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# Effect of Chemically Altered and Modified-Live Infectious Bovine Rhinotracheitis Vaccines on Fetal Retention in Beef Replacement Heifers During the First Four Months of Gestation

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**Abstract**

The objective of this study was to determine whether vaccination of pregnant heifers with either chemically altered or modified live infectious bovine rhinotracheitis (IBR) vaccine would cause abortion when previously vaccinated with a chemically altered IBR vaccine.

During pre-weaning processing and at weaning, 202 crossbred Brangus heifers were administered chemically altered infectious bovine rhinotracheitis virus (IBR) vaccines. At 60 to 120 days of gestation after first fall breeding, heifers were administered either a modified live virus (MLV) or a chemically altered IBR vaccine. Heifers at 60 to 90 days gestation, and those greater than 90 and up to 120 days gestation, were assigned by gestation category to one of three treatments: 1) a single IM injection of chemically altered IBR vaccine; 2) a single IM injection of modified live IBR vaccine; or 3) controls - no injections. Heifers were palpated 56 days after treatment to determine potential fetal loss. Subsequent calving information was used to confirm post-treatment palpation data. One heifer in each group aborted after treatment; these numbers did not differ among treatments (p=1.0) nor between gestation categories (p=1.0). Calving numbers verified that no fetuses were lost after post-treatment palpation. We concluded that a single dose of these vaccines in pregnant replacement heifers did not cause increased abortion rates compared to unvaccinated control heifers.

**Résumé**

L'objectif de cet étude était de déterminer si la vaccination de taures en gestation avec soit un vaccin chimiquement modifié ou soit un vaccin de type vivant modifié pour la rhino trachéite infectieuse bovine (IBR) allait entraîner l'avortement chez les sujets préalablement vaccinés avec un vaccin IBR chimiquement modifié.

Durant la période pré-sevrage et au moment du sevrage, 202 taures Brangus d'origine hybride ont reçu des vaccins IBR chimiquement modifiés. Après 60 ou 120 jours de gestation suite à la première mise à la reproduction à l'automne, les taures ont reçu soit un vaccin avec virus vivant modifié ou soit un vaccin IBR chimiquement modifié. Les taures entre 60 et 90 jours de gestation et celles excédant 90 jours mais précédant 120 jours de gestation ont été assignées par catégorie de gestation à l'un des trois traitements suivants : 1) une simple injection intra-musculaire du vaccin IBR chimiquement modifié; 2) une simple injection intra-musculaire du vaccin IBR vivant modifié, et 3) contrôle, sans injection. Les taures ont été palpées après 56 jours pour déceler des pertes fœtales potentielles. L'information sur les vêlages subséquents était utilisé pour confirmer le statut de gestation après la palpation suivant le traitement. Une taure dans chacun des groupes a avorté après le traitement; ces nombres n'étaient pas différents statistiquement entre les traitements (p = 1.0) ni entre les catégories de gestation (p = 1.0). Le nombre de vêlages indiquait qu'aucun fœtus n'avait été perdu après la palpation suivant le traitement. Nous concluons qu'une simple dose de ces vaccins pour les taures de remplacement en gestation n'a pas causé une augmentation du taux d'avortement comparé à celui des taures contrôles sans vaccination.

## Introduction

Bovine fetal and embryonic loss is caused by numerous factors, including viral infections associated with Bovine Respiratory Disease (BRD). To protect against infections, females are vaccinated with several antigens, including the virus that causes infectious bovine rhinotracheitis (IBR). Infectious bovine rhinotracheitis vaccines are available in various antigenic presentations including killed, chemically altered and modified live virus (MLV). Reviews of the vaccines and their use are available.[4,7,9,12]

The MLV presentations invoke a longer, and often greater, degree of immune response activity than the killed viral vaccines.[5,6,12] Moreover, a single dose of MLV vaccine can immunize, as opposed to two doses of killed vaccine.[3] Use of some MLV vaccines in pregnant females potentially causes viral replication and transmission across the blood-uterine barrier sufficient to induce varying degrees of embryo/fetal loss,[3] but other MLV products (non-replicating MLV) have been altered to avoid these complications.[13]

This trial studied potential fetal loss in gestating beef replacement heifers after a single injection of either a chemically altered[a] or MLV IBR[b] vaccine during the first four months of gestation.

