ANTIBODY RESPONSE TO VACCINES FOR RHINOTRACHEITIS, CALICIVIRAL DISEASE, PANLEUKOPENIA, FELINE LEUKEMIA, AND RABIES IN TIGERS (PANTHERA TIGRIS) AND LIONS (PANTHERA LEO)


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ANTIBODY RESPONSE TO VACCINES FOR RHINOTRACHEITIS, CALICIVIRAL DISEASE, PANLEUKOPENIA, FELINE LEUKEMIA, AND RABIES IN TIGERS (PANTHERA TIGRIS) AND LIONS (PANTHERA LEO)


Abstract: This article presents the results of a study of captive tigers (Panthera tigris) and lions (Panthera leo) vaccinated with a recombinant vaccine against feline leukemia virus; an inactivated adjuvanted vaccine against rabies virus; and a multivalent modified live vaccine against feline herpesvirus, calicivirus, and panleukopenia virus. The aim of the study was to assess the immune response and safety of the vaccines and to compare the effects of the administration of single (1 ml) and double (2 ml) doses. The animals were separated into two groups and received either single or double doses of vaccines, followed by blood collection for serologic response for 400 days. No serious adverse event was observed, with the exception of abortion in one lionness, potentially caused by the incorrect use of the feline panleukopenia virus modified live vaccine. There was no significant difference between single and double doses for all vaccines. The recombinant vaccine against feline leukemia virus did not induce any serologic response. The vaccines against rabies and feline herpesvirus induced a significant immune response in the tigers and lions. The vaccine against calicivirus did not induce a significant increase in antibody titers in either tigers or lions. The vaccine against feline panleukopenia virus induced a significant immune response in tigers but not in lions. This report demonstrates the value of antibody titer determination after vaccination of nondomestic felids.

Key words: Lion, Panthera leo, Panthera tigris, serology, tiger, vaccination.

INTRODUCTION

Infections due to feline panleukopenia virus (FPV), rabies, feline leukemia virus (FeLV), feline rhinotracheitis (FHV, feline herpesvirus type 1), and feline calicivirus (FCV) have been described in numerous species of exotic felids, both in the wild and in captivity, with clinical signs similar to those observed in the domestic cat (Felis catus). Serologic studies have also shown that these diseases are endemic in certain regions in the world, where they may pose a serious threat to wild and captive felid populations. The vaccination of nondomestic felids has long been practiced in zoos, but few studies have examined the immune response, tolerance, or quantity and frequency of vaccine required. This article presents the results of a study performed in tigers (Panthera tigris) and lions (Panthera leo) vaccinated with three vaccines manufactured for domestic cats. The aim of the study was to assess the immune response and safety of vaccines in these species and to compare the effects of the use of two different dosages.

MATERIALS AND METHODS

Vaccines and animals

The Feligen® CRP (Virbac S.A., Carros 06511, France) used in the study is a live attenuated vaccine, which combines FCV, FHV, and parvovirus (FPV) strains in a lyophilized form. The preparation is resuspended in a water diluent or with the Rabigen Mono vaccine prior to injection. The Feligen CRP vaccine contains the F9 viral strain of calicivirus, the F2 strain of FHV, and the LR72 strain of attenuated FPV. The titer is composed of between 10^5 and 10^7 TCID₅₀/ml for FCV and FHV, and between 10^3.7 and 10^5.7 TCID₅₀ per vial for FPV. Rabigen Mono is an inactivated, monovalent rabies vaccine, prepared using the Pasteur VP 12 strain. The vaccine is inactivated and contains an adjuvant (aluminium hydroxide). It has an activity of more than 5 IU per dose (the minimal activity recommended by the European Pharmacopeia is...
A refrigerated package for analysis was used. Serum samples were collected and frozen at −70°C (3,000 g for 15 min), each serum sample was centrifuged without dilution. The first vaccination injection; and then on day 21 before the second vaccination injection; and then on day 42, day 150, and day 400. After centrifugation, the second vaccination injection; and then on day 21 before the first injection; then on day 21, the animals were given a booster of the CRP vaccine (2 ml). The animals were randomly assigned to the two groups, and each group was subjected to the same vaccination protocol but with a double dose of the FeLV vaccine, separately, at the same dose.

