

EFFICACY OF A HALF-DOSE CANINE PARVOVIRUS AND DISTEMPER VACCINE IN SMALL ADULT DOGS: A PILOT STUDY

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ABBREVIATIONS

CAV-2 – canine adenovirus-2
CDV – canine distemper vaccine
CPV – canine parvovirus vaccine
DOI – duration of immunity
DPV – canine distemper and parvovirus vaccine
ELISA – enzyme-linked immunosorbent assay
FPV – feline panleukopenia virus

FCV – feline calicivirus
FHV – feline herpesvirus
HI – hemagglutination inhibition
MLV – modified live virus
OD – optical density
SN – serum neutralization
VAAE – vaccine-associated adverse events

ABSTRACT

Small adult dogs between 3 and 9 years of age, participated in a clinical research study to determine whether giving them just a half-dose of a bivalent canine distemper and parvovirus vaccine (DPV) generated a protective serum antibody titer response 1 and 6 months later in comparison to pre-vaccination titer levels. None of these dogs had received a vaccination for at least 3 years and all were healthy. The half-dose vaccine generated increased serum vaccine antibody titers for all of the dogs studied. Results varied quantitatively when titers measured on the undiluted serum were compared to endpoint titers determined on the same samples when the serum was serially diluted. The median titer and endpoint titer levels had a sustained increase in all dogs at 6 months post-vaccination. Results confirmed that receiving a half-dose of bivalent DPV was efficacious for this study cohort. Further investigations could address a larger number of smaller breed canines.

INTRODUCTION

Background: Vaccination has been and remains the single most important reason why most pet owners bring their pets to

veterinarians for an annual or more often “wellness visit” (1–8). Despite evidence indicating that annual vaccinations are not necessary for previously immunized pets, many practitioners are reluctant to change their current vaccination programs. This is likely because they rarely are taught applied clinical immunology and may not understand the principles of vaccinal immunity (that portion of immunity conveyed by vaccines) (1–3, 9). Clearly, the accumulated evidence indicates that vaccination protocols should no longer be considered as a “one size fits all” program (10).

Based upon nearly 5 decades of clinical and research experience with vaccinations in companion animals, we have accumulated the following information: the dose of canine distemper virus (CDV) and canine parvovirus (CPV) vaccines can be reduced to 50%, but not more, for small breed and mixed breed type dogs, based on body weight, and still convey full duration of immunity (1–4). This applies to puppies and older dogs of small breeds and breed types that weigh 12 pounds or less as adults. Serum vaccine antibody titers have also been performed 3 or more weeks

after vaccination. As reported for dogs given a full dose of vaccine (11), greater than 95% of the dogs given a full or a half half dose mounted what is considered to be protective antibody titers to both CDV and CPV (1). To the author's knowledge, there are no parallel published data on half-dose vaccines given to cats (12–14).

It makes little immunological sense to vaccinate toy- and giant-breed puppies and adult dogs, to exemplify the 2 size extremes, with the same dose of vaccine. These products are stated to provide a sufficient excess of antigen for the average-sized animal so they are likely to be either too much for the toy breeds or too little for the giant breeds (2). Although the minimum immunizing doses have been established (2, 5–7), the optimum dosages required for disease protection have yet to be determined. Researchers are still uncertain as to whether these dosages should be based on body mass (2, 6). It apparently depends to some extent upon whether the vaccine is of modified live virus (MLV) attenuated origin, or killed inactivated viral origin because of the differing immunogenic principles involved (2, 5, 6, 9). According to some experts, killed, inactivated vaccines should be adjusted for body mass, and yet even today, rabies vaccine — the most potent of all such vaccines — is required by law to be given at a full dose to dogs of all sizes (2, 3). More field evidence and clinical data are still needed today on this important issue.

Similarly, the administration of identical vaccine dosages for animals in all age groups is questionable (2, 3, 6, 13). The combination of certain specific viral antigens such as CDV with canine adenovirus-2 (CAV-2), for cross-protection against infectious canine hepatitis virus) and/or CPV has been shown to influence the immune system by reducing lymphocyte numbers and responsiveness (9) and causing thymic depletion (2, 3).

What is the potential effect of those findings on vaccine dosage or age of vaccination, given the wide divergence of size among dog breeds? Why has this been largely ignored by the research and clinical veterinary communities 25 years later? In humans, questions of the vaccine dosage necessary to elicit full protection in infants rather than adults have been addressed for hepatitis B vaccine (15). The investigation was made for economic reasons to determine whether the standard dosage could be split and still afford protection for more than one infant (to reduce

costs of vaccinating children in socioeconomically deprived countries). One fifth of the adult dose of hepatitis B vaccine was found to protect infants vaccinated during the first 6 months of life (15).

Tragically, a similar principle was applied to vaccinating children with a 10 to 50- fold higher titered measles virus vaccine in an attempt to overcome maternal immunity. Increased infant mortality resulted, especially in girls, who succumbed to other infections because their immune systems became suppressed (2).

