

Bovine Coronavirus prevalence & risks in EU dairy farms

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The Science of Healthier Animals®



The goals of this cross-sectional field study

The objective is to obtain a rough estimate of the farm prevalence of Coronavirus in dairy production in Europe

&

To characterize farm-level risk factors in management and biosecurity that are linked to BCoV infection in neonatal dairy calves and weaned dairy calves.

130 EU Dairy farms



Austria, Belgium, Czech Republic, Denmark, France, Greece, Hungary, Ireland, Italy, Netherlands, Poland, Portugal, Romania, Sweden, Spain, Slovakia, United Kingdom (Scotland)

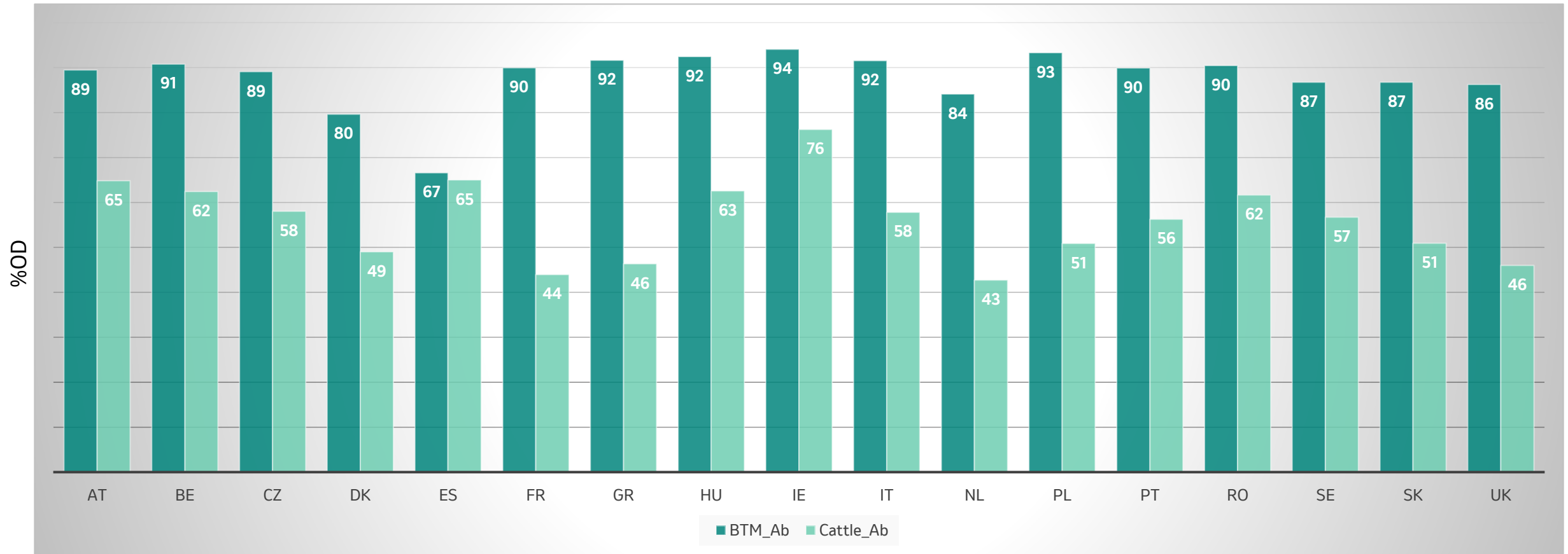


MATERIALS AND METHODS

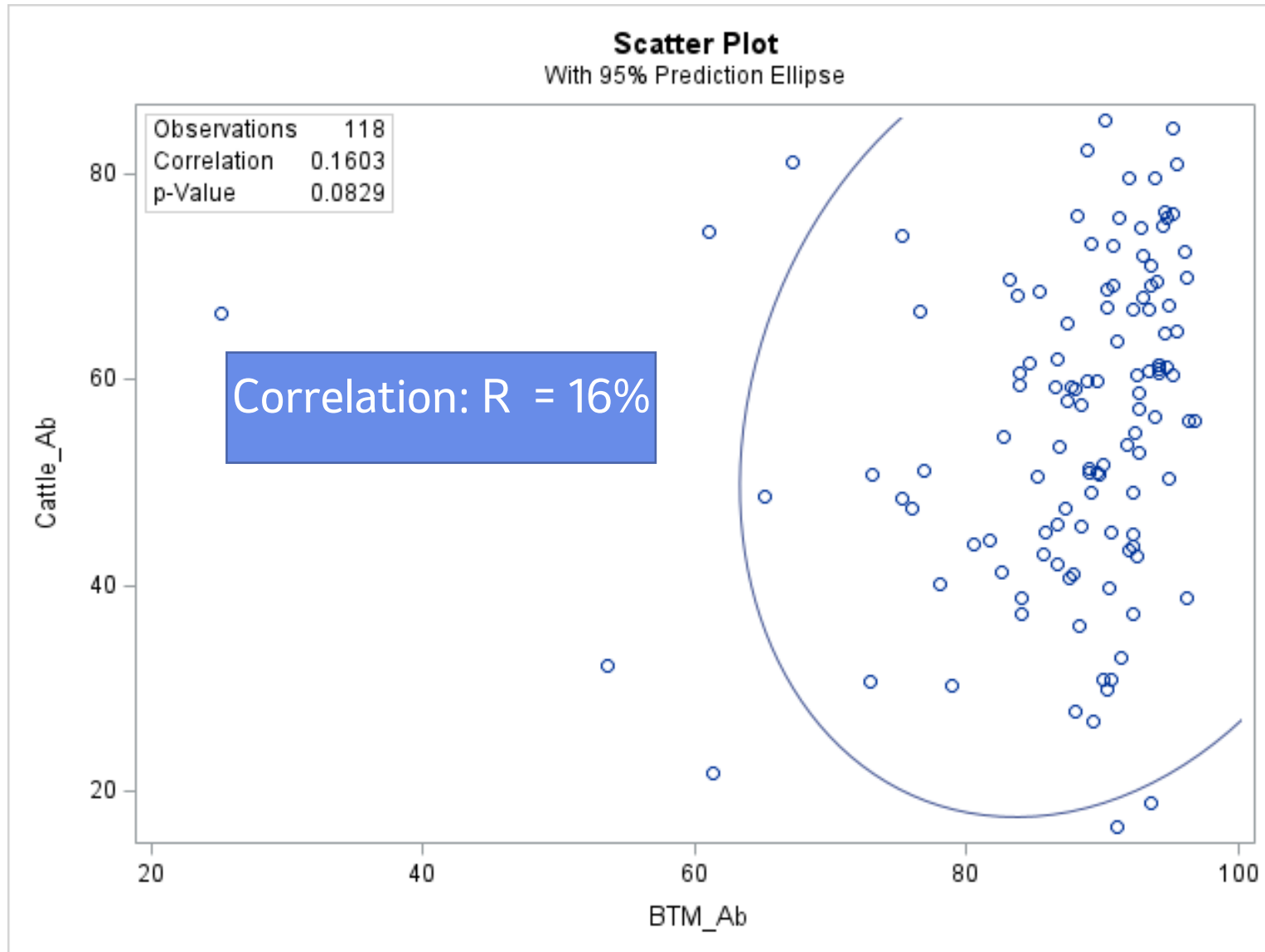
- ▶ Convenience sample of 130 European dairy farms with at least 100 lactating cows. Samples are taken between September 2021 and December 2022.
- ▶ From 10-20 neonatal calves, 10-20 recently weaned calves and 5-10 fresh cows. All samples are tested individually, no pooled samples.
- ▶ Nasal and faecal swabs : BCoV detection using semiquantitative Real Time PCR (RT-PCR)
- ▶ Blood samples : BCoV antibody detection (expressed in percent optical density (%OD))
- ▶ Bulk tank milk (BTM) samples : BCoV antibody detection (%OD)
- ▶ 2 questionnaires per farm :
 - General farm description and husbandry
 - Biosecurity (Biocheck survey, <https://biocheck.ugent.be>, Ugent, BE)
- ▶ Descriptive and interferential statistics were performed.

Farm BTM and cattle BCoV antibody levels

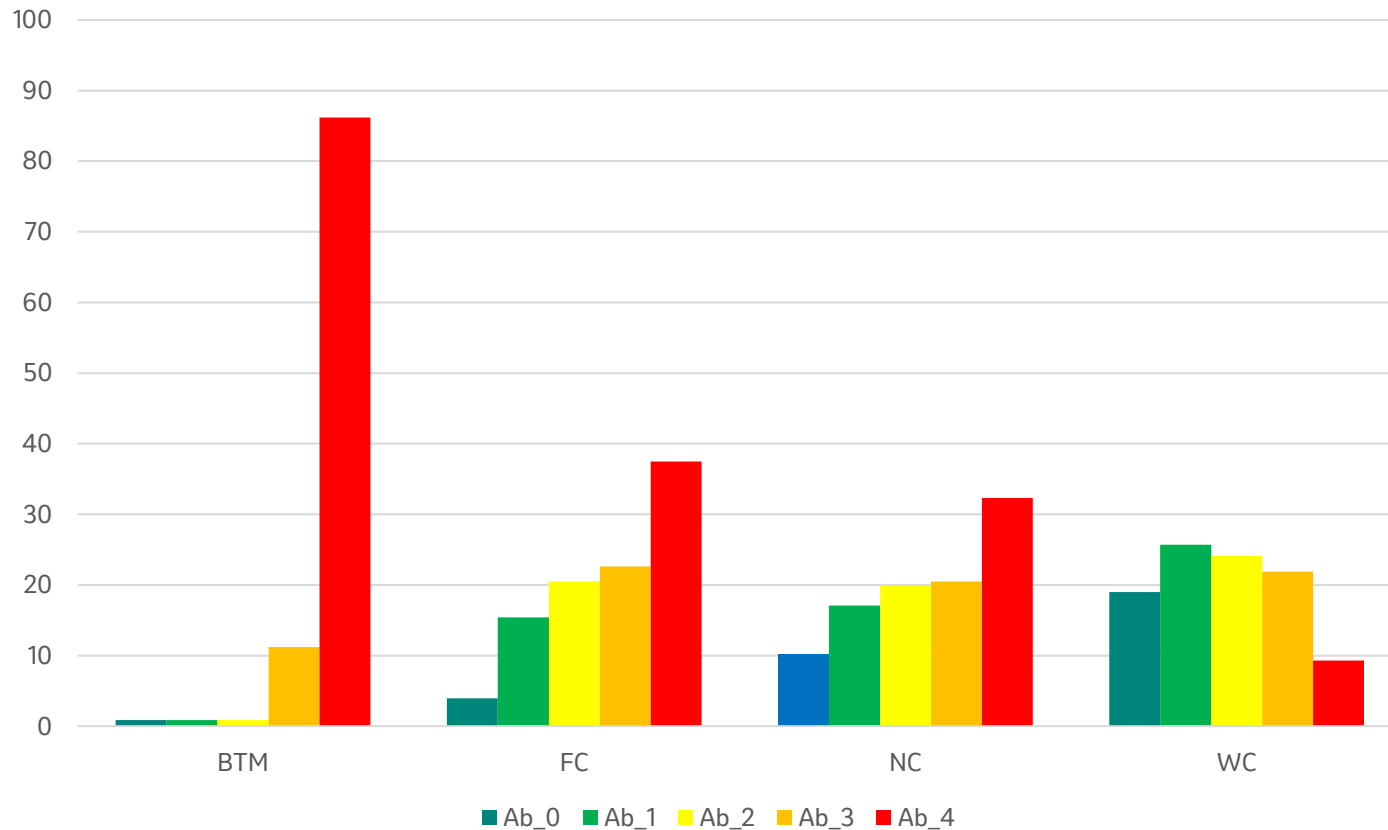
100% of the sampled farms were antibody positive



