Efficacy of Bovine Papilloma Virus Vaccination in Preventing Papillomas in Yearling Beef Bulls

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Cutaneous papillomas or warts are common lesions in young cattle. They usually occur in young animals (also on teats of mature cattle) and are white or tan firm protruding masses with a dry horny surface. They vary in size from I mm to 500 mm and may be single or multiple.[1] Species-specific papilloma viruses (subgroup of papova virus) are responsible for causing these warts. There are at least six BPV strains, designated BPV- I through BPV-6 and there are probably many more strains. These strains of warts have been classified as to the usual site of the lesions and the wart appearance but the authors admit that prediction of virus strain based on these characteristics is quite tentative.[2]

Warts are usually small benign growths that appear on young animals under 2 years of age, persist for 3 to 12 months, and then spontaneously regress without causing clinical signs (other than a blemish). In cattle warts on the teats, penis, or interdigital skin or in the alimentary tract have been reported to produce clinical signs of pain or occlusion. Occasionally individuals with defective cellular immunity may develop multiple extremely large warts that may result in weight loss.[1]

Fibropapillomas also occur on the bovine penis, sometimes affecting the bulls' breeding soundness and health.[3] These lesions are also reported to be associated with at least one strain of the bovine papilloma virus.[4]

The literature reports that vaccination against warts has been attempted in several settings. Smith reports that tissue can be removed and made into a crude autogenous vaccine (2 ml intradermally three times at weekly intervals) by homogenizing, grinding, freeze-thawing twice, filtering, and killing the virus with 0.5% formalin.[1] Autogenous vaccines are sometimes reported to be very effective[4] but failures have also been reported.[5] Autogenous vaccines are also reported to be capable of preventing new lesions caused by the same BPV strain in a herd. Commercial wart vaccines for cattle rarely seem to effectively result in lesion remission of existing warts, but they may be capable of preventing the development of new lesions if the same BPV strain is involved.[1] The immunity of cattle to papillomatosis has been studied but practical recommendations for other approaches to immunological control have not been forthcoming.[6]

Papillomatosis has been an ongoing problem at Virginia Bull Test Stations with occasional pen prevalence rates as high as 30% of all bulls. Some papillomas occur on the surfaces of the penis and prepuce with typical penile prevalence rates of 2 - 5% but in some cases as many as 10% of bulls have been affected with penile papillomas. Larger papillomas on the penis inhibit breeding soundness so bulls are not eligible for sale. The objective of this study was to assess the efficacy of vaccination against bovine papilloma virus in preventing outbreaks of papillomatosis in confined beef bulls undergoing rate-of-gain performance testing.

Methods

The study was carried out during the 1994-95 and 1995-96 bull test periods using 10 groups of bulls at three different locations. These bulls were part of a performance test-of-gain program and entered the test facilities in the late summer and fall. They were housed in pens of approximately 40 bulls per pen grouped, as much as possible, with bulls of similar age and breed. A 30 ml dose of commercial wart vaccine was administered to every other bull subcutaneously, as directed by the manufacturer, when they were received at the test station. Bulls that received vaccine were assigned an odd-numbered lot number while those that were not vaccinated were given even-numbered lot numbers. A booster dose of 30 ml of the same commercial vaccine was given to vaccinated bulls 14 days later. At the end of the test which was 128 days after initial vaccination for fall-born bulls and 154 days for spring-born bulls, all bulls were examined for the presence of warts on the skin surfaces and on the mucosa of the glans penis. Bulls were assigned a wart score from 0 to 3 based on the estimated number and size of warts found by examination at the end of the test period. The scores were defined as follows; O=no warts, 1 = few small warts (es-

timated to be less than 2 grams), 2 = moderate number of warts (2 to 10 grams), 3=severe wart invasion (more than 10 grams of warts estimated). The people assigning the wart scores were not aware of which bulls had been vaccinated. Bull age at the time of examination, breed, wart score, and lot number were recorded and entered into a computer spreadsheet and then transferred to statistical programs for analysis.

Statistical Analysis

Descriptive statistics and analyses of the data were done using SAS' (SAS/STAT User's Guide, Version 6. 4th ed. Cary, NC: SAS Institute Inc., 1990). A random effects logistic regression model was used to evaluate the effect of vaccination, breed and age on the occurrence of warts. For this analysis, the wart scores were converted to a dichotomous variable (O=no warts, 1=warts found). Logistic binomial regression for distinguishable data in EGRER(EGRET Reference Manual. Seattle, WA: Statistics and Epidemiology Research Corporation, 1993) was used for the analysis. Pen was included in the model as a random effect to account for the lack of independence among bulls within the same pen. To allow for a nonlinear relationship between age and the occurrence of warts, a categorical variable with 4 levels was created based on age quartiles. A secondary analysis was done at the pen level to look at the relationship between the percent of bulls vaccinated in a pen and the percent affected by warts.

Results

The period from vaccination to observation was 128 days for fall-born bulls and 154 days for spring-born bulls. There were 587 bulls included in the study during the 1994-95 test period and 618 during the 1995-96 period. Of the 1205 bulls, there were 750 (62.2%) Angus, 139 (11.50/o) Charolais, 135 (11.2%) Simmental, 101 (8.40/o) Polled Hereford, 54 Gelbvieh (4.50/o), and 26 (2.2%) other breeds (Limousine, Red Angus, Salers, Tarentaise). The bull age when examined for warts had a range of 341 to 495 days (median 406). The crude association of wart score with vaccination, age, and breed are shown in tables 1 through 3.

