Comparison of anamnestic responses to rabies vaccination in dogs and cats with current and out-of-date vaccination status

Michael C. Moore, DVM, MPH; Rolan D. Davis, MS; Qing Kang, PhD; Christopher I. Vahl, PhD; Ryan M. Wallace, DVM, MPH; Cathleen A. Hanlon, VMD, PhD; Derek A. Mosier, DVM, PhD

Objective—To compare anamnestic antibody responses of dogs and cats with current versus out-of-date vaccination status.

Design—Cross-sectional study.

Animals—74 dogs and 33 cats.

Procedures—Serum samples were obtained from dogs and cats that had been exposed to rabies and brought to a veterinarian for proactive serologic monitoring or that had been brought to a veterinarian for booster rabies vaccination. Blood samples were collected on the day of initial evaluation (day 0) and then again 5 to 15 days later. On day 0, a rabies vaccine was administered according to label recommendations. Paired serum samples were analyzed for antirabies antibodies by means of a rapid fluorescent focus inhibition test.

Results—All animals had an antirabies antibody titer ≥ 0.5 IU/mL 5 to 15 days after booster vaccination. Dogs with an out-of-date vaccination status had a higher median increase in titer, higher median fold increase in titer, and higher median titer following booster vaccination, compared with dogs with current vaccination status. Most (26/33) cats, regardless of rabies vaccination status, had a titer ≥ 12 IU/mL 5 to 15 days after booster vaccination.

Conclusions and Clinical Relevance—Results indicated that dogs with out-of-date vaccination status were not inferior in their antibody response following booster rabies vaccination, compared with dogs with current vaccination status. Findings supported immediate booster vaccination followed by observation for 45 days of dogs and cats with an out-of-date vaccination status that are exposed to rabies, as is the current practice for dogs and cats with current vaccination status. (*J Am Vet Med Assoc* 2015;246:205–211)

Each year in the United States, approximately 6,000 cases of rabies are documented in animals, primarily in the major wildlife reservoir species (ie, raccoons, bats, skunks, and foxes). These confirmed cases are invariably associated with 1 or more human and animal exposures to rabies. In addition, many domestic animals come into contact with sick wildlife or other animals that cannot be captured for rabies diagnostic testing and, depending on the geographic location and species of animal involved, may be considered potentially exposed to rabies. As a result, thousands of dogs and cats are known to be exposed or are potentially exposed to rabies each year in the United States.

From the Veterinary Diagnostic Laboratory (Moore, Davis, Hanlon) and the Department of Diagnostic Medicine and Pathobiology (Mosier), College of Veterinary Medicine, and the Department of Statistics, College of Arts and Sciences (Vahl), Kansas State University, Manhattan, KS 66506; Statistical Intelligence Group LLC, 117 Firethorn Ln, Manhattan, KS 66503 (Kang); and the CDC, 1600 Clifton Rd, Atlanta, GA 30333 (Wallace, Hanlon).

This manuscript represents a portion of a thesis submitted by Dr. Moore to the Kansas State University Graduate School as partial fulfillment of the requirements for a Master of Public Health degree.

Presented to the Compendium of Animal Rabies Prevention and Control Committee of the National Association of State Public Health Veterinarians, Nashville, Tenn, June 2014.

The authors thank Drs. Sue Nelson, John Teeter, and Don Dinges for assistance in procuring samples.

Address correspondence to Dr. Moore (mcmoore@vet.k-state.edu).

Regulations have been developed to minimize the public health risks that dogs and cats exposed or potentially exposed to rabies and potentially incubating the virus may pose. These regulations vary, depending on locality, but most public health officials refer to or rely on the Compendium of Animal Rabies Prevention and Control[1] for guidance in these situations.

According to the current version of the compendium, dogs and cats with current rabies vaccination status that have been exposed to an animal confirmed or suspected to be rabid should immediately receive a rabies booster vaccination and be observed for 45 days, most often, as allowed by jurisdictional authorities, under the owner's supervision with no contact restrictions. The recommendation for dogs and cats that have never been vaccinated against rabies and that have been exposed to a rabid animal is euthanasia or quarantine for 6 months in a specialized facility.