Poor correlation between BTM antibodies and cattle antibodies



% Antibody distributions to BCoV in bulk tank milk and cattle categories



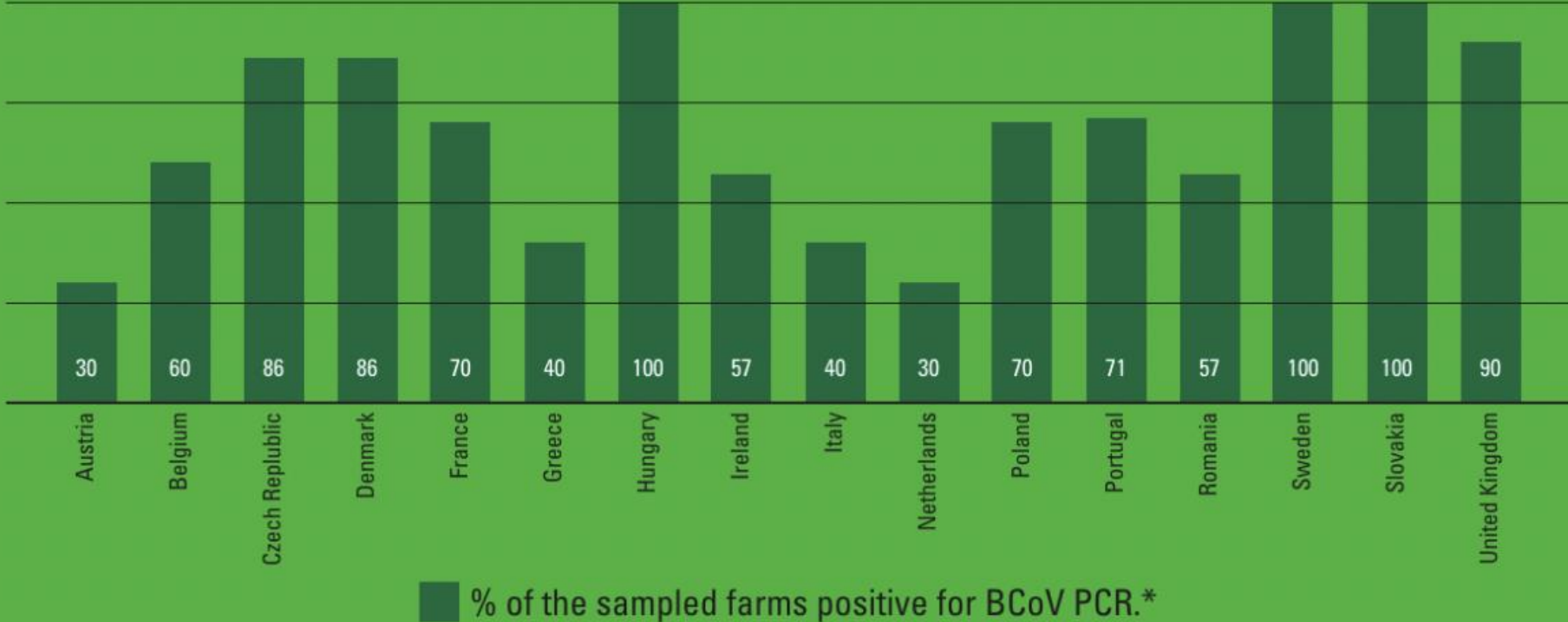
The Bulk tank milk samples nearly always show max levels of antibodies

The Fresh cows nearly all have some level of antibodies, and most farms have cows with high antibody levels

The Neonatal calves show similar antibody level distribution as the fresh cows, and most neonatal calves have high antibody levels

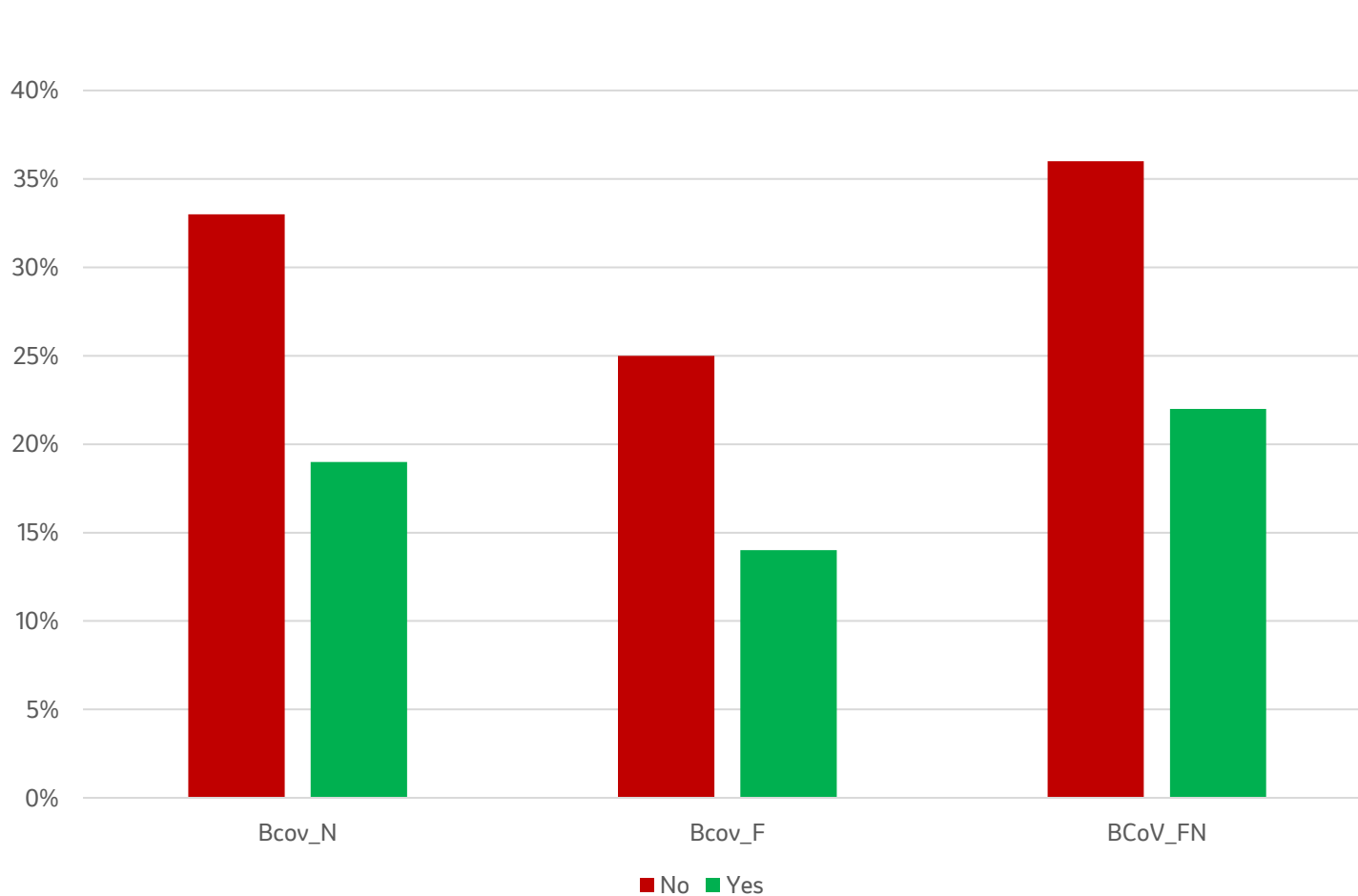
The weaned calves have the most calves with either no antibodies or low antibody levels.

Percentage of the sampled farms positive for bovine coronavirus PCR.*



Berge A.C., Vertenten G., PREVALENCE, BIOSECURITY AND RISK MANAGEMENT OF CORONAVIRUS INFECTIONS ON DAIRY FARMS IN EUROPE, European Buiatrics Congress, August 24-26, 2023, Berlin, Germany

BCoV recovered in calves under one month of age in herds with or without BCoV dry cow vaccination

