

Duration of serologic response to five viral antigens in dogs

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Objective—To determine whether vaccinated dogs either remained seropositive or responded serologically to revaccination for 5 key viral antigens after extended periods since their last vaccination.

Design—Serologic survey.

Animals—322 healthy client-owned dogs.

Procedure—Dogs were ≥ 2 years old and vaccinated against canine distemper virus (CDV), canine adenovirus-1 (CAV-1), canine adenovirus-2 (CAV-2), canine parainfluenza virus (CPIV), and canine parvovirus (CPV). On day 0, dogs were revaccinated with a vaccine from the same vaccine line as they had historically received. Antibody titers were measured in sera collected at day 0 (prevaccination titer) and 5 to 7 days later (postvaccination titer). Dogs were considered to have responded serologically if they had a day-0 serum neutralization titer to CDV $\geq 1:32$; a serum neutralization titer to CAV-1, CAV-2, or CPIV $\geq 1:16$; a hemagglutination inhibition titer to CPV $\geq 1:80$; or a ≥ 4 -fold increase in antibody titer after revaccination.

Results—The percentage of dogs that had titers at or greater than the threshold values or responded to revaccination with a ≥ 4 -fold increase in titer was 98.1% for CDV, 98.4% for CAV-1, 99.0% for CAV-2, 100% for CPIV, and 98.1% for CPV.

Conclusions and Clinical Relevance—In most dogs, vaccination induced a response that lasted up to and beyond 48 months for all 5 antigens. Although not equivalent to challenge-of-immunity studies as a demonstration of efficacy, results suggest that revaccination with the same vaccine provides adequate protection even when given less frequently than the traditional 1-year interval. The study provides valuable information for clinicians to help determine appropriate revaccination intervals. (*J Am Vet Med Assoc* 2004;224:55–60)

Instead of using the traditional 1-year revaccination interval for companion animals, veterinarians are increasingly designing protocols based on disease risk, degree and duration of serologic response to specific vaccines, interval since last vaccination, risk of adverse postvaccination events, and an increased understanding of the canine and feline immune systems. This more conservative approach seeks to minimize unnecessary vaccinations and the possibility of rare postvaccination sequelae such as anaphylaxis, autoimmune reactions,¹⁻³ immunosuppression,⁴ and, in cats, injec-

tion-site fibrosarcomas.⁵⁻⁷ Presently, regarding revaccination interval recommendations on product labeling, the USDA Center for Veterinary Biologics states that the role of sustained serologic titers in the prevention of disease has not been confirmed. Real-time, challenge-of-immunity studies conducted over multiyear periods are expensive and impractical to the extent that vaccine manufacturers do not ordinarily consider them except for rabies vaccines. Instead, there is a growing reliance on serologic data as indicators of susceptibility and appropriate revaccination intervals for individual animals in clinical settings.⁸⁻¹⁰ Serum titers for antibodies against canine distemper virus (CDV), canine adenovirus-1 (CAV-1), CAV-2, and canine parvovirus (CPV) correlate with protection,^{2,11-15} although the protective role of serum antibodies against canine parainfluenza virus (CPIV) is less clear-cut.

The purpose of the study reported here was to determine the duration of serologic response after vaccination for 5 viral antigens of clinical importance in dogs, namely CDV, CAV-1, CAV-2, CPIV, and CPV.

