The effects of maternal antibody and stress on responses to "Yersiniavax" in red deer calves

C Mackintosh, F Griffin and P Wilson

Abstract

Three trials were undertaken to investigate the effects of maternal antibody and the stress of weaning on the serological response of red deer calves to vaccination with "Yersiniavax"

Trial 1 measured the level of antibodies to *Yersinia pseudotuberculosis* antigens in unvaccinated red deer calves from 2 days to 12 weeks of age The results showed that there was a typical exponential decay rate for antibodies to somatic OI, OII and OIII and virulence antigens These were maximal in 2-day-old deer calves, they were still detectable at 2, 4 and 8 weeks of age but they had fallen to baseline levels by 12 weeks of age

Trial 2 compared the responses of four groups of red deer calves, born to mixed age hinds, that received their first dose of "Yersiniavax" at either 6, 9, 12 or 15 weeks of age and their second dose 3 weeks later. It showed that the group vaccinated initially at 12 weeks of age gave adequate primary and secondary responses to "Yersiniavax", while groups receiving their first dose at 6 or 9 weeks of age gave poorer primary and boost responses, especially to the somatic antigens There was a correlation between the presence of colostral antibody and poor response to vaccine

Trial 3 compared the responses of two groups of yearling's calves that received their first dose of "Yersiniavax" at either 3 weeks before weaning (when 9 weeks of age) or at weaning (when 12 weeks of age), and their second dose 3 weeks later Both groups gave poor responses to the somatic OI and OII antigens, but the group vaccinated at weaning gave slightly higher responses to somatic OIII and the virulence antigens (Crude V and Pure V)

These results strongly suggest that there is interference between circulating colostral antibodies in red deer calves and vaccination with "Yersiniavax" This effect was greatest with the somatic antigens, which are lipopolysaccharide and thus less immunogenic than the virulence antigens, which are proteins The levels of maternal antibody were minimal by 12 weeks of age Based on these results the authors recommend that the first dose of "Yersiniavax" is given to red deer at least 12 weeks of age to maximise the primary response to vaccination Weaning at the time of vaccination at 12 weeks of age did not appear to significantly reduce the response to vaccination

Farmers should be reminded that, although the bulk of calves are born from mid November to early December and can be vaccinated in early March, the vaccination of the calves born in mid to late December, especially yearling's calves, should be delayed till late March, when they are over 12 weeks old, if optimum protection is to be achieved

Introduction

Yersiniosis, caused by *Y. pseudotuberculosis,* is the most common bacterial disease of young red deer on deer farms in New Zealand. The organism is carried by a wide range of wildlife and domestic animals Almost all young farmed deer are exposed in their first autumn/winter and the majority experience subclinical infection However, concurrent stressors such as underfeeding, cold wet weather, storms or transport can precipitate clinical disease Outbreaks of disease can affect >20% of mobs of weaners (Mackintosh et al., 1984a 1984b, Mackintosh, 1992) The likelihood of outbreaks can be reduced by good husbandry, adequate feeding, provision of shelter and minimising stress A vaccine, "Yersiniavax", has been developed to further minimize the risk of serious outbreaks "Yersiniavax", is a killed bacterin, that contains formalin-killed cultures of the three common strains of *Y. pseudotuberculosis* (serotypes I, II and III) plus DEAE dextran adjuvant (Mackintosh et al., 1986, 1990, 1991, 1992, 1998).

It is estimated that between a quarter and a half of the weaner deer on New Zealand deer farms are immunised with a "Yersiniavax" annually It is essential that the timing and manner of vaccination of young deer with "Yersiniavax" is optimal to achieve the greatest immunological response, thereby providing the best protection Recently evidence of outbreaks of yersiniosis in vaccinated deer herds has been reviewed (Wilson *et al* 1999)

It must be acknowledged that vaccines against bacterial diseases are unlikely ever to be effective in reducing morbidity and mortality to zero. There are a number of factors that can reduce the immunological response of young animals to vaccination. These include the presence of maternal antibody and the timing of vaccination in relation to "stressful" procedures such as weaning. It is desirable to vaccinate deer calves as early as practicable in the late summer to ensure that they have adequate protection before the autumn/winter, when the maximum challenge with yersiniosis is expected. However, there is a potential problem with vaccinating at too young an age, when circulating levels of maternally derived antibodies may still be present and interfere with the response to the vaccine.

