Duration of serologic response to three viral antigens in cats

Douglas E. Mouzin, MS, MBA; Marianne J. Lorenzen, DVM; John D. Haworth, DVM, PhD; Vickie L. King, PhD

Objective—To determine whether vaccinated cats either remained seropositive or responded serologically to revaccination against 3 key viral antigens after extended periods since their last vaccination.

Design—Serologic survey.

Animals—272 healthy client-owned cats.

Procedure—Cats were ≥ 2 years old and vaccinated for feline panleukopenia virus (FPV), feline calicivirus (FCV), and feline herpesvirus (FHV). On day 0, cats were revaccinated with a vaccine from the same line of vaccines as they had historically received. Antibody titers were measured in sera collected on day 0 (prevaccination titer) and 5 to 7 days later (postvaccination titer). Cats were considered to have responded serologically if they had a day-0 hemagglutination inhibition titer to FPV ≥ 1:40, serum neutralization (SN) titer to FCV ≥ 1:32, SN titer to FHV ≥ 1:16, or ≥ 4-fold increase in antibody titer after revaccination.

Results—The percentage of cats that had titers at or above the threshold values or responded to revaccination with a ≥ 4-fold increase in titer was 96.7% for FPV, 97.8% for FCV, and 88.2% for FHV.

Conclusions and Clinical Relevance—In most cats, vaccination induced a response that lasted up to and beyond 48 months for all 3 antigens. Although not equivalent to challenge-of-immunity studies as a demonstration of efficacy, results suggest that revaccination with the vaccine used in our study provides adequate protection even when given less frequently than the traditional 1-year interval. The study provides valuable information for clinicians to determine appropriate revaccination intervals. (*J Am Vet Med Assoc* 2004;224:61–66)

Veterinary vaccines approved by the USDA have historically been granted a 1-year revaccination recommendation, although maximum duration of immunity has not been established (rabies vaccines with approved multiyear revaccination intervals are exceptions). The annual revaccination interval has greatly reduced the prevalence of infectious diseases in dogs and cats. In addition, the annual revaccination visit has provided veterinarians and pet owners with a convenient time for a periodic physical examination and a review and discussion of the pet's health status. However, in recent years, the annual revaccination interval has been increasingly questioned as being somewhat arbitrary and based on convenience and limited scientific data. It has instead been proposed to base revaccination intervals on disease risk, determination of which antigens are core components of a sound immunization program, duration of immunity conferred by specific vaccines, and the risk of postvaccination reactions.

The emergence during the past decade of an epidemiologic link between vaccination and injection-site fibrosarcomas in cats[1,2] has been a factor in prompting recommendations for feline revaccination intervals > 1 year.[3-5] The reported prevalence of injection site sarcoma varies. In 1 study, prevalence was established at 158 cases in 434,638 cats, or 3.6 cases/10,000 cats.[6] In another study, prevalence was reported at 1.9 cases/10,000 cats.[2] More recently, epidemiologists who used a database of 31,671 cats established a prevalence of 0.63 sarcomas/10,000 cats.[7] In addition to fibrosarcomas, possible links to vaccine-associated autoimmune diseases in dogs and cats have been reported.[8,9]

For most feline and canine diseases, the optimum revaccination interval is based on postvaccination duration of immunity. The definitive method for establishing duration of immunity is a real-time challenge study. However, efficacy of veterinary vaccines is usually evaluated by detecting short-term protection against challenge several weeks after primary vaccination. The most notable exceptions are rabies vaccines for which 1- to 3-year duration of immunity in dogs or cats must be proven as a public health safeguard. 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. The cost and difficulty of keeping animals in isolation for extended periods and concerns about the welfare of animals maintained at length under experimental conditions make it impractical to conduct multiyear, duration-of-immunity studies in a test population of sufficient size. In addition, certain factors inherent in the challenge-of-immunity model sometimes limit its relevance or practicality for proving efficacy. Susceptibility to some diseases can vary with the age of the animal (eg, older cats are more resistant than kittens to FeLV infection), and experimental isolation of animals creates an artificial environment that does not duplicate natural patterns of exposure and susceptibility. Thus, serologic response to vaccination has been proposed and used as a helpful alternative to real-time challenge studies in determining duration of immunity.[10-16] This approach is potentially valuable in diseases in which serologic data are indicative of protection.