In one study, adult household pets having adequate to very good serum antibody titers to one or more of CDV, CPV and CAV-2 were given an additional polyvalent booster vaccination (7). Two months later, serum antibody titers to these 3 viruses were measured again. Whereas titers to CDV and CAV-2 showed a significant increase, those for CPV did not (7), raising the question of whether these dogs were already well-immunized against CPV, or if some other immunological mechanism was being invoked. Regardless, the existing CPV antibody titers indicated that they all should remain protected against street CPV (5, 11).

Another study by these same Japanese investigators (6) assessed data from 3 different CDV, CPV, and CAV-2 vaccines that either included or did not include a killed, inactivated leptospirosis bacterin. The purpose of the study was to see if the simultaneous administration of leptospirosis vaccination had any influence upon the serum antibody titers elicited 11–13 months later. Additionally, this multivariate study examined 3 different adult age and body weight groups. Some conflicting results were obtained: there were significantly lower CPV antibody titers were found in dogs vaccinated with leptospirosis versus those not given leptospirosis vaccine for 2 of the vaccines given to the 2-yr old age group and for 1 vaccine given to the 7-yr and greater age group, but no significant differences were seen at the 3–6 yr-old ages (6). No significant differences were seen for CPV titers of any group with respect to body weight. For CDV, no differences were seen for any of the age groups, although a significantly lower CDV titer was seen in those receiving leptospirosis vaccines in the medium weight group but for only 1 vaccine product.

Results for CAV-2 titers also were lower in the leptospirosis vaccine group but for only 1 vaccine product in the 2-yr age group and also in the small dog size group (6).

What do the results of this complex multivariant study reveal? Solid conclusions are difficult to make, except that adding a leptospirosis bacterin to the polyvalent MLV vaccines reduced the subsequent serum antibody titers primarily against CPV. Does this reduction in antibody titer level leave these dogs susceptible to CPV disease? Probably not, as vaccine protection against the CPV, CDV and CAV-2 "core" vaccine antigens is known to be influenced by the age of the animal; with older animals being less susceptible to these viral diseases (11,13). However, separating leptospirosis vaccines from the rest of the "core" may be the most reliable way to ensure that adequate "core" vaccine immunity is sustained.

Study Objective: The purpose of the current study was to document the serum antibody titer responses from administering a half-dose of a bivalent CDV) and CPV (a) to small breed adult dogs that had not been vaccinated in at least 3 years.

METHODS

Eligible small breed adult dogs, being at least 3 years and not more than 9 years of age, were recruited by posting an announcement on the author's web site (b) and by e-mail to holistic veterinarians and small breed pet owner clients that

are entered into the author's company electronic Laboratory Information System (c).

Participating veterinarians were given an Instruction Sheet (Figure 1) and Informed Consent Form to be completed at the time of enrollment and signed by the dog owner (Figure 2).

Prior to receiving a half (½)-dose of the bivalent DPV vaccine (a), a pre-vaccination whole blood sample (3–5 ml) was collected by the participating veterinary clinic, and allowed to clot by placing it into a plain red-top glass tube (d). The clotted sample was centrifuged and the separated serum was decanted and placed into a labeled, empty glass or plastic tube for shipment, by first class or priority mail in a small padded box, to the author's laboratory (c).

Upon receipt at the laboratory, the serum samples were stored at 4°C until assayed in batches. Serum antibody titers were measured for CDV and CPV using previously established enzyme-linked immunosorbent assay (ELISA) methodology and optical density (OD) readings were obtained with a spectrophotometer (e) (10). The ELISA assay methods used for CDV and CPV have been shown

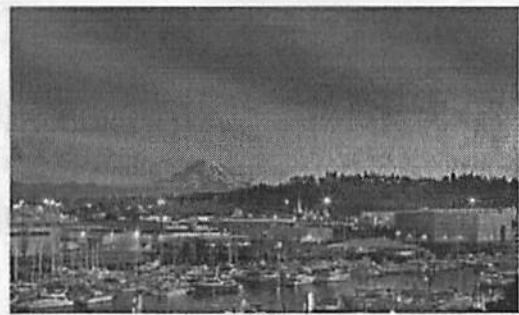


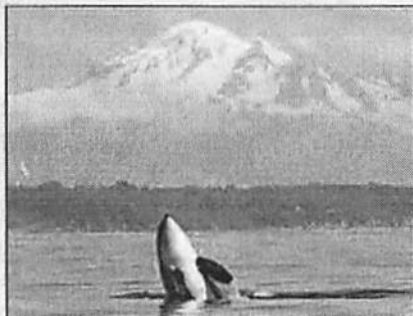
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to have high diagnostic accuracy in comparison to the reference standard assays of serum neutralization (SN) and hemagglutination inhibition (HI) (16).