All the blood samples were collected from the saphenous vein without anesthesia in a squeeze cage. Each animal was sampled on day 0 before the first injection; then on day 21 before the second vaccination injection; and then on day 42, day 150, and day 400. After centrifugation (3,000 g for 15 min), each serum sample was collected and frozen at −18°C before being sent in a refrigerated package for analysis.

Clinical monitoring of the vaccinated animals

The felids in the study underwent a physical examination and were dewormed with ivermectin (IVOMEC® Bovin, Merial, Villeurbanne 69623, France; 0.2 mg/kg i.m.) 21 days before vaccination and on day 0 (first vaccine injection). An initial blood sample was collected prior to vaccination to screen for FeLV and feline immunodeficiency virus (Speed Duo FeLV/FIV®, BVT, La Seyne-sur-Mer 83500, France). Regular physical examinations were performed over the 421 days of the study and in particular on each day of blood collection. All clinical signs, after vaccination, were recorded with a severity score (0–3) on a clinical record card (pain, pruritis, localized swelling, rectal temperature, food consumption, behavior, nasal and ocular discharge, vomiting, coughing, feces, cutaneous signs, clinical signs).

Serologic analyses

The assay of antirabies antibodies was undertaken at the national laboratory AFSSA (Agence Française de Sécurité Sanitaire et Alimentaire, city of Nancy, France) by seroneutralization in cell cultures (rapid fluorescent focus inhibition test). The results were expressed in IU/ml after comparison with reference serum supplied by the World Health Organization. The World Health Organization recommends serologic titers of >0.5 IU/ml to ensure protection against the virus irrespective of the animal species. The efficacy of the modified live CRP vaccine was assessed by measuring serum neutralizing antibodies against CRP, using a standard microtitration technique by inhibition of cytopathic effects on microassay plates. The seroneutralization titer corresponds to the highest dilution of serum that neutralizes the viruses and is calculated using the Spearman and Kärber method. Titters are expressed in 10exp. The positivity thresholds were 10^0.9 for anti-FCV antibodies, 10^0.3 for anti-FHV antibodies, and 10^0.1 for anti-FPV antibodies. If less than these values, the titers were not considered positive (false positive due to the in vitro method of titration). The assay of anti-FeLV antibodies was performed using ELISA on microassay plates by measuring antibodies against the antigen P45. An ELISA was done using cat-specific secondary antibodies. The titer corresponds to the first dilution with an optical density at 405 nm inferior to 0.5, after subtraction of the mean of the six control wells.
The statistical analysis of serology data was performed on R software, version 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria). Wilcoxon signed-rank tests were performed to compare intragroup data evolution between day 0 and day 42, day 42 and day 400, and day 0 and day 400. Mann-Whitney tests were performed to compare data between groups at day 0, day 42, and day 400. The differences were considered to be significant if $P \leq 0.05$. Animals showing titers inferior to the positivity threshold of the tests were considered negative (false positive) for the statistical analysis.

RESULTS

Clinical monitoring of the vaccinated animals

In the months preceding the study, no animal presented with any serious disease. However on day 0, 1 tiger (tiger 6) presented with a hematoma on the left shoulder and 1 lion (lion 18) presented with pyrexia and vomiting. The lion was treated empirically, and the symptoms regressed by the next day. After vaccination, and between day 0 and day 42, the clinical examinations did not reveal any abnormalities in any of the felids in the study. No clinical signs were observed after visual assessment and palpation of the injection sites.

