SMALL ANIMALS

Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus, and feline parvovirus infection in cats

Michael R. Lappin, DVM, PhD; Janet Andrews, PhD; Dan Simpson, BS; Wayne A. Jensen, DVM, PhD

Objective—To determine whether detection of virus-specific serum antibodies correlates with resistance to challenge with virulent feline herpesvirus 1 (FHV-1), feline calicivirus (FCV), and feline parvovirus (FPV) in cats and to determine percentages of client-owned cats with serum antibodies to FHV-1, FCV, and FPV.

Design—Prospective experimental study.

Animals—72 laboratory-reared cats and 276 client-owned cats.

Procedures—Laboratory-reared cats were vaccinated against FHV-1, FCV, and FPV, using 1 of 3 commercial vaccines, or maintained as unvaccinated controls. Between 9 and 36 months after vaccination, cats were challenged with virulent virus. Recombinant-antigen ELISA for detection of FHV-1-, FCV-, and FPV-specific antibodies were developed, and results were compared with results of hemagglutination inhibition (FPV) and virus neutralization (FHV-1 and FCV) assays and with resistance to viral challenge.

Results—For vaccinated laboratory-reared cats, predictive values of positive results were 100% for the FPV and FCV ELISA and 90% for the FHV-1 ELISA. Results of the FHV-1, FCV, and FPV ELISA were positive for 195 (70.7%), 255 (92.4%), and 189 (68.5%), respectively, of the 276 client-owned cats.

Conclusions and Clinical Relevance—Results suggest that for cats that have been vaccinated, detection of FHV-1-, FCV-, and FPV-specific antibodies is predictive of whether cats are susceptible to disease, regardless of vaccine type or vaccination interval. Because most client-owned cats had detectable serum antibodies suggestive of resistance to infection, use of arbitrary booster vaccination intervals is likely to lead to unnecessary vaccination of some cats. (*J Am Vet Med Assoc* 2002;219:38–42)

Recommended protocols for vaccination of cats have been under review ever since an association between SC or IM administration of vaccines and formation of soft tissue sarcomas was identified.[1-3] Rabies virus and feline leukemia virus vaccines containing adjuvants cause the most inflammation and have been linked most frequently to tumor production. However, soft tissue sarcomas reportedly can develop at the site of SC administration of modified-live or killed **feline herpesvirus 1 (FHV-1)**, **feline calicivirus (FCV)**, and **feline parvovirus (FPV)** vaccines.[4]

The duration of immunity in cats following administration of some killed rabies virus vaccines has been demonstrated to be at least 3 years,[5] and many believe the duration of immunity induced by other viral vaccines is similar. Because of this and because of the potential risks associated with vaccination, the **American Association of Feline Practitioners/Academy of Feline Medicine (AAFP/AFM)**, along with various others, has questioned the need for annual vaccination of cats against FHV-1, FCV, and FPV.[6-9] On the basis of a review of the literature and consultations with experts in the field, the AAFP/AFM has recommended that kittens ≥ 6 weeks old be vaccinated against FHV-1, FCV, and FPV every 3 to 4 weeks until they are ≥ 12 weeks old, followed by booster vaccination 1 year later and, for cats at minimal risk of infection, every 3 years after that.[7,8]

Feline herpesvirus 1, FCV, and FPV vaccines are thought to elicit both humoral and cell-mediated immune responses. Humoral immune responses can readily be measured by detecting virus-specific antibodies. In contrast, quantifying cell-mediated immune responses is difficult, and cell-mediated immune responses are not routinely measured. For many infectious agents, it is not known whether humoral or cell-mediated immune responses are more important in protecting against infection, although it is likely that both are involved to various degrees. It is also not currently known to what extent humoral or cell-mediated immunity is responsible for the protection elicited by vaccination against FHV-1, FCV, and FPV. Nevertheless, if the virus-specific antibody titer can be shown to be correlated with protection from challenge, then serologic screening of individual vaccinated cats could be used as an alternative to routine vaccination at arbitrary intervals.[9,10] In a previous study,[11] serum antibodies against FHV-1, FCV, and FPV could be detected in all cats inoculated twice with a combination killed FHV-1, FCV, and FPV vaccine 3 years previously. When these cats were challenged with virulent virus 7.5 years after vaccination, all were protected against FPV infection.[12] When cats were challenged with virulent FHV-1 and FCV, clinical signs of disease in the vaccinated cats were 52 and 63%, respectively, less severe, compared with signs in unvaccinated control cats.[12]

Various methods can be used to detect virus-specific antibody, including virus neutralization (FHV-1 and FCV) and hemagglutination inhibition (FPV) assays.[11,12] These assays are labor intensive and only

From the Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523 (Lappin); and Heska Corp, 1613 Prospect Pky, Fort Collins, CO 80525 (Andrews, Simpson, Jensen).

