Antibody Response to an Inactivated Vaccine for Rhinotracheitis, Caliciviral Disease, and Panleukopenia in Nondomestic Felids

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SUMMARY

The efficacy of an inactivated vaccine for the prevention of feline viral rhinotracheitis (FVR), feline caliciviral disease (FCVD), and feline panleukopenia (FPL) was tested in 27 nondomestic adult felids from 7 species. The vaccine was given IM at the standard domestic cat dose in 19 animals and double this dose in 8 others. The animals were vaccinated either 1, 2, or 3 times. Serum-neutralization (SN) antibodies to FVR (mean SN titer, 23) developed in all 15 animals that were previously seronegative, and SN antibodies to FCVD (mean SN titer, 11) developed in 19 of 21 animals that were previously seronegative. There was no significant increase of SN antibody titers by doubling the vaccine dose or by administering a 3rd vaccination. The optimal response could be obtained by using the domestic cat vaccination protocol of a single dose given twice, 4 weeks apart.

The critical evaluation of the SN antibody titer for FPL was complicated by preexisting titers to FPL from previous vaccinations, but in 23 animals the titers became higher, whereas they remained unchanged in only 4 animals.

The persistence of the SN titers was evaluated 7 to 9 months later and found to be satisfactory for FVR (mean SN titer, 18), FCVD (mean SN titer, 43), and FPL (mean SN titer, 517). Enhanced persistence of titer could not be demonstrated by doubling the dose or administering a 3rd vaccination.

VACCINATIONS ARE an important component of a preventive medical program in zoological collections, especially because of inherent problems associated with diagnosis and treatment of an uncooperative and dangerous patient.

The nondomestic felidae share some of the viral diseases of the domestic cat, notably feline panleukopenia (FPL),[1-3] feline viral rhinotracheitis FVR,[3-5] and feline caliciviral disease FCVD.[3-6] The disease of major concern has been FPL, but the respiratory viral diseases are becoming an emerging problem.

Vaccination for FPL in zoos has reduced markedly the incidence of the disease, but there is uncertainty as to which vaccine, what amount of vaccine for the larger felids, and which vaccination program to use.[7,8] These questions are further complicated when attempting to choose a vaccine and program to protect nondomestic felids against the feline respiratory diseases, namely FVR and FCVD. Few studies have been conducted to measure the antibody response of nondomestic felids to FPL[9] and/or FVR and FCVD.[10]

Of major concern is the use of a modified live-virus (MLV) vaccine in nondomestic felids. Inactivated vaccines have safety advantages, compared with MLV vaccines, and are preferred if they are capable of developing and sustaining immunity.

An inactivated vaccine[a] for protection of domestic cats against FVR, FCVD, and FPL has been tested for safety and efficacy against virulent virus challenge in the domestic cat and was found to induce good immunity.[11] The testing of this vaccine in nondomestic felids is the subject of this report.

Materials and Methods

The 27 study animals were from 7 species of adult felids on display at the National Zoological Park. They included 10 lions *(Panthera leo)*, 5 Bengal tigers *(Panthera tigris)*, 4 clouded leopards *(Neofelis nebulosa)*, 2 bobcats *(Felis rufus)*, 2 servals *(Felis serval)*, 2 puma *(Felis noncolor)*, and 2 jaguars *(Panthera onca)*. Each received a diet formulated to meet its particular needs. All animals were in a good nutritional state and free of clinical disease. They had each received an inactivated FPL vaccine[b] within the last 12 months as part of their preventive medical program.

Blood samples were collected from all animals prior to the study to establish prevaccination serum-neutralization (SN) antibody titers for FVR, FCVD, and FPL. The vaccine was administered IM, using the standard domestic cat dose (1 ml) for 19 felids, and the dose was doubled (2 ml) in 8 others (4 lions, 1 puma, 1 serval, and 2 tigers).

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[a]Felo-O-Vax PCT, Fort Dodge Laboratories, Fort Dodge, Iowa.
[b]Felocine, Norden Laboratories Inc, Lincoln, Neb.

TABLE 1—Mean Serum-Neutralization Antibody Titer Response to Various Vaccination Protocols

	No.	Feline viral rhinotracheitis	Feline caliciviral disease	Feline panleukopenia
Prevaccination titers	27	5	3	1,300
Protocol 1				
Response 4 weeks after 1 vaccination (single dose)	4	46 (4.5 X)	5 (4.0 X)	2,560 (4.0 X)
Titer 9 months later	1	2 (0.14 X)	12 (4.0 X)	192 (0.11 X)
Protocol 2				
Response 4 weeks after 2 vaccinations (single dose)	15	49 (7.5 X)	19 (5.0 X)	3,200 (4.5 X)
Titer 7–9 months later	2	8 (5.0 X)	10 (5.0 X)	555 (5.0 X)
Protocol 3				
Response 4 weeks after 2 vaccinations (double dose)	8	48 (7.0 X)	18 (4.0 X)	2,220 (3.5 X)
Titer 7–9 months later	2	11 (5.0 X)	5 (4.5 X)	192 (2.0 X)
Protocol 4				
Response 4 weeks after 3 vaccinations (single dose)	3	53 (5.0 X)	7 (4.5 X)	1,710 (0.5 X)
Titer 7–9 months later	13	25 (4.5 X)	66 (5.5 X)	639 (0.67 X)
Protocol 5				
Response 4 weeks after 3 vaccinations (double dose)	0		Not measured	
Titer 7–9 months later	6	16 (3.5 X)	30 (8.0 X)	485 (0.5 X)
Postvaccination titers 7–9 months later, regardless of protocol	26	18	43	517

( ) = Magnitude of increase from prevaccination titer.