It is also convenient to vaccinate deer calves at the times of year when they are being yarded for other management reasons, for example at weaning, weighing, tagging or anthelmintic treatment However, these can be stressful procedures that may diminish the immunological response of deer to vaccination, where farm and animal management is not optimal, and deer are not adapted to handling. Immunosuppression due to stress is more likely to reduce the response to novel antigens, which occurs at primary immunisation, than to booster vaccination. It is believed that the most stressful management procedure for deer calves is weaning and therefore this practice may have potentially the most profound effect on the immunological response to vaccination

The current recommendation is that the first vaccination should be given in late February or early March and the booster vaccination given 3 to 6 weeks later There are many farmers who would prefer to give the first dose in early February and the second dose in late February or early March prior to weaning, in order to minimise the possible stressful affects of weaning on vaccination However, it was not known to what extent maternal antibody interferes with immunisation. **Trials 1 and 2** were designed to investigate this question The effects of weaning stress on the response of deer calves to "Yersiniavax" have also not been measured and **Trial 3** was designed to investigate these effects

Materials and Methods

Vaccine used ""Yersiniavax"", Batch No 0 001 2, Expiry date 01 November 00

Vaccination The vaccine was administered via a vaccination syringe set at 2 ml and injected subcutaneously on the right side of the neck by one operator

Trial 1: Eighteen tame red deer hinds and their calves were closely monitored as part of a study of the effects of nutrition in late pregnancy on the growth rates of the calves in their first 12 weeks of life This allowed regular access to the hinds and their calves for sampling. Blood samples were collected from the calves from 2 days to 12 weeks of age and they were tested for antibodies to *Y pseudotuberculosis* somatic I, II and III and virulence antigens using an ELISA (Hibma and Griffin, 1988, Griffin et al , 1991)