## Materials and Methods

The trial used 202 pregnant, crossbred Brangus heifers bred during a 60-day fall breeding season. The animals originated from multiple management units in different locations in Texas, but were produced by one owner. Herd health practices prior to initiating this trial included administration of clostridial vaccines and internal parasite control as calves. Pre-weaning vaccines included a second clostridial vaccination and an injection of a combination vaccine containing chemically altered IBR virus.[a] At weaning, animals were administered this product a second time.

Post-weaning nutrition varied by origin, but included at least one week with free access to coastal bermuda-grass hay. An unknown portion of these animals also received a commercial starter ration for two weeks after weaning. Thereafter, all heifers were transported to a rearing unit and placed on coastal bermuda-grass pastures and cool season annuals with free access to hay or corn silage, as needed. They also were given a salt-limited 14% crude protein supplement. Thirty days prior to their first fall breeding season, heifers were treated for internal parasites and vaccinated against campylobacter and bacillary hemoglobinuria.

Heifers were palpated 60 days following the end of the breeding season to confirm pregnancy and estimate conception dates. To remove potential impact of gestation length on the data, heifers that were 60 to 90 days pregnant and those greater than 90 (up to 120) days were assigned to one of three treatments:

1. Vaccinated at palpation with a single dose of a vaccine containing a chemically altered IBR virus;[a]
2. Vaccinated at palpation with a single dose of a vaccine containing both modified live and killed IBR viruses;[b]
3. Unvaccinated at palpation (controls).

The lyophilized vaccine for each product was aseptically reconstituted with its associated diluent prior to injection. Additional vials were not reconstituted until the previous vial was empty. All vaccines were kept cold before rehydration and during use, and were protected from sunlight. Separate syringes and needles were used for each vaccine. Heifers could not be separated after treatment, but were commingled according to ranch practices.

All heifers were palpated again 56 days later to determine potential fetal loss due to vaccine treatment. Numbers of heifers aborting between vaccine treatment groups and between gestation categories were compared using Fisher's Exact test.[11] Power calculations[8] were performed to determine if the number of observations would effectively detect potential differences among treatments. Post-treatment pregnancy data were confirmed with subsequent calving information.

## Results and Discussion

At the start of treatment, there was more MLV product (not labeled for use in pregnant females or their nursing offspring) available for use, compared to the amount of chemically altered product. To comply with the herd owner's wishes, the extra MLV product was administered to heifers that were greater than 90 (up to 120) days gestation (Table 1). This inflated the number of heifers in the greater-than-90-days gestation category in the MLV treatment group (n=68) compared to control (n=38) and chemically altered vaccine (n=39) treatments. Nevertheless, data from the additional animals were included in the statistical analyses. The number of heifers at 60 to 90 days gestation were equal among the three treatments (n=19).

[a]Cattlemaster 4®, Pfizer Animal Health, Exton, PA 19341. This product contains chemically-altered IBR and parainfluenza-3 ($PI_3$) viruses, a modified live bovine respiratory syncytial virus (BRSV), and inactivated (killed) bovine viral diarrhea virus (BVDV).

[b]Fusion 4®, Merial, Ltd., Iselin, NJ 08830. This product contains modified live and killed forms of IBR virus, modified live $PI_3$ virus, and inactivated (killed) BRSV and BVD viruses.

**Table 1.** Fetal retention after injection with either chemically-altered or MLV IBR vaccines.

| Treatment | Chemically-altered[1] vaccine | | MLV[2] vaccine | | Control | |
|---|---|---|---|---|---|---|
| Days of gestation | 60-90 | >90 | 60-90 | >90 | 60-90 | >90 |
| Number of heifers[3] | 19 | 39 | 19 | 68 | 19 | 38 |
| Number aborted[4] (56 days post-treatment) | 1 | 0 | 0 | 1 | 1 | 0 |
| Number not calving[5] | 0 | 0 | 0 | 0 | 0 | 0 |

[1]Cattlemaster 4®, Pfizer Animal Health, Exton, PA 19341
[2]Fusion 4®, Merial, Ltd., Athens, GA 30601
[3]Due to available product, more heifers in the >90 MLV group were treated.
[4]Number aborted did not differ between vaccine treatment (p=1.0) nor gestational categories (p=1.0).
[5]Excludes the three heifers that aborted during the 56-day post-treatment period.

