Effect of Vaccination with Recombinant Canine Distemper Virus Vaccine Immediately before Exposure under Shelter-Like Conditions*

L. J. Larson, DVM
R. D. Schultz, PhD, DACVM

Department of Pathobiological Sciences
School of Veterinary Medicine
2015 Linden Drive
University of Wisconsin–Madison
Madison, WI 53706-1102

CLINICAL RELEVANCE

Vaccination with a modified-live virus (MLV) canine distemper virus (CDV) vaccine has historically been recommended for animals in high-risk environments because of the rapid onset of immunity following vaccination. Recombinant CDV (rCDV) vaccine was deemed a suitable alternative to MLV-CDV vaccination in pet dogs, but insufficient data precluded its use where CDV was a serious threat to puppies, such as in shelters, kennels, and pet stores. In this study, dogs experimentally challenged hours after a single dose of rCDV or MLV-CDV vaccine became sick but recovered, whereas unvaccinated dogs became sick and died. Dogs vaccinated with a single dose of rCDV or MLV-CDV vaccine 1 week before being experimentally challenged remained healthy and showed no clinical signs. Dogs given one dose of rCDV vaccine hours before being placed in a CDV-contaminated environment did not become sick. These findings support the hypothesis that rCDV vaccine has a similar time-to-immunity as MLV-CDV vaccines and can likewise protect dogs in high-risk environments after one dose.

INTRODUCTION

Canine distemper virus (CDV) is a member of the Paramyxoviridae family in the genus Morbillivirus and is closely related to the human measles virus and bovine rinderpest virus. CDV is highly contagious and has worldwide distribution. Before the emergence of canine parvovirus-2 (CPV-2) in 1978, CDV was the most prevalent and most important viral disease of dogs. CDV affects all members of the Canidae family as well as other carnivores (e.g., ferrets, raccoons, large cats) and even pandas.1–4 CDV infection in unprotected animals results in significant morbidity and mortality due to respiratory, gastrointestinal, and neurologic
disease. CDV-related morbidity ranges from 25% to 75%, and the fatality:case ratio can be as high as 90%.3

CDV is transmitted primarily via aerosolization of body secretion droplets from infected animals.4 Although only one CDV serotype exists, there are many biologically divergent CDV strains that cause differential dominating clinical signs. However, CDV-induced immunosuppression is a common feature with all virulent strains of CDV and is present as early as 3 days after infection and may be present for days to weeks before the onset of clinical signs of disease.5

Clinical signs of distemper manifest after an incubation period of 11 to 18 days following infection with the acute strains of CDV.4 Subacute strains of CDV, the predominant strains in the field today, have incubation periods ranging from approximately 2 weeks to longer than 4 weeks. After infection, pups are transiently febrile and leukopenic. Clinical signs of disease include conjunctivitis, rhinitis, coughing, diarrhea, vomiting, anorexia, dehydration, and weight loss; signs of acute encephalitis often, but not always, occur.4,6

Although widespread vaccination has now eliminated much of the disease, CDV remains a significant problem for unvaccinated animals and dogs in pet shops, puppy mills, and shelters. During the past 3 years, shelters nationwide have had recognized outbreaks of CDV because abandoned animals retrieved from city streets and relinquished to shelters typically have a history of no vaccination, and thus may be immunologically naïve to CDV.7 Once exposed, dogs can quickly succumb to the disease. CDV, CPV-2, canine adenovirus-2 (CAV-2), and rabies virus as core vaccines.9 This designation implies that all puppies should be vaccinated with these vaccines, thus, that “no pups should be left unvaccinated.” At the time the 2003 guidelines were written, data on the rCDV vaccine in Recombitek were incomplete. Therefore, rCDV vaccine was differentiated from the other major CDV vaccines. Specifically, time-to-immunity for dogs vaccinated with rCDV vaccine was unknown. Data generated for licensing the vaccine suggested that two doses of rCDV may be necessary to confer immunity, and, hence, the time-to-immunity would be too lengthy to make vaccination with rCDV feasible for animals in high-risk environments, such as shelters, commercial kennels, and pet

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shops. As a result, even though the rCDV vaccine was considered very safe and effective for use in pet dogs, the 2003 Guidelines did not recommend it for use where CDV is a serious threat. The purpose of this study was to assess the efficacy of the commercially available rCDV vaccine (Recombitek CDV) in puppies in shelter-like conditions and to specifically address whether this vaccine would protect puppies after one dose of vaccine, similar to what is seen with the traditional MLV-CDV vaccines.6

**MATERIALS AND METHODS**

Institutional Animal Care and Use Committee approval was obtained before conducting this study.

