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Technical Bulletin

Protection Against Bovine Respiratory Syncytial Virus in Calves Vaccinated with Adjuvanted Modified-Live Vaccine Administered in the Face of Maternal Antibody

Source: Kolb EA, Buterbaugh RE, Rinehart CL, et al. Protection against bovine respiratory syncytial virus in calves vaccinated with adjuvanted modified-live vaccine administered in the face of maternal antibody. *Vaccine* 2020;38(2):298–308. Available at: https://doi.org/10.1016/j.vaccine.2019.10.015. Accessed Dec. 12, 2019.

Key Findings

- PYRAMID® 5–vaccinated calves had decreased febrile response and significant reduction in the severity and presence of ocular discharge over time ($P < 0.01$).
- Calves in the PYRAMID 5 group had significant reduction in overall percentage of bovine respiratory syncytial virus (BRSV) lung involvement ($P = 0.04$) (Figure 1).
- BRSV was shed from the PYRAMID 5 group at lower levels and for fewer days, as compared to the control group.
- Detection of BRSV in nasal and lung samples by polymerase chain reaction (PCR) revealed a total reduction in viral presence following BRSV challenge in the vaccinated calves (Figure 2 and Figure 3).
- Over half of PYRAMID Vaccinates (9/17) had BRSV immunoglobulin A (IgA) antibody at 21 days post vaccination in nasal secretions compared to 0/16 of the controls. By eight days post challenge, all of the PYRAMID Vaccinates (17/17) were positive for the expression of IgA, while only 5/16 of the controls expressed IgA following challenge (Figure 4).
- A significant increase in BRSV-specific interferon-gamma (IFN-γ) levels were observed in the PYRAMID vaccine group at both 34 days post vaccination and eight days post challenge, demonstrating an immune memory response in the face of maternal antibody.

Introduction

Bovine respiratory disease (BRD) is one of the leading causes of beef and dairy calf morbidity and mortality in the United States, and is estimated to cost up to $900 million annually, due to reduced weaning weights, reduced average daily gains, increased treatment costs and increased feeding costs. Bovine respiratory syncytial virus (BRSV) is a significant viral pathogen often associated with BRD. In young beef and dairy calves, passive immunity is a critical component in protecting against disease, but may limit immune response to vaccination. Furthermore, once maternal antibodies are absent, the calf may not be adequately protected against disease caused by BRSV. The objective of this controlled study was to evaluate the efficacy of vaccination with PYRAMID 5 in the presence of adequate passive immunity.

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Objective

- To evaluate the efficacy of an adjuvanted modified-live virus (MLV) vaccine used in the presence of maternal antibodies against a BRSV challenge

Materials and Methods

- Holstein dairy calves were purchased from a local dairy and transported to the study site. Calves were randomly assigned to one of two treatment groups and housed in individual runs, with three feet of space on either side of the individual hut to eliminate nose-to-nose contact:

Table 1.

Treatment	# Calves
PYRAMID® 5 Vaccinates	17
Positive Control – sham vaccinated	16

- All calves were determined to be free of bovine viral diarrhea virus and persistent infection.
- Both groups were fed colostrum (1.9 L for the first three feedings) within 2 hrs of birth, 12 hrs, and 24 hrs, with known quantity of BRSV colostral antibodies.
- Seventeen calves were vaccinated with PYRAMID 5 at approximately 30 days old (30–38 days). Sixteen calves vaccinated with Positive Control received an equal dose (2.0 mL) of sterile diluent at approximately the same age.
- Serum neutralization (SN) titers for BRSV and all major respiratory viruses were measured in both groups at seven- to 14-day intervals for approximately eight weeks prior to challenge, the day before challenge (–1 Days post challenge (DPC)), and at necropsy (8 DPC). Blood samples were also collected for cell-mediated immunity (CMI) interferon-gamma (IFN-γ) assays.
- Challenge was performed when SN titers had declined to < 1:4, indicating that maternal antibody level had decreased to a level that would not be protective against BRSV. At 72 days post vaccination, all calves in the study were challenged with BRSV CA-1 strain, intranasally through the use of a nebulizer and mask to aerosolize the inoculant for inhalation, once a day for 2 consecutive days.
- Clinical signs including body temperature, attitude and general respiratory signs were monitored for eight days following challenge with BRSV CA-1 strain. Pyrexia was set at a body temperature ≥ 103.5 F. Clinical scores of 0–3 were assigned, based on signs of abnormal respiration, ocular discharge and depression. Nasal discharge was assessed on a scale of 0–4.
- Nasal secretions were obtained from all calves weekly for the first three weeks post vaccination. Secretions were also collected a total of four times during the challenge phase (–1, 3, 5, 8 DPC). Nasopharyngeal swabs were collected from all calves on days –1 and 3–8 DPC for virus isolation (VI) and BRSV polymerase chain reaction (PCR) assays.
- All calves were euthanized and necropsied eight days post challenge to assign a lung score by a board-certified pathologist.