Materials and Methods

Dogs—Dogs were client-owned animals maintained in domestic settings, allowing the serologic response to be assessed under conditions encountered in everyday practice. Dogs were selected for study after a thorough evaluation of their medical records; 322 dogs of both sexes, either sexually intact or neutered, of various ages, breeds, weights, lifestyles, and time since last vaccination were considered eligible and enrolled in the study. Dogs were required to be clinically normal, at least 2 years of age, not vaccinated within the past 12 months, and have no history of disease caused by CDV, CAV-1, CAV-2, CPIV, or CPV. Dogs had to have received a documented 2-dose primary vaccination series with a vaccine from the same vaccine line as the test vaccine,^a with or without a *Leptospira* Canicola-Icterohaemorrhagiae bacterin, administered 2 to 7 weeks apart as a puppy, and at least 1 revaccination dose of vaccine 8 to 16 months later. Occasionally, dogs were encountered that met the above requirements, but they had received combination vaccines against *Bordetella bronchiseptica*, CPIV, or CAV-2. These dogs were included in the study but excluded from analysis of responses against CPIV, CAV-1, and CAV-2. Dogs were also excluded if they had a history of vaccine intolerance such as allergy, severe systemic disease of any kind, were treated with an immunosuppressive agent within the past 60 days, pregnant, or treated with an anti-inflammatory drug within the past 30 days. Dogs were maintained by their owners in conventional domestic environments with or without other animals.

Site selection—The study was conducted at 44 companion animal veterinary clinics in the United States and Canada. These practices had clientele, vaccination use history, and records management that permitted compliance with the study protocol. At least 1 licensed veterinarian at each site was designated as the investigator or examining clini-

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cian. All participating practices provided affidavits attesting to exclusive use of a vaccine from the same vaccine line as the test vaccine during the period of historic vaccinations. Dog owners signed consent forms agreeing to participate in the study and comply with its protocol.

Test vaccine—A modified-live CDV-CAV-2-CPIV-CPV vaccine (ie, the test vaccine) combined with an *L. Canicola-Icterohaemorrhagiae* bacterin^a was used to revaccinate eligible dogs on day 0 of the study. The vaccine contained a CAV-2 strain that has been demonstrated to cross-immunize against CAV-1.¹¹ Vaccine was administered SC in a 1-mL dose. All prior vaccinations for CDV, CAV-1, CAV-2, CPIV, and CPV were with a vaccine from the same line of vaccines as the test vaccine, with or without the *Leptospira* bacterin. Some dogs received other manufacturers' vaccines that contained *B. bronchiseptica* combined with CAV-2 or CPIV antigens. Serologic assays for CAV-2, CAV-1, or CPIV for these dogs were not included in the study.

Serologic assays—Serum from each blood sample was frozen and sent to Cornell University Veterinary Diagnostic Laboratory (CUVDL) for testing. The laboratory was unaware of the vaccination history of any of the dogs. Each sample was evaluated for serum neutralization (SN) titers for antibodies against CAV-1, CAV-2, CDV, and CPIV and for hemagglutination inhibition (HI) titer for antibodies against CPV. Serial 2-fold dilutions were inoculated onto a 96-well microtiter plate, incubated, and evaluated for end point detection. Titration end points for viral agents were agglutination of swine RBCs, cytopathic effect (CPE) of CAV-1 and CAV-2 in Madin-Darby canine kidney cells, CPE of CDV in VERO cells, and CPE of CPIV in canine epidermal cells.

A serologic response to the respective viral test antigen was considered to have occurred if the dog was seropositive on day 0 or if analysis of the postvaccination serum sample revealed an anamnestic response (4-fold or greater increase in antibody titer vs the prevaccination [day 0] sample). Minimum antibody titers established by CUVDL were used to determine whether a sample was seropositive against a given antigen (SN titer for antibodies against CDV \geq 1:32; SN titer for antibodies against CAV-1, CAV-2, or CPIV \geq 1:16; and HI titer for antibodies against CPV \geq 1:80).

Lifestyle and disease risk questionnaire—On day 0, the dog owner completed a lifestyle and disease risk questionnaire for each dog. Dogs were categorized into high- and low-risk groups on the basis of questionnaire responses. A dog was included in the high-risk group if there were 5 or more instances during the past month of any certain behaviors, including roaming unsupervised; walking, exercising, or playing with other dogs not in the household; contact with wild animals; swimming or drinking from puddles or natural water sources; and oral-fecal contact with manure or another dog's feces. A high-risk classification was also made if the dog visited obedience classes, dog shows, field trials, a professional groomer, or a boarding facility at least once during the past month. Any dog not meeting the high-risk criteria was classified as low-risk.