The purpose of the study reported here was to

From Veterinary Medicine Biologicals Research and Development, Pfizer Animal Health, Pfizer Inc, 7000 Portage Rd, Kalamazoo, MI 49001.

The authors thank Dr. Edward J. Dubovi, Linda T. Benson, Mark Dana, and Lisa Bowen-Laue for technical assistance.

Address correspondence to Dr. Haworth.

determine duration of serologic response to the 3 viral pathogens most widely used for feline vaccination—**feline panleukopenia virus (FPV)**, **feline calicivirus (FCV)**, and **feline herpesvirus (FHV)**.[5,14] In several studies, vaccine-induced serum antibody responses to each of these antigens have been correlated with resistance to infection or clinical disease.[12,14,15] Cats were also grouped into high- and low-risk categories to determine whether lifestyle and disease risk correlated with serologic response.

Materials and Methods

Cats—Cats were selected for the study after a thorough evaluation of their medical records; 272 client-owned cats of both sexes, either sexually intact or neutered, and of various ages, breeds, weights, lifestyles, and intervals since last vaccination were enrolled in the study. Cats were required to be clinically normal, have negative results of a day-0 test result for FeLV and FIV, be at least 2 years old, not vaccinated within the past 12 months, and with no documented medical history of disease due to FPV, FCV, FHV, or *Chlamydia psittaci* (*Chlamydophila felis*) infection. In addition, cats must have received a documented 2-dose primary vaccination series with a vaccine from the same line as the test vaccine[a] administered 2 to 7 weeks apart as a kitten and at least 1 revaccination dose of vaccine at an 8- to 16-month interval. Cats were excluded if they had a history of vaccine intolerance such as allergy, severe systemic disease of any kind, were treated with an anti-inflammatory drug within the past 30 days or an immunosuppressive agent within the past 60 days, were pregnant, or had been given an FPV-FCV-FHV vaccine other than one from the same line as the vaccine used in the study. Cats were maintained by their owners in conventional domestic environments, which included multicat households in some instances.

Site selection—The study was conducted at 38 companion-animal veterinary clinics in the United States and 2 clinics in Canada. These practices had clientele, vaccination use history, and records management that permitted compliance with the study protocol. At least 1 veterinarian at each site was designated as the investigator or examining clinician. Investigators were encouraged to enroll cats that had not received a vaccine for an extended period. All participating practices provided affidavits attesting to exclusive use of a vaccine from the same vaccine line as the test vaccine in the test cats during the period of previous vaccinations. Cat owners signed consent forms agreeing to participate in the study and comply with its protocol.

Test vaccine—A modified-live FPV-FCV-FHV vaccine combined with *C psittaci*[a] (ie, the test vaccine) was used to revaccinate eligible test cats on day 0 of the study. Vaccine was administered per label instructions (1 mL, SC). All prior vaccinations for FPV, FCV, and FHV were with a vaccine from the same line as the test vaccine, with or without the *C psittaci* component.

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 the cats. Each sample was tested for **hemagglutination inhibition (HI)** titer for antibodies against FPV and **serum neutralization (SN)** titers for antibodies against FCV and FHV. Serial 2-fold dilutions were inoculated onto wells of a 96-well microtiter plate, incubated, and evaluated for endpoint detection. The VR953 strain of swine RBCs was used as the substrate for the HI assays. The C-14 strain of **Crandell feline kidney (CRFK)** cells was used as the substrate for FCV SN testing, and the C-27 strain of CRFK cells was used as the substrate for FHV SN testing. Cell substrates were obtained from the American Type Culture Collection. Titration endpoints were agglutination for HI assays and cytopathic effect for the SN assays.

A cat was considered to be a serologic responder to the respective test antigen if it was seropositive for antibodies against the antigen 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 cat was seropositive (HI titer for antibodies against FPV, ≥ 1:40; SN titer for antibodies against FCV, ≥ 1:32; and SN titer for antibodies against FHV, ≥ 1:16).

Lifestyle and disease risk questionnaire—On day 0, each cat owner completed a lifestyle and disease risk questionnaire for each cat. Cats were categorized into high- and low-risk groups on the basis of questionnaire responses. Cats were included in the low-risk group if they lived in households with 3 or fewer cats; if all of the cats in the household stayed indoors 100% of the time; and if they had not been to a kennel, groomer, or cat show for more than 24 hours during the preceding year. Any cat that did not meet the low-risk group criteria was classified as high-risk.