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available in specialized laboratories. Enzyme-linked immunosorbent assays incorporating whole virus or virus-infected cell preparations have been used to detect antibodies specific for FCV and FHV-1 and are potentially more sensitive than virus neutralization techniques.[13,14] In addition, ELISA are technically less complicated, can be standardized for use in multiple laboratories, and can be adapted for use in veterinary clinics. The purposes of the study reported here were to develop recombinant antigen-based ELISA for detection of antibodies specific for FHV-1, FCV, and FPV, to determine whether detection of virus-specific serum antibodies correlates with resistance to challenge with virulent virus, and to determine percentages of client-owned cats with serum antibodies to FHV-1, FCV, and FPV.

Materials and Methods

Detection of virus-specific serum antibodies—Sera were tested for FPV-specific antibodies by means of **hemagglutination inhibition (HI)** and for FHV-1- and FCV-specific antibodies by means of **virus neutralization (VN)**[11,12]; assays were performed at a commercial laboratory.[a] Results for the FPV HI, FCV VN, and FHV-1 VN assays were considered positive if titers were > 10, > 8, and > 8, respectively.

Sera were also tested for virus-specific antibodies by use of ELISA. In brief, wells on plastic 96-well microtitration plates[b] were coated with recombinant FCV capsid protein, FHV-1 glycoprotein C, or FPV VP2 protein. Proteins had been designed to contain the apparent immunodominant antigens and had been expressed in *Escherichia coli*.[15-17] Coated plates were incubated overnight at 4 C, and wells were washed 4 times with **phosphate-buffered saline solution containing 0.05% Tween 20 (PBST)** and then blocked for 1 hour at room temperature (approx 20 C).[c,d]

For detection of FCV-specific antibodies, sera were diluted 1:1,000, and 100-µl aliquots were added to capsid antigen-coated wells. For detection of FHV-1- and FPV-specific antibodies, sera were diluted 1:100, and 100 µl aliquots were added to glycoprotein C and VP2 antigen-coated wells, respectively. Plates were incubated for 1 hour at room temperature and then washed 4 times with PBST. One hundred microliters of a 100 ng/ml solution of horseradish peroxidase-conjugated goat anti-cat IgG (gamma chain specific)[e] was then added to each well, and plates were incubated for 1 hour at room temperature. Plates were again washed 4 times with PBST, and 100 µl of substrate (3,3',5,5'-tetramethylbenzidine)[e] was added to each well. Plates were incubated a final time for 30 minutes at room temperature, and the colorimetric reaction was then stopped by addition of 100 µl of 1.0*M* H_3PO_4 to each well. Optical density was read at 450 nm with an ELISA plate reader.[f]

The cutoff for the ELISA was determined with negative control serum samples from 54 unvaccinated specific-pathogen-free cats; for all negative control serum samples, results of HI assays for FPV antibodies and of VN assays for FHV-1 and FCV antibodies were negative. Results of the ELISA were considered positive if the optical density of the mean of the duplicate test wells was greater than the mean plus 3 SD optical density for the negative control serum samples.

Determination of interassay variation—Interassay variation was determined by assaying serum samples, using the FPV HI assay (n = 39), the FPV ELISA (39), the FHV-1 VN assay (40), the FHV-1 ELISA (40), the FCV VN assay (40), and the FCV ELISA (40), twice on separate days. The individual performing the second assay on each sample was not aware of the results of the first assay. For the VN and HI assays, interassay variation was determined by comparing titer magnitude. For the ELISA, the coefficient of variation was calculated.

Evaluation of concordance between results of HI or VN assays and ELISA—To assess concordance, results of the ELISA were compared with results of the HI or VN assay for serum samples from 73 (FPV and FHV-1) or 74 (FCV) vaccinated cats. Results were considered concordant if results for the 2 assays were the same (ie, both the ELISA and the VN or HI assay yielded positive results or both the ELISA and the VN or HI assay yielded negative results). Concordance was calculated by dividing the number of concordant results by the number of samples evaluated and multiplying by 100.

