

DURATION OF IMMUNITY FOR FELINE BIOLOGICS

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I. Introduction

A. Overview

Duration of immunity (DOI) for feline biologics is of increasing concern. There is an increased feeling among many scientists and some feline practitioners that we are "over vaccinating" in our effort to provide the best health care possible for the cat.

II. Duration of Immunity - Regulations

A. Historical perspective

Until recently, there was no requirement by Veterinary Biologics (VB) division of APHIS/USDA for a manufacturer of veterinary biologics to show any "duration of immunity" unless the label specifically stated that the vaccine would protect for a specified time such as "one", "two", or "three" years.

B. Annual revaccination

Manufacturers of veterinary biologics have routinely recommended "annual revaccination" for most vaccines without specific scientific information to either support a one year's duration of immunity, or that the vaccine would not protect for more than one year.

C. Rabies vaccines

Rabies vaccines have generally been the only feline biologics that have carried a specific label claim for duration of protection.

D. Current regulations

Recent changes in licensure requirements now include "duration of immunity" as well as potency and safety.

III. Cornell Studies on duration of immunity in a closed colony

A. Cats

1. SPF cat breeding colony established in December, 1990
 - a. Purchased 15 5-month-old kittens
 - 13 females
 - 2 males
 - b. Kittens had been vaccinated twice in October 1990 at approximately 9 and 12 weeks of age
 - c. Vaccine = commercial inactivated FP/FHV/FCV vaccine with an adjuvant
 - d. No vaccines given to cats after arrival at Cornell
 - e. As kittens from this colony became available, 17 additional queens were added to the breeding colony
 - f. Replacements were never vaccinated
 - g. Breeding cats were gang-housed with free contact between vaccinated and non-vaccinated cats.

B. Serological studies

1. Serum samples were obtained from all cats in colony:
 - a. January 1991 (5 months of age, 2 months after last vaccination)
 - b. October of 1993 (3 years after vaccination)
 - c. October 1994 (4 years after vaccination)
 - d. October 1995 (5 years after vaccination)
2. In March 1995, all cats were negative for FeLV antigen, FIV antibodies, feline coronavirus antibodies, and toxoplasma antibodies, and negative on isolation for chlamydia and pathogenic bacteria. All non-vaccinates were negative for FP, FHV, and FCV antibodies.

C. Results

1. **Table 1:** Table 1 lists the virus neutralizing antibody titers of the 15 vaccinated cats and the 17 non-vaccinated contact control cats from January 1991 (2 months after vaccination) until October 1995 (5 years after the last vaccination).
2. **FPV:** All 13 vaccinated cats tested had anti-FPV VN antibody titers of at least 1:5,000 two months after vaccination, and titers of at least 1:500 throughout the 5-year study.
3. **FHV:** All 13 vaccinated cats tested had anti-FHV-1 VN antibody titers of 1:2 to 1:96 two months after vaccination, with a mean antibody titer of 1:18. Titers remained low throughout the study, with mean titers gradually dropping to 1:4 among the 13 cats left on study after 5 years. Negative titers (<1:2) occurred in one cat at 3 years, 4 cats at 4 years, and 6 cats at 5 years. Four cats that had a negative titer at one sampling had a positive antibody titer on a subsequent year's sampling.
4. **FCV:** All 13 vaccinated cats tested had anti-FCV antibody titers of 1:24 to >1:256 2 months after vaccination (mean titer 1:145). All cats had positive titers at 3 and 4 years after vaccination. Twelve of 13 cats had VN titers of 1:3 to >1:256 5 years after vaccination (mean titer 1:45)

D. Conclusions

1. **FPV:** Two doses of inactivated, adjuvanted FPV vaccine produced solid and essentially permanent protection. A VN titer against FPV of 1:8 is considered to provide solid protection.
2. **FHV:** The vaccine tested produced average VN antibody titers against FHV-1 with titers of 1:2 to 1:96. These titers are consistent with those reported for other vaccines, including MLV FHV vaccines. At 3 years after vaccination, 14 of 15 cats had positive VN titers (mean titer 1:12). The negative cat at 3 years had a positive titer at 4 years. Antibody titers are not a good measure of immunity to FHV. It is generally considered that cell-mediated immunity is the

primary mechanism of immunity to this herpesvirus infection, and that any detectable titer is significant. In other studies, vaccinated cats may have a negative VN titer after vaccination, but be immune and have a rapid anamnestic response if exposed to virulent virus. It would appear from the results of this study that there is little difference in the immunity to FHV between 2 months and 3 years after vaccination.

4. **FCV:** Good, protective VN antibody titers against FCV were maintained for at least 4 years, with little difference in titers between 3 and 4 years.