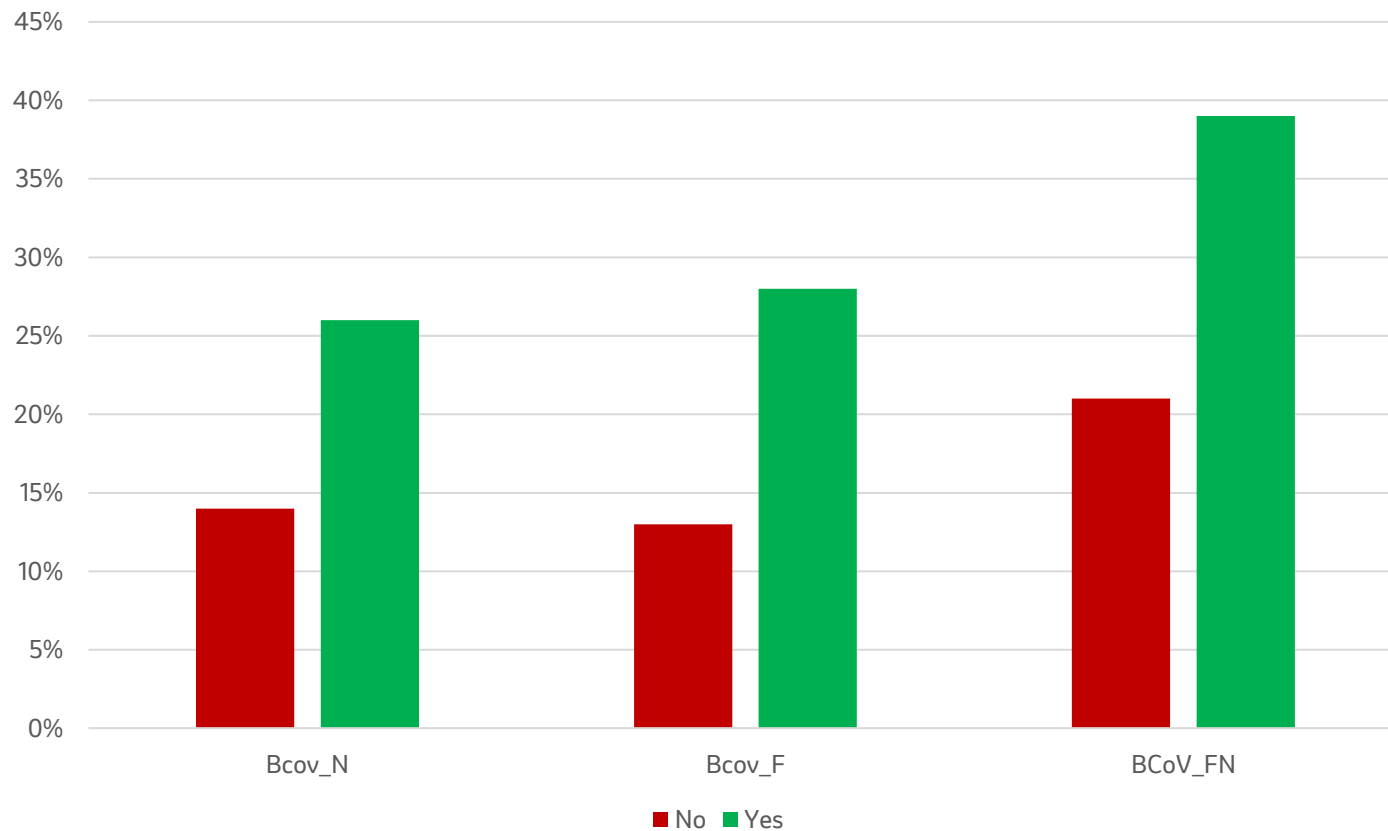


	BCoV in calves < 1 month			
Dam - Vac	Bcov_N	Bcov_F	BCoV_FN	Ab
No	33%	25%	36%	47
Yes	19%	14%	22%	69

61% reduction in neonatal calf shedding in herds that vaccinate their dry cows against BCoV

N = 1290
 BCoV_N = BCoV in nasal samples,
 BCoV_F = BCoV in faecal samples,
 BCoV_FN = BCoV in either nasal or faecal sample from calf
 Ab = Elisa antibody value.

BCoV recovered in weaned calves in herds with or without BCoV dry cow vaccination



	BCoV in calves weaned calves			
Dam - Vac	Bcov_N	Bcov_F	BCoV_FN	Ab
No	14%	13%	21%	39
Yes	26%	28%	39%	48

100% increase in weaned calf shedding in herds that vaccinate their dry cows against BCoV

N = 1388
 BCoV_N = BCoV in nasal samples,
 BCoV_F = BCoV in faecal samples,
 BCoV_FN = BCoV in either nasal or faecal sample from calf

Correlation nasal and fecal swabs (RT-PCR values)

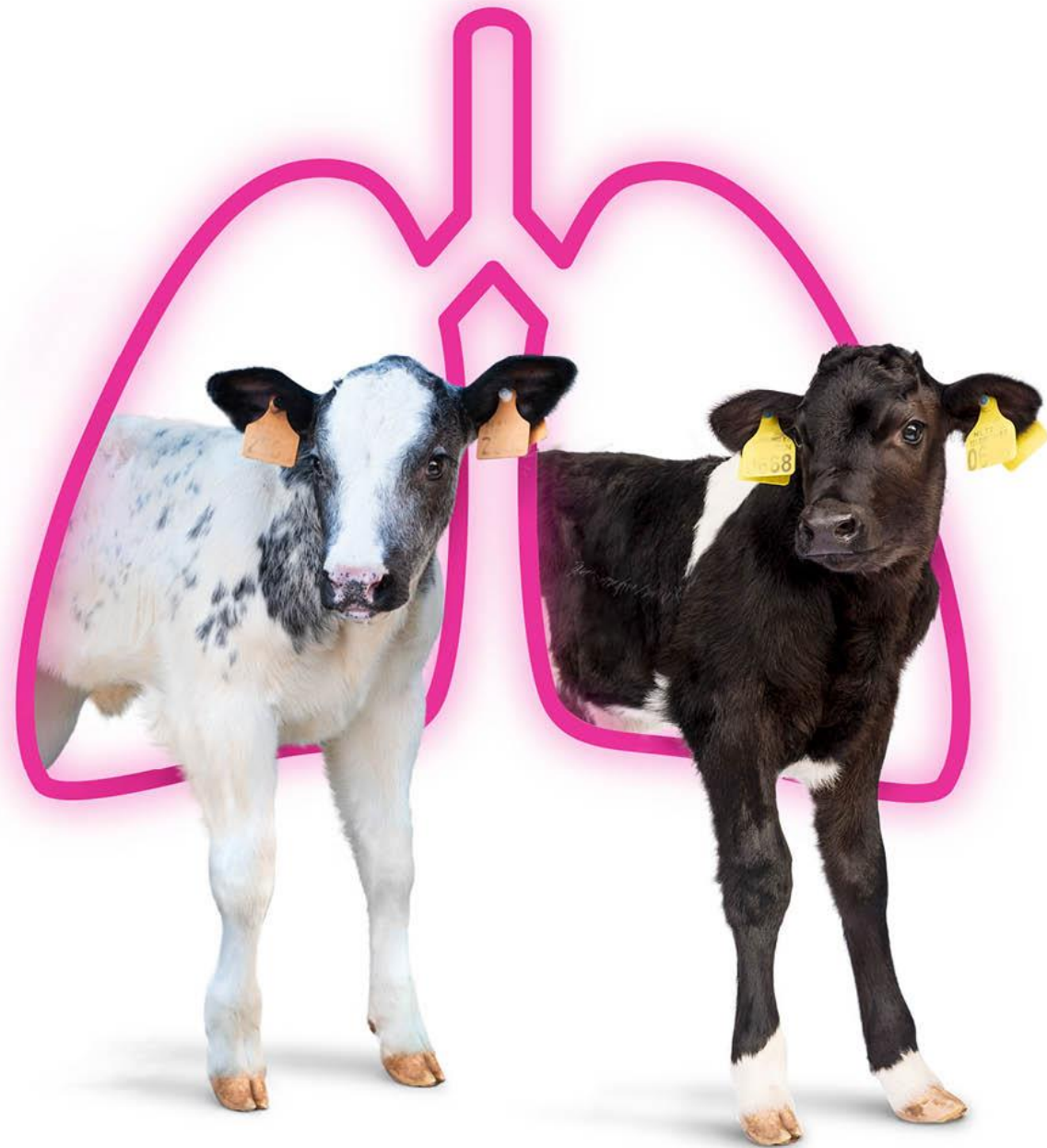
	BCoV-Feacal		
BCoV-Nasal	No	Yes	% BCoV-F+
No	2167	225	9%
Yes	291	423	59%
% BCoV-N +	12%	65%	
Chi-square P-value = 0.03			

Congruent results in 83% of sampled calves



Conclusions

1. Bovine Coronavirus (BCoV) is highly present in both the respiratory and enteric pathway in the dairy cattle population in Europe.
2. Preliminary results of field study found 80% of farms tested positive for BCoV
3. BCoV is associated with increased risk for Bovine Respiratory Disease (BRD).



BOVILIS EVENT

**THE NEXT
STEP IN
LUNG HEALTH**



Inhoud

1. Eigenschappen van het vaccin
2. Aanvang en duur van de immuniteit
3. Vaccinatie vanaf de geboorte
4. Invloed van maternale antistoffen
5. Gelijktijdig gebruik met Bovilis INtranasal RSP Live
6. In-Use Stabiliteit



Eigenschappen van het vaccin: Overzicht

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- Levend verzwakte BCoV stam CA25
- 2 ml per dosis is één spuit
- Toediening
- Vanaf de
- Snelle aa
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- Na recor
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Eerste respiratoir coronavirus vaccin voor runderen

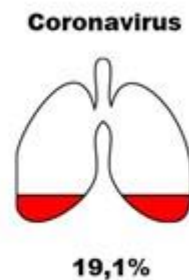
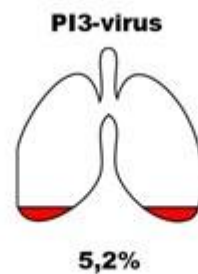


Griepbarometer

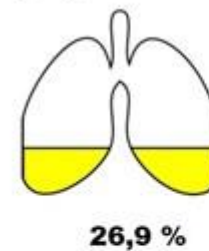
De Griepbarometer brengt de griepsituatie bij kalveren in beeld.

PERIODE: 1 december 2016 tot 14 augustus 2023

AANTAL GEVALLEN: 4086



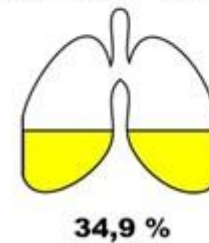
Mycoplasma bovis



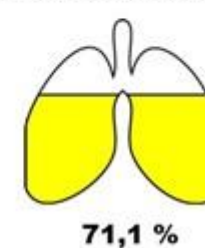
Histophilus somnus



Mannheimia haemolytica



Pasteurella multocida





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Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed



Prediction of respiratory disease and diarrhea in veal calves based on immunoglobulin levels and the serostatus for respiratory pathogens measured at arrival



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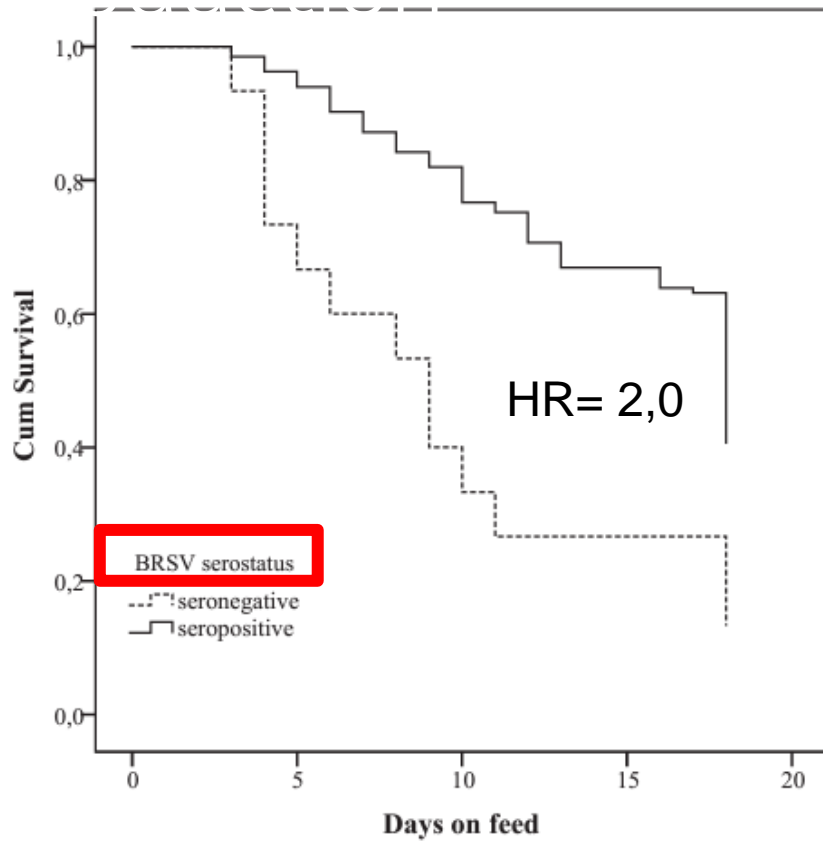