The participating veterinarians and dog owners had blood from the same dogs collected and processed as described above at 4 weeks and 6 months after each dog had received a half-dose of DPV vaccine. The samples were labeled as 4 weeks Post-DPV and 6 months Post-DPV, and shipped to the author's laboratory.

All 13 samples were assayed at each of the 3 sampling times for CDV and CPV titers; these were measured on the undiluted serum and then in serial dilutions until the endpoint titer was reached. At the 6-month time point, 5 of samples were inadvertently discarded before being assayed.

RESULTS

The pilot study enrolled 13 adult dogs that weighed 12 pounds or less and had not received any routine booster vaccines for at least 3 years. Two dogs were rejected because they were over 10 years of age, and another 3 were ineligible as they had received booster vaccinations less than 3 years ago.

Figure 1. Small Breed Vaccine Titer Study Instructions for Participating Veterinarian

INSTRUCTIONS FOR PARTICIPATING VETERINARIAN

HEMOPET / HEMOLIFE - W. JEAN DODDS, DVM
11901 S.W. 14TH AVE., GARDEN GROVE, CA 92645
Phone: (714) 991-2272 Fax: (714) 991-9123 BILLING: (714) 991-9222

DATE: _____
VETERINARIAN: _____
(Name MUST be provided)
Address: _____
City: _____ State: _____ Zip: _____
Phone: _____ FAX: _____ E-mail: _____

**** INFORMED CONSENT RELEASE FORM MUST BE SIGNED BY PET OWNER ****

OWNER: _____
Address: _____
City: _____ State: _____ Zip: _____
Phone: _____ FAX: _____ E-mail: _____

PET NAME: _____
Breed: _____
Age: _____ Sex: (circle) _____ F M MN Weight: (last more than 12 pounds) _____
ON REGISTRATION: YES NO If Yes, brief list: _____
HOW BLED: _____ HOW DIED: _____ BLOOD DRAWN: _____ (SEE POST-ILL)

INSTRUCTIONS: 1) Before giving the 1/2 dose of Nobivac DPV to your patient:
Draw blood (2 ml), place in EDTA to let it clot. Centrifuge and remove the serum; place into an empty EDTA or plastic tube.
Tape the closed top to provide extra security in transit.
You or your client can ship the separated serum sample to Hemopet by USPS Priority Mail in a small box with paper padding or bubble wrap. Please include a copy of the Test Request submission form, the signed Informed Consent form, and this instruction form with the sample.
2) Give the patient just 1/2 dose of the Nobivac DPV vaccine provided by us to your client.
3) Repeat the blood collection and processing steps described above: 4 weeks after the vaccination and again 6 months after the vaccination.
Thank you for participating in this clinical research study. Jean (W. Jean Dodds, DVM)

Figure 1: Instruction Sheet

Figure 2. Small Breed Vaccine Titer Study Informed Consent

ANNOUNCEMENT

Small Breed Vaccine Clinical Study

W. Jean Dodds, DVM
Hemopet, Garden Grove, CA



Minimizing the Volume of "Core" MLV Vaccines Given to Small Dogs

Clinical experience has shown that the dose of canine distemper virus (CDV) and canine parvovirus (CPV) vaccines can be reduced to 50%, but not more, for small breed type dogs, based on optimum body weight, and still convey the full duration of immunity.

Reducing the volume of vaccine and the number of antigens given together decreases the likelihood of an adverse event. Holistic veterinary medicine is now embracing a new standard of care by reducing the dosage of vaccine depending upon the weight of the pet and other factors.

We are now recruiting 20 small breed adult dogs to participate in a fully funded clinical pilot study. Any adult dog weighing less than 12 pounds that has not been vaccinated for either CDV or CPV in the prior 12 months is eligible to enroll. There is no charge to the participants.

A signed Informed Consent Form is required from each dog's owner/guardian, prior to entering the study (copy below).

Blood samples will be collected from all 20 enrolled dogs before, 4 weeks after, and 6 months after they have been vaccinated with a half-dose (0.5 ml) of a licensed bi-valent distemper and parvovirus vaccine (Nobivac DPV; Merck Animal Health; available in 25-dose packs).

INFORMED CONSENT:

Minimizing the Volume of MLV "Core" Vaccines Given to Small Dogs

One of the Principal Investigators has nearly five decades of clinical and research experience with vaccinations in companion animals. This experience has shown that the dose of canine distemper virus (CDV) and canine parvovirus (CPV) vaccines can be reduced to 50%, but not more, for small breed and breed type dogs, based on body weight, and still convey full duration of immunity. This applies to puppies and older dogs of small breeds and breed types that weigh 12 pounds or less as adults. This investigator has personally followed up on these vaccines with serum vaccine titers performed 3 or more weeks after vaccination. As reported for dogs given a full dose of vaccine (Twark and Dodds, JAVMA 217:1021-1024, 2000), greater than 95% of the dogs given a half dose mounted what is considered to be protective antibody titers to both CDV and CPV.