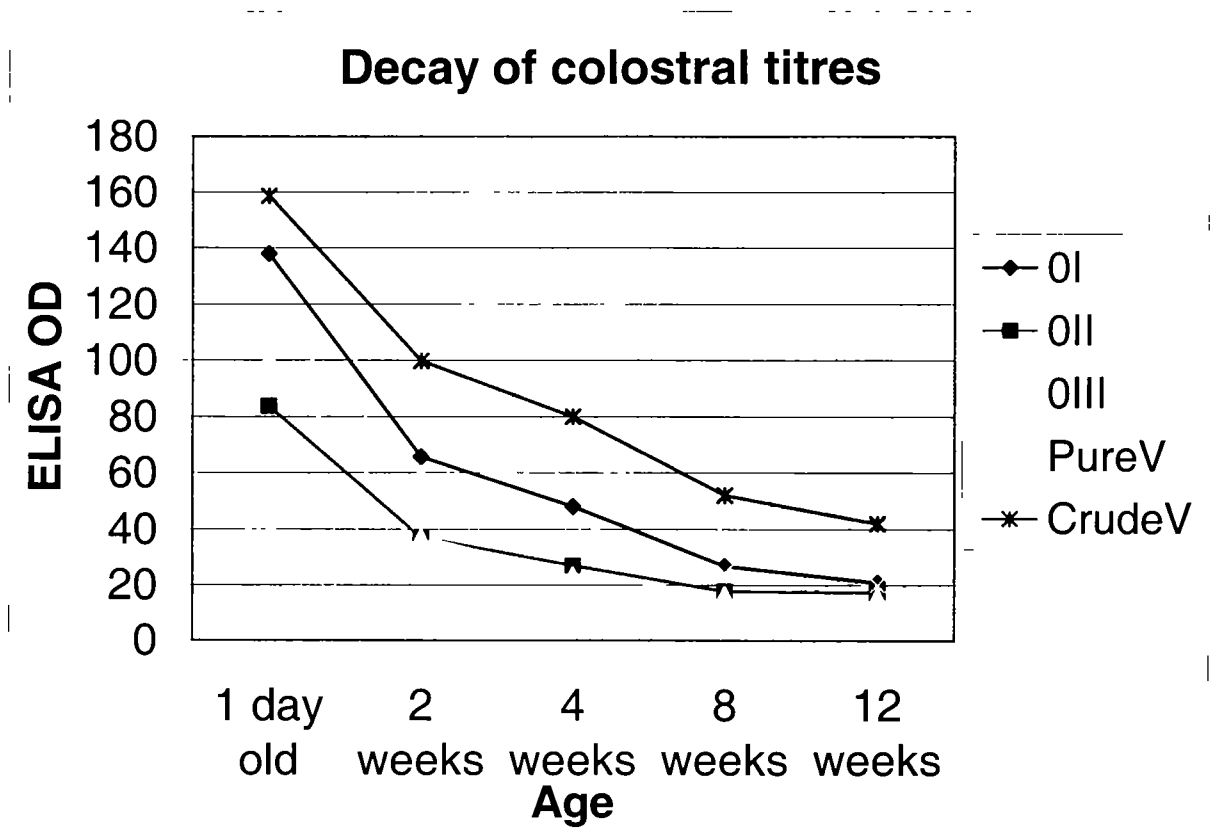
Trial 2: The calves from a group of adult red hinds were tagged at birth and 60 of them that were born over a 3 week period from November 17 to December 7, 1999 were used in this study. Most of these calves (51/60) were born over a 2 week period, Nov 20 to Dec 3 They were stratified by birth date and randomly allocated to four groups of 15 animals They received two 2 ml doses of "Yersiniavax" 3 weeks apart at the following mean ages· Group A at 6 and 9 weeks of age, Group B at 9 and 12 weeks of age, Group C at 12 and 15 weeks of age, and Group D at 15 and 18 weeks of age The calves were weaned at 13 weeks of age and received a dose of 5-in-1 clostridial vaccine at 14 weeks of age Blood samples were taken at 6, 9, 12, 15, and 18 weeks of age and tested for antibodies.

Trial 3: The calves from a group of yearling hinds were tagged at birth and 30 born over a 3 week period from December 2 to 22, 1999 were used in this study They were stratified by birth date and randomly allocated to two groups of 15 animals Group E received their first dose of "Yersiniavax" 3 weeks before weaning, when 9 weeks old, and their second dose at weaning Group F received their first dose of "Yersiniavax" at weaning, when 12 weeks old, and their second dose 3 weeks later Blood samples taken at 9, 12, 15, and 18 weeks of age were tested for antibodies

Results

Trial 1: The serological results showed that there was a typical exponential decay rate for antibodies to somatic OI, OII and OIII and virulence antigens (see Fig 1) These were maximal in 2-day-old deer calves, they were still detectable at 2, 4 and 8 weeks of age, but by 12 weeks of age they had fallen to base-line levels of around 20 OD units for OI, OII, OIII and Pure V and 40 OD units for Crude V

Fig. 1: Decay of red deer calves' colostral titres to *Y pseudotuberculosis* OI, OII and OIII somatic and "Pure V" and "Crude V" virulence antigens, expressed in optical density (OD) units



Trial 2: The serological results show that the unvaccinated deer had mean titres well above baseline levels (~20 OD units for OI, OII, OIII and Pure V and ~40 for Crude V) at 6 and 9 weeks of age (see Table 1) Base line levels were reached by 12 weeks of age

Table 1 Mean ELISA OD values for unvaccinated deer at 6, 9, 12 and 15 weeks of age for the *Y pseudotuberculosis* antigens OI, OII, OIII, Pure V and Crude V

	Weeks of age			
	6 weeks	9 weeks	12 weeks	15 weeks
OI	35	22	19	19
OII	27	20	20	17
OIII	26	22	17	19
Pure V	38	23	21	21
Crude V	82	45	35	36

