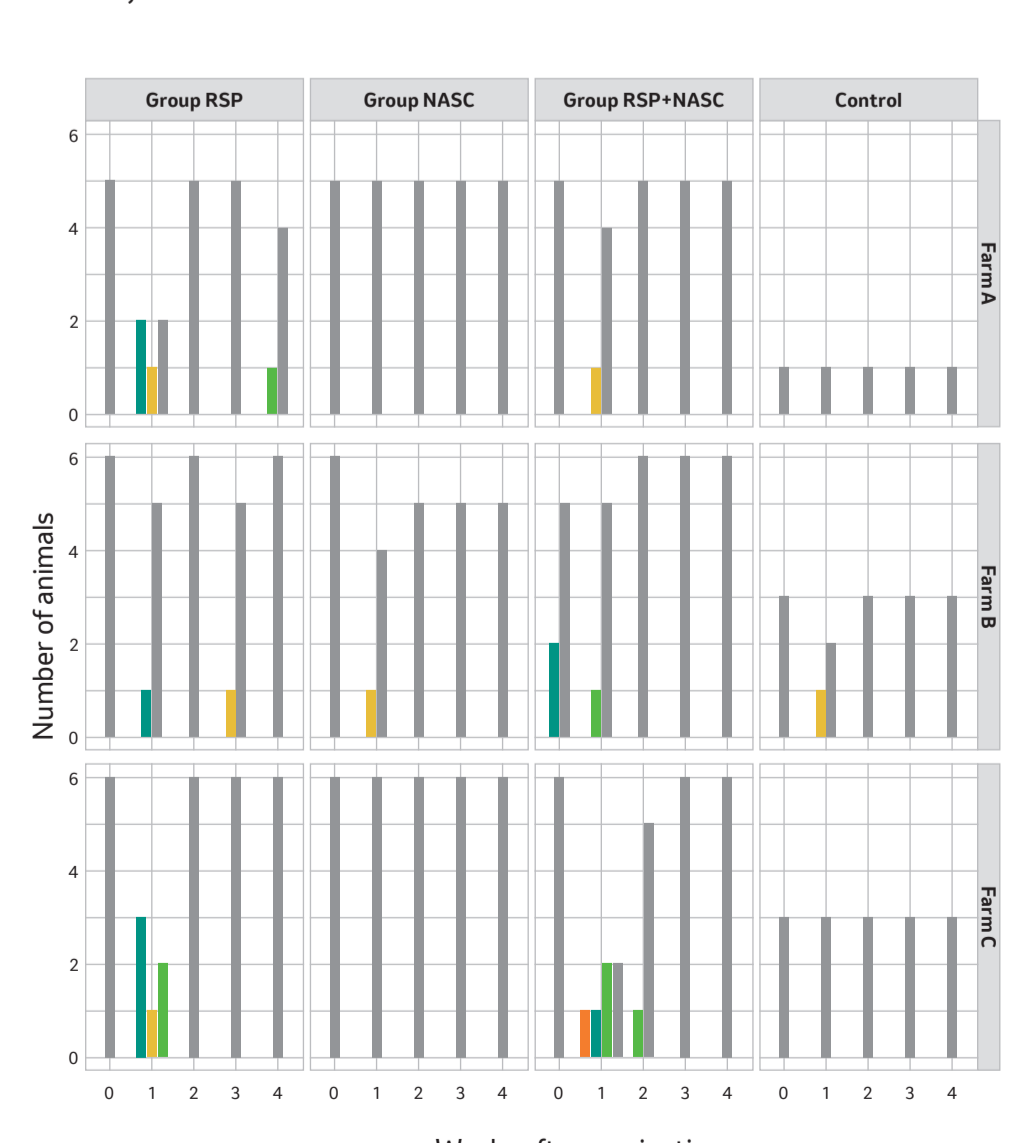


## RESULTS

### PI-3 vaccine and wild-type virus

- ▶ On farm B, PI3 wild type virus was detected before intranasal vaccination and seemed to persist for three weeks.
- ▶ On the other two farms PI3 virus was only detected in calves which received an intranasal vaccination containing PI3 and this for maximum of two weeks after the vaccination.
- ▶ In one calf on farm A, PI3 virus was detected in nasopharyngeal secretions and in lung lavage fluid four weeks after the vaccination. Vaccine strain specific RT-qPCR revealed that this was wild type virus.

FIGURE 3. RT-qPCR values for PI3 in nasal swabs from newborn calves vaccinated intranasally with live attenuated vaccines against BRSV, PI3 and BCoV.