Percentages of client-owned cats with virus-specific antibodies—Serum samples from 276 client-owned cats were assayed for virus-specific antibodies, using the FHV-1, FCV, and FPV ELISA. Samples from these cats had originally been submitted for detection of *Dirofilaria immitis*-specific antibodies.[g] Because all cats were owned, most had probably been vaccinated against FHV-1, FCV, and FPV; however, vaccination history was not known.

Association between detection of virus-specific antibodies and protection from challenge—Four experiments were performed to determine whether cats with detectable virus-specific serum antibodies were protected from challenge with virulent virus. Cats used for these experiments were from several sources. All cats were housed in a SPF facility; serologic status was determined prior to challenge by use of the HI (FPV) or VN (FHV-1 and FCV) assay.

Experiment 1 consisted of 24 cats. Fourteen of the cats were vaccinated once intranasally with a trivalent vaccine[h]; the other 10 were not vaccinated. All cats were sequentially challenged, at monthly intervals, with FPV, FHV-1, and FCV (9, 10, and 11 months, respectively, after vaccination for the 14 cats that were vaccinated). Prior to challenge, the unvaccinated cats were seronegative for antibodies to FHV-1, FCV, and FPV, and attempts to isolate FHV-1 and FCV from throat swab specimens[i] did not yield any virus. Results of serologic testing for antibodies against FPV were not available for 1 vaccinated cat, and data for this cat were excluded from these analyses.

Experiment 2 consisted of 16 cats. Twelve of the cats were vaccinated by SC administration of a modified-live FHV-1, FCV, FPV vaccine[j] at 12 to 16 weeks, 16 to 20 weeks, and 14 to 15 months of age; the remaining 4 cats were not vaccinated. All cats were sequentially challenged with FPV and FHV-1 (30 and 31 months, respectively, after the last vaccination for the 12 cats that were vaccinated). Prior to challenge, the unvaccinated cats were seronegative for antibodies to FHV-1 and FPV but were seropositive for antibodies to FCV, presumably as a result of natural exposure; attempts to isolate viruses from throat swab specimens did not yield FHV-1 but did yield FCV.

Experiment 3 also consisted of 16 cats, all of which were challenged with FCV. Twelve of the cats were vaccinated by SC administration of a modified-live or killed FHV-1, FCV, FPV vaccine[j,k] 2 to 4 times, with the last booster vaccination given 36 months prior to challenge. The remaining 4 cats had not been vaccinated and were seronegative for antibodies to FHV-1, FCV, and FPV prior to challenge; attempts at isolation of FCV and FHV-1 from throat swab specimens collected prior to challenge did not yield any virus.

Experiment 4 consisted of 16 cats, all of which were challenged with FCV. Twelve of the cats were vaccinated by SC administration of a killed FHV-1, FCV, FPV vaccine[k] 2 or 3 times, with the last booster vaccination given 24 to 30 months prior to challenge. The remaining 4 cats had not been vaccinated and were seronegative for antibodies to FCV, FHV-1, and FPV prior to challenge.

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Challenge inoculation—Viruses used for challenge exposures were obtained from the Center for Veterinary Biologics Laboratory[l] and maintained frozen at –70 C until used. United States Department of Agriculture protocols[18] for challenge exposure of cats with FCV, FPV, and FHV-1 were used. For each challenge, cats were sedated with 20 mg of ketamine hydrochloride and 0.05 mg of acepromazine, IV. For challenge with FPV, the virus was administered intraperitoneally. For challenge with FHV-1 and FCV, the virus was administered with an atomizer; half the challenge volume was administered into the oropharynx, and a quarter of the volume was administered into each nostril.

Monitoring—For evaluating responses to challenge with FPV, blood samples were collected into tubes containing EDTA on days –5, –3, 0, 3, 5, 7, 10, 14, and 21, and CBC were performed.[8] For evaluating responses to challenge with FHV-1 or FCV, clinical scores were assigned, as described,[19] daily for 14 days after challenge. The individual assigning scores was not aware of whether cats had been vaccinated. At the end of this 2-week observation period, a cumulative clinical score was calculated for each cat.