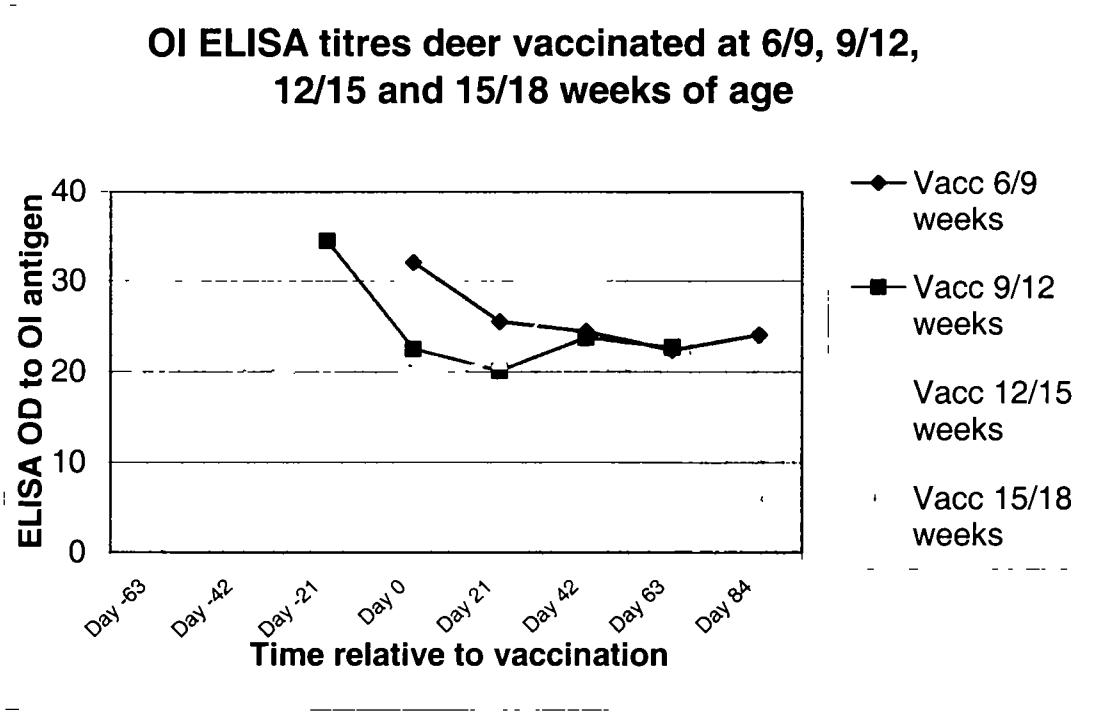
The results (see Table 2) show that Group C calves vaccinated at 12 and 15 weeks of age gave typically small primary responses seen 21 days later, but good secondary responses seen 21 days after boosting (Day 42) The Group D calves vaccinated at 15 and 18 weeks of age gave a similar primary response to Group C However, the Group A calves, vaccinated at 6 and 9 weeks of age, had significant levels of colostral antibody present at the time of vaccination and gave relatively poor primary and boost responses, especially to somatic antigens The Group A titres for the somatic antigens declined between Day 0 and Day 21 and either declined or rose slightly between Day 21 and Day 42 The titres to the virulence antigens declined from Day 0 to Day 21 and rose significantly less from Day 21 to Day 42 than the Group C deer The Group B calves vaccinated at 9 and 12 weeks of age also had detectable levels of colostral antibody and gave similarly poor primary and boost responses to somatic OI and OII antigens Group A animals had the lowest responses to the virulence antigens and Group B animals were intermediate between Groups A and C The ELISA values for OIII antigen were low in all four groups