In contrast, the compendium guidelines are less clear when it comes to recommendations for dogs and cats overdue for a booster vaccination (ie, dogs and cats with out-of-date rabies vaccination status), suggesting that these animals be evaluated on a case-by-case basis that takes into account the severity of the exposure, time since the last rabies vaccination, number of rabies vaccinations received previously, current health status of the animal, and local rabies epidemiology.[1] Unfortunately, this recommendation for a case-by-case risk as-

sessment coupled with concerns for public safety, a fear of liability, and the lack of published clinical data regarding response to rabies vaccination in dogs and cats with an out-of-date rabies vaccination status commonly leads to conservative handling of these animals. Most often, this means that public health officials consider these animals to be unvaccinated, resulting in either euthanasia or a 6-month quarantine.

The present study was designed to provide greater insight into the appropriate handling of dogs and cats with out-of-date rabies vaccination status that have been exposed to rabid animals. Specifically, the purpose of the study reported here was to compare anamnestic antibody responses of dogs and cats with current versus out-of-date rabies vaccination status.

Materials and Methods

Sample acquisition—The first phase of the study involved serum samples from 10 dogs and 2 cats, from 8 states, that had been exposed to rabies and for which the attending veterinarian or owner had contacted the Rabies Diagnostic Laboratory at Kansas State University between March 2010 and June 2012 for help in assessing the immune state of the animal. The remainder of the study involved serum samples from an additional 64 dogs and 31 cats that had been exposed to rabies and brought to a veterinarian for proactive serologic monitoring or that had not been exposed to rabies and had been brought to a veterinarian for booster rabies vaccination. In total, serum samples from 74 dogs and 33 cats from 13 states collected over a period of 3.75 years were included. The study protocol was approved by the Kansas State University Institutional Animal Care and Use Committee (protocol No. 3193).

For each animal included in the study, a 2-mL serum sample was obtained at the time of initial evaluation (day 0) and then again 5 to 15 days later. On day 0, a rabies vaccine of the attending veterinarian's choice was administered to the animal according to label recommendations. Serum samples were shipped fresh to the Rabies Diagnostic Laboratory and analyzed for antirabies antibody titer by means of a rapid fluorescent focus inhibition test.

Classification of rabies vaccination status—All dogs and cats included in the study were classified as having a current or out-of-date rabies vaccination status. Rabies vaccination status was classified as current if the animal had received initial rabies vaccination and the initial (ie, day 0) serum sample was obtained < 1 year after the initial vaccination or if the animal had received both an initial rabies vaccination and a rabies booster vaccination and the initial (day 0) serum sample was obtained < 3 years after the last vaccination. Otherwise, rabies vaccination status was classified as out of date.

A cutoff of 3 years since the last vaccination was used regardless of whether the last vaccine administered had been licensed for a 1-year or 3-year duration, because the antigenic mass, carrier, adjuvant, and other characteristics of 1-year and 3-year vaccines from 2 companies[2,a] were reportedly identical. One animal that received a 1-year vaccine was excluded from the data analysis because the company[b] that manufactured the vaccine would neither confirm nor deny that their 1-year and 3-year formulations were identical.

Rapid fluorescent focus inhibition test—The rapid fluorescent focus inhibition test,[3] a serum neutralization test, was used to determine the titer of rabies neutralizing antibodies in all serum samples. Briefly, rabies virus was mixed with serial dilutions of each serum sample, and the resulting mixture was incubated at 37°C for 90 minutes. Baby hamster kidney cells suspended in Eagle minimum essential medium with 10% fetal bovine serum were then added, and the mixture was incubated for 20 to 24 hours at 37°C. Following fixation with 80% acetone, a conjugate of antirabies antibody labeled with fluorescein isothiocyanate was added to the cells. After washing, cells were counted by means of fluorescent microscopy to determine the ratio of infected to noninfected cells at each dilution. Results were compared with results for a standard control sample containing a known neutralizing antibody concentration to determine the titer for each test sample.