Statistical analyses—The USDA has defined panleukopenia as a decrease in WBC count to ≤ 4,000 cells/µl or a decrease to < 25% of the mean for 3 or more counts prior to challenge. In addition, the USDA considers a panleukopenia vaccine to be effective if ≥ 80% of the control cats and ≤ 10% of the vaccinated cats develop panleukopenia. For the present study, cats were considered resistant to challenge with FPV if they failed to develop panleukopenia.

Vaccination against FHV-1 and FCV does not block infection; rather, it lessens the severity of clinical signs of disease. Therefore, efficacy of FHV-1 and FCV vaccines is determined by comparing severity of clinical signs of disease in vaccinated versus unvaccinated cats. The USDA considers an FHV-1 or FCV vaccine to be effective if clinical scores for vaccinated cats are significantly less than clinical scores for unvaccinated control cats, using the nonparametric Mann-Whitney modification of Wilcoxon's 2 sample test.[19] For the present study, relative efficacy of vaccination in each cat was calculated by use of the following formula: 100 X (mean clinical score for control cats – clinical score for test cat)/(mean clinical score for control cats). Cats were considered resistant to challenge with FHV-1 or FCV if relative efficacy was > 50%.

For each virus, results of the HI (FPV) or VN (FCV or FHV-1) assay and of the virus-specific ELISA were compared with results of challenge with that virus. Predictive values of positive and negative tests were then calculated for each assay, using results for vaccinated cats.[20]

Results

Concordance of assay results—Results of the HI or VN assay were concordant with results of the ELISA for 78, 93, and 75%, respectively, of the samples tested for antibodies to FHV-1, FCV, and FPV **(Table 1)**. Most of the discordant results for assays of antibodies to FPV were attributable to positive HI assay and negative ELISA results. Most of the discordant results for assays of antibodies to FHV-1 were attributable to positive ELISA and negative VN assay results.

Interassay variation—In evaluating interassay variation of the FPV HI assay, results for serum samples from all 14 unvaccinated control cats were negative both times samples were assayed. Replicate titers varied ≤ 2-fold for serum samples from 20 of the 25 (80%) vaccinated cats and by up to 16-fold for the remaining 5 cats. For 4 cats, titers varied sufficiently to change the interpretation of the FPV HI assay result from positive to negative (3 cats) or from negative to positive (1). For the FPV ELISA, the mean coefficient of variation was 7% for samples from the 25 vaccinated cats and 17% for samples from the 14 unvaccinated control cats. For 1 of the unvaccinated control cats for which assay results differed, results were positive the first time a sample was assayed and negative the second time. For the other unvaccinated control cat for which assay results differed, results were positive both times samples were assayed.

Table 1—Concordance between results of a hemagglutination inhibition (HI) assay and results of an ELISA for serum antibodies against feline parvovirus (FPV) and between results of virus neutralization assays and ELISA for serum antibodies against feline herpesvirus 1 (FHV-1) and feline calicivirus (FCV) in serum samples from cats

Assay results		No. of cats		
ELISA	HI or VN	FPV	FHV-1	FCV
+	+	45	41	63
+	–	7	15	3
–	+	11	1	2
–	–	10	16	6
Total		**73**	**73**	**74**
Concordant results (%)		**75**	**78**	**93**

For the FHV-1 VN assay, results for serum samples from all 14 unvaccinated control cats were negative both times samples were assayed. Replicate titers varied ≤ 2-fold for serum samples from 21 of 26 (81%) vaccinated cats and by up to 4-fold for the remaining 5 cats. For 4 cats, titers varied sufficiently to change the interpretation of the FHV-1 VN assay result from positive to negative. For the FHV-1 ELISA, the mean coefficient of variation was 5% for samples from the 26 vaccinated cats and 12% for samples from the 14 unvaccinated control cats. For 1 of the vaccinated cats, results were negative the first time the sample was assayed and positive the second time. For 2 unvaccinated control cats, results were negative the first time samples were assayed and positive the second time.

For the FCV VN assay, replicate titers varied ≤ 2-fold for 23 of 26 (89%) vaccinated cats and by up to 4-fold for the remaining 3 cats. For 7 of 14 unvaccinated control cats, results of the FCV VN assay were negative the first time samples were assayed and positive the second time. For the FCV ELISA, the mean coefficient of variation was 7% for samples from the 26 vaccinated cats and 23% for samples from the 14 unvaccinated control cats. For the FCV ELISA, all samples that yielded positive results the first time they were assayed yielded positive results the second time, and all samples that yielded negative results the first time they were assayed yielded negative results the second time.