The purpose of the current proposal is to document this experience with half-dose vaccines in a formal research grant study with the intent of publishing the results in a veterinary journal as well as presenting the data at veterinary meetings.

1. I have read and understood the above paragraphs explaining the collaborative study of giving minimal vaccine dosage (0.5 ml = 1/2 vaccine manufacturer's dose) to small breed dogs weighing less than 12 pounds as adults.
2. I also understand that my dog will have a small (3 ml) blood sample collected before, four (4) weeks after and again six (6) months after the vaccination to check the serum antibody titer levels against canine distemper virus and parvovirus.
3. I appreciate the importance of this study in advancing our understanding of the amount of vaccine needed for small breed dogs, and the duration of immunity conferred by this dose of vaccine.
4. I understand that any information I give about myself or my dog will be held in strict confidence.
5. I understand that this research may not benefit my animal directly, but in the future may be of benefit to other animals.
6. I understand that the results of this study may be presented and/or published at scientific meetings and in journals.

Name of Animal Owner (Guardian): _____

Address: _____

Phone # _____ FAX # _____ E-mail: _____

Signed: _____ Date: _____

Figure 2: Informed Consent Form

The 13 enrolled dogs completed the pre-vaccination testing and the 4 week post-½-dose DPV testing, and 8 of them completed the 6 month post-vaccination follow up titer measurement. The remaining 5 dogs had samples drawn at 6 months but these were inadvertently discarded.

Titers on Undiluted Serum (Figures 3a and 3b; Table 1)

Results indicated that all 13 dogs (not vaccinated for at least 3 years), had measurable serum antibody titers to both CPV) and CDV.

Canine Parvovirus (CPV)

Pre-Vaccination The pre-vaccination titers for CPV were all above the positive control with 12 of 13 being well above that OD level, when measured on the undiluted serum samples (Figure 3a), The median titer level was 125 (range 73–125) (Table 1).

4 Weeks Post-½-Dose Vaccination Four weeks after receiving the ½ dose of DPV vaccine, CPV titers went up in 9 of the 13 dogs and stayed essentially the same in the other 4 dogs,

Table 1. AHVMF Small Breed Half-Dose Vaccine Study for CPV & CDV Titers *			
Serum Titers	Pre-Vaccine Titers n = 13	4 Week Post-Vaccine Titers n = 13	6 Months Post-Vaccine Titers n = 8
CPV, Undiluted	125 ± 22 (73–156)	136 ± 14 (110–162)	169 ± 58 (96–257)
CPV, Endpoint Dilution	116 ± 87 (32–256)	94 ± 65 (32–256)	240 ± 183 (64–512)
CDV, Undiluted	89 ± 31 (55–143)	148 ± 33 (106–199)	148 ± 71 (110–257)
CDV, Endpoint Dilution	21 ± 26 (2–64)	80 ± 38 (32–128)	97 ± 87 (8–256)

* Median ± SD and Ranges

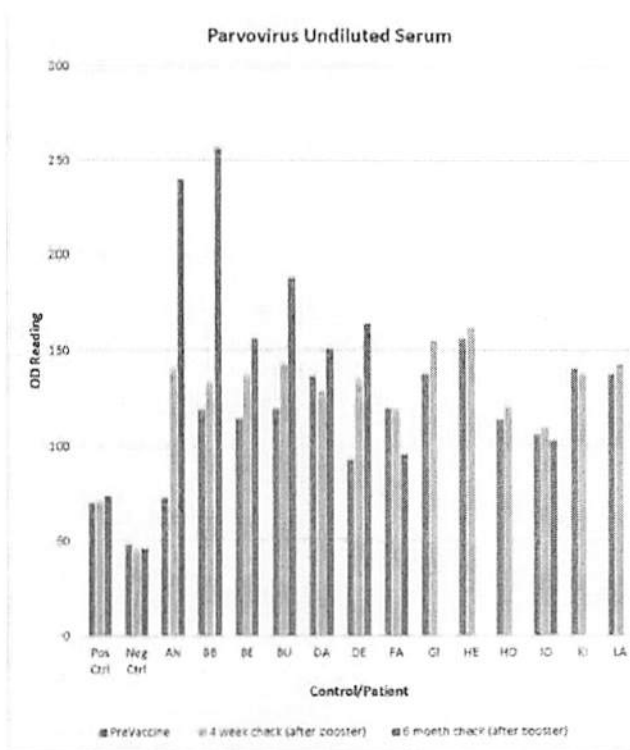


Figure 3a: Small Breed Vaccine Study
Serum Vaccine Titers for CPV on Undiluted Serum.