Study procedure—When each test cat was enrolled in the study (day 0), it was examined for general health, and a 0.5-mL sample of blood was obtained for FeLV and FIV diagnostic testing. A standard in-clinic ELISA test kit for FeLV p27 antigen and antibodies against FIV[b] was used to determine exposure to these agents. If the results of the FeLV and FIV ELISA were negative and the cat was confirmed to meet all inclusion criteria, approximately 5 mL of blood was collected from the jugular vein or other peripheral vein. Blood was collected in a serum separator tube, centrifuged, and the serum was placed in a plastic shipping tube labeled with the study, case number, and date, and stored frozen at –20°C. Immediately after blood sample collection, each cat was vaccinated per label instructions (1 mL, SC). Five to 7 days after vaccination, each cat was reexamined and a second blood sample was obtained and processed as before. Serum samples were frozen prior to shipment. The 2 serum samples were shipped on ice packs together to the diagnostic laboratory for serologic testing. Cats were observed for adverse reactions immediately after vaccination and monitored by the owners for 5 to 7 days after vaccination for development of adverse effects. After the second blood sample was collected, the cat's participation in the study was concluded.

On the basis of the period of **time since last vaccination (TSLV)**, cats were categorized into 1 of the following 6-month groups: 12 to 18, 19 to 24, 25 to 30, 31 to 36, 37 to 42, 43 to 48, or > 48 months. The serologic response to the 3 test antigens was determined for each cat, and the antibody titer was assigned to the respective TSLV category.

Statistical analyses—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 (GM)** 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 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

Cats enrolled in the study ranged in age from 2 to 17 years. On the basis of responses to the lifestyle and disease risk questionnaire, 86 of the 272 (32%) cats were classified as low risk and 186 (68%) were classified as high risk. The majority of cats (57.7%) had been vaccinated within the preceding 2 years, but more than one-fourth had not been vaccinated for 3 years or more, and 12.1% had not been vaccinated for 4 years or more. Geometric mean antibody titers and antibody titer ranges for each of the 3 antigens on day 0 at each 6-month TSLV interval were determined. Although some cats had antibody titers less than the minimum seropositive values recommended by CUVDL, GM antibody titers exceeded the minimum values for all antigens at all TSLV intervals.

FPV—For FPV, 263 of 272 (96.7%) cats were responders (ie, day-0 FPV HI titer ≥ 1:40 or a ≥ 4-fold increase in HI titer after day-0 vaccination) regardless of lifestyle. Eighty-four of 86 (97.7%) cats in the low-risk group and 179 of 186 (96.2%) cats in the high-risk group responded serologically (**Table 1**). For all TSLV categories, a nonsignificant increase in GM HI titers was detected after day 0 vaccination, except for the 12- to 18-month group, which had a nonsignificant decrease from 1,036 to 1,009. The only significant differences between high- and low-risk category cats for GM HI titers were in the prevaccination sample in the 31- to 36-month TSLV group and the prevaccination and postvaccination samples in the 43- to 48-month TSLV group; the low-risk category had higher GM HI titers.

FCV—For FCV, 266 of 272 (97.8%) cats were responders (day-0 SN titer ≥ 1:32 or 4-fold increase in SN titer after day-0 vaccination) regardless of lifestyle. Eighty-three of 86 (96.5%) cats in the low-risk group and 183 of 186 (98.4%) cats in the high-risk group responded serologically (**Table 2**). The GM titers at day 0 did not necessarily decline as TSLV increased. Comparison of GM titers before and after day-0 vaccination indicated that a significant serologic response to FCV occurred in all TSLV categories, except the 43- to 48-month and > 48-month groups. The only significant differences between high- and low-risk category cats were in the prevaccination sample in the 19- to 24-month TSLV group and the prevaccination and postvaccination samples in the 37- to 42-month TSLV group; the low-risk category had lower GM titers.