Percentages of client-owned cats with virus-specific antibodies—Results of the FHV-1, FCV, and FPV ELISA were positive for 195 (70.7%), 255 (92.4%), and 189 (68.5%), respectively, of the 276 client-owned cats.

Challenge with FPV—In experiments 1 and 2, all 14 unvaccinated control cats developed panleukopenia after challenge with FPV, but none of the 25 vaccinated cats did. Thus, for both experiments, the challenge

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protocol met the criteria for USDA approval of FPV vaccines. All 14 unvaccinated control cats had negative VN assay results (titer ≤ 10) prior to challenge exposure, whereas 19 of the 25 vaccinated cats had positive VN assay results (titer > 10), and 6 had negative results.

Two of the unvaccinated control cats had positive FPV ELISA results prior to challenge, and 12 had negative results. Both unvaccinated control cats with positive FPV ELISA results developed panleukopenia following challenge; therefore, results for these 2 cats were falsely positive. Fifteen of the 25 vaccinated cats had positive FPV ELISA results prior to challenge, and 10 had negative results.

For the vaccinated cats, the predictive values of positive VN assay and ELISA results were 100% (ie, none of the cats with positive results developed panleukopenia following challenge). The predictive values of negative VN assay and ELISA results were 0%, because all 6 vaccinated cats with negative FPV HI assay results and all 10 vaccinated cats with negative FPV ELISA results were resistant to FPV infection.

Challenge with FHV-1—In experiments 1 and 2, all 14 unvaccinated control cats developed persistent severe clinical signs of disease after challenge with FHV-1. In addition, clinical scores for vaccinated cats were significantly less than scores for unvaccinated cats. Therefore, for both experiments, the challenge protocol met the criteria for USDA approval of FHV-1 vaccines.

For all 14 unvaccinated control cats, results of the VN assay and ELISA were negative prior to challenge, and all cats were classified as susceptible to infection (relative efficacy ≤ 50%). For vaccinated cats in experiment 1, in which the vaccine was administered intranasally, mean relative efficacy was 63% (range, 26.3 to 94.7%). For vaccinated cats in experiment 2, in which the vaccine was administered SC, mean relative efficacy was 67% (range, 50.7 to 76.8%). For the 2 experiments combined, 4 of 26 vaccinated cats were classified as susceptible to disease.

Twenty-three vaccinated cats had positive VN assay results prior to challenge (2 were susceptible to disease), and 3 had negative results (2 were susceptible to disease). Thus, for the FHV-1 VN assay, the predictive value of a positive test result was 91%, and the predictive value of a negative test result was 67%.

Twenty-one vaccinated cats had positive ELISA results prior to challenge (2 were susceptible to disease), and 5 had negative results (2 were susceptible to disease). Thus, for the FHV-1 ELISA assay, the predictive value of a positive test result was 90%, and the predictive value of a negative test result was 40%.

Challenge with FCV—In experiments 1, 3, and 4, unvaccinated control cats developed persistent severe clinical signs of disease after challenge with FCV, and clinical scores for vaccinated cats were significantly less than scores for unvaccinated cats. Therefore, for all 3 experiments, the challenge protocol met the criteria for USDA approval of FCV vaccines.

Results of the FCV VN assay were negative for 15 of the 18 unvaccinated control cats and positive for 3. All 3 cats with positive results were classified as susceptible to disease (relative efficacy ≤ 50%), and results for these 3 cats were considered falsely positive. Two unvaccinated control cats for which results of the VN assay were negative were classified as resistant to disease. Results of the FCV ELISA were negative for all 18 unvaccinated control cats, but 2 of the 18 were classified as resistant to disease.

For the 14 cats that received the FCV vaccine intranasally, mean relative efficacy was 92% (range, 61.7 to 100%), whereas for the 24 cats that received the FCV vaccine SC, mean relative efficacy was 94% (range, 80.4 to 100%). None of the cats were classified as susceptible to disease.

All 38 vaccinated cats had positive VN assay and ELISA results, and all were classified as resistant to disease. Therefore, for these vaccinated cats, the predictive values of positive VN assay and ELISA results were 100%. Because none of the vaccinated cats had negative results, predictive values of negative VN assay and ELISA results could not be calculated.

