Infectious Bovine Rhinotracheitis Virus Antibody Responses to Vaccines Used in Combination

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Merlin Kaeberle, professor, veterinary medicine
Ronald Sealock, superintendent, Rhodes Farm

Summary
The objective of this experimentation was to determine if circulating antibody titers to parainfluenza type-3 (PI-3) and infectious bovine rhinotracheitis (IBR) viruses could be enhanced by a combination of vaccines. The vaccines utilized were a modified live virus vaccine administered by the intranasal route and an inactivated virus vaccine injected intramuscularly. Virus neutralization tests were conducted on sera obtained at intervals before and following vaccination. Unfortunately, the calves were apparently exposed naturally to PI-3 virus, and the responses to that virus were inconclusive. However, antibody responses to IBR virus were dramatically enhanced by the combination of the two vaccines.

Introduction
Immunization of young calves against respiratory disease presents a major problem because the presence of maternal antibodies may block the response to vaccination. Antibodies to infectious bovine rhinotracheitis (IBR) and parainfluenza type 3 (PI-3) viruses may persist in calves until several weeks of age due to natural infection or vaccination of cows in the herd. Modified live virus vaccines administered by the intranasal route have potential to induce immune responses when some level of circulating maternal antibodies are still present. However, the level of systemic antibodies produced to these vaccines is minimal and the duration of immunity may be limited. The objective of this research was to determine if an intranasal modified live virus vaccine utilized in combination with an oil adjuvanted killed virus vaccine would enhance the level of circulating (serum) antibodies in calves.

Materials and Methods
Seventy-one spring calves averaging about 90 days of age were weaned and randomly assigned to one of four treatment groups. The number of animals in each group and vaccination schedule are indicated in Table 1. The vaccines were a modified live IBR and PI-3 virus vaccine (Nasalgen IP, Coopers Animal Health, Inc., Mundelein, IL) administered intranasally and an inactivated virus vaccine (Vira Shield 5, Grand Laboratories Inc., Larchwood, IA) administered intramuscularly. The reduced number of calves vaccinated at day 37 was due to the death of a few calves and the reserving of 2 or 3 calves in each group as controls to monitor for natural infection. Modified live virus vaccines (Groups C and D) were in one corral separated from controls or inactivated virus vaccines (Groups A and B) in another corral for the first 30 days of experimentation.

Calves were bled for serum on days 0, 37 and 63. The serum was stored at –20°C until tested for antibodies to IBR and PI-3 viruses by microtiter virus neutralization tests.

Table 1. Groups of calves and vaccination schedule.

<table>
<thead>
<tr>
<th>Group</th>
<th>Vaccine</th>
<th>Number*</th>
<th>Vaccine</th>
<th>Number</th>
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</thead>
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<tr>
<td>A</td>
<td>None</td>
<td>18</td>
<td>VS 5**</td>
<td>12</td>
</tr>
<tr>
<td>B</td>
<td>VS 5</td>
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<td>15</td>
</tr>
<tr>
<td>C</td>
<td>N***</td>
<td>17</td>
<td>VS 5</td>
<td>15</td>
</tr>
<tr>
<td>D</td>
<td>N+VS 5</td>
<td>18</td>
<td>VS 5</td>
<td>15</td>
</tr>
</tbody>
</table>

*Number = Number of calves
**VS 5 = Vira Shield 5
***N = Nasalgen IP

Results and Discussion
A small number of calves, two or three in each group, were not vaccinated on day 37 to monitor for natural infections. By that time calves in Group I (unvaccinated controls) had enhanced titers to PI-3 virus indicating natural exposure of the calves to this virus. Therefore, data on PI-3 virus antibodies were inconclusive and are not presented. There was no indication of IBR virus infection in the calves.

Mean IBR virus antibody titers for the various groups of calves are provided in Figure 1. At day 37 antibody titers in Group A animals (unvaccinated controls) had declined, and antibody responses of calves in Groups B and C were minimal. We anticipate that the response of Group C calves (modified live virus) had peaked at this time although there was potential for increasing titers in Group B calves administered the oil adjuvanted killed virus vaccine. Antibody titers of the Group D calves were much higher than in calves in the other groups. This enhancement was pronounced at day 63 following a booster dose of killed virus vaccine as indicated by the titers developed by calves in Groups C and D.

This experimentation demonstrated a priming effect by the intranasal vaccine, which may have the potential to immunize in the presence of some level of maternal antibodies. The priming effect is evident from the enhanced response of Group C calves that received the inactivated virus vaccine at day 37. Administration of the two vaccines at the same time followed by a booster of inactivated virus vaccine...
proved to be the best protocol. The intranasal vaccine has recognized ability to establish local or mucosal immunity. Also, the vaccine has been reported to induce interferon production, which can provide early protection against viral infection. Use of these vaccines in combination should be considered for immunization of young calves. Primary vaccination with the intranasal vaccine provides early resistance to the viruses.

Secondary vaccination with inactivated virus vaccine markedly enhances circulating antibody titers and probably persisting resistance.

Acknowledgments
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Figure 1. Mean neutralizing IBR virus antibody titers in groups of calves vaccinated with several protocols. Group A: No vaccination on day 0, Vira Shield 5 on day 37. Group B: Vira Shield 5 on day 0 and day 37. Group C: Nasalgen on day 0 and Vira Shield 5 on day 37. Group D: Nasalgen plus Vira Shield 5 on day 0 and Vira Shield 5 on day 37.