End point dilution was not used to determine the specific antibody titer for samples that resulted in complete neutralization of the virus at the highest serum dilution used. However, the maximum possible titer varied between test runs depending on the control sample's ability to neutralize the challenge virus. Standard operating procedures for the test method defined a priori an acceptable range of titers for the control sample, with testing repeated if the titer for the control sample was outside the acceptable range. Because the lowest titer for control samples used in the present study was 12 IU/mL, for calculation purposes, we reported results for test samples > 12 IU/mL as 12 IU/mL. In the statistical analysis, all titers reported as ≥ 12 IU/mL were treated as right censored. For comparison, a rabies neutralizing antibody titer ≥ 0.5 IU/mL is considered by the World Health Organization to be an adequate vaccine response for dogs and cats traveling to rabies-free areas.[4]

Data analysis—Rabies neutralizing antibody titers following booster vaccination (ie, days 5 to 15) were compared between dogs with current versus out-of-date vaccination statuses by modeling the proportions of animals with titers exceeding various given values (sometimes referred to as a reverse cumulative distribution). This approach was selected to account for the right censoring of titers for some animals. A proportional hazards model[c] was used to compare distributions of titers between the 2 groups (current vaccination status versus out-of-date vaccination status), with current vaccination status as the reference. In essence, the proportional hazards ratio represented the comparative ability of the 2 groups to reach a particular titer after booster vaccination on day 0. If the ratio was equal to 1, the 2 groups were considered identical. If the ratio was > 1, then the response to booster vaccination in animals with an out-of-date vaccination status was considered to be not as robust as the response in animals with a current vaccination status. Conversely, if the ratio was < 1, the response to booster vaccination in animals with an out-of-date vaccination status was considered superior to the response in animals with a

current vaccination status. For purposes of the present study, we assumed the response to booster vaccination in animals with an out-of-date vaccination status was not clinically worse than the response in animals with a current vaccination status if the hazard ratio was < 1.25. On the basis of an analysis of data from Mansfield et al,[5] this choice of noninferiority margin was determined to be conservative. Formally, in the hypothesis test of noninferiority, the null hypothesis was that the ratio was ≥ 1.25 (ie, out-of-date vaccination status was inferior to current vaccination status), and the alternative hypothesis was that the ratio was < 1.25 (ie, out-of-date vaccination status was noninferior to current vaccination status). Diagnostic graphs indicated the proportional hazard model was appropriate for these data.

Results

Rabies neutralizing antibody titers for the 10 dogs and 2 cats in the first phase of the study were summarized (**Table 1**). For all 12 animals, antibody titers 5 to 15 days after booster vaccination were > 0.5 IU/

Table 1—Rabies neutralizing antibody titers immediately prior to (baseline) and 5 to 15 days after booster vaccination in 10 dogs and 2 cats that had been exposed to an animal confirmed or suspected to be rabid.

Species	Exposure description	> 1 vaccine dose previously	Label duration of last vaccine (y)	Time since last vaccination (mo)	Rabies vaccination status	Baseline titer (IU/mL)	Titer after booster vaccination (IU/mL)
Dog*	Contact with skunk	Yes	3	39.0	OOD	9.7	12
Dog	Exposed to rabid skunk	Yes	UK	9.0	C	0	12
Dog*	Raccoon bite	Yes	3	41.4	OOD	12	12
Dog*	Raccoon bite	Yes	1	18.1	C	0.7	3.4
Dog*	Exposed to rabid skunk	No	1	36.0	OOD	0.6	12
Dog	Exposed to rabid skunk	Yes	3	15.6	C	12	12
Dog*	Exposed to rabid skunk	No	1	15.6	OOD	0.2	12
Dog*	Exposed to rabid skunk	No	1	15.4	OOD	0.6	12
Dog*	Raccoon bite	Yes	1	30.5	C	1.8	12
Dog	Exposed to rabid skunk	Yes	3	10.7	C	3.1	12
Cat*	Raccoon bite	Yes	3	38.7	OOD	0.3	12
Cat*	Exposed to bat	Yes	3	44.9	OOD	12	12

*Quarantined for 6 months after rabies exposure; no animals developed signs of rabies-associated disease during quarantine, and all 12 animals survived.