Study procedure—When each test dog was enrolled in the study (day 0), it was examined for general health, and a 10-mL sample of blood was obtained for serologic testing. Blood was collected in a serum separator tube and centrifuged, and the serum was placed in a plastic shipping tube labeled with the study, case number, and date and kept frozen at -20°C . Immediately after blood sample collection, each dog was vaccinated per label instructions (1 mL, SC). All dogs were vaccinated with a modified live CDV-CAV-2-CPV-CPIV vaccine from the same vaccine line as that used by that practice historically. Five to 7 days after vaccination, each

dog was reexamined, and a second blood sample was obtained and processed as described. The 2 serum samples were frozen and shipped together on ice to the diagnostic laboratory for serologic evaluation. Dogs were observed for adverse reactions immediately after vaccination and monitored by the owners for the 5 to 7 days after vaccination for adverse effects. After the second blood sample was collected, the dog's participation in the study was concluded.

On the basis of the period of time since last vaccination (TSLV), dogs were categorized into 6-month groups as follows: 12 to 18, 19 to 24, 25 to 30, 31 to 36, 37 to 42, 43 to 48, and $>$ 48 months. The serologic response to the 5 test antigens was determined for each dog, and the antibody titer was assigned to the respective TSLV category. Distribution of serologic responses was calculated for all dogs and dogs within the high- and low-risk groups.

Statistical analyses—Geometric mean (GM) antibody titers for each TSLV interval were calculated and used to determine duration of serologic response. Antibody titer values were transformed by a logarithm base 2 and analyzed with a general linear repeated-measures mixed model. The fixed effects of the model were the 6-month TSLV category, pre- or postvaccination sample time, and TSLV category by sample time interaction were determined. For each antigen, the prevaccination titer was compared with the postvaccination titer within the TSLV category if the sample time or TSLV category by sample time interaction was significant ($P \leq 0.05$). For each antigen, the TSLV categories were compared within sample time if the TSLV category or TSLV category by sample time interaction was significant ($P \leq 0.05$). Geometric mean antibody titers for each antigen at each sample time for each TSLV group were calculated by back-transforming the least-squares means. The number of samples, GM values, and range of antibody titers were calculated for each TSLV category and sample time. A frequency distribution of the prevaccination antibody titers was calculated for each TSLV and each risk category. In addition, GM values were compared between high- and low-risk categories within each TSLV category and sample time with a general linear repeated-measures mixed model.

Results

Of the 322 dogs for which a lifestyle and disease risk questionnaire was completed, 151 (47%) were classified as low risk and 171 (53%) as high risk. All 322 dogs were evaluated for antibodies against CDV and CPV, 313 were evaluated for antibodies against CAV-1 and CAV-2, and 260 were evaluated for antibodies against CPIV. The risk category did not significantly affect serologic response to any test antigens at any TSLV interval except for CPIV. In the prevaccination sample for the 37- to 42-month TSLV interval, the high-risk category had a higher CPIV GM titer than the low-risk category (149.1 vs 57.0; $P = 0.048$). The high-risk category also had higher CPIV GM titers in the postvaccination sample in the TSLV intervals 37 to 42 months, 43 to 48 months, and $>$ 48 months than the low-risk category (282.0 vs 76.6, 676.6 vs 101.4, and 313.8 vs 103.3, respectively; $P \leq 0.03$). Because dogs were excluded if they had a clinical history of disease caused by CDV, CAV-1, CAV-2, CPIV, or CPV, there was probably minimal opportunity for adventitious exposure to enhance the serologic response.