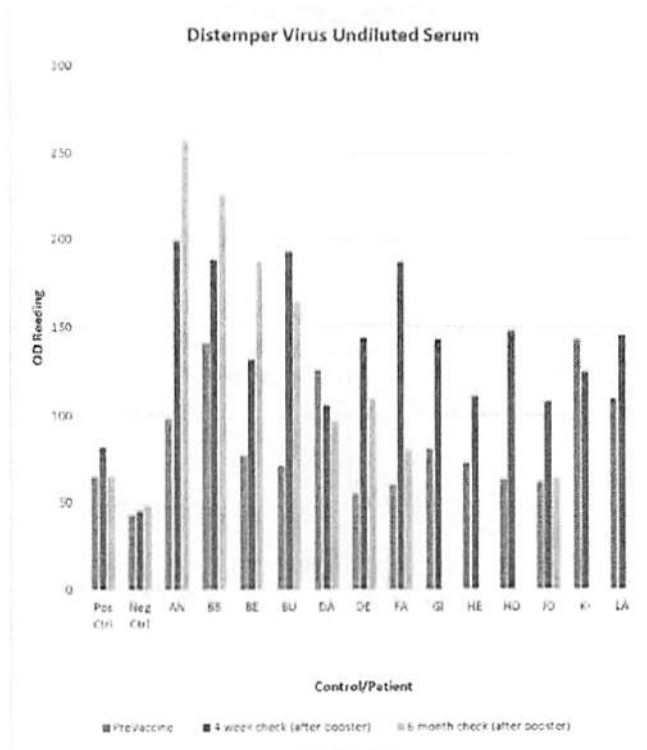


Figure 3b: Small Breed Vaccine Study
Serum Vaccine Titers for CDV on Undiluted Serum.

whose pre-booster titers were already high or very high (Figure 3a). The median titer level was 136 (range 110–162) (Table 1).

Results of the final serum CPV titers measured on undiluted serum at 6 months after the ½ dose vaccination showed the following (Figure 3a):

6 Months Post-½-Dose Vaccination Six of the 8 dogs showed a rise in CPV OD from the 4-weeks sample. The other 2 dogs had lower 6-month OD titers for CPV, although one of these dogs had essentially the same high titer level at all 3 time points (Figure 3a). The median titer level was 169 (range 96–257) (Table 1).

Canine Distemper Virus (CDV)

Pre-Vaccination The pre-vaccination titers for CDV were lower than those of CPV relative to the positive control OD; 2 of these were just below the positive control but above the negative control OD, and another 6 samples were at or slightly above the positive control OD. Thus, only 5 dogs had high pre-vaccination CDV titers (Figure 3b). The median titer was 89 (range 55–143) (Table 1).

4 Weeks Post-½-Dose Vaccination For CDV titers, 11 of 13 dogs had significantly boosted titers after vaccination, and the other 2 dogs had slightly lower post-vaccination titers but their pre-vaccination titer levels were already high or very high (Figure 3b). The median titer level was 148 (range 106–199) (Table 1).

Results of the final serum CDV titers measured on undiluted serum at 6 months after the ½-dose vaccination showed the following (Figure 3b):

6 Months Post-½-Dose Vaccination For CDV, 3 of the 8 dogs had higher OD titers at 6 months than at 4 weeks post-vaccination. The other 5 had lower OD titer readings than at 4 weeks, and were still high except for one dog. The median titer level was also 148 (range 110–257) (Table 1).

Endpoint Titers on Serially Diluted Serum (Figures 4a and 4b; Table 1)

Canine Parvovirus (CPV)

Pre-Vaccination The pre-vaccination endpoint titers for CPV were all above the positive control with 12 of 13 being well

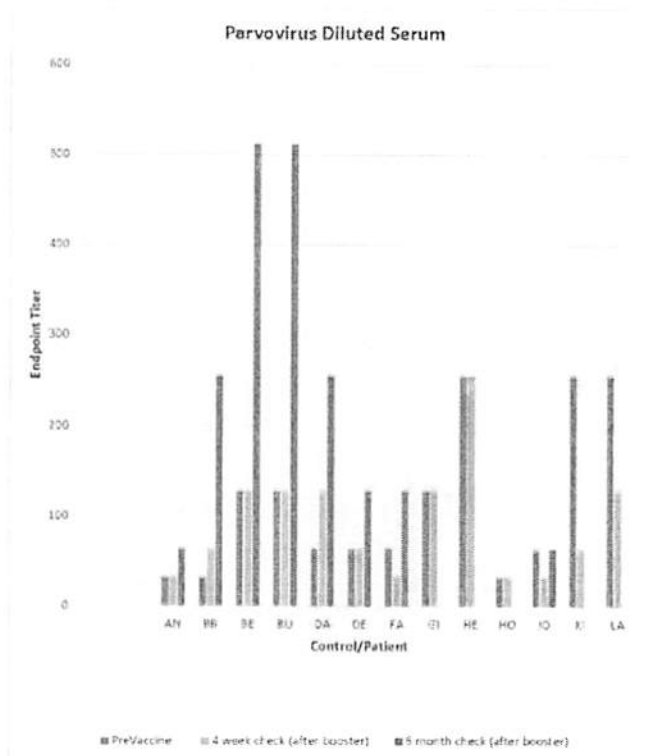


Figure 4a: Small Breed Vaccine Study Serum Vaccine Endpoint Titers CPV on Diluted Serum.