C = Current. OOD = Out of date. UK = Unknown.

Rabies vaccination status was classified as current if the animal had received an initial rabies vaccination and the initial serum sample was obtained < 1 year after the initial vaccination or if the animal had received both an initial rabies vaccination and a rabies booster vaccination 1 year later and the baseline serum sample was obtained < 3 years after the last vaccination. Otherwise, rabies vaccination status was classified as out of date. A cutoff of 3 years since the last vaccination was used regardless of whether the last vaccine administered had been licensed for a 1-year or 3-year duration, because formulations of the 1-year and 3-year vaccines were confirmed by the manufacturer to be identical.

Table 2—Rabies neutralizing antibody titers immediately before (baseline) and 5 to 15 days after booster vaccination in 74 dogs and 33 cats classified as having a current or out-of-date rabies vaccination status.

Species and vaccination status	Baseline titer (IU/mL)*	Titer after booster vaccination (IU/mL)*	Median increase (IU/mL)	Median fold rise
Dog				
Current (n = 55)	2.6 (0–12)	11.1 (0.5–12)	3.1	0
Out of date (n = 19)	2.0 (0–12)	12.0 (0.5–12)	8.1	2
Cat				
Current (n = 7)	2.4 (0.1–12)	12.0 (2.6–12)	9.4	2
Out of date (n = 26)	6.3 (0.3–12)	12.0 (2.9–12)	2.4	0

*Data are given as median (range).
See Table 1 for remainder of key.

Table 3—Number (percentage) of dogs and cats in Table 2 with rabies neutralizing antibody titers 5 to 15 days after booster vaccination that equaled or exceeded various benchmarks above 0.5 IU/mL.

	Titer (IU/mL)					
Species and vaccination status	0.5	1.0	2.0	4.0	8.0	12.0
Dog						
Current (n = 55)	55 (100)	53 (96)	50 (90)	40 (72)	34 (61)	26 (47)
Out of date (n = 19)	19 (100)	18 (94)	18 (94)	16 (84)	13 (68)	13 (68)
Cat						
Current (n = 7)	7 (100)	7 (100)	7 (100)	6 (85)	6 (85)	6 (85)
Out of date (n = 26)	26 (100)	26 (100)	26 (100)	23 (88)	23 (88)	21 (80)

Data are given as number (%).
See Table 1 for remainder of key.

mL. Five of the animals were classified as having a current vaccination status, and 7 were classified as having an out-of-date vaccination status. All 7 animals with an out-of-date vaccination status and 2 animals with a current vaccination status were quarantined for 6 months, during which time no rabies-associated clinical disease was reported. All 12 animals survived following rabies exposure. The 2 animals with current vaccination status that were quarantined had been exposed > 1 year (but < 3 years) after receiving a rabies vaccine labeled for 1-year duration. However, the manufacturer confirmed that the 1-year and 3-year formulations of this product were identical; therefore, for purposes of the present study, both animals were classified as having a current vaccination status.

Table 4—Rabies neutralizing antibody titers immediately before (baseline) and 5 to 8 days after booster vaccination in 14 dogs and 2 cats with a titer < 0.5 IU/mL prior to booster vaccination.

Species and vaccination status	Baseline titer (IU/mL)	Time between samples (d)	Titer after booster vaccination (IU/mL)
Dog			
Out of date	0.2	8	12
	0.2	7	12
	0	5	12
	0.4	7	2.4
	0	8	0.5
Current	0	7	12
	0.4	7	4.4
	0.3	5	11.1
	0.4	7	0.5
	0.1	7	1.3
	0.1	7	6.1
	0	7	2
	0.1	5	4
	0.3	6	0.5
Cat			
Out of date	0.3	5	12
Current	0.1	6	12

Median titer after booster vaccination was 12 IU/mL for dogs with an out-of-date vaccination status and 4 IU/mL for dogs with a current vaccination status.

See Table 2 for key.