Most dogs (56.2% to 57.3%, depending on the antigen) had been vaccinated during the 2 years preceding day 0, whereas 16.1% to 17.3% had not been vaccinated for 3 years or more. Geometric mean anti-

body titers and antibody titer ranges for each antigen on day 0 were calculated for each 6-month TSLV interval from 12 to > 48 months. At each TSLV interval, GM titers for all antigens exceeded minimum seropositive values. Antibody titers in some dogs at day 0 were below the seropositive threshold at slightly more than half of all TSLV intervals for all antigens. However, all dogs were seropositive for antibodies against CAV-1 at 25 to 30 months and 37 to 42 months (Table 1); CAV-2 at 25 to 30 months, 31 to 36 months, and 37 to 42 months (Table 2); CDV at 25 to 30 months and 43 to 48 months (Table 3); CPV at 37 to 42 months (Table 4); and CPiV at all 7 TSLV intervals (Table 5).

CAV-1—Three hundred eight of 313 (98.4%) dogs were responders to CAV-1 (Table 1). Twelve dogs had

SN titers < 1:16 at day 0. Geometric mean SN titers at day 0 (ie, before revaccination) were not significantly different among the first 6 TSLV categories and declined by 28% from 1:218 at 12 to 18 months to 1:157 at 43 to 48 months. At the > 48-month TSLV interval, the GM SN titer had declined by 56.4% from the 12- to 18-month TSLV interval, to 1:95 ($P = 0.014$). In all TSLV categories, a significant increase in GM SN titers was detected after day 0 vaccination except the 37- to 42-month group ($P = 0.091$), which had a non-significant increase. The increase was > 2-fold for 4 of the 7 TSLV categories, which represented 127 dogs.

CAV-2—For CAV-2, 310 of 313 (99.0%) dogs were responders (Table 2). Five dogs had SN titers < 1:16 at day 0. Geometric mean SN titers at day 0 did not differ

Table 1—Geometric mean (GM) serum neutralization (SN) titers against canine adenovirus type 1 in dogs on day 0 and days 5 to 7 after revaccination. Dogs were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 313)	6-month interval since last vaccination						
		12–18 (119)	19–24 (58)	25–30 (46)	31–36 (39)	37–42 (21)	43–48 (11)	> 48 (19)
Day 0 GM titer	NA	218	206	213	149	164	157	95
Day 0 titer range	NA	4–2,048	4–2,048	16–2,048	12–2,048	32–1,536	4–2,048	8–2,048
Day 5 to7 GM titer	NA	339	420	300	325	225	386	238
Day 5 to 7 titer range	NA	12–3,072	32–7,680	24–2,048	16–1,536	32–3,072	16–3,072	32–3,072
No. of responders* overall	308	115	58	46	38	21	11	19
% Responder*	98.4	96.6	100	100	97.4	100	100	100
No. low risk (responders*)	147 (144)	56 (54)	23 (23)	23 (23)	20 (19)	8 (8)	8 (8)	9 (9)
No. high risk (responders*)	166 (164)	63 (61)	35 (35)	23 (23)	19 (19)	13 (13)	3 (3)	10 (10)

*Based on prevaccination (day 0) SN titer \geq 1:16 or \geq 4-fold increase in postvaccination SN titer. NA = Not applicable.

Table 2— Geometric mean SN titers against canine adenovirus type 2 in dogs on day 0 and days 5 to 7 after revaccination. Dogs were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 313)	6-month interval since last vaccination						
		12–18 (119)	19–24 (58)	25–30 (46)	31–36 (39)	37–42 (21)	43–48 (11)	> 48 (19)
Day 0 GM titer	NA	190	181	210	200	139	138	103
Day 0 titer range	NA	4–2,048	12–7,680	16–1,536	16–2,048	24–3,072	12–1,024	12–1,536
Day 5 to7 GM titer	NA	345	315	344	359	265	388	249
Day 5 to 7 titer range	NA	12–4,096	24–10240	12–1,536	32–2,048	16–4,096	24–2,048	24–2,048
No. of responders* overall	310	118	57	46	39	21	10	19
% Responder*	99.0	99.2	98.3	100	100	100	90.9	100
No. low risk (responders*)	147 (146)	56 (56)	23 (23)	23 (23)	20 (20)	8 (8)	8 (7)	9 (9)
No. High risk (responders*)	166 (164)	63 (62)	35 (34)	23 (23)	19 (19)	13 (13)	3 (3)	10 (10)

See Table 1 for key.