A few animals presented with general disorders during the months after vaccination. Wounds on the tail (tiger 4 on day 42) and the claw (lion 18 on day 42) were noted. Between day 34 and day 51, some gastrointestinal signs were observed (transient anorexia, vomiting and/or melena, and transient prostration) in three animals (lion 14 on day 34, lion 10 on day 40, lion 12 on day 51) that responded to empirical therapy. One case of stillbirth (1 cub) and neonatal death (2 cubs) was observed in a lioness between days 18 and 20 (lion 17).

Serology results

For all the vaccines tested, there was no significant difference in antibody response in tigers and lions receiving 1-ml versus 2-ml vaccine doses.

FeLV and FIV: ELISAs for the detection of FeLV and FIV were negative for all animals tested. The anti-FeLV serologies were all negative at day 0 and day 42.

Rabies (Table 1): On day 0, before vaccination, none of the tigers exhibited a significant antirabies titer ($\leq 0.04$ IU/ml). On day 42, all of the tigers (TA and TB) presented with a significant increase in antibodies ($P = 0.03$ in both cases) with titers superior to the threshold of protection (>0.5 IU/ml). On day 400, all of the tigers (TA and TB) presented with titers >0.1 IU/ml (mean = 0.53 IU/ml, $S = 0.28$, and mean = 0.66 IU/ml, $S = 0.3$, respectively). The drop in antibody titer between day 42 and day 400 was not significant for TA ($P = 0.14$) or TB ($P = 0.11$). Between day 0 and day 400, the titers were significantly higher on day 400 in both groups ($P = 0.03$ in both cases).

On day 0, prior to vaccination, the lions in groups LA and LB presented with zero or negligible rabies antibody levels ($\leq 0.05$ IU/ml), except one (14; no significant difference between LA and LB [$P = 0.44$]). On day 42, all of the lions (LA and LB) presented with a significant increase in the titers ($P = 0.02$ in both cases) and titers superior to the threshold of protection (>0.5 IU/ml). On day 400, all of the lions (LA and LB) presented with titers greater than 0.1 IU/ml.

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**Table 1.** The 19 tigers and lions by study inclusion number, gender, and age and their rabies neutralizing antibody titers on day 0, day 42, and day 400 after vaccination.

<table>
<thead>
<tr>
<th>Animal and group</th>
<th>Gender</th>
<th>Age (yr)</th>
<th>Titersb Day 0</th>
<th>Titersb Day 42</th>
<th>Titersb Day 400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tigers TAc</td>
<td>Mn</td>
<td>7</td>
<td>&lt;0.02</td>
<td>2.88</td>
<td>0.42</td>
</tr>
<tr>
<td>2</td>
<td>Mn</td>
<td>7</td>
<td>&lt;0.02</td>
<td>0.55</td>
<td>0.95</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>7</td>
<td>&lt;0.02</td>
<td>0.95</td>
<td>0.42</td>
</tr>
<tr>
<td>4</td>
<td>Mn</td>
<td>7</td>
<td>0.04</td>
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<td>0.32</td>
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<tr>
<td>Tigers TBd</td>
<td>Mn</td>
<td>7</td>
<td>0.03</td>
<td>0.95</td>
<td>0.95</td>
</tr>
<tr>
<td>1</td>
<td>Mn</td>
<td>7</td>
<td>&lt;0.02</td>
<td>1.26</td>
<td>0.24</td>
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<tr>
<td>6</td>
<td>Mn</td>
<td>7</td>
<td>&lt;0.02</td>
<td>3.79</td>
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<td>M</td>
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<tr>
<td>8</td>
<td>M</td>
<td>7</td>
<td>&lt;0.02</td>
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</tr>
<tr>
<td>Lions LAc</td>
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<td>5.00</td>
</tr>
<tr>
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<td>Mn</td>
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<td>&lt;0.02</td>
<td>8.69</td>
<td>0.42</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>3</td>
<td>&lt;0.02</td>
<td>15.1</td>
<td>5.00</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>4</td>
<td>0.05</td>
<td>8.69</td>
<td>0.42</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
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<td>&lt;0.02</td>
<td>15.1</td>
<td>5.00</td>
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<tr>
<td>Lions TBd</td>
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<td>&lt;0.02</td>
<td>8.69</td>
<td>0.32</td>
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<td>9</td>
<td>Mn</td>
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<td>&lt;0.02</td>
<td>8.69</td>
<td>1.26</td>
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<tr>
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<td>0.05</td>
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<td>2.88</td>
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<tr>
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<td>3.79</td>
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<tr>
<td>18</td>
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<tr>
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<td>F</td>
<td>7</td>
<td>ND</td>
<td>8.69</td>
<td>0.95</td>
</tr>
</tbody>
</table>