FHV—For FHV, 240 of 272 (88.2%) cats were responders (day-0 SN titer ≥ 1:16 or 4-fold increase in SN titer after day-0 vaccination) regardless of lifestyle. Eighty of 86 (93.0%) cats in the low-risk group and 160 of 186 (86.0%) cats in the high-risk group responded serologically (**Table 3**). Titers at day 0 were

Table 1—Geometric mean (GM) serum hemagglutination inhibition (HI) titers against feline panleukopenia virus in cats on day 0 and days 5 to 7 after revaccination. Cats were categorized by the 6-month interval since their last vaccination

		6-month interval since last vaccination (months)						
Serologic response category	**Overall (n = 272)**	**12–18 (108)**	**19–24 (49)**	**25–30 (25)**	**31–36 (19)**	**37–42 (25)**	**43–48 (13)**	**> 48 (33)**
Day 0 GM titer	NA	1,036	732	1,026	654	617	659	472
Day 0 titer range	NA	10–12,800	40–5,120	20–7,680	40–5,120	10–3,840	10–5,120	10–9,600
Days 5 to 7 GM titer	NA	1,009	787	1,246	719	665	698	600
Days 5 to 7 titer range	NA	10–7,680	40–5,120	20–5,120	40–3,840	30–3,840	10–5,120	10–12,800
No. of responders* overall	253	104	49	24	19	24	12	31
% Responder*	96.7	96.3	100	96.0	100	96.0	92.3	93.9
No. low risk (responders*)	86 (84)	36 (34)	14 (14)	7 (7)	4 (4)	8 (8)	7 (7)	10 (10)
No. high risk (responders*)	186 (179)	72 (70)	35 (35)	18 (17)	15 (15)	17 (16)	6 (5)	23 (21)

*Based on prevaccination HI titer ≥ 1:40 or ≥ 4-fold increase in postvaccination HI titer. NA = Not applicable.

Table 2—Geometric mean serum neutralization (SN) titers against feline calicivirus in cats on day 0 and days 5 to 7 after revaccination. Cats were categorized by the 6-month interval since their last vaccination

		6-month interval since last vaccination (months)						
Serologic response category	**Overall (n = 272)**	**12–18 (108)**	**19–24 (49)**	**25–30 (25)**	**31–36 (19)**	**37–42 (25)**	**43–48 (13)**	**> 48 (33)**
Day 0 GM titer	NA	430	433	219	180	323	430	687
Day 0 titer range	NA	4–81,920	24–6,144	16–4,096	24–2,048	8–6,144	64–10,240	32–30,720
Days 5 to 7 GM titer	NA	554	555	393	349	458	517	877
Days 5 to 7 titer range	NA	12–30,720	32–8,192	12–6,144	64–3,072	8–6,144	96–3,840	48–40,960
No. of responders* overall	266	107	49	24	19	21	13	33
% Responder*	97.8	99.1	100	96.0	100	84.0	100	100
No. low risk (responders*)	86 (83)	36 (36)	14 (14)	7 (7)	4 (4)	8 (5)	7 (7)	10 (10)
No. high risk (responders*)	186 (183)	72 (71)	35 (35)	18 (17)	15 (15)	17 (16)	6 (6)	23 (23)

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

Table 3—Geometric mean (GM) SN titers against feline herpesvirus virus in cats on day 0 and days 5 to 7 after revaccination. Cats were categorized by the 6-month interval since their last vaccination

Serologic response category	Overall (n = 272)	6-month interval since last vaccination (months) 12–18 (108)	19–24 (49)	25–30 (25)	31–36 (19)	37–42 (25)	43–48 (13)	> 48 (33)
Day 0 GM titer	NA	41	46	41	39	27	45	36
Day 0 titer range	NA	4–512	6–1,024	4–256	6–256	4–128	16–512	4–256
Days 5 to 7 GM titer	NA	53	67	66	57	43	71	46
Days 5 to 7 titer range	NA	4–768	16–768	8–256	8–512	12–256	16–512	4–512
No. of responders* overall	240	91	47	23	18	20	13	28
% responder*	88.2	84.3	95.9	92.0	94.7	80.0	100	84.8
No. low risk (responders*)	86 (80)	36 (33)	14 (14)	7 (7)	4 (3)	8 (8)	7 (7)	10 (8)
No. high risk (responders*)	186 (160)	72 (58)	35 (33)	18 (16)	15 (15)	17 (12)	6 (6)	23 (20)

*Based on prevaccination SN titer ≥ 1:16 or ≥ 4-fold increase in postvaccination SN titer. *See* Table 1 for remainder of key.

relatively constant, within a 2-fold dilution, across all TSLV categories ($P > 0.05$). After day-0 vaccination, a significant increase in titers developed in all TSLV categories. There were no significant differences in titers between the high- and low-risk categories.