Table 3—Geometric mean SN titers against canine distemper virus in dogs on day 0 and days 5 to 7 after revaccination. Dogs were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 322)	6-month interval since last vaccination						
		12–18 (119)	19–24 (62)	25–30 (47)	31–36 (42)	37–42 (22)	43–48 (11)	> 48 (19)
Day 0 GM titer	NA	548	407	427	385	417	453	264
Day 0 titer range	NA	16–4,096	16–6,144	32–4,096	8–4,096	24–4,096	64–4,096	16–3,072
Day 5 to7 GM titer	NA	689	565	549	475	447	853	449
Day 5 to7 titer range	NA	16–4,096	24–6,144	24–4,096	16–6,144	64–2,048	192–2,048	48–6,144
No. of responders* overall	316	118	59	47	41	22	11	18
% Responder*	98.1	99.2	95.2	100	97.6	100	100	94.7
No. low risk (responders*)	151 (147)	56 (56)	25 (23)	24 (24)	20 (19)	9 (9)	8 (8)	9 (8)
No. high risk (responders*)	171 (169)	63 (62)	37 (36)	23 (23)	22 (22)	13 (13)	3 (3)	10 (10)

*Based on prevaccination SN titer \geq 1:32 or \geq 4-fold increase in postvaccination SN titer. See Table 1 for remainder of key.

Table 4—Geometric mean hemagglutination inhibition (HI) titers against canine parvovirus in dogs on day 0 and days 5 to 7 after revaccination. Dogs were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 321)	6-month interval since last vaccination						
		12–18 (119)	19–24 (62)	25–30 (47)	31–36 (42)	37–42 (21)	43–48 (11)	> 48 (19)
Day 0 GM titer	NA	601	465	415	295	462	170	238
Day 0 titer range	NA	10–6,400	20–3,840	20–5,120	20–3,840	80–2,560	40–640	40–2,560
Day 5 to 7 GM titer	NA	961	974	744	593	855	518	528
Day 5 to 7 titer range	NA	20–7,680	120–5,120	40–5,120	30–5,120	160–5,120	80–3,840	160–3,840
No. of responders* overall	315	117	62	46	40	21	10	19
% Responder*	98.1	98.3	100	97.9	95.2	100	90.9	100
No. low risk (responders*)	151 (147)	56 (55)	25 (25)	24 (23)	20 (19)	9 (9)	8 (7)	9 (9)
No. high risk (responders*)	170 (168)	63 (62)	37 (37)	23 (23)	22 (21)	12 (12)	3 (3)	10 (10)

*Based on prevaccination HI titer \geq 1:80 or \geq 4-fold increase in postvaccination HI titer. See Table 1 for remainder of key.

Table 5— Geometric mean SN titers against canine parainfluenza virus in dogs on day 0 and days 5 to 7 after revaccination. Dogs were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 260)	6-month interval since last vaccination						
		12–18 (101)	19–24 (48)	25–30 (32)	31–36 (34)	37–42 (18)	43–48 (10)	> 48 (17)
Day 0 GM titer	NA	206	119	110	101	98	59	65
Day 0 titer range	NA	24–2,048	24–1,024	24–512	24–768	16–2,048	16–256	16–1,024
Day 5 to 7 GM titer	NA	307	254	162	222	165	163	169
Day 5 to 7 titer range	NA	32–4,096	24–1,536	48–768	64–1,024	24–2,048	32–1,536	32–4,096
No. of responders overall*	260	101	48	32	34	18	10	17
% Responder*	100	100	100	100	100	100	100	100
No. low risk (responders*)	133 (133)	53 (53)	21 (21)	18 (18)	19 (19)	7 (7)	7 (7)	8 (8)
No. high risk (responders*)	127 (127)	48 (48)	27 (27)	14 (14)	15 (15)	11 (11)	3 (3)	9 (9)

See Table 1 for key.

significantly among the 7 TSLV intervals. In all TSLV categories, a significant increase in GM SN titer after day 0 vaccination was detected; the increase was > 2-fold for the 43- to 48-month and > 48-month groups.