Rabies neutralizing antibody titers before (day 0) and after (day 5 to 15) booster vaccination for all 74 dogs and 33 cats included in the study were summarized, along with median increase in titer and median fold increase (**Table 2**). Dogs with out-of-date vaccination status had a higher median increase in titer, higher median fold increase in titer, and higher median titer following booster vaccination, compared with dogs with current vaccination status. However, statistical analyses were not performed on these parameters.

The percentages of dogs and cats in each vaccine category with titers that equaled or exceeded various benchmarks above 0.5 IU/mL were summarized (**Table 3**). All animals in the study had a titer ≥ 0.5 IU/mL 5 to 15 days after booster vaccination. This included the 14 dogs (9 with current vaccination status and 5 with out-of-date vaccination status) and 2 cats (1 with current vaccination status and 1 with out-of-date vaccination status) that had titers < 0.5 IU/mL prior to booster vaccination (day 0; **Table 4**). Median increase in titer for dogs (**Table 5**) and cats (**Table 6**) with an out-of-date vaccination status was higher for those that had previously received only a single dose of vaccine, compared with those that had previously received ≥ 2 doses of vaccine. Again, however, no statistical analyses were performed on this parameter.

Reverse cumulative distributions of titers 5 to 15 days after booster vaccination were calculated for dogs with current vaccination status and dogs with out-of-date vaccination status (**Figure 1**). The hypothesis test for noninferiority was significant ($P = 0.029$), with out-of-date dogs shown to be noninferior to current dogs, and the proportional hazards ratio (with current vaccination status as the reference) was 0.53 (95% confidence interval, 0.20 to 1.12). Because the upper limit of the 95% confidence interval was < 1.25, the response to booster vaccination in dogs with an out-of-date vaccination status was considered to be noninferior to the response in dogs with a current vaccination status.

Table 5—Rabies neutralizing antibody titers immediately before (baseline) and 5 to 15 days after booster vaccination for 15 dogs with an out-of-date vaccination status classified on the basis of number of rabies vaccinations received previously.

No. of vaccine doses received previously	Baseline titer (IU/mL)	Time between samples (d)	Titer after booster vaccination (IU/mL)	Time overdue for vaccination (mo)	Increase in titer (IU/mL)
≥ 2	0.6	6	2.8	0.2	2.2
	0.4	7	2.4	0.3	2
	9.7	15	12	3	2.3
	4	7	5.9	4.8	1.9
	12	6	12	7.5	0
	3.9	7	12	10.6	8.1
	2.9	7	7.8	14.9	4.9
	0	8	0.5	19.7	0.5
	2	7	12	22.8	10
1	3.4	7	12	0.3	8.6
	0.6	10	12	3.4	11.4
	0.2	8	12	3.6	11.8
	0	5	12	5.9	12
	0.6	7	12	24	11.4
	0.2	7	12	36.1	11.8

Median increase in titer was 2.2 IU/mL for dogs that had previously received ≥ 2 doses of vaccine and was 11.6 IU/mL for dogs that had previously received only a single dose of vaccine.

Table 6—Rabies neutralizing antibody titers immediately before (baseline) and 5 to 15 days after booster vaccination for 24 cats with an out-of-date vaccination status classified on the basis of number of rabies vaccinations received previously.

No. of vaccine doses received previously	Baseline titer (IU/mL)	Time between samples (d)	Titer after booster vaccination (IU/mL)	Time overdue for vaccination (mo)	Increase in titer (IU/mL)
≥ 2	12	8	12	0.1	0
	6.1	7	11.3	0.1	5.2
	12	8	12	0.1	0
	3.4	7	12	0.2	8.6
	12	7	12	0.2	0
	5.4	6	12	0.9	6.6
	6.4	7	9	1.1	2.6
	12	7	12	2.3	0
	12	7	12	2.5	0
	0.3	5	12	2.7	11.7
	3.4	7	3.7	2.9	0.3
	12	7	12	2.9	0
	8.9	7	12	3.2	3.1
	12	7	12	3.7	0
	12	7	12	5.6	0
	2.5	7	12	5.6	9.5
	2.4	7	12	8.4	9.6
	12	8	12	8.9	0
	2.4	6	12	15.9	9.6
	3	6	3.3	34.6	0.3
	0.6	7	2.9	46.1	2.3
1	0.6	5	12	4.9	11.4
	9.6	6	12	21.2	2.4
	2.7	6	12	38.5	9.3

Median increase in titer was 0.3 IU/mL for cats that had previously received ≥ 2 doses of vaccine and was 9.3 IU/mL for cats that had previously received only a single dose of vaccine.