Fig. 3. Survival graph for occurrence of BRD in rosé veal calves in the first weeks after arrival, according to the serostatus for bovine respiratory syncytial virus (BRSV) measured upon arrival (Log Rank test: $\chi^2 = 13.8$, $df = 1$; $P < 0.001$)

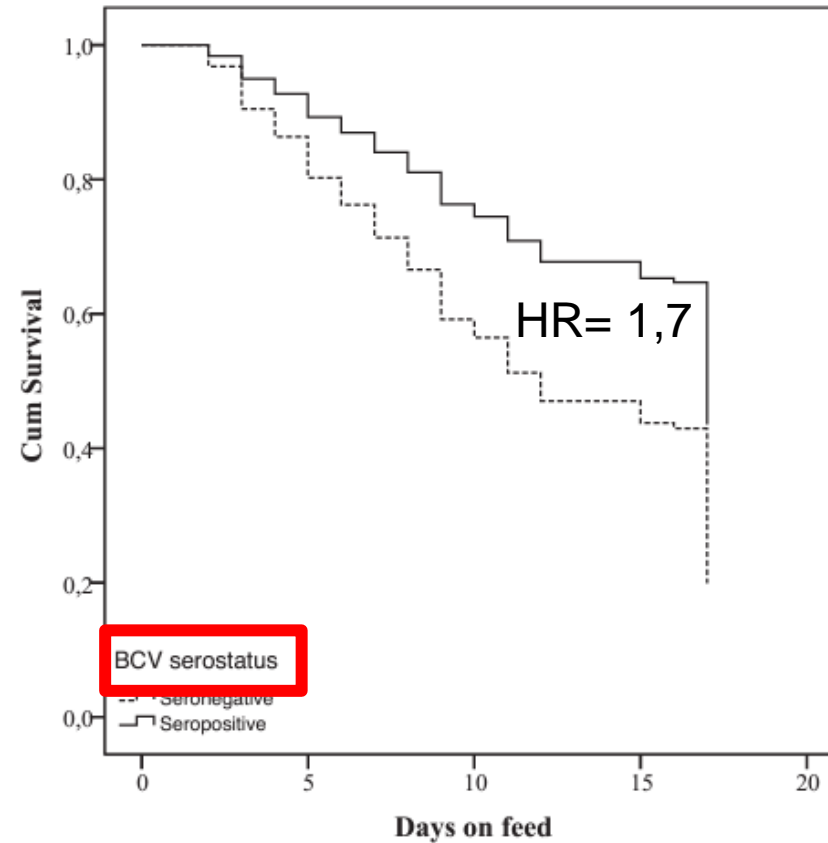
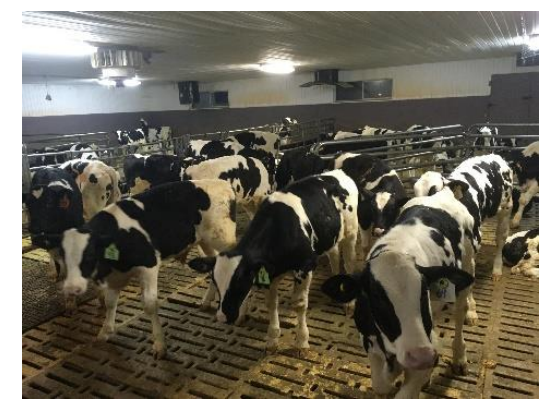


Fig. 4. Survival graph for occurrence of BRD in rosé veal calves in the first weeks after arrival, according to the serostatus for bovine coronavirus (BCV) measured upon arrival (Log Rank test: $\chi^2 = 10.7$, $df = 1$; $P < 0.01$).





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Pathogen-specific risk factors in acute outbreaks of respiratory disease in calves

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ABSTRACT

Respiratory tract infections (bovine respiratory dis-

VIRALE AGENTIA: **BCoV 38.4%**
 BRSV 29.4%
 PI3 8.1%

BACTERIËLE AGENTIA: **Pasteurella multocida 89.1%**
 Mannheimia haemolytica 41.2%
 Histophilus somni 36.4%
 Mycoplasma Bovis 33.3%

Histophilus somni were detected in 33.3, 41.2, 89.1, and 36.4% of the herds, respectively. Specific risk factors for



Table 5. Final multivariable logistic regression model describing the association between risk factors and detection of bovine coronavirus by PCR on pooled broncho-alveolar lavage samples from epidemic respiratory disease in calves¹

Independent variable	Category	n	% positive	b	SE	OR	95% CI	P-value
Intercept				-1.8	0.5			<0.001
<i>Mannheimia haemolytica</i>	Negative	50	34.0	Referent				
	Positive	36	55.6	1.0	0.5	2.8	1.1–7.5	0.03
Detection of coronavirus in neonatal calves in the last year	No	66	37.8	Referent				
	Yes	20	60.0	1.3	0.6	3.6	1.2–11.1	0.03
Herd size (per increase of 100 animals)		86		0.3	0.1	1.3	1.0–1.8	0.03

¹b = regression coefficient; OR = odds ratio.



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Preventive Veterinary Medicine



Subclinical respiratory disease ???

or

Prec
imm
mea

Thoracic ultrasound scanning ???

CrossMark

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European Buiatrics Congress Berlijn 2023

Serologic predictors for pneumonia in male dairy veal calves

G. Hoflack, T. Lowie, S. Jourquin, F. Debruyne, L. Chantillon, J. Clinquart, M. L. Pas, R. Boone, G. Vertenten, B. Sustronck, B. Pardon

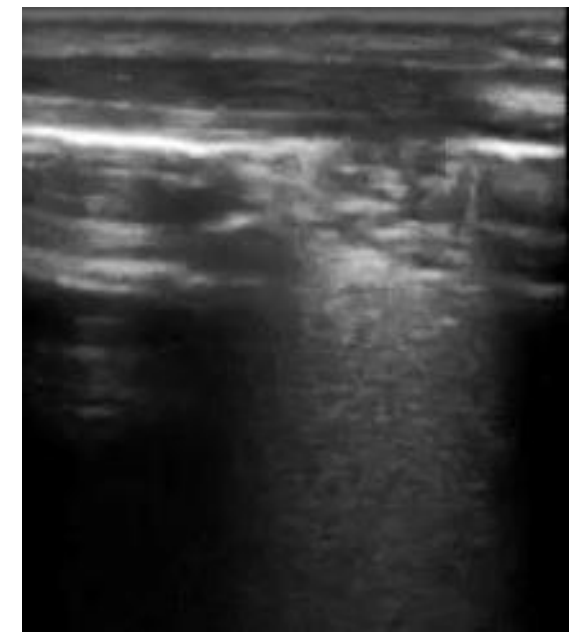
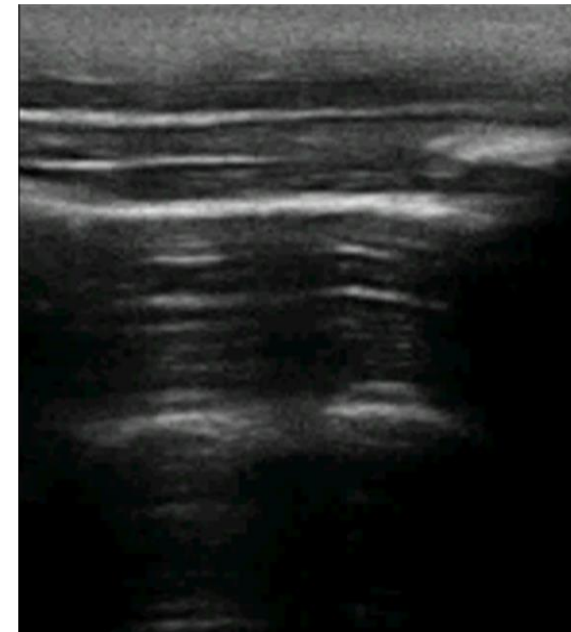


Serologic predictors for veal calf pneumonia



Calf Health Scoring Criteria			
0	1	2	3
Rectal temperature			
100-100.9	101-101.9	102-102.9	≥103
Cough			
None	Induce single cough	Induced repeated coughs or occasional spontaneous cough	Repeated spontaneous coughs
Nasal discharge			
Normal serous discharge	Small amount of unilateral cloudy discharge	Bilateral, cloudy excessive mucous discharge	Copious bilateral mucopurulent discharge
			
Eye scores			
Normal	Small amount of ocular discharge	Moderate amount of unilateral discharge	Heavy ocular discharge
			
Ear scores			
Normal	Ear flick or head shake	Slight unilateral droop	Head tilt or bilateral droop
			

Wiconsin-Score ≥ 5 : Klinische BRD



Consolidatie diepte ≥ 1 cm : Pneumonie (qTUS positief)





Serologic predictors for veal calf pneumonia

BCoV seronegatieve kalveren bij aankomst hebben een 2.4 keer hogere odds om pneumonie te ontwikkelen binnen de eerste weken na aankomst

BRSV seronegatieve kalveren bij aankomst hebben een 1.6 keer hogere odds om pneumonie te ontwikkelen binnen de eerste weken na aankomst

BRSV seropositieve kalveren bij aankomst hebben een 2.6 keer meer kans op afwezigheid van pneumonie na de eerste metafylactische behandeling



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- 2 ml per dosis in één spuit
- Toediening via de neus
- Vanaf de geboorte
- Snelle aanpak
- Lange duur
- Stimulatie van de aangeboren immuniteit
- Werkzaam tegen BCoV
- Na record van 2017
- Gelijktijdig toe te dienen met Bovilis INtranasal RSP live

Levend verzwakte BCoV stam CA25

Stimulatie van de aspecifieke aangeboren immuniteit




vaccines



Article

Early Activation of the Innate Immunity and Specific Cellular Immune Pathways after Vaccination with a Live Intranasal Viral Vaccine and Challenge with Bovine Parainfluenza Type 3 Virus

Piet Nuijten, Natalie Cleton, Jeroen van der Loop, Birgit Makoschey, Wilco Pulskens and Geert Vertenten * 

