2.11 ± 1.00 for CVDLS dairy breeds (r=0.31) and 3.43 ± 1.50 for beef breeds (r=0.58). Both the SH ratios were significantly greater than the CVDLS dairy breed ratio.

Based on these results, breed and source location should be taken into account when interpreting Se content. Fetal liver Se content should only be used as a screening test and combined with whole blood Se content to make judgements about herd Se status.

Pasteurella haemolytica Vaccines and Their Effectiveness

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Abstract

Pasteurella haemolytica **biotype A, serotype 1 (Ph1) bacterins and bacterin-toxoids formulated in oil adjuvants induce protective immune responses approaching those induced by virulent Ph1. In comparison, aluminum hydroxide based adjuvants induce lower protective and serological immune responses. Bacterin-toxoid vaccines formulated in water-in-oil adjuvants induced high levels of protective immunity against transthoracic and field challenge. Bacterin-toxoid with oil-in-water adjuvant induced high protective immunity against transthoracic challenge and was superior to Ph1 bacterin-toxoid with $Al(OH)_3$ adjuvant. Reactions at the point of inoculation vary with formulations, are usually inapparent if intramuscular, manageable if subcutaneous and disappear with time.**

Introduction

The effectiveness of Ph1 vaccines is determined by antigen content and the presentation of these antigens to the bovine immune system. Of the methods of antigen presentation for stimulating immune responses oil adjuvant formulations have been very effective. Here the effectiveness of oil adjuvants for stimulating protective immune responses to Ph1 will be presented with a discussion of available direct comparisons to other adjuvants.

The newer USDA licensed Ph1 vaccines induce protective immune responses in calves as demonstrated by experimental challenge. Consistent protection in field trials and in veterinary practice, however, has not always followed. Reasons for this lack of consistent protection in field challenge studies include herd variation in susceptibility, differences in potential pathogenic flora in source herds, superimposed infections by bacteria other than Ph1 and uncontrolled variations in stress levels. Also contributing to this inconsistency is the use of vaccines too late in the infection and disease process and use of vaccines that induce only marginal protection.

Inoculation of healthy animals with fully pathogenic Ph1 results in solid protective immunity and is typically the "gold standard" to which the immune responses to Ph1 vaccines are compared. Loan and Purdy reported on the effectiveness of Ph1 bacterin-toxoids with oil adjuvants for the prevention of *Pasteurella*-induced pneumonia and bovine respiratory disease complex (BRDC) in 1986.[1] Such bacterin toxoids gave significant protection in both experimental and field challenge studies. This led to a reevaluation of oil adjuvants in Ph1 vaccines and to additional reports on the effectiveness of water-in-oil adjuvant formulations.[2,3] In subsequent studies by Loan and Tigges[4] purified Ph1 capsular polysaccharide in oil adjuvant stimulated higher titers of IgG1 and IgG2 compared to the same antigen with $Al(OH)_3$ adjuvant, suggesting a possible mechanism for the enhanced stimulation of immunity by oil adjuvants. Other studies also indicated the superior enhancing effect of oil adjuvants compared to other commonly used adjuvants on the immune responses of calves to Ph1 antigens. Such antibody responses may be higher than those to fully virulent Ph1.[2]

In comparisons of Ph1 bacterins with oil adjuvants to live Ph1, bacterins induced protection approximately equivalent to that induced by high doses of attenuated live *P. haemolytica* vaccine[5]. In a broader comparison of vaccine efficacy,[2] bacterin with oil adjuvant had the same protective efficacy as live *P. haemolytica* when protection was measured by experimental challenge. In the same study, aluminum hydroxide in gel and trehalose dimycolate (in oil) did not stimulate protective immune responses. Oil adjuvants have been used also in combination bacterins containing Ph1[6].

Oil adjuvants have been studied in the bovine animal using antigens other than those of Ph1. Vaccines formulated with oil adjuvants stimulated higher antibody responses and significantly greater protection against foot and mouth disease when compared to the more traditional vaccines with alum and aluminum hydroxide with or without added saponin or quil A.[7,8]

Almost without exception, vaccines with oil adjuvants stimulate higher antibody titers and/or higher levels of protection against other diseases in cattle where these have been tested.[7]

Methods

Protection studies at Texas A&M University were conducted by experimental challenge of Ph1 immunity by transthoracic challenge.[9] Field challenge of immunity was via the "Tennessee-Texas Connection" wherein stocker-feeder calves were purchased in Eastern Tennessee, placed in a simulated salebarn market situation, intermixed with other calves and shipped 1100 miles to an experimental feedlot in Bushland, Texas.[1] Time in the simulated market system was approximately 6 days.