**Part 1**

Twelve CDV antibody–negative beagle puppies (10 to 12 weeks old) were housed in isolation rooms and allowed to acclimate for 7 days before study initiation. Physical examinations on all pups revealed no abnormalities. The puppies were negative for CDV antibody as shown by virus neutralization test. Puppies were divided into three groups of four pups each and vaccinated according to the schedule in Table 1; the groups were composed as follows:

- **Group 1**—Two pups were vaccinated with rCDV vaccine and two with MLV-CDV vaccine 1 week before challenge.
- **Group 2**—Two pups were vaccinated with rCDV vaccine and two with MLV-CDV vaccine 15 minutes to 4 hours before challenge.
- **Group 3**—Pups remained unvaccinated and served as virus challenge controls.

All 12 pups were challenged IV with 1 ml of virulent CDV (1 × 10^4.5 TCID<sub>50</sub> [50% tissue culture infective dose]).

**Part 2**

Four 12-week-old CDV-antibody negative beagle pups were housed in isolation and acclimated for 7 days before study initiation. Physical examinations revealed no abnormalities. Puppies were vaccinated with Recombitek C6 (Merial) according to the manufacturer’s instructions. Four hours after vaccination, the puppies were exposed to an environment contaminated with CDV by co-housing them with six CDV-infected dogs in various stages of clinical disease; the infected dogs were being used for a separate vaccine study. The isolation room was not cleaned for 24 hours before the dogs were commingled, thereby ensuring intimate contact not only between the rCDV-vaccinated dogs and diseased animals and but also with the viral-contaminated environment. For animal welfare reasons, no unvaccinated control dogs were placed in this environment. Physical examinations were performed on CDV-diseased animals every 6 to 8 hours, and

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**TABLE 1. Part 1 Group Designations**

<table>
<thead>
<tr>
<th>Puppy Group</th>
<th>No. of Puppies</th>
<th>Time of Vaccination before Challenge</th>
<th>Type of Vaccination</th>
<th>Virulent CDV Challenge (IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>4</td>
<td>1 wk</td>
<td>rCDV or MLV-CDV</td>
<td>+</td>
</tr>
<tr>
<td>Group 2</td>
<td>4</td>
<td>15 min to 4 hr</td>
<td>rCDV or MLV-CDV</td>
<td>+</td>
</tr>
<tr>
<td>Group 3</td>
<td>4</td>
<td>N/A</td>
<td>None</td>
<td>+</td>
</tr>
</tbody>
</table>

N/A = not applicable.
Clinical signs of disease were recorded. Diseased dogs were euthanized as required based on severity of disease.

The rCDV-vaccinated puppies were examined daily for clinical signs of CDV for 4 weeks. Clinical signs were recorded, and pups were assigned a clinical score based on severity of such clinical signs as lethargy, vomiting, diarrhea, dehydration, muscle tremors, anorexia, and convulsions. The rCDV-vaccinated dogs were in intimate contact with diseased dogs for 5 days, by which time all the diseased dogs had been euthanized because of the severity of their disease.

**Vaccines**

The recombinant product was Recombitek C4 or C6 (Merial), and the MLV-CDV vaccine was Galaxy D (Schering-Plough Animal Health).

**Statistical Analysis**

The Fisher exact test (two-tailed) was used to compare morbidity and mortality among the groups of experimentally challenged animals.

**RESULTS**

**Part 1**

Group 1 pups vaccinated 1 week before IV challenge infection remained healthy with no clinical signs of disease throughout the study. Group 2 pups vaccinated with either rCDV or MLV-CDV vaccine developed certain clinical signs consistent with CDV disease within 14 days of exposure via IV challenge. Clinical signs ranged from mild to moderate and included diarrhea, lethargy, and anorexia. Severity of disease was similar among the Group 2 pups regardless of vaccine type. None of the dogs in Group 2 developed central nervous system disease. All pups in the group recovered and were free of clinical signs of CDV infection by 4 weeks postchallenge. All pups in Group 3 developed severe disease, including central nervous system disease that resulted in 100% mortality by 21 days postchallenge with the acute biotype of CDV.