IV. "Cats Only Veterinary Clinic" study

A. The study

1. Cornell Feline Health Center has an on-going study to determine antibody titers against FPV, FHV-1, and FCV in cats presented to a multiperson feline practice (*Cats Only Veterinary Clinic*, Columbus, Ohio)
2. Veterinarians in the clinic were concerned that they were over vaccinating. They were seeing what they believed to be excess adverse vaccination reactions following routine annual vaccination.
3. A collaborative study was established between "Cats Only" and the "Cornell Feline Health Center"
4. Cats presented for annual physical exams are routinely sampled, with serum and detailed vaccination history sent to Cornell. Multiple yearly samples from the same cat are obtained where possible.
5. Unless there is an unknown vaccination history, or the cats are from a "high risk" situation, cats are not routinely vaccinated for FPV/FHV/FCV.

B. Serology

1. Virus neutralizing (VN) antibody titers against FPV, FHV-1, and FCV are determined on serum samples.
2. Results are periodically reported back to Cats Only, but any negative results are immediately reported so that these cats can be revaccinated.

C. Results

VN antibody titers against FPV, FHV-1, and FCV are summarized in Table 2 for the 347 cats that were tested for the first time, the 36 cats that were tested twice, and 11 cats that have been tested 3 times. All but 7 cats had positive and protective VN titers against FPV, and these 7 cats had no or unknown vaccination histories. Similar results were determined for FCV, with only 4 cats with negative titers in the first sample group. For FHV, 63 of 347 had negative VN antibody titers. These results will be discussed.

| CAT No. | FPV 1/91 | | FPV 10/93 | | FPV 10/94 | | FPV 10/95 | | FHV 1/91 | | FHV 10/93 | | FHV 10/94 | | FHV 10/95 | | FCV 1/91 | | FCV 10/93 | | FCV 10/94 | | FCV 10/95 | |
|-----------------|----------|---------|-----------|-------|-----------|-------|-----------|-------|----------|---------|-----------|-------|-----------|-------|-----------|-------|----------|---------|-----------|-------|-----------|-------|-----------|-------|
| | 1/6 YPV | 1/6 YPV | 3 YPV | 3 YPV | 4 YPV | 4 YPV | 5 YPV | 5 YPV | 1/6 YPV | 1/6 YPV | 3 YPV | 3 YPV | 4 YPV | 4 YPV | 5 YPV | 5 YPV | 1/6 YPV | 1/6 YPV | 3 YPV | 3 YPV | 4 YPV | 4 YPV | 5 YPV | 5 YPV |
| Controls | | | | | | | | | | | | | | | | | | | | | | | | |
| A002 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | 3 |
| A012 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A013 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A014 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | 2 | <2 | <2 | <2 | <2 | <2 |
| A021 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A022 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A031 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | 2 |
| A032 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A061 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A082 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A101 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A102 | -- | -- | <10 | <10 | <10 | <10 | -- | -- | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | -- |
| A171 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A242 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A401 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A402 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| A481 | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |
| Mean | -- | -- | <10 | <10 | <10 | <10 | <10 | <10 | -- | <2 | <2 | <2 | <2 | <2 | <2 | <2 | <2 | -- | <2 | <2 | <2 | <2 | <2 | <2 |

-- = Not Tested; YPV = Years post vaccination

TABLE 2: Virus neutralizing antibody titers against feline parvovirus, feline herpesvirus-1, and feline calicivirus in cats presented to a private feline practice for routine annual vaccination.

| Sample # | # Cats Tested | Virus Neutralizing Antibody Titer | | | | | |
|-----------------------------|---------------|-----------------------------------|--------|-----------|--------------|---------|--|
| | | <10 | 10-100 | 101-1,000 | 1,001-10,000 | >10,000 | |
| Feline Parvovirus | | | | | | | |
| 1 | 347 | 7 | 8 | 36 | 93 | 201 | |
| 2 | 36 | 0 | 3 | 3 | 10 | 20 | |
| 3 | 11 | 0 | 0 | 1 | 3 | 7 | |
| Feline Herpesvirus-1 | | | | | | | |
| | | <2 | 2-10 | 11-50 | 51-100 | >100 | |
| 1 | 347 | 63 | 103 | 116 | 32 | 28 | |
| 2 | 36 | 5 | 5 | 18 | 4 | 4 | |
| 3 | 11 | 0 | 3 | 3 | 1 | 4 | |
| Feline Calicivirus | | | | | | | |
| | | <2 | 2-10 | 11-100 | 101-1,000 | >1,000 | |
| 1 | 347 | 4 | 22 | 82 | 133 | 105 | |
| 2 | 36 | 1 | 3 | 15 | 13 | 4 | |
| 3 | 11 | 0 | 1 | 2 | 7 | 1 | |