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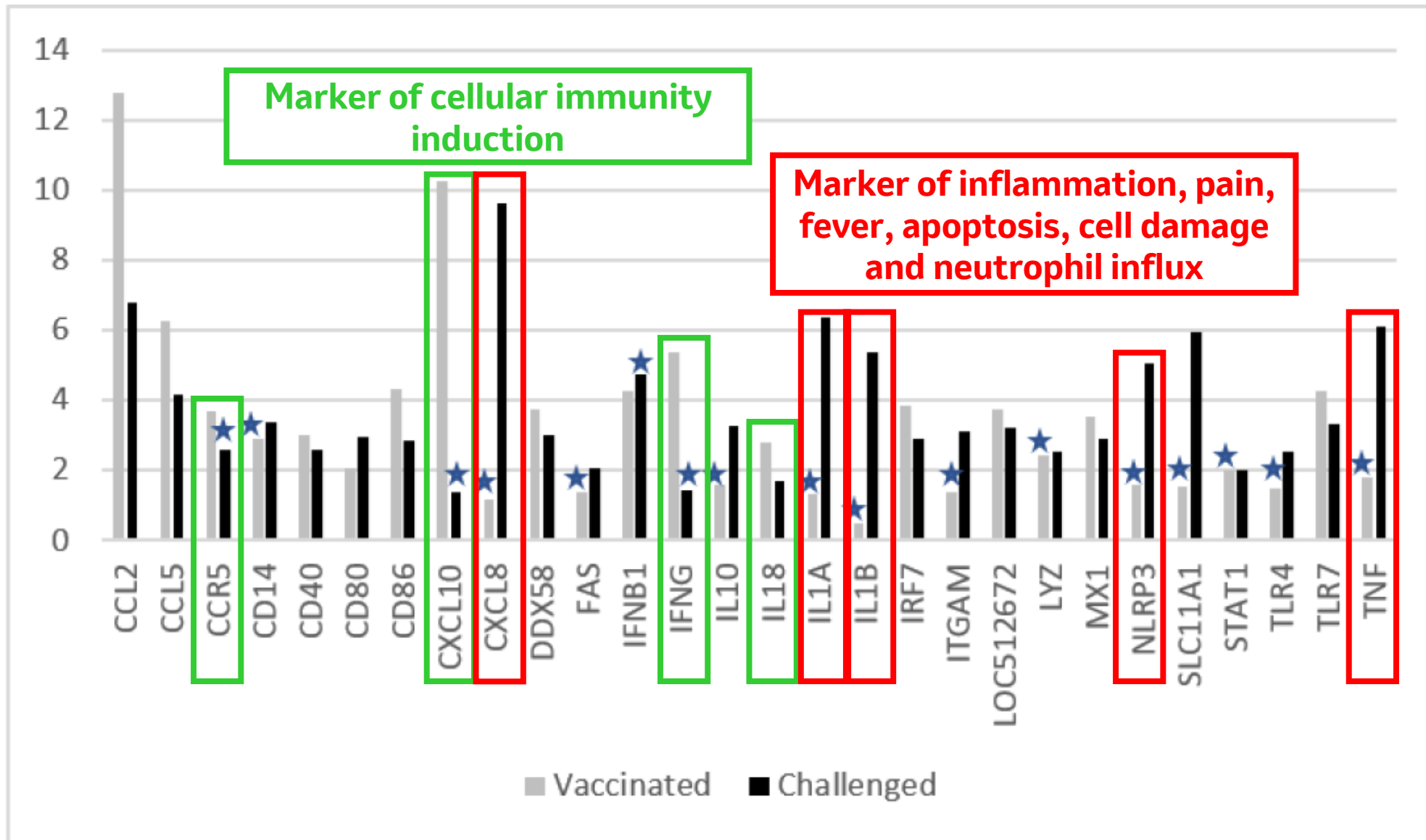


Figure 3. Comparison of gene expression (fold-change on Y-axis) of vaccinated- versus nonvaccinated-challenged animals. Genes are shown which had significant changes in Ct values five days after vaccination or five days after challenge (see materials and methods). Asterisks indicate non-significant changes according to the arbitrary criteria described in the materials and methods section.



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Vanaf de dag van de geboorte



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Veterinary Vaccine

journal homepage: www.elsevier.com/locate/vetvac

Vaccination of calves at day of birth with attenuated vaccines against bovine respiratory syncytial virus, bovine parainfluenza type 3 virus and respiratory bovine coronavirus

Mark H. van Rooij^a, Mélodie Schmitz^b, Joris M.H. Meessen^a, Pieter A.W.M. Wouters^c,
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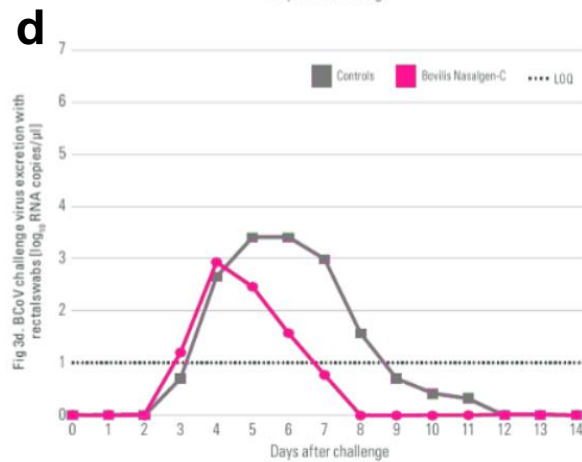
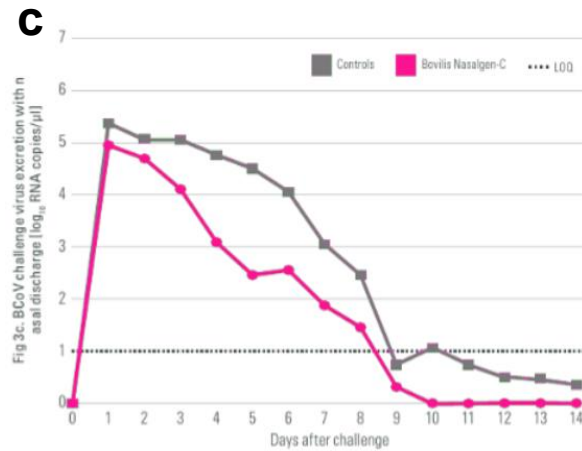
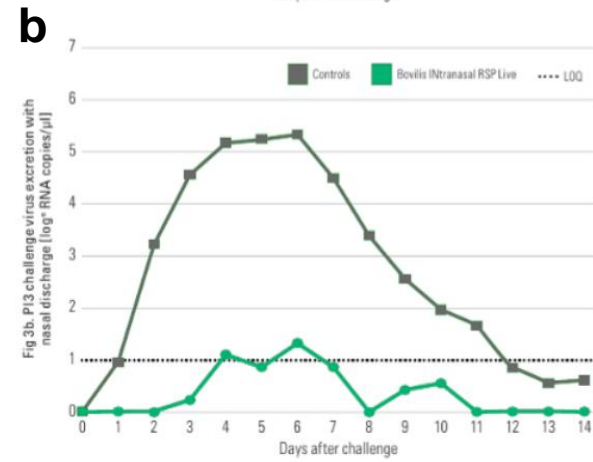
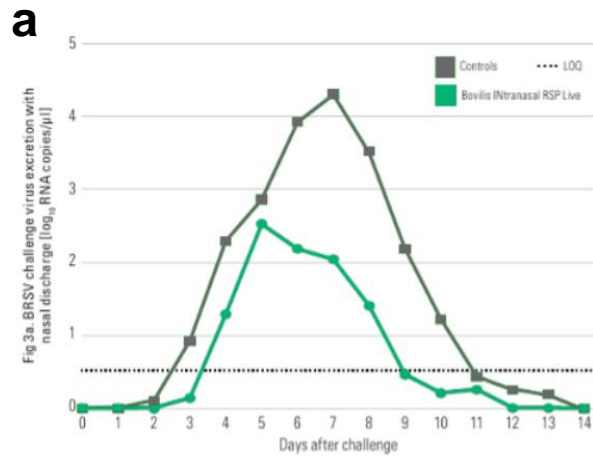


Study / Group	Number of animals	Vaccination (D0/D1)		Challenge	
		Vaccine	Route	Study day	Virus
BRSV control	6	Not vaccinated		D 6	BRSV
BRSV IN	6	BRSV/PI3	IN		
PI3 control	5	Not vaccinated		D 7	PI3
PI3 IN	5	BRSV/PI3	IN		
BCoV control	5	Not vaccinated		D 5	BCoV
BCoV IN	5	BCoV	IN		





Administratie van Bovilis Nasalgen-C en Bovilis Intranasal Live RSP vanaf de geboorte



Virus hoeveelheid in nasale swabs significant lager bij de gevaccineerde dieren (Fig a-c)

BCV virus hoeveelheid in rectale swabs significant lager bij de gevaccineerde dieren (Fig d)



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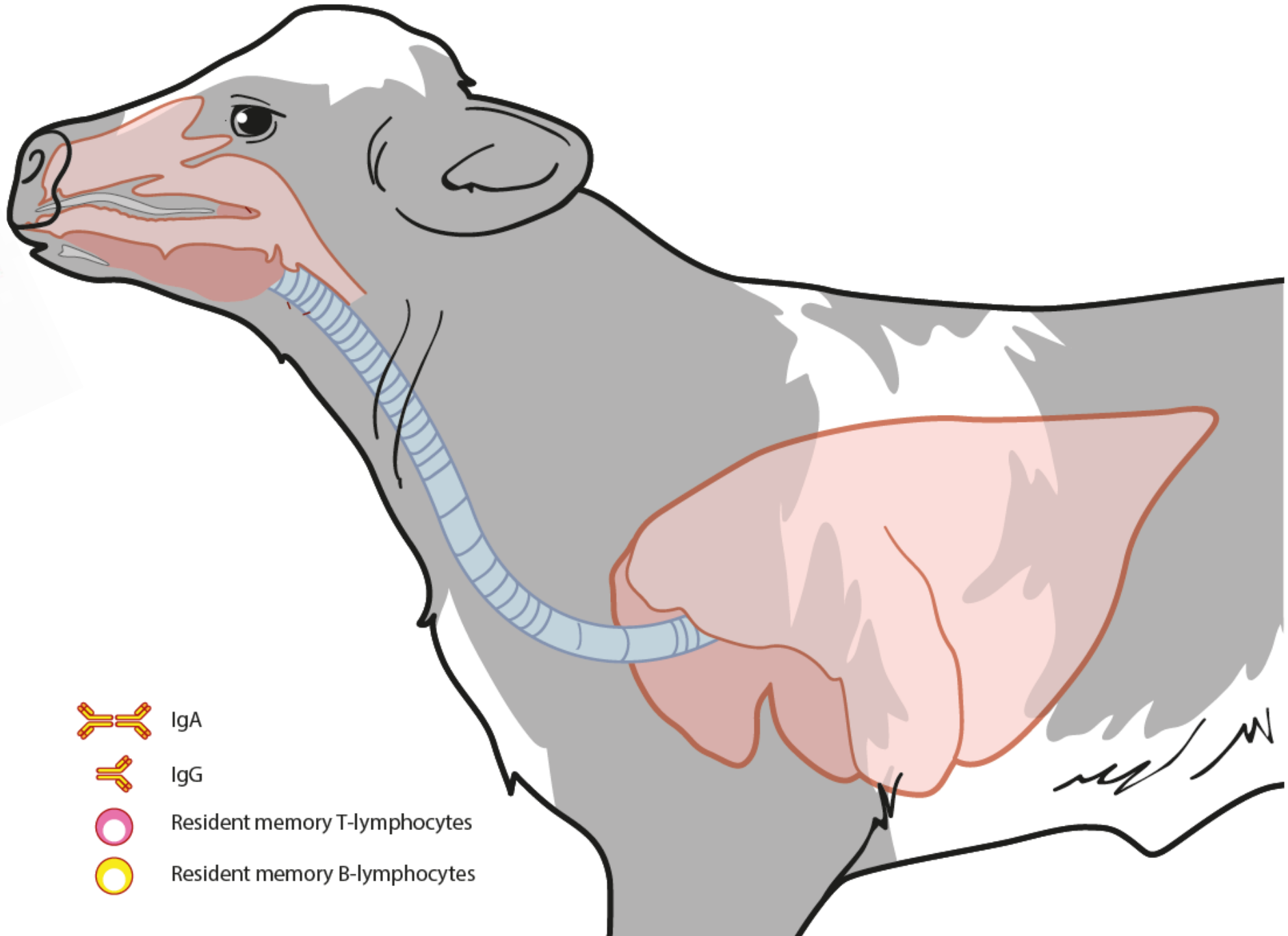
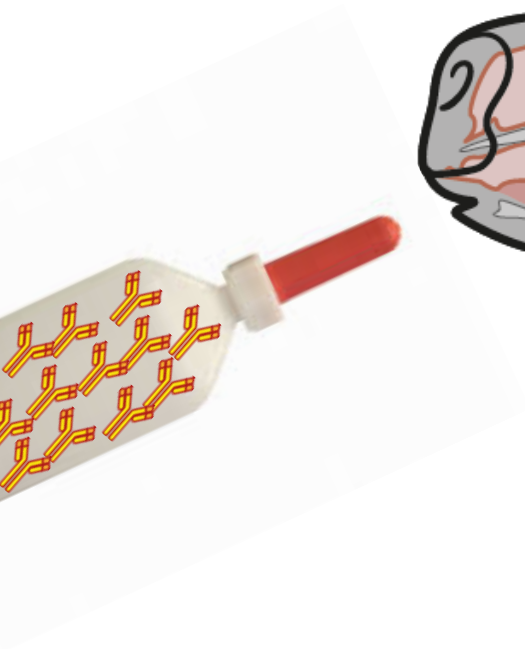