CDV—For CDV, 316 of 322 (98.1%) dogs were responders. Eleven dogs had SN titers < 1:32 at day 0. Geometric mean SN titers at day 0 were not significantly different among TSLV intervals. In all TSLV categories, a significant increase in GM SN titer after day 0 vaccination was detected except for the 31 to 36-month and 37- to 42-month groups.

CPIV—For CPIV, all 260 dogs included in the analysis were serologic responders, and all were seropositive prior to vaccination on day 0. Geometric mean SN titers at day 0 had declined significantly by 68.4% from 1:206 for the 12- to 18-month TSLV interval to 1:65 for the > 48-month TSLV interval. In all TSLV categories, a significant increase in GM SN titer was detected after day 0 vaccination; the increase was > 2-fold for 4 of the 7 TSLV groups (19 to 24 months, 31 to 36 months, 43 to 48 months, and > 48 months).

CPV—For CPV, 315 of 321 (98.1%) dogs were responders. Sixteen dogs had HI titers < 1:80 at day 0. Geometric mean HI titers at day 0 had declined significantly by 71.7% for the 43- to 48-month TSLV interval and 60.4% for the > 48-month TSLV interval. In all TSLV categories, a significant increase in GM SN titer was detected after day 0 vaccination; the increase was > 2-fold for the 19- to 24-month, 43- to 48-month, and > 48-month groups.

Adverse events—Adverse events after day-0 vaccination were reported in 13 dogs. These sequelae included signs of nausea, coughing, lethargy, pruritis, facial-cervical edema, enteritis lasting 1 to 2 days, nocturnal tremors lasting 4 days, and conjunctivitis lasting 6 days. Clinical signs resolved in all dogs either spontaneously or with appropriate treatment. Whether there was a causative relationship between these adverse events and vaccination was not established.

Discussion

Results of our study indicated that vaccination consistently induced a serologic response up to and beyond 48 months for all 5 antigens. The GM anamnestic response to revaccination was significant for most TSLV categories. A more pronounced serologic response was not necessarily expected because pre-existing antibodies may neutralize vaccine antigens.^{15,16}

For vaccination against CDV and CPV, other investigators have detected a serologic response of long duration in a high percentage of dogs. McCaw et al¹⁸ found that 73% of 122 dogs vaccinated from 9 months to 4.6 years earlier had protective CPV antibody titers (HI titer \geq 1:80) and that 79% of 117 dogs had protective CDV antibody titers (SN titer \geq 1:96). In another study,¹⁰ 95.1% of 1,441 dogs vaccinated with various commercial vaccines had protective CPV antibody titers (HI titer \geq 1:80), and 97.6% had protective CDV antibody titers (SN titer \geq 1:32) 1 to 7 years after vaccination. The consensus from these and other studies^{12,16} is that CPV and CDV vaccination generally confers reliable multiyear protection.