Discussion

In the present study, the predictive values of positive test results for vaccinated cats were 100% for both FPV and both FCV assays, 91% for the FHV-1 VN assay, and 90% for the FHV-1 ELISA. The 2 vaccinated cats that were susceptible to FHV-1 challenge (relative efficacy ≤ 50%) but for which results of the FHV-1 VN assay and ELISA were positive had lower clinical scores (relative efficacy, 37 and 26%) than did the control cats, suggesting that they were at least partially protected. Thus, although it has not been determined whether FHV-1-, FCV-, and FPV-specific antibodies are responsible for protection from challenge, results of the present study do suggest that detection of FHV-1-, FCV-, and FPV-specific antibodies is predictive of whether cats are susceptible to disease.

For some unvaccinated cats in the present study, results of the FCV VN assay or of the FPV ELISA were falsely positive. Positive results in these cats were likely a result of nonspecific binding of unknown substances in the serum of these cats to test reagents, and false-positive results are inherent to all antibody detection assays. Most positive results for vaccinated cats in the present study were true-positive results, in that most cats with positive results were resistant to challenge. We conclude, therefore, that serum antibody testing should not be used to predict resistance to FHV-1, FCV, or FPV infection in cats for which the vaccination history is unknown and suggest that cats for which vaccination history is unknown be vaccinated according to guidelines published by the AAFP/AFM.[8]

All 15 vaccinated cats in the present study for which results of the FPV ELISA were positive, all 38 vaccinated cats for which results of the FCV ELISA were positive, and 19 of the 21 vaccinated cats for which results of the FHV-1 ELISA were positive were resistant to challenge with these organisms. Because results of these ELISA appear to be predictive of protection from disease in vaccinated cats, use of these ELISA to detect virus-specific antibody in previously vaccinated cats may help in the development of ratio-

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nal booster vaccination regimens for adult cats. The assays used in this study are currently available.[a,g]

Several vaccinated cats in this study for which results of the FPV or FHV-1 assays were negative were, nevertheless, resistant to challenge, suggesting that the absence of detectable antibody is not predictive of susceptibility to disease. These results also suggest that cell-mediated immunity or the ability to rapidly regenerate humoral immunity can maintain protection even when serum antibodies have declined to undetectable levels. Thus, if serologic testing for virus-specific antibodies is used to determine whether cats require booster vaccination against FHV-1, FCV, and FPV, some cats will be vaccinated unnecessarily. However, the number would still be less than the number of cats that would be vaccinated unnecessarily if an arbitrary booster vaccination interval of 1 or 3 years were used. In the present study, virus-specific antibodies suggestive of resistance to infection with FHV-1, FCV, and FPV were found in 195 (70.7%), 255 (92.4%), and 189 (68.5%) of 276 client-owned cats, respectively. Results suggest that most of these cats would not require booster vaccination.

Whether results of serologic assays used to predict resistance to infection with FHV-1, FCV, and FPV would be affected by route of vaccine administration or vaccination interval was previously unknown, because results of only a single long-term study using only a single vaccine have been reported.[12] In the present study, 2 FPV and FHV-1 vaccines and 3 FCV vaccines were used. Additionally, the interval between vaccination and challenge varied from 9 to 31 months for FHV-1 and FPV and from 9 to 36 months for FCV. Positive predictive values of the serologic assays were similar regardless of the vaccine or vaccine interval.

The ELISA used in this study were designed to detect antibodies against the immunodominant antigens for each organism.[15-17] This may help explain the generally good correlation between results of these ELISA and results of the VN and HI assays. Many of the discordant results for the FPV and FHV-1 assays were attributable to positive ELISA results and negative HI or VN assay results. This suggests that the FHV-1 and FPV ELISA used in this study may be more sensitive than the VN and HI assays.

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[a]New York State Diagnostic Laboratory, Ithaca, NY.
[b]Nunc Immuno Plate Maxisorb, Nalge Nunc International Corp, Rochester, NY.
[c]StabilCoat immunoassay stabilizer, Surmodics Inc, Eden Park, Minn.
[d]ProClin 300 (0.5%), Supelco, Bellefonte, Pa.
[e]Kirkegaard & Perry Laboratories Inc, Gaithersburg, Md.
[f]SpectroMax 250, Molecular Devices, Sunnyvale, Calif.
[g]Heska Veterinary Diagnostic Laboratories, Fort Collins, Colo.
[h]Trivalent intranasal/intraocular vaccine, Heska Corporation, Fort Collins, Colo.
[i]Diagnostic Laboratory, Colorado State University, Fort Collins, Colo.
[j]Eclipse 4, Schering-Plough, Union, NJ.
[k]Felovax, Fort Dodge Laboratories Inc, Fort Dodge, Iowa.
[l]USDA, Animal and Plant Health Inspection Services, Veterinary Services, Center for Veterinary Biologics Laboratory, Ames, Iowa.