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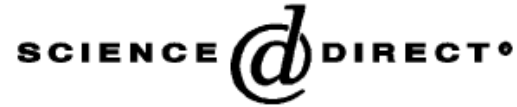
Werkzaam in aanwezigheid van maternale antistoffen



-  IgA
-  IgG
-  Resident memory T-lymphocytes
-  Resident memory B-lymphocytes



Available online at www.sciencedirect.com



Veterinary Immunology and Immunopathology 98 (2004) 85–89

Veterinary
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The neonatal Fc receptor (FcRn) is expressed in the bovine lung

Balázs Mayer^a, Zsuzsanna Kis^a, Győző Kaján^a, László V. Frenyó^a,
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Received 10 July 2003; accepted 22 October 2003



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Balázs Mayer^a, Zsuzsanna Kis^a, Győző Kaján^a, László V. Frenyó^a,
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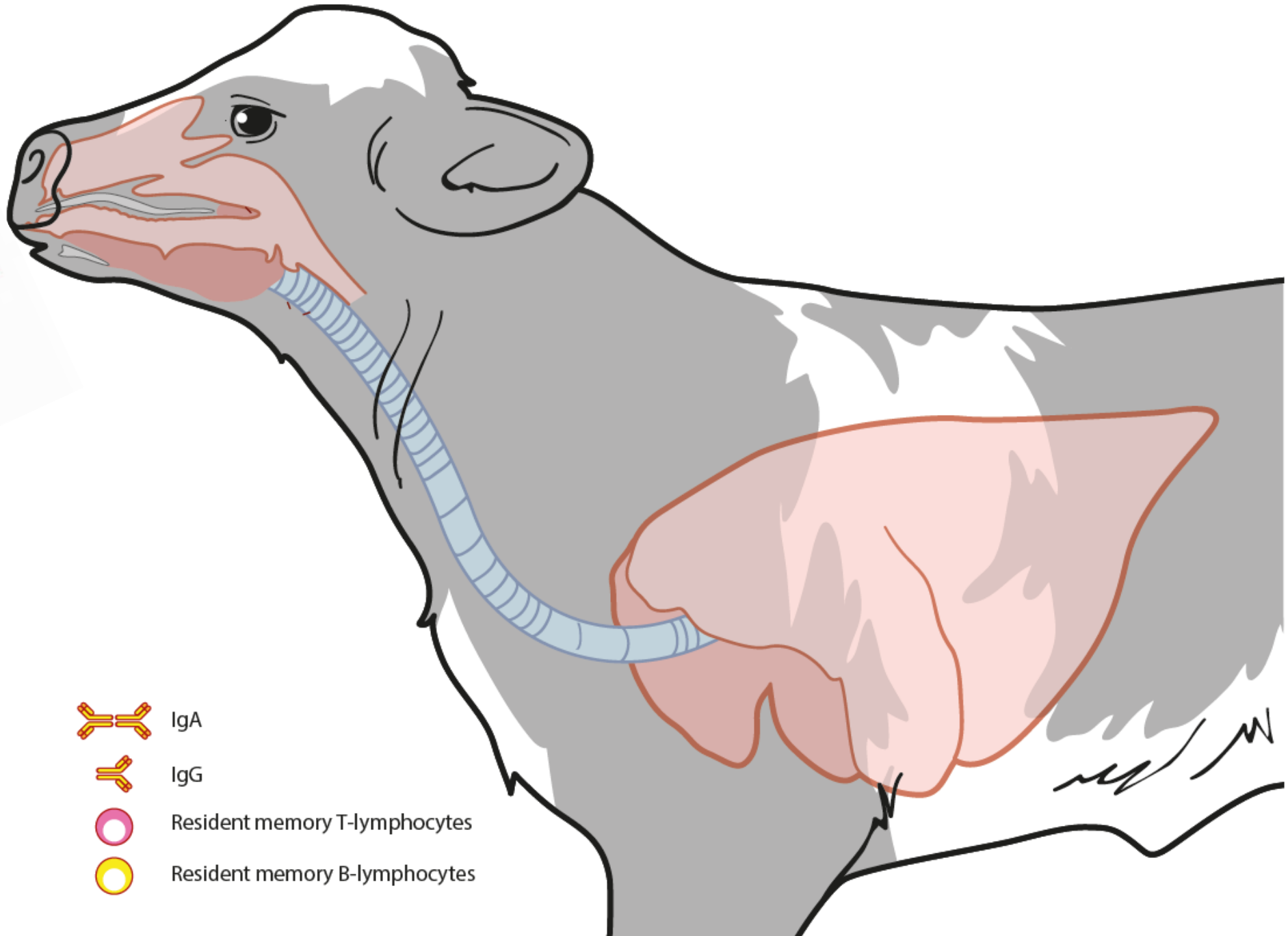
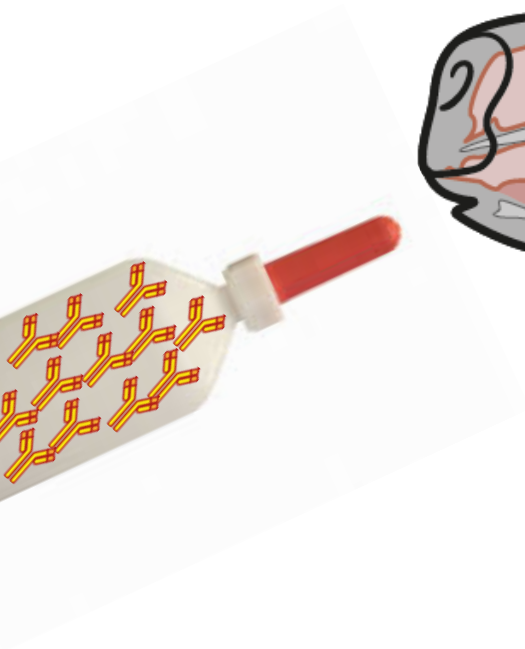
Abstract





In neonatal calves, maternal immunoglobulin (Ig) is transferred into respiratory secretion which contributes to protection against pathogens. The early predominance of IgG I in respiratory tract secretions is progressively reduced in favor of IgA by age but in the lower, bronchoalveolar system secreted IgG remains the dominant secreted Ig even in adulthood. The trans-epithelial transport of secretory IgA into mucosal secretions is carried out by the polymeric Ig receptor. However, the mechanism by which IgG crosses epithelial cells to provide defense on mucosal surfaces is still unknown. In order to investigate the possibility that the neonatal Fc receptor, FcRn is involved in this transport we have first analyzed the localization of this receptor in the upper and lower respiratory tracts.

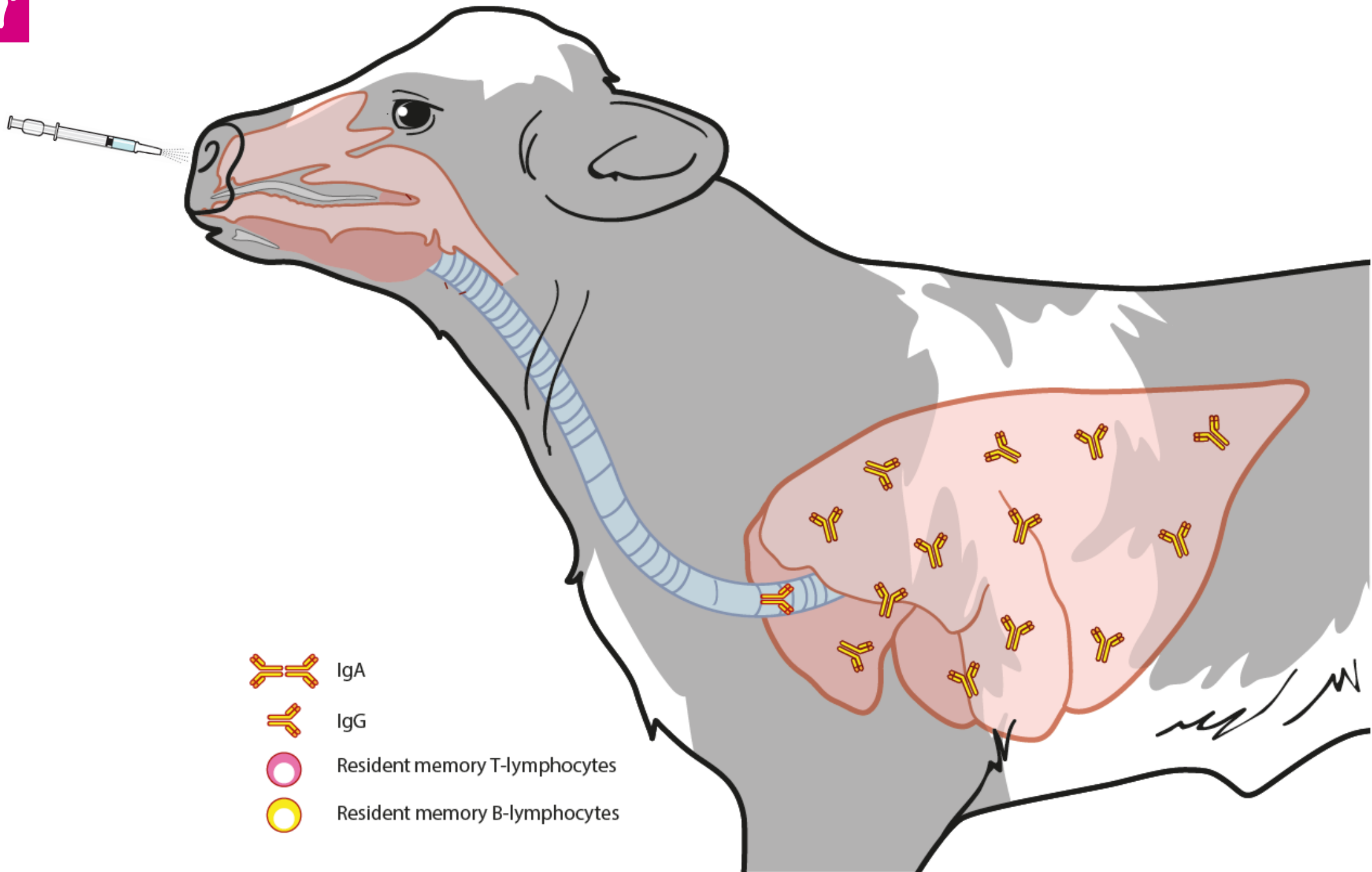
Consistent with the *in situ* hybridization data, immunohistochemistry showed undetectable expression in the tracheal epithelial cells, relatively weak expression in epithelial cells of the bronchi, apparent staining those lining the bronchioli and randomly scattered signal over the alveolar tissue. The bovine FcRn may thus play a role in IgG transport across mucosal epithelial barriers as a trafficking receptor and ensure IgG predominance in the lower respiratory tract.