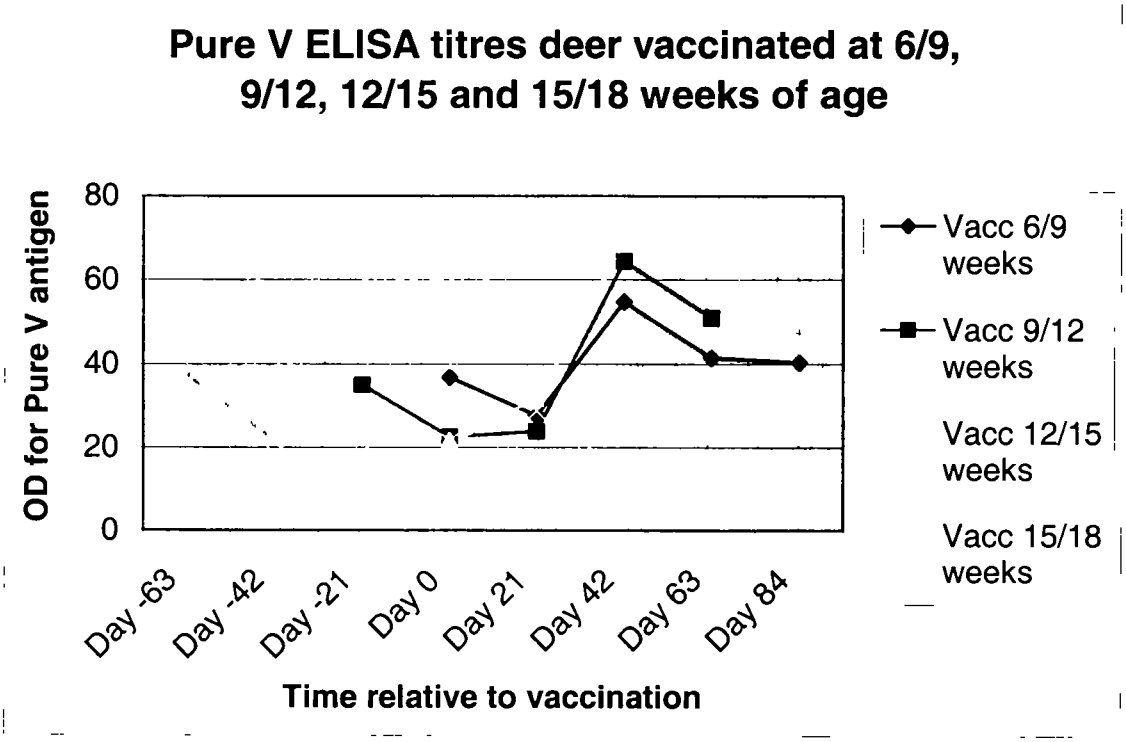
Table 2 ELISA OD values for the three somatic antigens OI, OII and OIII and Crude V and Pure V virulence antigens for the four groups of calves (A, B, C and D), presented in columns with respect to days before and after primary vaccination (Day 0) and boosting (Day 21)

Antigen	Group	Vacc. wks	Day -63	Day -42	Day -21	Prime Day 0	Boost Day 21	Peak Day 42	Day 63	Day 84
OI	A	6 and 9				32 1	25 5	24 4	22 4	24 0
	B	9 and 12			34 5	22 5	20 1	23 8	22 7	
	C	12 and 15		36 6	23 5	19 5	21 2	30 6		
	D	15 and 18	35 2	20 6	19 4	18 6	21 1			
OII	A	6 and 9				25 8	22 4	25 1	20 9	25 4
	B	9 and 12			27 1	19 6	19 7	23 8	23 9	
	C	12 and 15		29 2	20 7	19 6	20 6	31.9		
	D	15 and 18	24 9	18 9	20 3	16 8	21 9			
OIII	A	6 and 9				25 1	24 1	21 4	21 5	20 2
	B	9 and 12			26 5	21 3	17 3	21 7	20 6	
	C	12 and 15		27 5	23 0	16 8	20 8	21 0		
	D	15 and 18	24 2	20 3	17 4	19 2	20 5			
Crude V	A	6 and 9				76 7	73 2	105 5	89 0	81 5
	B	9 and 12			83 8	44 9	54 5	122 7	101 7	
	C	12 and 15		92 4	49 5	35 4	71 0	127 7		
	D	15 and 18	73 9	41 4	35 1	36 3	47 3			
Pure V	A	6 and 9				36 8	27 6	54 8	41 5	40 4
	B	9 and 12			35 0	22 6	23 8	64 3	51 1	
	C	12 and 15		43 3	24 3	21 7	31 6	68 8		
	D	15 and 18	37 4	21 7	21 2	21 5	28 8			