References

1. Kass PH, Barnes WG, Spangler WL, et al. Epidemiologic evidence for a causal relationship between vaccination and fibrosarcoma tumorigenesis in cats. *J Am Vet Med Assoc* 1993;203:396–405.

2. Hendrick MJ, Brooks JJ. Postvaccinal sarcomas in the cat: histology and immunohistochemistry. *Vet Pathol* 1994;31:126–129.

3. Hendrick MJ, Shofer FS, Goldschmidt MH, et al. Comparison of fibrosarcomas developed at vaccination sites and at nonvaccination sites in cats: 239 cases (1991–1992). *J Am Vet Med Assoc* 1994;205:1425–1429.

4. Burton G, Mason KV. Do postvaccinal sarcomas occur in Australian cats? *Aust Vet J* 1997;75:102–106.

5. Jenkins SR, Auslander M, Conti L, et al. Compendium of animal rabies prevention and control, 2000. *J Am Vet Med Assoc* 2000; 216:338–343.

6. Schultz RD. Current and future canine and feline vaccination programs. *Vet Med* 1998;3:233–254.

7. Elston T, Rodan I, Flemming D, et al. 1998 Report of the American Association of Feline Practitioners and Academy of Feline Medicine Advisory Panel on Feline Vaccines. *J Am Vet Med Assoc* 1998;212:227–241.

8. Richards J, Rodan I, Elston T, et al. Feline vaccine selection and administration. *Compend Contin Educ Pract Vet* 2001;23:71–80.

9. Richards J, Rodan I, Elston T, et al. Feline vaccine liability and management. *Compend Contin Educ Pract Vet* 2001;23:116–126.

10. Tizard I, Ni Y. Use of serologic testing to assess immune status of companion animals. *J Am Vet Med Assoc* 1998;213:54–60.

11. Scott FW, Geissinger C. Duration of immunity in cats vaccinated with an inactivated feline panleukopenia, herpesvirus, and calicivirus vaccine. *Feline Pract* 1997;25(4):12–19.

12. Scott FW, Geissinger CM. Long-term immunity in cats vaccinated with an inactivated trivalent vaccine. *Am J Vet Res* 1999;60: 652–658.

13. Hill SL, Lappin MR, Carman J, et al. Comparison of methods for estimation of *Toxoplasma gondii*-specific antibody production in the aqueous humor of cats. *Am J Vet Res* 1995;56:1181–1187.

14. Dawson DA, Carman J, Collins J, et al. Enzyme-linked immunosorbent assay for detection of feline herpesvirus 1 IgG in serum, aqueous humor, and cerebrospinal fluid. *J Vet Diagn Invest* 1998;10:315–319.

15. Tohya Y, Yokoyama N, Maeda K, et al. Mapping of antigenic sites involved in neutralization on the capsid protein of feline calicivirus. *J Gen Virol* 1997;78:303–305.

16. Maeda K, Yokoyama N, Fujita K, et al. Identification and characterization of the feline herpesvirus type 1 glycoprotein C gene. *Virus Genes* 1997;14:105–109.

17. Lopez de Turiso JA, Cortes E, Ranz A, et al. Fine mapping of canine parvovirus B cell epitopes. *J Gen Virol* 1991;72:2445–2456.

18. 56 Federal Register 66784, 66786 (Dec 26, 1991) (codified at 9 CFR 113).

19. *Supplemental assay method for scoring feline rhinotracheitis virus in cats following challenge, supplemental assay method for scoring feline calicivirus in cats following challenge*. Ames, Iowa: Center for Veterinary Biologics and National Veterinary Services Laboratories, 2001.

20. Griner PF, Mayewski RJ, Mushlin AI, et al. Selection and interpretation of diagnostic tests and procedures: principles and application. *Ann Intern Med* 1981;94:533–600.

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