Adverse events—Adverse events that were possibly related to day-0 vaccination were reported in 8 cats. These sequelae were all characterized as mild and included signs of lethargy, pyrexia, alopecia, anorexia, weight loss, and hematuria. Clinical signs resolved in 6 cats either spontaneously or with appropriate treatment. Outcomes of the other 2 cats with lethargy, anorexia, or pyrexia were unknown. Whether there was a causative relationship between these adverse events and vaccination was not established.

Discussion

The central finding of our study was that for most cats, vaccination induced a serologic response to all 3 viral antigens that exceeded presumed protective values for an extended period, lasting in some instances 4 years or more. Results of other studies indicate that seropositive status for FPV, FCV, and FHV correlates with protection. Scott and Geissinger[14] found that detectable postvaccination **virus neutralizing (VN)** antibodies against FCV and FHV provided substantial protection against virulent challenge for 3 years or more. They also determined that postvaccination VN titers for FPV antibodies provided complete protection against challenge administered up to 7.5 years later. The seropositive thresholds for those VN assays were ≥ 1:10 for FPV, ≥ 1:4 for FCV, and ≥ 1:2 for FHV. Lappin et al[12] found that regardless of vaccine type or postvaccination interval, if detectable antibodies against FPV, FCV, or FHV were detected, cats were protected against virulent challenge. Minimum seropositive values in that study were HI titers for FPV > 1:10, and VN titers for FCV or FHV > 1:8. Interassay variation may exist in the serologic methods used in those studies versus those used in our study. However, the essential results of those studies are that even very low FPV, FCV, or FHV serum antibodies concentrations correlate with protection. Others have determined that a dog or cat that has developed an immune response after vaccination will possess immune memory cells that will activate a rapid and effective serologic response to exposure even if serum antibody titers have declined to low or undetectable concentrations.[15]

Serologic response to vaccination can vary depending on vaccine potency, strain variations, and whether a live or killed agent is used.[11,17] In our study, records verified that all cats were vaccinated with a vaccine from the same line of FPV-FHV-FCV vaccines throughout their lifetime, thus avoiding variations in immunizing antigens (in some cats, the vaccine included a *C psittaci* component). Cats were excluded if there was a known history of clinical disease caused by FPV, FHV, or FCV, minimizing the chance that serologic response was because of natural exposure. The same diagnostic laboratory was used for all serologic testing to ensure that uniform assay methods were used. Inclusion in the study was limited to adult cats, removing the chance that antibody titers were maternally induced. Prescreening procedures excluded cats considered at risk for immunosuppressive diseases or cats receiving medications that would influence serologic response. Thus, there was reasonable assurance that selection criteria or variations in methods and materials did not measurably influence duration and degree of serologic response to a specific FPV-FHV-FCV vaccine.

With the understanding that disease risk may be influenced by urban versus rural location, results of the lifestyle questionnaire suggested that most cats had substantial contact with other cats or environments that were a potential source of infectious disease. However, in our study, the greater opportunities for exposure among cats in the high-risk category did not appear to be associated with serologic response to vaccination at any of the 6-month TSLV intervals. This was possibly attributable to exclusion of cats with a clinical history of FPV, FCV, or FHV-related diseases. It has been hypothesized that high-risk cats are likely to encounter natural exposure and have resulting increases in antibody titers. Results of our study do not seem to support that contention for FCV, because we found only 3 intervals for which cats in the low-risk category had lower GM SN titers than those in the high-risk category. In all of these examples, the GM HI titers were > 1:32.

Although postvaccination increases in GM titers were < 4-fold for any TSLV interval, revaccination of seropositive cats often results in little or no serologic response because vaccine antigen is neutralized somewhat by preexisting antibodies. In a study[5] of 106 dogs that were vaccinated within the previous 1 to 4 years

with canine parvovirus, despite the fact that this virus is highly immunogenic,[17] only 1 dog had a 4-fold or greater increase in antibody titer after revaccination. Scott and Geissinger[14] reported strong anamnestic responses after FPV, FCV, or FHV challenge in vaccinated cats, but these marked increases did not appear until 14 to 28 days after exposure. Had antibody titers been measured beyond 5 to 7 days after revaccination in our study, somewhat greater serologic responses may have been detected.