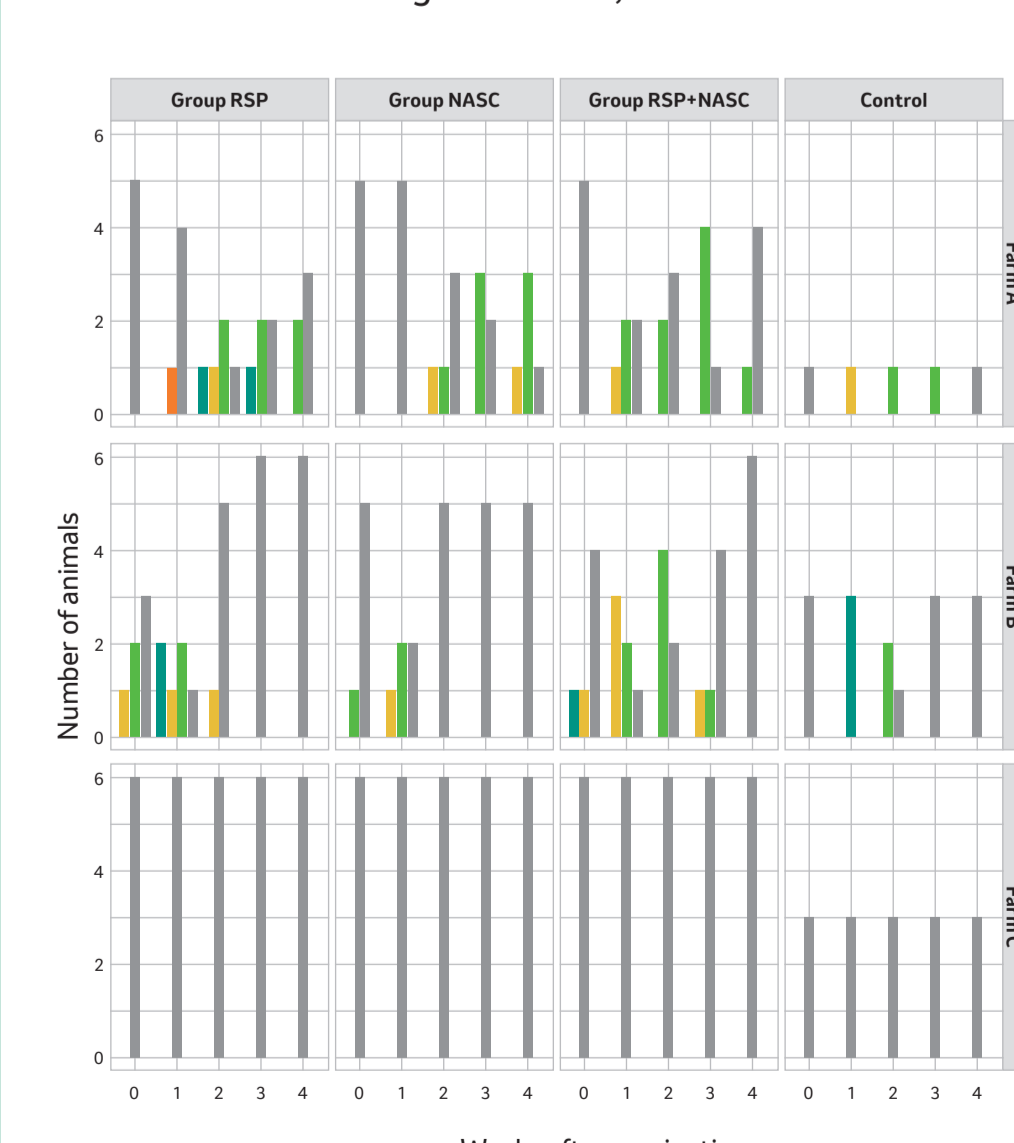


## RESULTS

### BCoV vaccine and wild-type virus

- ▶ On farm A, wild type BCoV was detected one week after intranasal vaccination and persisted for the complete study period, whereas on farm B wild type BCoV was already detected before vaccination and persisted for three weeks thereafter.
- ▶ The results on farm C showed that in absence of wild virus circulation no vaccine virus could be detected in nasopharyngeal secretions after intranasal vaccination.

FIGURE 4. RT-qPCR values for BCoV in nasal swabs from newborn calves vaccinated intranasally with live attenuated vaccines against BRSV, PI3 and BCoV.



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