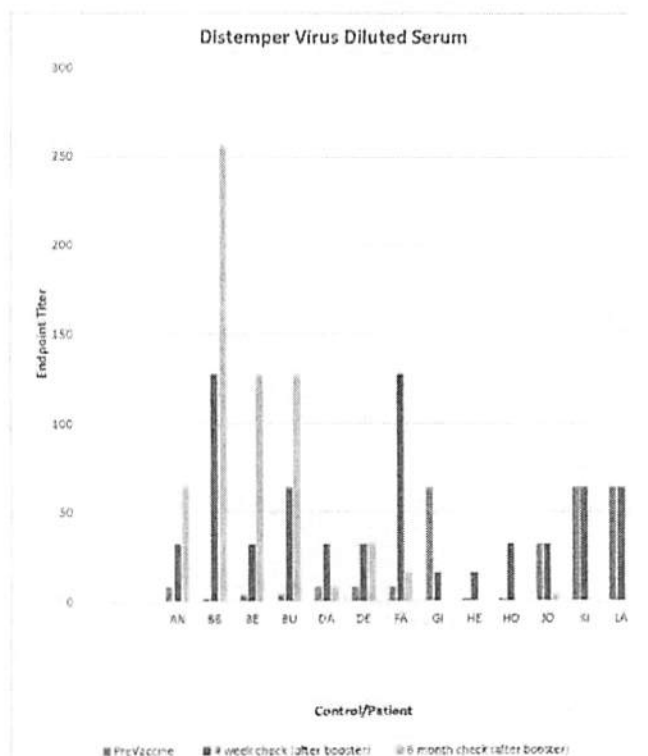


Figure 4b: Small Breed Vaccine Study Serum Vaccine Endpoint Titers CDV on Diluted Serum.

above that OD level, when measured on the diluted serum samples (Figure 4a). The median endpoint titer level was 116 (range 32–256) (Table 1).

4 Weeks Post-½-Dose Vaccination Two of 13 dogs had boosted endpoint titers levels at 4 weeks, with a high titer level of 1:256 (Figure 4a). The median endpoint titer level was 94 (range 32–256) (Table 1).

6 Months Post-½-Dose Vaccination For CPV, 7 of the 8 dogs had boosted endpoint titers levels at 6 months with endpoint titer dilutions as high as 1:512. Seven of the 13 dogs had essentially the same endpoint titer levels at 4 weeks as they had pre-vaccination, with the highest level at 1:256. The other 4 of 13 dogs had lower endpoint titer levels at 4 weeks than they had prior to the ½-dose vaccination. The median titer level was 240 (range 64–512) (Table 1).

Canine Distemper Virus (CDV)

Pre-Vaccination The pre-vaccination endpoint titers for CDV were lower than those of CPV relative to the positive control OD; 2 of these were just below the positive control but above the negative control OD, and another 6 samples were at or slightly above the positive control OD. Only 3 dogs had higher pre-vaccination CDV endpoint titers (Figure 4b). The median endpoint titer level was 21 (range 2–64) (Table 1).

4 Weeks Post-½-Dose Vaccination For CDV titers, 9 of 13 dogs had significantly boosted endpoint titers after vaccination, and the other 4 dogs had equivalent or lower post-vaccination endpoint titers but their pre-vaccination endpoint titer levels were already high (Figure 4b). The median endpoint titer level was 80 (range 32–128) (Table 1).

6 Months Post-½-Dose Vaccination For CDV, 4 of 8 dogs had markedly boosted endpoint titer levels at 6 months, with the highest level at 1:256 (Figure 4b). The median endpoint titer level was 97 (range 8–256) (Table 1).

DISCUSSION

The rationale for the present study was prompted by the fact that adverse reactions to vaccines, also called vaccine-associated adverse events (VAAE), can still cause serious illness, suffering and death (2, 3, 15, 17–23). They remain relatively rare, however, based upon the published human and veterinary literature and personal clinical experience (2, 3, 15, 17–23).

Viral vaccines are intended to provide an immune response similar in duration to that following a natural infection. These anti-viral adaptive immune responses typically result in the development of sterilizing immunity that not only prevents clinical disease but also prevents infection; and the duration of immunity (DOI) generated here is often lifelong. In contrast to viruses, adaptive immunity to bacteria, fungi or parasites develops more slowly with a generally shorter DOI; and development of sterilizing immunity is less common. Older dogs and cats rarely die from vaccine-preventable infectious diseases, especially when they have been vaccinated and immunized as young adults (5, 11, 18, 19). Young animals, however, can still become seriously ill and die from these infectious diseases, most often because vaccines were given too early in life when the presence of their residual maternally derived antibody partially neutralized the effects of the vaccine, leaving the youngster inadequately protected.