Despite the generally long-lived serologic response to vaccination, a few cats were encountered in 16 of the 21 TSLV categories that had antibody titers less than the protective threshold on day 0. Even in the group with the shortest interval since last vaccination (12- to 18-month group), some cats had antibody titers on day 0 that were less than protective values and did not have a postvaccination anamnestic response for FPV (3.7% nonresponders), FCV (0.9% nonresponders), or FHV (15.7% nonresponders). Failure of some cats to develop a robust serologic response 12 to 18 months after vaccination suggests that annual revaccination for 2 years after a 2-dose primary regimen may be beneficial for a young cat with an immune system that may not be fully developed, especially if vaccination history is unknown. Other factors that can negatively affect an animal's ability to respond to vaccination include maternal antibodies, congenital or acquired immunodeficiencies, concurrent diseases, inadequate nutrition, immunosuppressive medications, and stress.

Although our study focused on serologic responses to vaccination, it should be noted that serum antibodies are not the sole source of protection. Cell-mediated immunity and rapid immune memory-cell response to revaccination, even when serum antibodies are undetectable, also contribute to protection.[5,10,14,15] Thus, failure to detect serum antibodies in vaccinated cats does not necessarily correspond with susceptibility to disease.[10-12] Antibodies are an indirect indication of the cell-mediated, T lymphocyte arm of the immune response, which is enabled by B lymphocytes. Thus, serum antibodies, even when detected months to years after vaccination, indicate that the animal has sufficient immunologic memory for a rapid anamnestic cellular or antibody response. Although serum antibodies may not be directly responsible for nullifying intracellular viral infection, they contribute to host defenses and are considered a viable indicator of immunity.[15]

Other studies have examined duration of serologic response to FPV, FCV, and FHV prior to experimental challenge. Scott and Geissinger[14] found that 2 primary doses of an inactivated FPV-FCV-FHV vaccine induced detectable VN titers for ≥ 3 years for all 3 antigens (n = 9 cats) and that VN titers for antibodies against FPV persisted ≥ 7 years.[14] Variable protection against virulent FCV or FHV challenge in those cats was observed, although all cats remained clinically normal after challenge with FPV. Lappin et al[12] found that 3 FPV, FCV, and FHV vaccines induced specific antibodies detectable by use of ELISA from 9 to 36 months after vaccination in some cats and that seropositive results had positive predictive value for protection against virulent challenge. In that study, all 15 vaccinated cats that were seropositive to FPV, all 38 vaccinated cats that were seropositive to FCV, and 19 of 21 vaccinated cats that were seropositive to FHV were resistant to challenge.

Determination of duration of immunity for human vaccines is conducted by collecting data on disease incidence and adjusting the vaccination frequency on the basis of the results. For example, the World Health Organization plans to discontinue oral poliomyelitis vaccination after no wild-type poliovirus transmission is detected in the world for 3 consecutive years by use of surveillance programs that are able to detect 1 case of nonpoliomyelitis-associated acute flaccid paralysis per 100,000 children who are < 15 years of age.[18] Hsia et al[19] have determined that the prevalence of Lyme disease must exceed 10% before vaccination with yearly boosters becomes more effective than no vaccination. A similar method to prospectively evaluate prevalence of disease in the large population of pets impacted by current vaccination protocols would encounter difficulties in collecting and analyzing the data.

The distribution of cats among the TSLV intervals revealed that 39.7% of cats received the traditional regimen of annual revaccination for the 3 core feline antigens, whereas 26.1% were vaccinated on a triennial or less frequent basis. Veterinarians often encounter cats that are vaccinated infrequently. One of the peripheral questions our study sought to answer was the risk of susceptibility associated with irregular or extended vaccination intervals in a natural exposure setting for high- versus low-risk cats. Thus, we selected a high percentage of cats that had been vaccinated at intervals > 1 year. The American Association of Feline Practitioners and Academy of Feline Medicine now recommend revaccination against FPV, FCV, and FHV at 3-year intervals after primary vaccination and annual revaccination the first year,[3] and the data in our study seem to support that recommendation, regardless of the cat's lifestyle-associated risks. Recently, similar recommendations were made by the AVMA Council on Biologic and Therapeutic Agents.[4]

It should also be recognized that historic immunization practices based on annual revaccination have resulted in excellent disease control for the antigens evaluated in this study. The effects of moving to extended interval vaccination on feline 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[20] revealed that the incidence of pertussis was lower by a factor of 10 to 100 in countries in which high vaccine coverage was maintained than in countries in which vaccination programs were compromised by antivaccine movements.