Results and Discussion

Ph1 bacterin toxoids with water-in-oil adjuvants induced 80 to 100% protection against experimental transthoracic challenge.(Table 1) A bacterin-toxoid formulated with oil-in-water adjuvant induced 100% protection compared to 60% protection induced by the same bacterin-toxoid with $Al(OH)_3$ adjuvant. In field studies, Ph1 bacterin-toxoids with water-in-oil adjuvants decreased BRDC morbidity by 35% to 70% and treatment days 50% to 80%.(Table 2) Sick days were significantly reduced in 4 of the 6 trials. In one other trial no calves developed BRDC; in the remaining trial early deaths from BRDC in the nonvaccinated group prevented a valid comparison. Where no BRDC occurred, vaccination reduced the rate of colonization of the nasal passages by Ph1 significantly. This could be important for interrupting the infection cycle and for clearing cow-calf herds of Ph1 nasal carrier status. In 274 vaccinated calves in 5 trials there were no deaths due to BRDC. In nonvaccinated controls there were death losses in 3 trials. This lends support to anecdotal reports from practitioners concerning the beneficial effect of vaccination for reducing death losses.

The mechanism for stimulation of protective immunity and reduction in nasal colonization attributable to the use of bacterin-toxoids with oil adjuvants is unknown at this time. Several attributes of Ph1 vaccines with oil adjuvants which may contribute to this protection include the observed enhanced overall antibody responses to Ph1 antigens[2] and the high relative stimulation of IgG1 antibody production.[4]

Some of the less popular features of vaccines with oil adjuvants include difficulties in injection and reactions at the injection sites. Newer oil adjuvant formulations, however, are easy to inject, induce reactions at the site of injection comparable to other adjuvants, are manageable by the industry, and disappear with time.[7]

Table 1. Protection Against Transthoracic Challenge by Differing Formulations of *P. haemolytica* Bacterin-Toxoids

Vaccination Status	Adjuvant and Route	No. of Calves	Challenge Result	Significance*
V(2X)	W/O IM	8	58 cm^3**	p<.05
NV		8	831cm^3**	
V(2X)	W/O IM	5	67 cm^3**	p<.05
NV		5	234cm^3**	
V(2X)	W/O IM	8	8⁺	p<.001
NV		8	1⁺	
V(1X)	W/O SC	5	5⁺	p<.05
NV⁺⁺		5	1⁺	
V(2X)	O/W IM	5	5⁺	p<.05
V(2X)	$AlOH_3$IM	5	3⁺	
NV⁺⁺		5	1⁺	

V(1X)- vaccinated 1 time; V(2X)- vaccinated 2 times; NV- not vaccinated. W/O- water-in- oil; O/W- oil in water. IM- intramuscular; SC- subcutaneous. *Significant difference compared to nonvaccinates. **Average lung lesion volume. ⁺Surviving calves. ⁺⁺Survivors had clinical signs.

Table 2. Protection Against Field Challenge by Differing Formulations of *P. haemolytica* Bacterins

Vaccination Status	Adjuvant and Route	Number of Calves	Percent Morbidity	Percent Mortality	Sick Days
V	W/O IM	50	22	0	36*
NV		50	34	2	72
V	W/O IM	23	30**	0*	24*
NV		23	74	17	75
V	W/O IM	50	6*	0	9**
NV		50	20	0	45
V	W/O SC	50	4	0	18
NV		50	8	4	16⁺
V	W/O SC	51⁺⁺	0	0	—
NV		50	0	0	—
V	W/O IM	50	20**	0	64**
NV		50	46	0	134

V- vaccinated twice; NV- not vaccinated. W/O- water-in-oil; O/W- oil-in-water. IM-intramuscular; SC- subcutaneous *Significantly different than nonvaccinates p<.05.

**Significantly different than nonvaccinates p<.01. ⁺Deaths in nonvaccinates invalidated comparison. ⁺⁺*P. haemolytica* isolations from nasal cavity reduced, 11 vs. 37 (p<.05)

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What's Going on in Bovine Viral Vaccines: Do Both Killed and Modified Live Vaccines Induce Cell Mediated Immunity?

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The spectrum of immunity from inactivated bovine viral vaccines has often been discounted because of the lack of a cell mediated response. With the advent of newer adjuvants, the effect of an inactivated BRSV, BVDV PI3, IBR vaccine (Vira Shield™ 5: Grand Laboratories, Freeman, SD) on cell mediated and cytotoxic T cell response against IBR and BRSV was measured. Our results indicated that cattle vaccinated with an inactivated vaccine mounted and maintained a cellular proliferative response against both viruses at all time points measured up to 9 months post vaccination and a cytotoxic T cell response for 3 months against BRSV and for 4 months against IBR post vaccination. Studies are ongoing on the long term effect of this immune response on a sequential challenge with IBR, BRSV and BVDV. The efficacy of this immune response on protection against disease and virus shedding will be discussed.