Postexposure rabies prophylaxis protocol for domestic animals and epidemiologic characteristics of rabies vaccination failures in Texas: 1995–1999

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Objective—To determine whether postexposure rabies prophylaxis (PEP) in domestic animals, as mandated by the state of Texas, has continued to be effective and to evaluate PEP and preexposure rabies vaccination failures from 1995 through 1999.

Design—Retrospective study.

Animals—830 unvaccinated domestic animals (621 dogs, 78 horses, 71 cats, and 60 cattle) that received PEP and 4 animals (3 dogs and 1 horse) that had preexposure rabies vaccination failure.

Procedure—Zoonotic incident case reports from 1995 through 1999 were reviewed for information regarding unvaccinated domestic animals that received PEP according to state protocol after exposure to a rabid animal; reports were also reviewed for information regarding preexposure rabies vaccination failures. The PEP recommendations were to immediately vaccinate the animal against rabies, isolate the animal for 90 days, and administer booster vaccinations during the third and eighth weeks of the isolation period. Rabies vaccines used in the PEP protocol were administered via the route prescribed by the USDA.

Results—From 1995 through 1999, 830 animals received PEP; 4 failures were recorded. Additionally, 4 preexposure rabies vaccination failures were recorded.

Conclusions and Clinical Relevance—Results of this study indicate that an effective PEP protocol for unvaccinated domestic animals exposed to rabies includes immediate vaccination against rabies, a strict isolation period of 90 days, and administration of booster vaccinations during the third and eighth weeks of the isolation period. This PEP schedule has proven to be effective for control of rabies in domestic animals. (*J Am Vet Med Assoc* 2001;218: 522–525)

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As indicated in a previous study,[1] there are many considerations to be addressed when deciding on the disposition of an unvaccinated domestic animal that has been exposed to a rabid animal. This issue poses a quandary for all involved participants, including the attending veterinarian, the animal's owner, animal control officials, and public health authorities. Although concern for public health is of paramount importance, the emotional and monetary value of a domestic animal cannot be disregarded. The National Association of State Public Health Veterinarians, Inc recommends that unvaccinated dogs and cats exposed to a rabid animal be euthanatized or kept in strict isolation for 6 months and vaccinated against rabies 1 month prior to release from isolation. Immediate slaughter or a 6-month period of close observation is recommended for unvaccinated livestock, without vaccination during or after the observation period.[2] The state of Texas, however, has developed, studied, and evaluated additional options for **postexposure rabies prophylaxis (PEP).**

One reason for the need for alternative postexposure recommendations stems from the questions of the exposed animal's owner, who will possibly suffer adverse emotional and monetary consequences if the animal must be euthanatized, as to why PEP is widely accepted and highly effective in humans but not in animals. The standard PEP protocol for humans includes immediate administration of rabies immune globulin and a series of 5 doses of rabies vaccine over a 1-month period (administered on days 0, 3, 7, 14, and 28).[3] Additionally, the World Health Organization has approved options that reduce postexposure treatment in humans and has advocated the need to develop an effective and inexpensive PEP schedule for animals.[4] Questions also arise from animal owners, who may not understand the dynamics of anamnestic response, as to why the national recommendations allow vaccinated animals exposed to rabies to be immediately vaccinated but do not recommend immediate vaccination for unvaccinated animals exposed to rabies.[2]

The need for postexposure management alterna-

tives for exposed unvaccinated domestic animals has been recognized in Texas. For instance, south Texas has experienced a rabies epizootic in canines that began in 1988.[5] The canine variant of rabies is readily transmitted from coyotes to domestic dogs and between domestic dogs; rabies in a domestic animal population increases the chances for human exposure. According to previous reports from the **Texas Department of Health (TDH)**, for all nonnegative animals tested for rabies (ie, determined by the laboratory to be either positive or unsuitable for testing because of decomposition or destruction of required tissue), 5 to 10 times as many people were exposed to rabies for each domestic animal tested than for each wild animal tested.[6,a] These estimates have remained true for the years 1995 through 1999.[b] San Antonio, a heavily populated city threatened by its proximity to the rabies epizootic in south Texas, had an estimated 25% rabies vaccination coverage of its pet population,[7] despite Texas state law, which states that owners are required to vaccinate their dogs and cats against rabies annually.[8]

In 1979, the Rabies Control Act of the Texas Health and Safety Code[8] was enacted, and the accompanying administrative Rules of the Board of Health, Rabies Control and Eradication created under this law included a protocol for exposed unvaccinated animals for which a USDA-approved vaccine was available. The recommendations from 1979 through 1987 were to either humanely euthanatize the animal exposed to rabies or to immediately vaccinate the animal against rabies, keep it in strict isolation for 6 months, and administer a booster vaccination to the animal 1 month prior to its release from isolation. A dose of rabies immune globulin was not included in these recommendations, because, in addition to being expensive and having limited availability for domestic animals, it could cause adverse reactions.[1]

In 1988, the state recommendations regarding PEP were amended; exposed unvaccinated domestic animals were to be humanely euthanatized or receive a rabies vaccination immediately and be kept in strict isolation for 90 days, with booster vaccinations administered during the third and eighth weeks of the isolation period. For animals < 3 months of age, additional vaccinations were to be administered to ensure that the animal received at least 2 vaccinations at or after the minimum age designated by the USDA for the vaccine administered.