Table 1. The association of wart score with vaccination status.

	Wart Score				
Vaccination status	**0**	**1**	**2**	**3**	**Total**
Unvaccinated (No.)	514	67	23	3	607
Unvaccinated (%)	84.7	11.0	3.8	0.5	
Vaccinated (No.)	510	63	22	3	598
Vaccinated (%)	85.3	10.5	3.7	0.5	
Total (No.)	1024	130	45	6	1205
Total (%)	85.0	10.8	3.7	0.5	100.0

Table 2. The association of age category by wart score.

	Wart Score				
Age category	**0**	**1**	**2**	**3**	**Total**
Youngest quartile (No.)	246	43	9	2	300
Youngest quartile (%)	82.0	14.3	3.0	0.7	
Youngest mid quartile (No.)	249	32	13	1	295
Youngest mid quartile (%)	84.7	11.0	3.8	0.5	
Oldest mid quartile (No.)	267	24	14	3	308
Oldest mid quartile (%)	84.7	11.0	3.8	0.5	
Oldest quartile (No.)	262	31	9	0	302
Oldest quartile (%)	85.3	10.5	3.7	0.5	
Total	1024	130	45	6	1205

Table 3. The association of breed by wart score.

	Wart Score				
Breed category	**0**	**1**	**2**	**3**	**Total**
Angus (No.)	601	105	39	5	750
Angus (%)	80.1	14.0	5.2	.7	
Charolais (No.)	132	6	1	0	139
Charolais (%)	95.0	4.3	0.7	0	
Gelbvieh (No.)	51	1	2	0	54
Gelbvieh (%)	94.4	1.9	3.7	0	
Misc. breeds (No.)	25	0	1	0	26
Misc. breeds (%)	96.2	0	3.8	0	
Polled Hereford (No.)	91	9	1	0	101
Polled Hereford (%)	90.1	8.9	1.0	0	
Simmental (No.)	124	9	1	1	135
Simmental (%)	91.9	6.7	0.7	0.7	
Total	1024	130	45	6	1205

The logistic regression analysis showed that vaccination had no effect on the occurrence of warts. This was true both considering the effect of vaccination alone (P = O.98) or when controlling for breed and age (P = O.8). Breed had a significant effect on warts (P<0.001) with non-Angus breeds having lower risk(see Table 4). There was not an association between age and warts when considering it alone nor when controlling for the effect of breed (p=0.3).

Looking at the two years separately did not affect the conclusions about vaccine efficacy or breed, but the association with age was different for the two years with older bulls having lower risk of warts in the 1994-95 period.

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Table 4. Linear regression analysis for the effect of breed on presence of warts.

Term	Coefficient	Std Err	P-value	OR	95% Lower Bound	95% Upper Bound
Intercept	-1.5	0.2	<0.001			
Angus	0		1			
Charolais	-1.5	0.5	<0.001	0.2	0.07	0.4
Gelbvieh	-1.8	0.7	0.02	0.2	0.06	0.8
P Hereford	-0.8	0.4	0.05	0.4	0.2	1.0
Simmental	-0.9	0.4	0.02	0.4	0.2	0.9
Other	-1.8	1.1	0.1	0.2	0.02	1.4
EBV*	0.6	0.1	<0.001			

*Extra binomial variation (the significance of this term shows that pen was a significant source of variation in the occurrence of warts).

Pen-Level Analysis

There were 30 pens of bulls in the study. The proportion of bulls in pens diagnosed with warts ranged from 0 to 0.43 (median=O. 1 4) and the proportion of bulls vaccinated by pen had a range of 0.29 to 0.60 (median- 0. 5). Although not statistically significant, pens with lower percentages of bulls vaccinated tended to have more bulls with warts (Spearman's rho=-O.32, p-0.08). This relationship persisted when adjusting for the average pen age and proportion Angus bulls in the pen. The moderate correlation was dependent on two pens with less than 40% vaccinated bulls in the 1994-95 test period. This observation may be due to chance alone, but it would be interesting to do a study at the pen level (vaccination assigned at random to pens) in order to find out what the effect of wart vaccination is on the occurrence of warts in pens rather than individual bulls.

Summary

Vaccination of these yearling age bulls with a commercial vaccine directed against papillomatosis had no protective effect against the development of warts nor against the severity of the wart infestations which they developed. Although Smith[1] states that commercial vaccines may prevent the development of papillomatosis he does not cite literature which documents this. There may exist little proof that these vaccines prevent warts from developing. Several reasons for this failure may be postulated. Failure of the vaccine to contain antigens for the wart strain that was present in these test stations is one possibility. A second possibility is that subcutaneous vaccination does not stimulate the appropriate immune response for protection. Note that the successful treatment of warts by an autogenous vaccination utilized the intradermal route.

The breed predisposition to warts is a previously unpublished finding. That this relationship is an inherent characteristic of Angus cattle is substantiated by the finding that even bulls penned with Angus bulls were not at increased risk of developing warts. The characteristics of this breed that make it more susceptible to papillomatosis remain unknown.

At present, management or immunological techniques to prevent the development of infectious papillomatosis in a setting where young cattle from various sources are commingled and managed together remain illusive.

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