Five vaccination protocols were used in this study. Blood samples were obtained to measure the SN antibody response 4 weeks after the last vaccination in 4 of the 5 protocols. Blood samples were again collected to measure SN antibody titers 7–9 months after the last vaccination in all protocols.

Protocol 1—Four animals were vaccinated once, using a 1-ml dose of vaccine.

Protocol 2—Fifteen animals were vaccinated twice 4 weeks apart, using a 1-ml dose of vaccine.

Protocol 3—Eight animals were vaccinated twice 4 weeks apart, using a 2-ml dose of vaccine.

Protocol 4—Thirteen animals were vaccinated 3 times, 4 weeks apart, using a 1-ml dose of vaccine.

Protocol 5—Six animals were vaccinated 3 times, 4 weeks apart, using a 2-ml dose of vaccine.

Several animals were represented in more than 1 protocol (ie, blood sample collected 4 weeks after 1st, 2nd, and possibly a 3rd vaccination from 1 animal).

The tests for FVR and FCVD antibodies were performed in a microneutralization system, using constant virus (100 median tissue culture infective doses) and 2-fold serum dilutions, as previously described.[12] Neutralizing antibody titers to FPL virus were assayed in cell culture, using a direct fluorescent antibody technique to detect end points.[13–14]

Results

Before vaccination, 15 nondomestic felids were seronegative to FVR. After vaccination, the mean SN titer was 23. In 11 of 12 with preexisting titer for FVR, the mean titer increased from 11 to 78 after vaccination, whereas one lion maintained a titer of 12. Before vaccination, 21 nondomestic felids were seronegative to FCVD. For 19 of them, the mean SN titer after vaccination was 11; 2 lions remained seronegative. For 6 of the 7 animals with preexisting titer to FCVD, the mean titer increased from 16 to 42 after vaccination, whereas 1 lion had a drop in titer from 6 to 4. All 27 animals had high titers to FPL, attributable to previous vaccinations, but the titer increased in 23 animals and remained constant in the other 4 after vaccination.

The mean SN antibody response to the various vaccination protocols and the persistence of these titers are shown in Table 1. There was no significant difference in the mean postvaccinal titer for FVR, FCVD, or FPL between any of the vaccination protocols, as evaluated by Student's *t* test. The resultant titers at 7–9 months after the last vaccination were also comparable regardless of the vaccination protocol used.

To evaluate further each felid's response to the vaccinations, especially animals with preimmunization titers to any of the 3 antigens, the resultant increase or decrease in SN titer to each of the antigens after vaccination was reported as the "fold change" from the individual's preimmunization titer (ie, titers that increased from 2 to 4 or 16 to 32 each represented a 2-fold increase; Table 1). The initial responses to the vaccination, as expressed by the fold change in the titer, were comparable regardless of the protocol for FVR and FCVD, whereas the FPL results were erratic because of the preexisting titers. When the fold change from the prevaccinal titer was compared 7–9 months after vaccination, the results were again comparable, with persistent increases in titer except for the 1 animal (bobcat) that received only 1 dose of the vaccine.

There was no diagnosis of any infectious disease or major medical problems in these animals during the study period.

Discussion

Critical evaluation of a vaccine-induced antibody titer and protective capability depend on virulent virus challenge. This is not possible in a zoological environment when dealing with rare and endan-

gered species. Therefore, it becomes necessary to extrapolate from studies in domestic felids, wherein certain titers have been proved protective to virulent virus challenges. For FVR, a mean titer of 1:6 has been shown to be protective[15]; for FCVD, a mean titer of 1:8.2 provides protection[11]; and for FPL, titers greater than 1:8 have been repeatedly demonstrated to provide protection on challenge of immunity.[13-14]

The SN antibody response produced by a single dose of the inactivated vaccine 4 weeks apart in nondomestic felids for FVR and FCVD was protective. This protocol also increased the titer to FPL in 85% of the animals and remained constant, at a protective titer (mean SN titer, 853), in the remaining 15%. The SN antibody response was not increased significantly by doubling the dose of the vaccine or by a 3rd vaccination 4 weeks after the 2nd. This indicates that the vaccination protocol for the domestic cat produces the same protection in the larger felids (lions and tigers) as in the domestic cat. This is contrary to previous ideas that the dose of an inactivated vaccine had to be increased in larger species to elicit a satisfactory antigenic response, and that the MLV vaccines, because of viral replication after inoculation, required only a standard dose for an acceptable antigenic response.

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