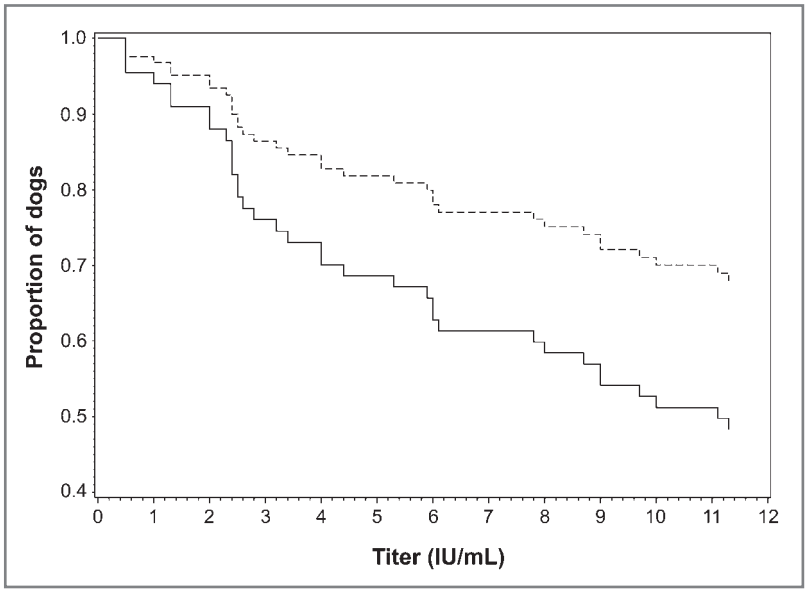

Figure 1—Reverse cumulative distributions of rabies neutralizing antibody titers 5 to 15 days after booster vaccination in dogs with a current (n = 55; solid line) or out-of-date (19; dashed line) rabies vaccination status. The reverse cumulative proportion represents, for any given titer, the proportion of dogs with a titer equal to or greater than that titer. The hypothesis test for noninferiority was significant (P = 0.029), with out-of-date dogs shown to be noninferior to current dogs.

Because of the small number of cats in the study and the fact that most cats, regardless of whether they had a current (6/7) or out-of-date (21/26) vaccination status, had a titer ≥ 12 IU/mL 5 to 15 days after booster vaccination, proportional hazards analysis could not be used to analyze the response to booster vaccination in cats with current versus out-of-date vaccination status.

Discussion

Results of the present study indicated that the anamnestic responses of dogs and cats with an out-of-date rabies vaccination status were similar to the responses in animals with a current rabies vaccination status. Specifically, titers 5 to 15 days after booster vaccination in dogs with an out-of-date vaccination status were shown to be noninferior to titers in dogs with a current vaccination status. Also, dogs with an out-of-date vaccination status had a higher median increase in titer, higher median fold increase in titer, and higher median titer following booster vaccination, compared with dogs with current vaccination status; however, statistical analyses were not performed to compare these parameters between groups.

The noninferiority margin of 1.25 used in the present study was selected because it has commonly been used in other studies as a conservative margin for hazard ratio analyses. On the basis of an analysis of results reported by Mansfield et al[5] for dogs and cats vaccinated with 3 rabies vaccines, we determined that a margin of 1.25 corresponded to a difference in titer between animals with an out-of-date vaccination status and naïve

animals that was at least 88% of the difference in titer between animals with current vaccination status and naïve animals. Ng[6] recommends that the noninferiority margin preserve at least 80% of the advantage the active treatment holds over placebo. Therefore, we believe that the noninferiority margin of 1.25 used in the present study was conservative.