Studies in dogs (18) and cats (19) assessed the DOI in previously vaccinated pets that had not received a booster vaccination in as long as 9 years. When the dogs were challenged with CDV, CPV, and CAV-2 and the cats were challenged with feline panleukopenia virus (FPV), feline calicivirus (FCV) and feline herpesvirus (FHV), both species resisted infection and/or disease. Thus, even a single dose of these MLV canine or feline “core” vaccines, when administered at 16 weeks or older, should provide long-term immunity in a very high percentage of animals, while also increasing the overall herd (population) immunity (18, 19).

But factors associated with the age and weight of pet animals being vaccinated are also important, not only for affording protection against these diseases, but also for helping to assure the well-being of those vaccinated.

The risk of a VAAE in this large canine study population was inversely related to the dog’s weight, such that for dogs weighing < 10 kg, the actual VAAE rate was underestimated (18). This weight-response relationship was previously suggested by a study in which dogs of toy breeds had significantly more suspected VAAEs than other dogs, although body weight was not reported (18). Vaccines, in contrast to virtually all veterinary pharmaceuticals, are prescribed on a one-dose-fits-all basis, rather than by body weight (2, 5, 11, 20). Even when adjusted for body weight, there was a nearly linear increase in VAAE rate when the number of vaccine antigens given simultaneously was increased (18). This suggests that vaccine

components other than the primary antigen may contribute to adverse events (14–19). In a published study (9), 8 of 18 dogs that developed immediate-type allergic reactions had high concentrations of specific serum IgE against the vaccines, and 7 also had specific IgE antibodies against fetal calf serum (9, 11, 12, 14–16).

Further, the canine study found that young adult small-breed neutered dogs receiving multiple vaccines per office visit were at greatest risk of a VAAE within 72 hours after vaccination (18). The authors concluded that these factors should be considered in risk assessment and risk communication with clients regarding vaccination of dogs (18).

Parallel data were documented by these same investigators two years later for cats (19), where the risk of VAAE significantly increased as the number of vaccines administered per office visit increased. The risk was greatest for cats about 1 year of age, and overall risk was greater for young adult neutered versus sexually intact cats (19). The most commonly diagnosed VAAE was lethargy with or without fever. The authors concluded that veterinarians should incorporate these findings into risk communications and limit the number of vaccinations administered concurrently to cats (19).

For these special cases, appropriate alternatives to current vaccine practices include (10, 11, 13, 16, 20–22):

- measuring serum antibody titers;
- avoidance of unnecessary vaccines or over vaccinating;
- caution in vaccinating sick or febrile individuals; and
- tailoring a specific minimal vaccination protocol for dogs and cats of breeds or families known to be at increased risk for adverse reactions.
- starting the vaccination series later, such as at 8–10 weeks of age when the immune system is more able to handle antigenic challenge;
- alerting the caregiver to pay particular attention to the puppy and kitten behavior and overall health after the second or subsequent boosters; and
- avoiding revaccination of individuals already experiencing a significant adverse event. Littermates of affected puppies and kittens should be closely monitored after receiving additional vaccines in a series, as they too are potentially at higher risk.

Canine Vaccine Adverse Events (18)

- retrospective cohort study; 1.25 million dogs vaccinated at 360 veterinary hospitals
- 38 adverse events per 10,000 dogs vaccinated
- inversely related to dog weight
- vaccines prescribed on a 1-dose-fits-all basis, rather than by body weight.
- increased for dogs up to 2 yr of age, then declined
- greater for neutered versus sexually intact dogs
- increased as number of vaccines given together increased
- increased after the 3rd or 4th vaccination
- genetic predisposition to adverse events documented

Feline Vaccine Adverse Events (19)

- retrospective cohort study; 0.5 million cats vaccinated at 329 veterinary hospitals
- 51.6 adverse events per 10,000 cats vaccinated
- inversely related to cat weight
- increased for cats about 1 yr of age
- greater for neutered versus sexually intact cats
- increased as number of vaccines given together increased
- lethargy with or without fever was most common sign

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Some veterinarians have challenged the validity of using vaccine titer testing to assess the immunologic status of animals against the common, clinically important infectious diseases (10–12).