Our data, which revealed persistence of serologic responses to CAV-1 and CAV-2 for > 48 months, are noteworthy. To our knowledge, no other published data indicate duration of response to these antigens exceeding 2 years after vaccination.¹² Although we found that titers for antibodies against CPIV lasted > 48 months after vaccination, the protective value of circulating antibodies for this antigen has not been established. Clinical infection by CPIV is countered primarily by mucosal immunity and often involves concurrent infection with other infectious agents such as CAV-2 and *B bronchiseptica*, making it difficult to experimentally measure the efficacy of CPIV vaccine. Nevertheless, the importance of serologic responses to antigens in the respiratory tract should not be discounted, even for those responses that provide immunogenicity from secretory IgA. Ellis et al,^{17,18} for example, found that vaccine-induced serum antibodies for *B bronchiseptica* correlated well with immunity in dogs after parenteral vaccination, intranasal vaccination, or both. In addition, parenteral vaccination against CPIV provides a serologic response and subsequent reduction in shedding of challenge virus.¹⁹

Results of our study suggest a rationale for revaccination intervals longer than 1 year for the antigens we tested, based on serologic data. However, it is important that such data be considered vaccine-specific. Vaccines differ in their immunizing strains, potency, adjuvant used (if any), degree of attenuation, and whether or not the vaccine is an inactivated or modified live-virus preparation. Any of these factors can affect postvaccination duration of immunity. Care was taken in our study to ensure that all dogs received the same vaccine viral antigens throughout their lifetimes, ensuring that the serologic data were valid for the vaccine tested.

Canine distemper virus, CPV, and CAV-2 are considered core antigens recommended for routine vaccination of dogs.^{2,12,16} In addition, routine vaccination for CPIV is sometimes recommended.² In the absence of real-time, duration-of-immunity studies, which involve maintaining animals in experimental isolation for long periods of time and are of questionable applicability to real-life environments, vaccine-specific serologic persistence data may assist in determining the appropriate revaccination interval for each of these antigens. Recently, recommendations made by the American Animal Hospital Association²⁰ and the AVMA Council on Biologics and Therapeutic Agents²¹ reinforce the concept of core vaccinations, with clinicians using judgment, experience, and the best science available to determine the vaccination requirements for each individual animal.

Based on serologic response, our data indicate that the modified-live CDV-CAV-2-CPIV-CPV vaccine that we tested is suitable for primary vaccination, revaccination 1 year later, and revaccination at multiyear intervals thereafter. Although the data may suggest that revaccination at intervals longer than 3 years is justified, to do so may be associated with unnecessary risk of disease. Particularly for canine distemper, extended or widespread lapses in vaccination inevitably result in declining population immunity and disease out-

breaks.^{8,22-24} For respiratory pathogens such as CAV-2 and CPIV, there may be continual risk of exposure, making it important to maintain constant immunity. Serologic data, such as that obtained in our study, provide a rational basis for assessing immune status and form a database that can be continuously updated. However, serology, with its inherent limitations, should be used conservatively in determining revaccination intervals.

It should also be recognized that historic practices based on annual revaccination have resulted in excellent disease control for the antigens evaluated in this study. The effects of extended-interval vaccination on canine population immunity are unknown. In humans, as pertussis (a respiratory disease readily controlled by an efficacious vaccine) became rarer, attention shifted from disease prevention to possible adverse events associated with vaccination and resulted in antivaccine movements in some countries. One study revealed that the incidence of pertussis was lower by a factor of 10 to 100 in countries in which a high rate of vaccination was maintained, compared with countries in which vaccination programs were compromised by antivaccine movements.²⁵

For many clinicians, deviating from the traditional 1-year revaccination interval in favor of multiyear intervals represents a new immunization paradigm. In some instances, veterinarians may consider administering certain noncore vaccines (*B bronchiseptica*, *Borrelia burgdorferii*, *Leptospira canicola*, *L icterohaemorrhagiae*, and other *Leptospira* serovars) at clinic visits interspersed between those in which vaccination for core antigens is performed. Annual revaccination for respiratory antigens that confer short-term immunity and those with a seasonal occurrence is justifiable and can be used to construct a staggered vaccination protocol in which core and certain noncore vaccines can be given on an alternating basis. Whatever approach is taken, it is appropriate that vaccination be considered and promoted to pet owners as part of a total health care program that emphasizes examination, testing, diagnosis, treatment, and prevention.

^aVanguard Plus 5/L, Pfizer Inc, New York, NY.

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