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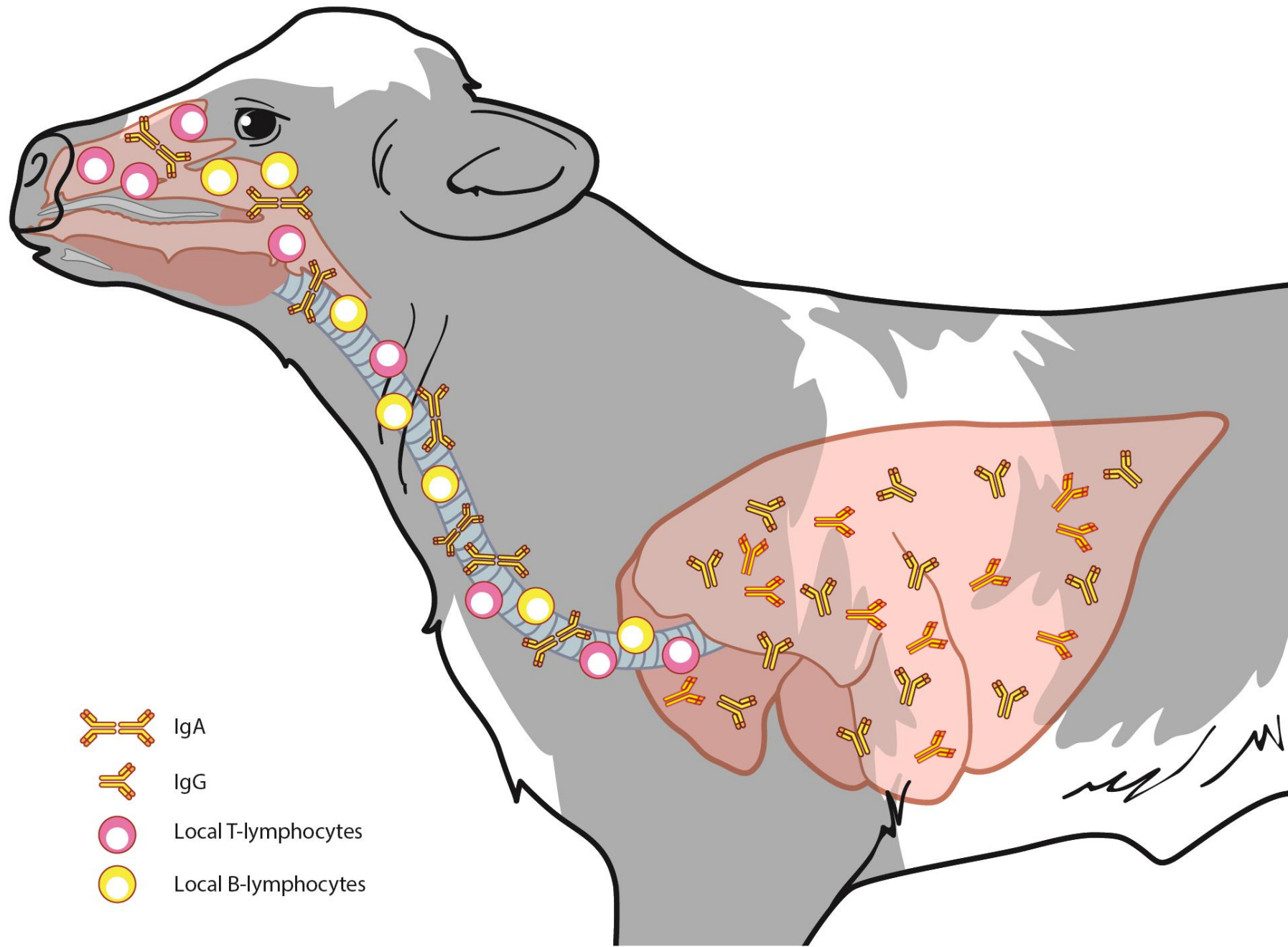
Keywords: Neonatal Fc receptor; Lung; Respiratory tract; IgG transport; Cow







-  IgA
-  IgG
-  Resident memory T-lymphocytes
-  Resident memory B-lymphocytes



-  IgA
-  IgG
-  Resident memory T-lymphocytes
-  Resident memory B-lymphocytes



-  IgA
-  IgG
-  Local T-lymphocytes
-  Local B-lymphocytes



Bovilis Nasalgen-C en invloed van maternale antistoffen

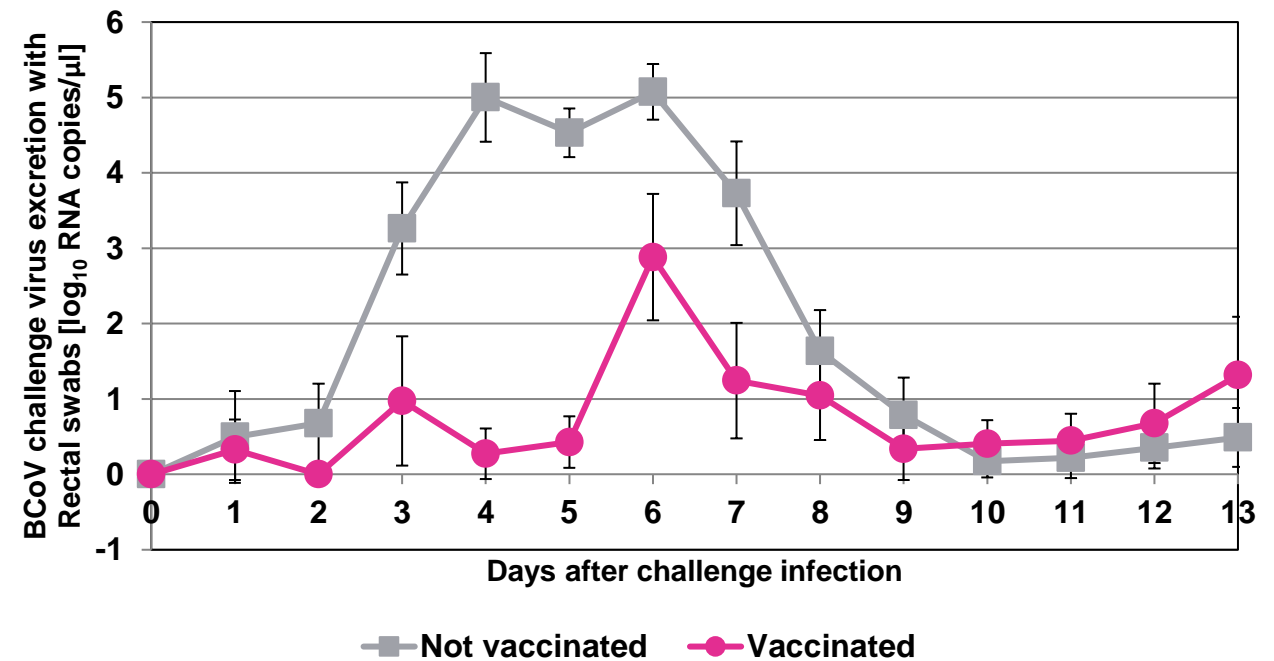
- Twaalf conventionele kalveren (tussen 5 en 8 dagen oud bij vaccinatie)
 - Groep A: niet gevaccineerd
 - Groep B: Bovilis Nasalgen-C intranasaal
- Aerosol challenge met BCV veld virus 3 weken na vaccinatie
- Dagelijkse opvolging van algemene, respiratoire, and enterische klinische symptomen
- Staalnames voor BCV :
 - Dagelijks nasale swabs
 - Dagelijks rectale swabs
 - Broncho-alveolaire lavage 3 dagen na challenge



Bovilis Nasalgen-C en invloed van maternale antistoffen

- Significante reductie van de hoeveelheid BCoV in
 - Nasale swabs ($p < 0.02$)
 - BALs ($p < 0.04$)
 - Rectale swabs ($p < 0.04$)

Gemiddeld aantal BCoV RNA copies in rectale swabs





Eigenschappen van het vaccin: Overzicht

- Eerste respiratoir corona virus vaccin voor runderen
- Levend verzwakte BCoV stam CA25
- 2 ml per dosis in één neusgat
- Toediening met of zonder nozzle
- Vanaf de dag van de geboorte
- Snelle aanvang van de immuniteit (5 days)
- Lange duur van de immuniteit (12 weeks)
- Stimulatie van de aspecifieke aangeboren immuniteit
- Werkzaam in aanwezigheid van maternale antistoffen
- Na reconstitutie 24 uur houdbaar
- Gelijktijdig toe te dienen met Bovilis INtranasal RSP live