Research has shown that once an animal's titer stabilizes it is likely to remain constant for many years. Properly immunized animals have sterilizing immunity that not only prevents clinical disease but also prevents infection, and only the presence of antibody can prevent infection (10–14, 16, 24–27). As stated by eminent expert Dr. Ronald Schultz in discussing the value of vaccine titer testing, these tests "show that an animal with a positive test has sterilizing immunity and should be protected from infection. If that animal were vaccinated it would not respond with a significant increase in antibody titer, but may develop a hypersensitivity to vaccine components (e.g. fetal calf serum). Furthermore, the animal doesn't need to be revaccinated and should not be revaccinated since the vaccine could cause an adverse reaction (hypersensitivity disorder). You should avoid vaccinating animals that are already protected. It is often said that the antibody level detected is "only a snapshot in time". That's simply not true; it is more a "motion picture that plays for years" (10).

Furthermore, protection as indicated by a positive titer result is not likely to suddenly drop-off unless an animal develops a medical problem such as cancer or receives high or prolonged doses of immunosuppressive drugs. Viral vaccines prompt an immune response that lasts much longer than that elicited by classic antigen. Lack of distinction between the two kinds of responses may be why practitioners think titers can suddenly disappear (10, 14, 16).

But, not all vaccines produce sterilizing immunity (3, 10, 13). Those that do include: CDV, CPV, and CAV-2 in the dog, and FPV in the cat. Examples of vaccines that produced non-sterile immunity would be leptospirosis, bordetella, rabies virus, FCV and FHV — the latter two being upper respiratory viruses of cats. While non-sterile immunity may not protect the animal from infection, it should keep the infection from progressing to severe clinical disease (3, 10, 25).

Therefore, interpreting titers correctly depends upon the disease in question. Some titers must reach a certain level to indicate immunity, but with other agents like those that

produce sterile immunity, the presence of any measurable antibody shows protection (10, 11, 20, 24). The positive titer test result is fairly straightforward, but a negative titer test result is more difficult to interpret, because a negative titer is not the same thing as a zero titer and it doesn't necessarily mean that animal is unprotected. A negative result usually means the titer has failed to reach the threshold of providing sterile immunity. This is an important distinction, because for the clinically important CDV and CPV of dogs, and FPV of cats, a zero antibody titer indicates that the animal is not protected against CPV and may not be protected against CDV or FPV (10–14, 24–27).

Finally, a decade of experience with vaccine titer testing reveals the following: Published studies in refereed journals show that 90–98% of dogs and cats that have been properly vaccinated develop good measurable antibody titers to the infectious agent measured (10–13, 24–27). So, in contrast to the concerns of some practitioners (4, 6, 7), using vaccine titer testing as a means to assess vaccine-induced protection will likely result in the animal avoiding needless and unwise booster vaccinations.

The author's study (11), evaluated 1441 dogs for CPV antibody titer and 1379 dogs for CDV antibody titer. Of these, 95.1 % were judged to have adequate CPV titers, and nearly all (97.6 %) had adequate CDV titers. Vaccine histories were available for 444 dogs (CPV) and 433 dogs (CDV). Only 43 dogs had been vaccinated within the previous year, with the majority of dogs (268 or 60%) having received a booster vaccination 1–2 years beforehand. On the basis of these data, we concluded that annual revaccination is unnecessary (11). Comprehensive studies of the duration of serologic response to 5 viral vaccine antigens in dogs (26) and 3 viral vaccine antigens in cats (27) were published a decade ago by researchers at a major pharmaceutical company (f), and found a sustained DOI of at least 3 years in both dogs and cats, so why hasn't the veterinary profession at large followed suit?

When an adequate immune memory has already been established, there is little reason to introduce unnecessary antigen, adjuvant, and preservatives by administering booster vaccines. By titring triennially or more often, if needed, one can assess whether a given animal's humoral immune response has fallen below levels of adequate immune memory. In that event, an appropriate vaccine booster can be administered (20–24).

CONCLUSIONS

This study addressed whether small breed adult dogs, vaccinated at least 3 years previously, could be adequately immunized and protected by receiving less than a full dose of a bivalent DPV vaccine. A half-dose of this vaccine was given and generated increased serum vaccine antibody titers for all of the dogs studied. Results varied quantitatively when titers measured on the undiluted serum (standard method) were compared to endpoint titers determined on the same samples when the serum was serially diluted. The median

titer and endpoint titer levels had a sustained increase in all dogs at 6 months post-vaccination. As the presence of measurable CPV and CDV serum antibody titers reflects immunity to these viruses, and given that vaccines are known to cause adverse events, especially in smaller dogs, results of this study confirmed that receiving a half-dose of bivalent DPV vaccine was efficacious for this study cohort. Further investigations could address a larger number of smaller canines. 🐾

ENDNOTES

- a. Nobivac DPV; Merck Animal Health, Madison, NJ.
- b. www.hemopet.org; Garden Grove, CA.
- c. www.hemalife.org; Garden Grove, CA.
- d. Vacutainer, RTT; Becton-Dickinson, East Rutherford, NJ.
- e. TiterChek; Zoetis US, Florham Park, NJ.
- f. Pfizer Animal Health, Kalamazoo, MI.

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