* Mn, male neutered; M, male; F, female; ND, not done (by mistake; not included in the statistical tests concerning Day 0).  
* Rabies titers in IU/ml; an adequate rabies titer is believed to be >0.5 IU/ml.  
* Cats received 1-ml dose of vaccine on Day 0.  
* Cats received 2-ml dose of vaccine on Day 0.
Table 2. The 19 tigers and lions by study inclusion number, gender, and age and their calicivirus (FCV), herpesvirus (FHV), and feline panleukopenia virus (FPV) neutralizing antibody titers on day 0, day 42, and day 400 after vaccination.

<table>
<thead>
<tr>
<th>Animal and group</th>
<th>Gender</th>
<th>Age (yr)</th>
<th>FCV antibody titers</th>
<th>FHV antibody titers</th>
<th>FPV antibody titers</th>
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<td></td>
<td></td>
<td></td>
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<td>Day 400</td>
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<td>Tigers TA</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Mn</td>
<td>7</td>
<td>1.96</td>
<td>1.51</td>
<td>1.87</td>
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<tr>
<td>3</td>
<td>Mn</td>
<td>7</td>
<td>1.40</td>
<td>(–)</td>
<td>1.05</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>7</td>
<td>1.03</td>
<td>1.02</td>
<td>1.57</td>
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<tr>
<td>5</td>
<td>Mn</td>
<td>7</td>
<td>1.63</td>
<td>1.62</td>
<td>1.75</td>
</tr>
<tr>
<td>Tigers TB</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Mn</td>
<td>7</td>
<td>1.86</td>
<td>1.64</td>
<td>1.52</td>
</tr>
<tr>
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<td>Mn</td>
<td>7</td>
<td>1.40</td>
<td>1.04</td>
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</tr>
<tr>
<td>7</td>
<td>Mn</td>
<td>9</td>
<td>1.03</td>
<td>1.24</td>
<td>1.15</td>
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<tr>
<td>8</td>
<td>M</td>
<td>7</td>
<td>1.27</td>
<td>1.04</td>
<td>1.40</td>
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<tr>
<td>Lions LA</td>
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<td>10</td>
<td>M</td>
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<td>1.75</td>
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<td>12</td>
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<td>0.95</td>
<td>(–)</td>
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<tr>
<td>13</td>
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<td>(–)</td>
<td>(–)</td>
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</tr>
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<td>16</td>
<td>F</td>
<td>7</td>
<td>(–)</td>
<td>(–)</td>
<td>0.93</td>
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<tr>
<td>Lions LB</td>
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<tr>
<td>9</td>
<td>M</td>
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<td>(–)</td>
<td>(–)</td>
<td>(–)</td>
</tr>
<tr>
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<td>ND</td>
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<td>0.93</td>
</tr>
</tbody>
</table>

* Mn, male neutered; M, male; F, female; ND, not done (by mistake; not included in the statistical tests concerning Day 0).
* Cats received 1-ml dose of vaccine on Day 0, followed by a 1-ml booster on Day 21.
* (–), inferior to the threshold of positivity for the titration method.
* Cats received 2-ml dose of vaccine on Day 0, followed by a 2-ml booster on Day 21.

(mean = 3.0 IU/ml, S = 2.3, and mean = 1.9 IU/ml, S = 1.31, respectively). The drop in antibody titer between day 42 and day 400 was significant for LA and LB (P = 0.04 and P = 0.03, respectively). The titers were still significantly higher on day 400 than on day 0 in both groups (P = 0.02 in both cases).