Vaccines should be administered via the same principles that apply to pharmaceuticals. They should be selected thoughtfully, administered appropriately, and the animal should be monitored for response. The objectives of companion animal vaccination are to protect the maximum number in the population at risk, vaccinate each animal no more frequently than neces-

sary, and vaccinate only for infectious agents for which a reasonable risk of exposure and disease exists.

[a]Felocell 4, Pfizer Inc, New York, NY.
[b]Snap FIV antibody/FeLV antigen test, IDEXX Laboratories, Westbrook, Me.

References

1. Hendrick MJ, Goldschmidt MH, Shofer FS, et al. Postvaccinal sarcomas in the cat: epidemiological and electron probe microanalytical identification of aluminum. *Cancer Res* 1992;52:5391–5394.
2. Kass PH, Barnes WG Jr, Spangler WL, et al. Epidemiologic evidence for a causal relation between vaccination and fibrosarcoma tumorigenesis in cats. *J Am Vet Med Assoc* 1993;203:396–405.
3. Richards J, Rodan I, Elston T, et al. Feline vaccine selection and administration. *Compend Contin Educ Pract Vet* 2001;23:71–80.
4. Klingborg DJ, Hustead DR, Curry-Galvin EA, et al. AVMA Council on Biologic and Therapeutic Agents' report on cat and dog vaccines. *J Am Vet Med Assoc* 2002;221:1401–1407.
5. Schultz RD. Current and future canine and feline vaccination programs. *Vet Med* 1998;93:233–254.
6. Coyne MJ, Postorino Reeves NC, Rosen DK. Estimated prevalence of injection-site sarcomas in cats during 1992. *J Am Vet Med Assoc* 1997;210:249–251.
7. Gobar GM, Kass PH. World Wide Web-based survey of vaccination practices, postvaccinal reactions, and vaccine site-associated sarcomas in cats. *J Am Vet Med Assoc* 2002;220:1477–1482.
8. Greene CE, Schultz RD, Ford RB. Canine vaccination. *Vet Clin North Am Small Anim Pract* 2001;31:473–492.
9. Scott-Moncrieff JC, Azcona-Olivera J, Glickman NW, et al. Evaluation of antithyroglobulin antibodies after routine vaccination in pet and research dogs. *J Am Vet Med Assoc* 2002;221;515–521.
10. Feline vaccine liability and management. *Comp Contin Educ Pract Vet* 2001;23:116–126, 165.
11. Coyne MJ, Burr JHH, Yule TD, et al. Duration of immunity in dogs after vaccination or naturally acquired infection. *Vet Rec* 2001;149:509–515.
12. Lappin MR, Andrews J, Simpson D, et al. Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus, and feline parvovirus infection in cats. *J Am Vet Med Assoc* 2002;220: 38–42.
13. McCaw DL, Thompson M, Tate D, et al. Serum distemper virus and parvovirus antibody titers among dogs brought to a veterinary hospital for revaccination. *J Am Vet Med Assoc* 1998;213:72–75.
14. Scott FW, Geissinger CM. Long-term immunity in cats vaccinated with an inactivated trivalent vaccine. *Am J Vet Res* 1999;60: 652–658.
15. Tizard I, Ni Y. Use of serologic testing to assess immune status of companion animals. *J Am Vet Med Assoc* 1998;213:54–60.
16. Twark L, Dodds WJ. Clinical use of serum parvovirus and distemper virus antibody titers for determining revaccination strategies in healthy dogs. *J Am Vet Med Assoc* 2000;217:1021–1024.
17. Carmichael LE. Canine viral vaccines at a turning point—a personal perspective. *Adv Vet Med* 1999;41:289–307.
18. Technical Consultative Group to the World Health Organization on the Global Eradication of Poliomyelitis. "Endgame" issues for the global polio eradication initiative. *Clin Infect Dis* 2002; 34:72–77.
19. Hsia EC, Chung JB, Schwartz JS, et al. Cost-effectiveness analysis of the Lyme disease vaccine. *Arthritis Rheum* 2002;46: 1651–1660.
20. Gangarosa EJ, Galazka AM, Wolfe CR, et al. Impact of anti-vaccine movements on pertussis control: the untold story. *Lancet* 1998;351:356–361.