Results

- **Clinical Signs:** Decreased febrile response and significant reduction in ocular discharge over time ($P < 0.01$).
- **Lung Lesions:** Significant reduction ($P = 0.04$) in overall percentage of BRSV lung involvement (Figure 1).
- **BRSV Virus Isolation (VI):** BRSV in the PYRAMID® vaccine group was shed at lower levels and for fewer days than the control group. Peak nasal shedding was four times higher in the control group.
- **BRSV PCR:** Total reduction in viral presence in the nasal samples and lungs of the vaccinated calves following direct BRSV challenge (Figure 2 and Figure 3).
- **BRSV Nasal IgA:** Over half of vaccinates (9/17) had BRSV immunoglobulin A (IgA) antibody at 21 days post vaccination in nasal secretions compared to 0/16 of the controls. By eight days post challenge, all vaccinates (17/17) were positive for the expression of IgA, while only 5/16 of the controls expressed IgA following challenge (Figure 4).
- **Interferon Gamma Analysis:** Significant boost ($P < 0.001$) in BRSV-specific IFN-γ levels occurred at both 34 days post vaccination and eight days post challenge in vaccinates when compared to controls.

Figure 1.

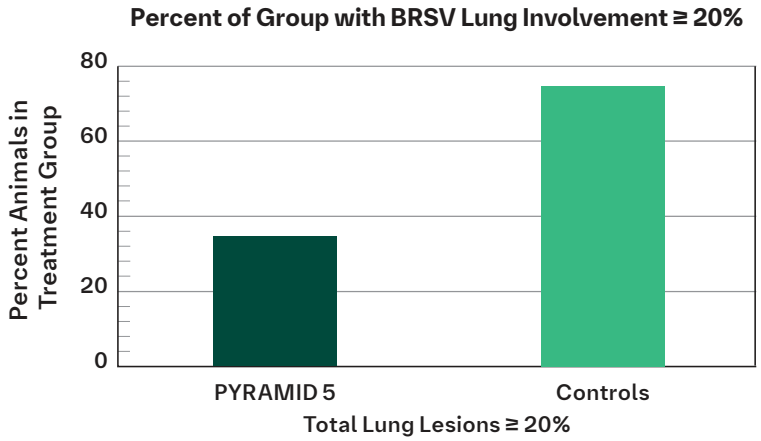

Figure 1: PYRAMID® 5 Vaccinates and Controls. Indicates the percentage of calves within each group with a total lung lesion involvement of 20% or more. PYRAMID® 5 Vaccinates had a significant reduction in lung lesions compared to the controls ($P < 0.05$).

Figure 2.

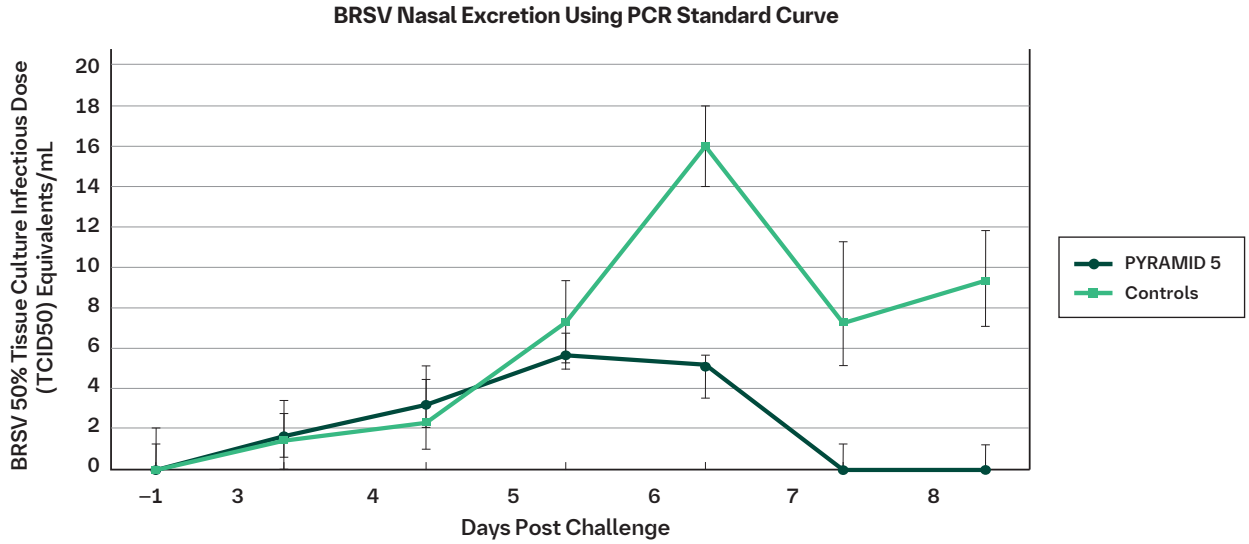

Figure 2: BRSV RNA in nasal samples post challenge. PYRAMID® 5 Vaccinates and Controls. There was an overall effect of treatment ($P = 0.05$) and an effect of time ($P < 0.0001$) noted.