FCV (Table 2): On day 0, all of the tigers presented with anti-FCV antibodies, but there was no significant difference between TA and TB (P = 0.56). For TA as for TB, the variations in titers were not significant between day 0 and day 42 (P = 0.95 for TA and P = 0.97 for TB), between day 42 and day 400 (P = 0.47 for TA and P = 0.14 for TB), or between day 0 and day 400 (P = 0.86 for TA and P = 0.36 for TB).

On day 0 before vaccination, 40% of all of the lions sampled presented with antibodies against FCV, but there was no significant difference between LA and LB (P = 0.16). For LA as for LB, the variations in titers were not significant between day 0 and day 42 (P = 0.16 for LA and P = 0.18 for LB), between day 42 and day 400 (P = 0.79 for LA and P = 0.22 for LB), or between day 0 and day 400 (P = 0.21 for LA and P = 0.23 for LB).

FHV (Table 2): On day 0, all of the tigers in group A and 3 of the 4 tigers from group B presented with antibodies against FHV. On day 0, there was no significant difference between TA and TB (P = 0.38). Between day 0 and day 42, a significant increase in the antibody levels of TA and TB was observed (P = 0.03 in both cases). All of the tigers (TA and TB) presented with antibodies on day 42 and on day 400. For all the tigers from groups A and B, the titters decreased between day 42 and day 400, but the differences were not significant (P = 0.07 in both cases). Nevertheless, between day 0 and day 400, a significant increase in the level of antibodies of TA and TB was still observed (P = 0.03 in both cases).

On day 0, prior to vaccination, all of the lions sampled presented with antibodies against FHV. On day 0, there was no significant difference between LA and LB (P = 1). Between day 0 and day 42, there was a significant increase in the level of antibodies in both LA and LB (P = 0.02 in both cases).
cases). On day 42 and day 400, all of the lions presented with antibodies. Between day 42 and day 400, the antibodies decreased for LA and LB \((P = 0.07)\). Between day 0 and day 400, the increase in antibodies was less marked for LA and LB \((P = 0.07 \text{ in both cases})\) than between day 0 and day 42.

**FPV (Table 2):** On day 0, prior to vaccination, none of the tigers presented with antibodies against FPV. Between day 0 and day 42, the levels of antibodies increased significantly for TA \((P = 0.03)\) but not significantly for TB \((P = 0.16)\). Between day 42 and day 400, the levels of antibodies did not vary significantly for TA \((P = 0.72)\) or for TB \((P = 0.14)\). However, there was a significant increase in titers between day 0 and day 400 for TB \((P = 0.03)\).

On day 0, 40% of the lions sampled presented with antibodies against FHV; there was no significant difference between LA and LB \((P = 0.91)\). The variations of LA and LB between day 0 and day 42 were not significantly different \((P = 0.33 \text{ and } P = 0.67, \text{ respectively})\) or between day 42 and day 400 \((P = 0.18 \text{ and } P = 0.46, \text{ respectively})\). Between day 0 and day 400, there was no significant variation in the titers in group LA \((P = 0.16)\), whereas there was a trend towards an increase in group LB \((P = 0.05)\).

## DISCUSSION

### Serologic response

In the domestic cat, these vaccines are effective and safe when used alone or in combination, after two injections given 2–4 wk apart for the live combined CRP and the FeLV vaccines, and a single injection for the rabies vaccine, followed by annual boosters.13,18,19,22,23,29,40

The presence of anti-FCV, anti-FHV, and anti-FPV antibodies in some of the lions and tigers on day 0 could be explained by natural exposure to the virus, prior to the first vaccination. The animals that were born in the zoo had never been vaccinated. Those that were acquired at 1 yr of age may have been vaccinated before their arrival. The production of antibodies could then have been maintained by repeated exposure to the virus. The repeated clinical examinations did not reveal any symptoms of upper respiratory tract disease or FPV in any of the animals.