In the present study, we used 3 methods to compare anamnestic responses to rabies vaccination in dogs and cats with current versus out-of-date vaccination status: fold rise in titer, absolute increase in titer, and absolute titer following booster vaccination. Evaluating the fold rise in titer gives an advantage to animals with a low starting titer. Therefore, because many animals in the present study with an out-of-date vaccination status had lower starting titers, we were not surprised that they had a higher fold rise in titer, compared with animals with a current vaccination status.

Although absolute increase in titer following booster vaccination provides some information on the anamnestic response to vaccination, it may not represent a true measure of protection. Assuming that neutralizing antibody titer is a measure of protection,[7,8] then a rabies neutralizing antibody titer of 5.5 IU/mL should afford better protection than a titer of 0.5 IU/mL. However, when evaluating absolute increase in titer, an increase from 0.1 to 0.5 IU/mL is the same as an increase from 5.1 to 5.5 IU/mL.

In contrast to fold rise or absolute increase in titer, absolute titer following booster vaccination should provide a good indication of the level of protection achieved. In the present study, we found that the response for dogs with an out-of-date vaccination status was noninferior to the response for dogs with a current vaccination status ($P = 0.029$). Unfortunately, we could not perform the same analyses for cats in the present study because of the low number of cats enrolled and the fact that most cats, regardless of whether they had a current or out-of-date vaccination status, achieved the maximum titer (≥ 12 IU/mL) after booster vaccination. Given these high titers, even if a difference had been found between groups, it likely would not have been clinically meaningful.

Results of the present study may help clarify recommendations in the Compendium of Animal Rabies Prevention and Control[1] for postexposure management of dogs and cats overdue for a booster vaccination that are exposed to an animal confirmed or suspected to be rabid. Currently, the guidelines recommend that such animals be evaluated on a case-by-case basis on the basis of the following 5 criteria: severity of the exposure, time since the last rabies vaccination, number of rabies vaccinations received previously, current health status of the animal, and local rabies epidemiology.

Importantly, the guidelines do not recommend altering postexposure management for dogs and cats with a current vaccination status on the basis of severity of the exposure. Considering that dogs and cats in the present study responded to rabies booster vaccination in a similar manner regardless of whether they had a current or out-of-date vaccination status, we believe that postexposure management should be the same for dogs and cats with current versus out-of-date vaccination status, regardless of the severity of exposure.

With respect to time since the last rabies vaccination, we did not identify a difference in anamnestic response between animals with current versus out-of-date vaccination status. In fact, dogs with an out-of-date vaccination status generally had higher responses than did dogs with a current vaccination status.

Similarly, with respect to the number of rabies vaccinations received previously, we did not find a substantial difference in anamnestic responses between dogs and cats that had previously received only a single dose of vaccine and those that had received ≥ 2 doses previously. However, age could have been a confounding factor, given that animals vaccinated only once had a median age of 3 years, whereas animals vaccinated multiple times had a median age of 6 years, and immunosenescence in dogs and cats is well documented.[9]

We did not evaluate the effect of health status on anamnestic responses in the present study, and all animals were generally healthy. However, we recommend that, regardless of vaccination status, public health officers should be cautious when managing immunocompromised dogs and cats that have been exposed to rabid animals.

Finally, in suggesting that public health officials take local rabies epidemiology into consideration in the postexposure management of dogs and cats with an out-of-date vaccination status that have been exposed to an animal suspected to be rabid, the compendium acknowledges that although rabies is endemic in the United States, the incidence varies widely from one location to the next. Thus, without confirmatory testing, the risk that a dog bitten by a wild raccoon has truly been exposed to rabies is much lower in, for example, Illinois than in Alabama. Nevertheless, given that the response to rabies booster vaccination in the present study was similar regardless of rabies vaccination status, we believe that postexposure management should be the same.