Only three heifers (one in each treatment) aborted in the 56 days after the vaccines were administered (Table 1). In one of the three, palpated at 56 days after treatment, recent abortion was evident from placental membranes protruding from the vulva. This was a 1.72% fetal loss for heifers in the chemically altered group; 1.15% fetal loss in the modified live group; and 1.75% loss in the control group. These losses were within expected spontaneous abortion rates of 0-3% reported in the literature[1,2,10,14] and did not differ among treatments (p=1.0) nor between gestation categories (p=1.0).

For calculating a power value in a one-tailed test,[8] it was assumed that an increase in abortion rate of seven percentage points above spontaneous rates (0-3%) would be significant. An alpha value of 0.01 was used. Given the number of observations per treatment (n=57 or more) and an assumed standard deviation value of two, a power value of 0.969 resulted. Power values of 0.75 or higher are generally accepted as sufficient to prevent a Type II error.[8] Calving numbers confirmed no additional fetuses were lost after post-treatment palpation.

The lack of increased abortions above previously reported spontaneous rates following vaccination with the chemically altered IBR vaccine is not surprising, since it is approved for use in pregnant females or their nursing offspring. The lack of increased abortion rate following vaccination with the MLV product suggests that no infection and replication occurred. Previous research indicates that MLV products are generally not expected to infect and replicate in previously immunized animals.[12] However, no serology was done in this study to measure pre- and post-treatment antibody titers. Consequently it is unknown if the heifers in this trial were indeed immune because of the chemically altered IBR vaccinations given at pre-weaning and weaning, and thus assumed to be safe from potential viral infection and replication after receiving MLV vaccine at first gestation (start of treatment).

The vaccines were administered under typical field conditions, and the virus titer in the MLV product was not assessed prior to administration. An additional concern is that heifers were commingled after treatment. This could have confounded the data since potential viral shedding from MLV-vaccinated heifers may have occurred post-treatment. Nevertheless, the MLV product used in this trial did not cause increased abortions above reported spontaneous rates.

## Conclusions

We conclude that, under the field conditions of this trial, one injection of either chemically altered infectious bovine rhinotracheitis virus vaccine or modified live infectious bovine rhinotracheitis virus vaccine given to previously vaccinated beef replacement heifers at 60 to 120 days of gestation did not increase the incidence of fetal loss above expected spontaneous rates.


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# Abstracts

## Evidence for the Transmission of Scrapie to Sheep and Goats from a Vaccine against *Mycoplasma agalactiae*

M. Caramelli, G. Ru, C. Casalone, E. Bozzetta, P. L. Acutis, A. Calella, G. Forloni
*Veterinary Record* (2001) 148:531-536

An accidental infection from a vaccine was suggested as the explanation for the sudden increase in outbreaks of scrapie in Italy in 1997 and 1998. This paper describes a recent outbreak of scrapie in sheep and goats which were exposed to the same vaccine. No ewes or goats had been imported into the herd since 1992, but a vacccine against *Mycoplasma agalactiae* had been administered twice, in 1995 and 1997. High rates of crude mortality and scrapie incidence were experienced by both species, all birth cohorts were involved and a large proportion of aged animals was affected. A pattern of brain lesions was observed, with slight differences between the sheep and goats, which was very similar to the pattern observed in animals previously exposed to the same vaccine but clearly different from that observed in the brains of sheep with scrapie in a flock not exposed to the vaccine. Regardless of their exposure status, genotype analysis of the sheep showed the presence of polymorphism only at codon 171. The patterns of both incidence and brain lesions provide evidence that the epidemic of scrapie was due to the use of the vaccine.

## Ultrasonographic Appearance of the Superficial Supramammary Lymph Nodes in Lactating Dairy Cattle

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The superficial supramammary lymph nodes of 54 lactating dairy cows were examined ultrasonographically with a 7.5 MHz linear transducer; each node was measured in two planes within 24 hours of recording the milk somatic cell count. In most cows, the nodes were well demarcated from the surrounding tissue. The parenchyma of the nodes ranged from hypoechoic to anechoic, with a central bright hyperechoic area, and a thin hyperechoic line surrounded the nodes. The size of the nodes varied, but their internal architecture remained relatively consistent. Their mean length was 7.4 cm (range 3.5 to 15 cm) and their mean depth was 2.5 cm (range 1.2 to 5.7 cm). They were significantly larger in cows with more lactations ($p<0.05$), but there were no correlations between their size and either the time calved or the milk somatic cell count. The lymph nodes on sides which were positive in a California milk test were significantly larger than those on sides which were negative ($p<0.05$).