The FeLV vaccine did not produce a serologic response in any of the animals in this current study, whether given as a single or double dose. However, because the FeLV ELISA was performed using domestic cat-specific secondary antibodies, it is possible that the test did not cross-react with lion antibodies, thus giving false-negative results. Other studies have demonstrated that another type of vaccine based on subunits and cell membrane antigens induces an immune response in tigers and cheetahs \((Acinonyx jubatus)\) that had received three injections of a single or double dose given via i.m. injection.7,9 A new study using a different antibody detection method, with higher doses administered i.m., should therefore be considered.

The rabies vaccine induced a serologic response in all of the animals in our study from day 42 after 2 injections given 3 wk apart. The titers are considered protective, in accordance with the recommendations of the World Health Organization \((\text{titer } >0.5 \text{ IU/ml})\).41 At day 400, 4 tigers and 2 lions did not meet this minimal titer. On the assumption that a rabies titer of \(>0.5 \text{ IU/ml}\) is desirable in all species, it may be advisable to administer a booster vaccine 1 yr after primary vaccination. By comparing this current study with that of Haigh and Field,21 who successfully tested an inactivated vaccine in double doses in lynx \((Lynx lynx)\) and lions, it does not seem necessary to use a double dose of the vaccine or the i.m. route with Rabigen Mono.

Concerning the vaccination against FCV, the antibody titers varied randomly and the serologic variations were not significant for TA, TB, LA, and LB. The presence of a large number of seropositive animals on day 0 explains these results. These variations could be due to new exposures to the virus or to a vaccine booster effect or, for some of them, to a progressive decrease in antibodies in the absence of antigenic contact. The vaccine could also have been neutralized by circulating antibodies. This observation is comparable to that of Wack et al.,22 who did not observe any variations in the titers of cheetahs that were seropositive prior to vaccination. In a similar study, Spencer and Burroughs36 observed an increase in titers in only 49% of cheetahs that had been seropositive prior to vaccination. The number of seronegative animals on day 0 was not sufficient to statistically assess their serologic response. It is therefore not possible to make conclusions on the efficacy of FCV vaccination in this study.

Despite the presence of numerous seropositive animals on day 0, a significant increase in the antibody titers against FHV was observed between day 0 and day 42 for all of the animals, after two injections 3 wk apart. Therefore, it can be concluded that there was an immune response to
the vaccine with a booster effect or that all of the animals were exposed to the wild virus during the course of the study. However, no signs of FHV infection were detected, and there was no known exposure to stray cats during the course of the vaccine trial. It is therefore probable that the combined CRP vaccine triggered an anamnestic serologic response in all of the tigers and lions in our study. This study shows that it may not be necessary to double the vaccine dose, which confirms the results of the multidose study undertaken by Bush et al. Other studies involving vaccines against FCV and FHV undertaken in exotic cats show that in the majority of cases the antibody titers obtained with inactivated or modified vaccines are short lived; an intensive primary vaccination campaign with boosters at 3 or 6 mo are often recommended.

Concerning the vaccination against FPV, overall the tigers in group A responded quicker than the tigers in group B, with a significant increase in titers in group A between day 0 and day 42, whereas the significant increase of titers in group B was only visible between day 0 and day 400. It can therefore be concluded that there is a significant serologic response to the vaccine after the first or the second injection. However, natural exposure to the wild virus could also be responsible for these results. Because no signs of clinical disease or exposure to stray cats were observed, it is likely that the vaccine induced a serologic response. The percentage of seroconversion or increase in antibody titers was 100% in the tigers in this study. Our study shows that it is unnecessary to double the vaccine dose in tigers, which confirms the study undertaken by Bush et al. On day 400, antibodies were detected in the three individuals that had been seronegative on day 0 and day 42. In a study with this vaccine in the domestic cat, the animals had shown zero antibody titers on day 0 and day 42, followed by significant seroconversion after day 42. The same may have occurred in the tigers in this current study, which were seronegative on day 42 but seropositive on day 400.