In conclusion, results of the present study indicated that the anamnestic response to rabies booster vaccination in dogs and cats with an out-of-date vaccination status is similar to the response for dogs and cat with a current vaccination status. Thus, we believe that postexposure management of any previously vaccinated dog or cat exposed to a confirmed or suspected rabid animal should be the same, regardless of vaccination status. Specifically, we believe that appropriate postexposure management for dogs and cats with an out-of-date vaccination status is immediate booster vaccination followed by observation for 45 days, rather than euthanasia or quarantine for 6 months. If additional reassurance is needed, titers could be measured prior to and again 5 to 7 days after booster vaccination to determine whether an anamnestic response has occurred.

a. Rainforth R, Merck, White House Station, NJ: Personal communication, 2014.
b. Menardi R, Merial, Duluth, Ga: Personal communication, 2014.
c. Proc PHREG, SAS/STAT, version 9.3, SAS Institute Inc, Cary, NC.

References

1. Brown CM, Conti L, Ettestad P, et al. Compendium of animal rabies prevention and control, 2011. *J Am Vet Med Assoc* 2011;239:609–617.

2. Lau E. States consider controlling rabies vaccination intervals (2011). Veterinary Information Network. Available at: news.vin.com/VINNews.aspx?articleId=19501. Accessed Apr 23, 2014.
3. Smith JS, Yager PA, Baer GM. A rapid reproducible test for determining rabies neutralizing antibody. *Bull World Health Organ* 1973;48:535–541.
4. World Organisation for Animal Health. Chapter 2.1.13. Rabies. In: *OIE terrestrial manual*. Paris: World Organisation for Animal Health, 2013;1–28. Available at: www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.13_RABIES.pdf. Accessed Jun 1, 2014.
5. Mansfield KL, Burr PD, Snodgrass R, et al. Factors affecting the serological response of dogs and cats to rabies vaccination. *Vet Rec* 2004;154:423–426.
6. Ng TH. Non-inferiority hypotheses and choice of non-inferiority margin. *Stat Med* 2008;27:5392–5406.
7. Aubert MF. Practical significance of rabies antibodies in cats and dogs. *Rev Sci Tech* 1992;11:735–760.
8. Hooper DC, Morimoto K, Bette M, et al. Collaboration of antibody and inflammation in clearance of rabies virus from the central nervous system. *J Virol* 1998;72:3711–3719.
9. Day MJ. Ageing, immunosenescence and inflammageing in the dog and cat. *J Comp Pathol* 2010;142:S60–S69.

From this month's *AJVR*

Associations between early radiographic and computed tomographic measures and canine hip joint osteoarthritis at maturity

Anemone A. Andronescu et al

Objective—To evaluate associations of measures assessed by radiography, 2-D CT, and 3-D CT of the hip joints of immature dogs with osteoarthritis in the same joints at maturity.

Animals—46 hound-type dogs from a colony predisposed to osteoarthritis.

Procedures—Images of hip joints (1/dog) were obtained at 16, 32, and 104 weeks of age. Radiographic measures included Norberg angle, distraction index, and osteoarthritis score. Two-dimensional CT measures included acetabular index; percentage of femoral head coverage; and center edge, horizontal toit externe, acetabular anteversion, and ventral, dorsal, and horizontal acetabular sector angles. Three-dimensional CT measures were femoral head and neck volume, femoral neck angle, and femoral head and neck radius. Differences among measures at 16 and 32 weeks in dogs with different osteoarthritis scores at later time points, relationships among variables at each time point, and relationships of single and combined measures with the presence of osteoarthritis at 104 weeks were evaluated.

Results—The 16- and 32-week distraction index, center edge angle, dorsal acetabular sector angle, horizontal acetabular sector angle, percentage of femoral head coverage, acetabular index, and Norberg angle and the 32-week femoral neck angle varied significantly with osteoarthritis severity at 104 weeks. Presence of osteoarthritis in mature dogs was most strongly associated with 16-week combined measures of distraction index and center edge angle and 32-week combined measures of dorsal acetabular sector angle and Norberg angle.

Conclusions and Clinical Relevance—Changes in hip joint morphology associated with radiographic signs of osteoarthritis were detectable as early as 16 weeks of age and varied with osteoarthritis severity in adult dogs. The use of combined hip joint measures may improve early identification of dogs predisposed to hip joint osteoarthritis. (*Am J Vet Res* 2015;76:19–27)

January 2015

See the midmonth issues of *JAVMA* for the expanded table of contents for the *AJVR* or log on to avmajournals.avma.org for access to all the abstracts.