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Figure 3.

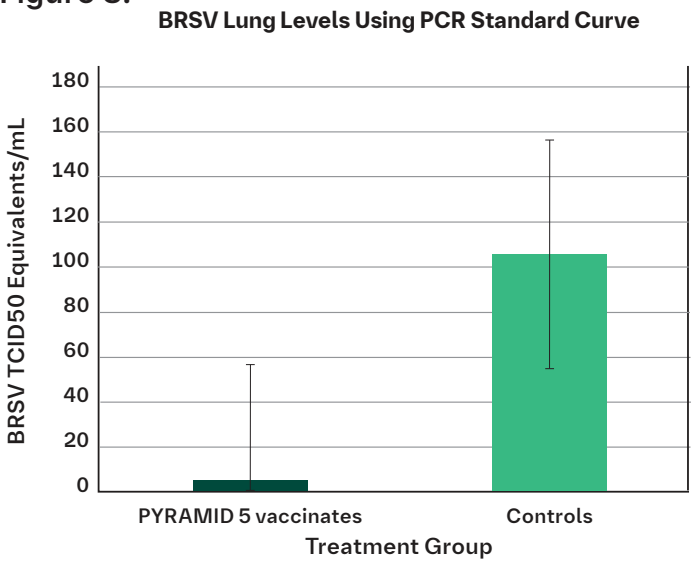

Figure 4.

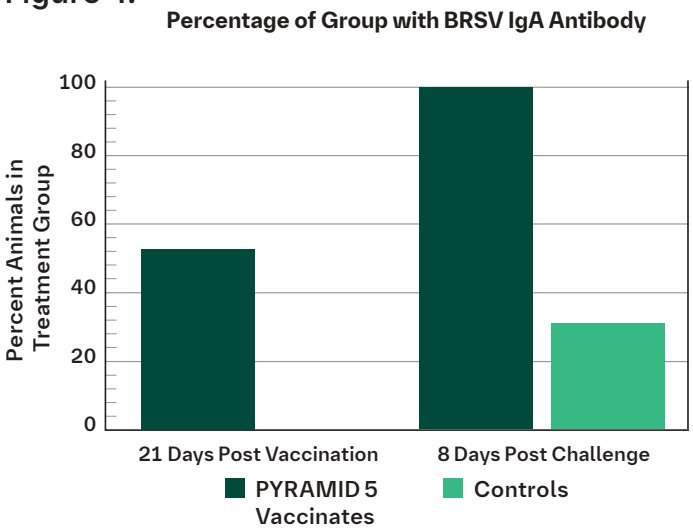

Figure 3: BRSV RNA in lungs from PYRAMID® 5 and Controls. Lung levels of BRSV RNA were significantly lower (PYRAMID 5 = 3.97 vs. Controls = 105.85 TCID50/mL, $P < 0.05$) in PYRAMID 5.

Discussion

The results of this controlled study established that calves vaccinated with an adjuvanted MLV (PYRAMID 5) in the face of maternal antibodies could be protected against BRSV when challenged. This was demonstrated through vaccination by a reduction in the severity of fever, reduction of clinical signs, decreased lung pathology, and decreased viral shedding. Activation of the adaptive immune system plays an essential role in protecting against viral respiratory pathogens, specifically BRSV. This study revealed that calves vaccinated with PYRAMID 5 in the face of well-defined maternal antibody levels experienced an activation of the adaptive immune system.

This activation generated local mucosal immune response and memory response, demonstrated by the presence of IgA and IFN-γ expression.

The noticeable difference in IgA levels in the PYRAMID group is especially important to note, as the vaccine was not administered intranasally, indicating that parenteral adjuvanted MLV vaccination can create both a systemic and mucosal response. This also indicates that adjuvants may be critical to the successful activation of the immune response in the face of maternal antibodies and subsequent disease protection.

Conclusion

- Administration of PYRAMID 5 vaccine to calves approximately 30 days of age and fed colostrum containing BRSV antibodies decreased the severity and duration of clinical signs after direct BRSV challenge.
- Vaccination with PYRAMID 5 generated local mucosal immune response and memory response, demonstrated by the presence of IgA and IFN-γ expression.

Learn more about PYRAMID research by visiting **PYRAMIDVaccines.com**

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