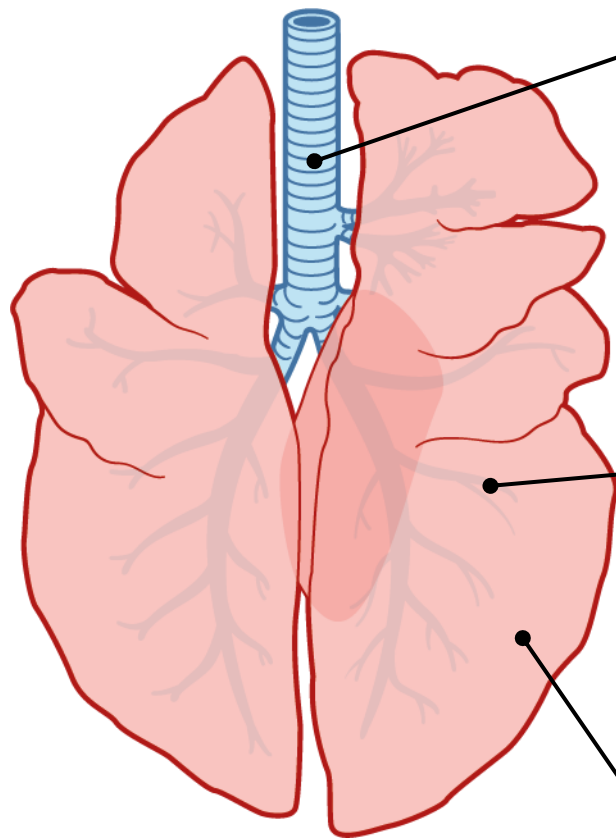




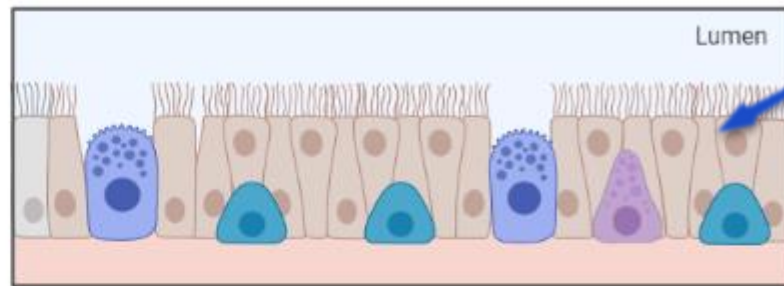
Eigenschappen van het vaccin: Overzicht

- Eerste respiratoir corona virus vaccin voor runderen
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- Toediening
- Vanaf de
- Snelle aa
- Lange du
- Stimulat
- Werkzaa
- Na recor
- Gelijktijdig toe te dienen met Bovilis INtranasal RSP live

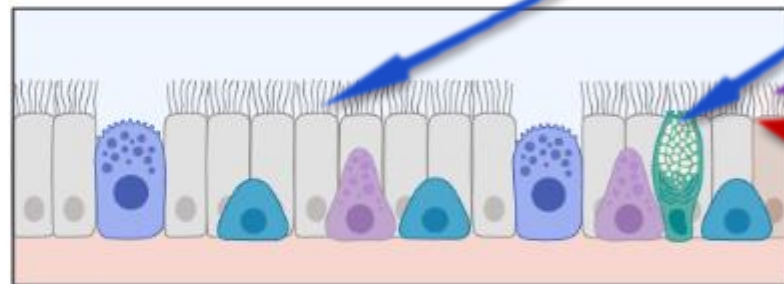
Gelijktijdig toe te dienen met Bovilis INtranasal RSP live



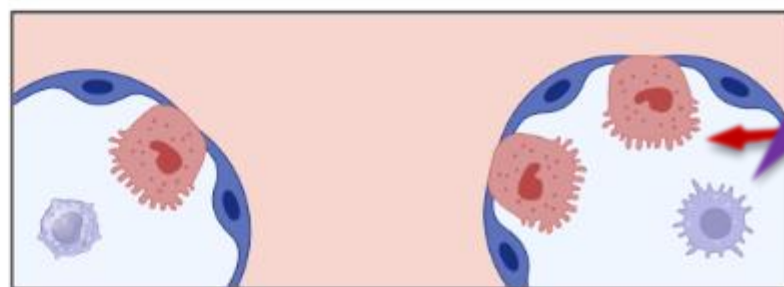
Trachea, Bronchi



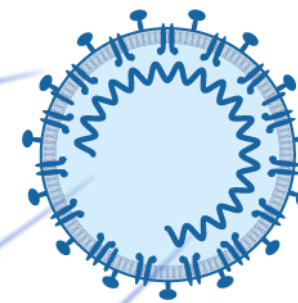
Bronchioles to alveoli



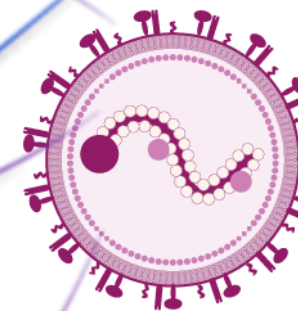
Alveoli



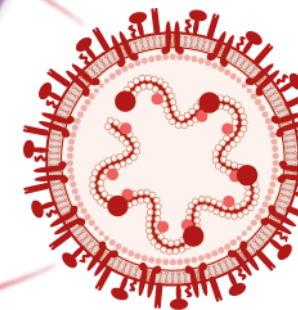
- Ciliated cell
- Club cell
- Goblet cell
- Basal cell
- Alveolar macrophage
- PNEC
- Type I pneumocyte
- Type II pneumocyte



BCoV



PI-3



BRSV



Gelijktijdige toediening van Bovilis Nasalgen-C en Bovilis INtranasal RSP Live

- Twee studies bij colostrum vrije kalveren (6 dieren per groep, leeftijd 4 – 9 dagen bij vaccinatie):
 - Groep A: niet gevaccineerd.
 - Group B: IN vaccinatie met Bovilis Nasalgen-C (studie 1) of Bovilis® INtranasal RSP® Live (studie 2).
 - Group C: IN vaccinatie gelijktijdig met Bovilis Nasalgen-C en Bovilis® INtranasal RSP® Live
- Studie 1: BCV challenge 3 weken na vaccinatie.
- Studie 2: opeenvolgende challenge met PI3 (1 week na vaccinatie) en BRSV (3 weken na vaccinatie).

Observations	Study 1	Study 2
Daily observation for general, respiratory and enteric clinical signs	yes	yes
Lung lesions	no	yes

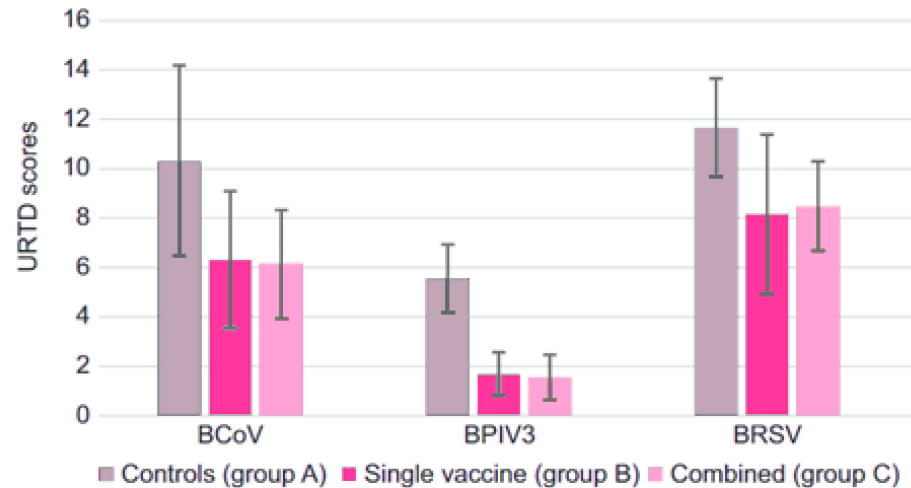
Sampling and testing for viral load after challenge	Study 1	Study 2
Daily nasal swabs	yes	yes
Daily rectal swabs	yes	no
Broncho-alveolar lavage	4 days post challenge	5 days post challenge (only BRSV)



Gelijktijdige toediening van Bovilis Nasalgen-C en Bovilis INtranasal RSP Live

Bovenste luchtweg score (URTD) lager bij gevaccineerde dieren

FIGURE 1. Scores of upper respiratory tract disease (URTD) after challenge infection three (BCoV, study 1), one (BPIV3, study 2) and three (BRSV, study 2) weeks post vaccination.

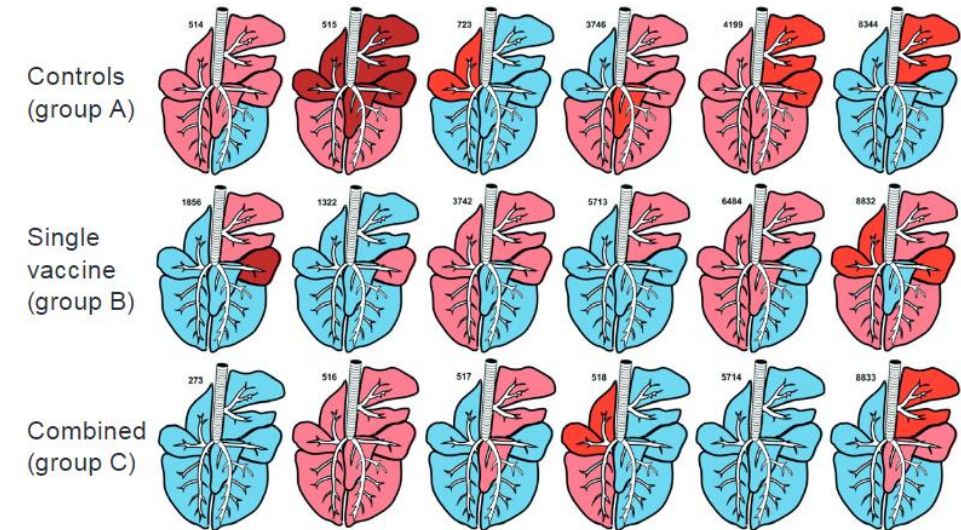


The columns represent the average value per group and the bars mark the standard error of the mean.

Long consolidatie na BRSV challenge aanzienlijk lager in de gevaccineerde groepen

FIGURE 2. Extent of gross pneumonic consolidation 14 days post BRSV challenge expressed as percentage affected area per lung lobe.

-	0
+	<5
++	>5 <10
+++	>10





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Eigenschappen van het vaccin: Overzicht

- Eerste respiratoir corona virus vaccin voor runderen
- Levend vaccin
- 2 ml per runder
- Toediening via neusgat
- Vanaf de geboorte
- Snelle aanpak
- Lange duur
- Stimulerend effect
- Werkzaam tegen
- Na record
- Gelijktijdig

2ml één neusgat

Met of zonder nozzle

24 uur houdbaar na oplossen

Bescherming na 5 dagen gedurende 12 weken





- ✓ **EERSTE RESPIRATOIR CORONAVIRUS VACCIN**
- ✓ **ÉÉN NEUSGAT 2ml**
- ✓ **MET OF ZONDER NOZZLE**
- ✓ **VANAF DE GEBOORTE**
- ✓ **GELIJKTJDIG MET BOVILIS INTRANASAL RSP LIVE**
- ✓ **24 UUR HOUDBAAR NA OPLOSSEN**