Mean OD values for somatic OI and pure V responses are presented in figures 2 and 3, respectively

Figs. 2 and 3: Mean ELISA values of the four groups of calves to somatic OI antigen and Pure V antigen expressed in OD units and graphed with respect to the time of the blood sampling occasions before and after the first vaccination (Day 0) and the second vaccination (Day 21)





Trial 3: Both groups gave poor responses to the somatic OI and OII antigens, but Group F, vaccinated at weaning, gave slightly higher responses to somatic OIII and the virulence antigens (see Table 3). Group F, vaccinated at weaning, had similar responses to the Group C in Trial 2 that were also vaccinated at 12 weeks of age but were not weaned until a week later

Table 3 ELISA OD values for the three somatic antigens OI, OII and OIII and Crude V and Pure V virulence antigens for the two groups of calves (E and F), presented in columns with respect to days before and after primary vaccination (Day 0) and boosting (Day 21)

					Prime	Boost		
	GROUP	Vaccination	Age at vaccination	Day -21	Day 0	Day 21	Day 42	Day 63
OI	E	3 wks pre-weaning	9 and 12 weeks		26.7	24 7	26 6	21 7
	F	weaning	12 and 15 weeks	23 6	21 1	23 3	25 5	
OII	E	3 wks pre-weaning	9 and 12 weeks		23 6	27 7	25 4	23 2
	F	weaning	12 and 15 weeks	27 2	26 5	23 1	28.4	
OIII	E	3 wks pre-weaning	9 and 12 weeks		17 4	21 6	29 8	25 3
	F	weaning	12 and 15 weeks	18 6	19 6	24 8	37 3	
Crude V	E	3 wks pre-weaning	9 and 12 weeks		61 3	89 4	126 3	96 4
	F	weaning	12 and 15 weeks	57 2	53 6	87 2	132 4	
Pure V	E	3 wks pre-weaning	9 and 12 weeks		25 2	33 2	59.8	44 2
	F	weaning	12 and 15 weeks	25 3	27 4	30 6	69 3	

Discussion

The correlation between the presence of colostral antibody and poor response to vaccine suggests cause and effect, although it is possible that there could be some effect of age *per se* The results strongly suggest that there is interference between circulating colostral antibodies in red deer calves and response to vaccination with "Yersiniavax" This effect was greatest with the somatic antigens, which are lipopolysaccharide and thus less immunogenic than the virulence antigens, which are proteins. The levels of maternal antibody were minimal by 12 weeks of age Based on these results the authors recommend that to maximise the primary response to vaccination, the first dose of "Yersiniavax" is given to red deer at least 12 weeks old. Weaning at the time of vaccination at 12 weeks of age did not appear to significantly reduce the response to vaccination

It is not uncommon to get interference with vaccination in animals less than three months old, due to the presence of maternal antibody, although there is some variability in the magnitude of the effect between vaccines and species For example the response to vaccination with clostridial vaccines is stronger in calves vaccinated at 3-4 months of age compared with those vaccinated at 1-2 months of age (Schipper et al , 1978) In dogs, maternal antibody interferes with distemper vaccination, but the effect is less with high titre vaccines and the maternal antibody wanes quicker in faster growing dogs (Chappuis, 1995). There is a strong association between the level of maternal antibody and the degree of interference with rabies vaccination in hamsters (Bernard and Ito, 2000)

Farmers should remember that, although the bulk of calves are born from mid November to early December to mature hinds (median usually Nov 26-Dec4), the calves of yearling hinds tend to be born about 2 weeks later. Therefore, while most calves could be vaccinated in early to mid March and achieve optimum antibody response, the vaccination of the calves born in mid to late December, especially yearling's calves, should be delayed till late March when they are over 12 weeks old. As a practical guide, calves less than about 30 kg are likely to be younger than 12 weeks of age

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