The serologic variations observed between day 0 and day 42 were not significant in the lions. The presence of a large number of seropositive animals on day 0 explains these results. These variations could be due to new exposures to the virus, to a vaccine booster effect, or, for some of them, to a progressive decrease in antibodies in the absence of antigenic contact. The vaccine could also have been neutralized by circulating antibodies. This observation is comparable to that of Spencer and Burroughs: only 58% of the cheetahs that were seropositive before vaccination presented with an increase in their antibody levels and only 36% seroconversion was observed in a group in which 81% were seronegative. Similarly, Wack et al. did not find any significant difference between the means of the titers of seropositive cheetahs receiving one injection of a vaccine against FPV. Due to the small population in this study, a study of the seronegative individuals alone could not be performed. The presence of seropositive individuals at day 0 and the small size of the population in this current study prevented definitive conclusions regarding the efficacy of the FPV in the lion. In serologic studies in nondomestic cats, vaccination against FPV is generally considered to be effective and lasting, although some of the studies in young cats and occasionally in adults have been discredited.

Safety of the vaccines

None of the animals in the study presented with any apparent local reactions or pain on examination after vaccination. The wounds observed did not bear any relation to the vaccine injection site. Concerning the possible systemic reactions, the vaccines used did not seem to be the cause in the majority of cases. Only six animals presented with illness during this study. The gastrointestinal disorders observed in three lions could possibly have been related to the FPV vaccine (return to virulence). However, these clinical signs were delayed (between day 34 and day 51), of short duration (1–5 days), and responded rapidly to symptomatic treatment. The stillbirth and neonatal deaths observed in one lioness between day 18 and day 20 could have been a secondary effect of the vaccination against FPV. The lioness had received a double dose of the vaccine at the end of the gestation period. The risk of abortion is well recognized in the domestic cat, and the vaccination of pregnant cats is a contraindication given by the manufacturer. This was therefore a serious adverse event linked to the incorrect and off-label use of the vaccine. Finally, no deleterious effect of the vaccination was observed in the lioness that presented with fever and vomiting on day 0.

All of the vaccination studies against FeLV have demonstrated good tolerance in nondomestic cats. In the cheetah, minimal secondary reactions have been reported: mandibular lymphadenomegaly and mild postvaccination depression. Antirabies vaccination trials using inactivated vaccines have shown very good toler-
ance in the lynx and the lion. Cases of vaccine-induced infections have been observed in wild carnivores after the administration of live attenuated vaccines. Modified live vaccines and an inactivated agent against FHV and FCV have been tested without any deleterious secondary effects in more than 20 species of exotic cats. However, other studies have reported adverse reactions (vaccine-induced infection and anaphylactic reactions) after the use of live modified vaccines. The risks linked to the use of the live attenuated FPV vaccine remain controversial, with the exception of pregnant females and young animals less than 4 wk of age, in which their use remains inadvisable. Live attenuated vaccines have been tested without secondary reactions in more than 25 species of nondomestic cats. However, some deleterious results have been observed in other studies (return of virulence and mortality). Inactivated vaccines have often proved to be safe in nondomestic cats, with the exception of an anaphylactic reaction in a Brazilian jaguar (Panthera onca) and postvaccination myocarditis in a young tiger.

Finally, it should be mentioned that lack of postvaccine viral challenge in this current study does not allow assessment of the protection induced. Cellular immunity was not studied here and should also be taken into account. Moreover, the lack of an unvaccinated control group makes it impossible to rule out the possibility of natural exposure to the viruses. In conclusion, seroconversion was highly suspected after vaccination against rabies, FHV, and FPV (for tigers only). The negative results for FeLV vaccination could be due to the use of a domestic cat–specific serologic technique. The lack of seroconversion observed for FCV and FPV (for lions) could be due to the presence of seropositive animals before vaccination.

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LITERATURE CITED


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