Using the Fisher exact test, differences based on mortality were significant ($P < .029$) between Group 3 and Groups 1 and 2. Differences based on morbidity were also significant ($P < .029$) between Group 3 and Group 1 when the MLV-CDV and rCDV vaccinated dogs were combined, whereas no significance was found between Group 3 and the combined MLV-CDV- and rCDV-vaccinated Group 2 dogs.

**Part 2**

The four CDV antibody negative pups vaccinated with rCDV before being housed in a room containing CDV and CDV-infected and diseased dogs showed no signs of distemper infection at any time for 4 weeks after exposure to the CDV-infected dogs. Unvaccinated controls were not placed in the same environment, but the assumption was made that the prolonged contact (5 days) would result in infection in nonvaccinated dogs.
DISCUSSION

Experimental CDV infection with the challenge isolate used in this study (Snyder Hill) is associated with 100% morbidity rates in unvaccinated dogs and mortality rates between 80% and 100% from respiratory, gastrointestinal, and/or neurologic abnormalities and/or anorexia. The AAHA Canine Vaccine Task Force recommends that all puppies be vaccinated with a MLV-CDV vaccine with the last dose administered at 12 weeks of age or older. The Task Force further recommended revaccination at 1 year of age and then no more often than every 3 years through the animal’s life. In the 2003 Guidelines, it was recommended that when rCDV vaccine is used, at least four doses should be administered, with the third dose given when the pup is 12 weeks or older and the fourth dose administered 3 to 4 weeks later. Because there were no published studies demonstrating duration of immunity (DOI) beyond 3 to 4 months after vaccination, yearly revaccination was recommended with the rCDV vaccine. The proven ability of MLV-CDV vaccines to induce rapid protection after one dose in animals that lacked passively acquired maternal antibodies lead the Canine Vaccine Task Force to recommend it as the vaccine of choice for animals in high-risk environments as shelters, kennels, and pet stores. Data on rCDV and its ability to protect animals immediately after vaccination was lacking at the time those recommendations were made. In the original minimum protective dose studies, rCDV produced very low or no antibody titers in animals, and so it was thought that rCDV did not routinely provide a serum antibody level that would inhibit viral replication (sterile immunity). Because of these data, it was thought that two doses of rCDV vaccine and more time may be necessary to protect immunologically naïve dogs; hence, rCDV was not recommended in environments where CDV posed a serious threat.

This study demonstrates that, as occurs with one dose of MLV-CDV vaccine, one dose of rCDV vaccine protects pups exposed hours after vaccination from death and those exposed 7 days after vaccination are completely protected from disease. This information is especially important for immunologically naïve dogs in shelter-like settings or in any situation where CDV poses a major threat. The results of this study and other studies by one of the authors (R. D. S.) led to a change in the 2006 AAHA Canine Vaccine Task Force recommendations. The rCDV vaccine recommendations in the recently updated guidelines published in March 2006 are similar to those for MLV-CDV vaccines.

CONCLUSION

This study demonstrates that rCDV vaccine protects puppies exposed to CDV and performs similarly to the MLV-CDV vaccines, even in the face of severe challenge. As is true with MLV-CDV vaccines, the rCDV vaccine time-to-immunity in pups is sufficient to protect the animals from death when administered within minutes to hours before experimental IV challenge or natural exposure to CDV. Importantly, one dose of rCDV vaccine given to shelter-like settings or in any situation where CDV poses a major threat. The results of this study and other studies by one of the authors (R. D. S.) led to a change in the 2006 AAHA Canine Vaccine Task Force recommendations. The rCDV vaccine recommendations in the recently updated guidelines published in March 2006 are similar to those for MLV-CDV vaccines.

*Results of our rCDV studies were presented at the 2004 ACVIM Forum in Minneapolis and the 2004 AVMA Convention in Philadelphia.*

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pups 7 days before experimental IV challenge completely protected them from CDV disease, similar to the protection provided by a single dose of MLV-CDV vaccine. Therefore, rCDV vaccine can now be recommended for use in shelters, breeding colonies, kennels, and puppy facilities, similar to the recommendations for MLV-CDV vaccines.

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**REFERENCES**