Rabies and the opportunity for exposure to rabid animals continue to be prevalent in Texas. From 1979 through 1987 (the period that included the first version of PEP recommendations), there were 6,568 laboratory-confirmed cases of rabies in animals in Texas, including 856 domestic animals. From 1988 through 1994 (the second period included in the previous study),[1] there were 3,150 confirmed cases, including 618 domestic animals. From 1995 through 1999, there were 1,910 confirmed cases of rabies, including 286 domestic animals (in 109 dogs, 66 cats, and 111 livestock).[9] The purposes of the study reported here were to determine whether the effectiveness of the PEP recommendations, as mandated by the state of Texas, has continued from 1995 through 1999 and to investigate PEP and preexposure rabies vaccination failures during this period.

Criteria for Selection of Cases

Completed zoonotic incident reports from the TDH filed from 1995 through 1999 were reviewed; each of the 1,910 reports corresponded with an investigation of a laboratory-confirmed case of rabies in an animal. Reports of all unvaccinated (without history of vaccination) domestic animals that received PEP in accordance with the rules associated with the Rabies Control Act[8] after exposure to a rabid animal were included in the analysis. The PEP failures, in which an exposed unvaccinated animal began PEP and subsequently developed rabies, were evaluated. To be classified as a true PEP failure, the rabies vaccine had to be one approved by the USDA and had to have been administered in accordance with Texas' PEP protocol. Reports in which preexposure rabies vaccination failure in a domestic animal was documented also were evaluated. For a preexposure rabies vaccination failure, the rabies vaccine had to have been administered at least 30 days prior to the onset of clinical signs of rabies.

Procedures

Each laboratory-confirmed case of rabies was investigated by TDH Zoonosis Control Division personnel, and the standardized zoonotic incident case investigation report was completed. The report included date, location, and description of the incident that caused rabies to be suspected, the rabid animal's medical history (if known) and vaccination status, and any human or domestic animal rabies exposures and their disposition or PEP status. The completed reports were then reviewed by additional division personnel for accuracy.

Rabies vaccines used in the PEP protocol were administered via the route prescribed by the USDA. In some instances, rabies vaccines approved for animals 12 weeks of age or older were administered to animals < 12 weeks of age as allowed for in the PEP protocol. On January 26, 1996, Texas state law[8] mandated that vaccines with a 3-year duration of immunity be used in dogs and cats on an annual basis. On July 12, 1998, the law was amended; annual vaccination of cats could be executed with vaccines licensed for 1 or 3 years. Use of either type of vaccine, if approved by the USDA, has been allowed in other domestic animals.

When an animal received PEP, the attending veterinarian and the owner were instructed to report to the TDH if the animal developed rabies or clinical signs associated with those of rabies during its life. To assess the interval between administration of pre- or postexposure rabies vaccination and the development of rabies, the period including the day the vaccine was administered through the day prior to the rabies incident date was measured. The rabies incident date refers to the day the animal died or was euthanatized.

Results

From 1995 through 1999, the PEP protocol that had been amended in 1988 was in effect and being

Table 1—Data from unvaccinated domestic animals that received postexposure rabies prophylaxis (PEP)

Species	No. receiving PEP	No. that developed rabies	PEP failure rate
Dogs	621	4	0.6%
Cats	71	0	0.0%
Horses	78	0	0.0%
Cattle	60	0	0.0%
Total	**830**	**4**	**0.5%**

implemented (ie, a rabies vaccination administered immediately, strict isolation for 90 days, and booster vaccinations administered during the third and eighth weeks of the isolation period). During this 5-year period, 621 unvaccinated dogs received PEP, with a range of 70 to 224 dogs/y (mean, 124.2 dogs/y). Seventy-one unvaccinated cats received PEP, with a range of 11 to 17 cats/y (mean, 14.2 cats/y). In livestock, there were 138 animals that had not been vaccinated previously and received PEP; the range was 11 to 43 livestock/y (mean, 27.6 livestock/y). Of the 138 livestock that received PEP, 78 (57%) were horses, and 60 (43%) were cattle (**Table 1**). Four unvaccinated goats also received PEP. However, USDA-approved rabies vaccines for goats do not exist; therefore, administration in this species would be considered off-label use of the vaccine.

During the same period, 826 (99.5%) of the 830 animals that received PEP did not develop rabies (Table 1). None of the cats, horses, or cattle that received PEP developed clinical signs of rabies; additionally, the 4 goats that received PEP did not develop rabies. Four PEP failures were recorded during this period (**Table 2**). One case in which the animal developed rabies involved an 8-month-old puppy (dog 1); 9 days had lapsed between the rabies exposure and administration of the initial and only postexposure rabies vaccination. Another case involved a 1-year-old dog (dog 2); this dog died 11 days following the first and only postexposure vaccination. An 8-week-old puppy (dog 3) and a 5-week-old puppy (dog 4) also had received one postexposure rabies vaccination each and developed rabies; the ages cited here reflect the age at the time of the rabies incident (ie, the age at which they died or were euthanatized). Both of these puppies were < 3 months of age when the initial and only postexposure vaccination was administered (at 6 and 2 weeks, respectively)[10]; additionally, there was an 8-day delay in administration of the vaccine to dog 3.

Dog 1 was bitten by a stray dog on the suspected exposure date; the stray escaped and was not tested for rabies. Dog 3 had been bitten by a fox on the suspected exposure date, but the fox was not submitted for rabies testing. In the dog that exposed dog 2 and the skunk that exposed dog 4, rabies was confirmed by the TDH Bureau of Laboratories. Results of the monoclonal antibody test[11] used revealed that dog 1 was infected with the Texas fox-domestic dog/coyote variant of rabies virus, and dog 4 was infected with the south central skunk variant. Polymerase chain reaction[11] was used to determine that dog 2 was infected with the domestic dog/coyote variant, and dog 3 was infected with the Texas fox variant of rabies virus.

Four preexposure rabies vaccination failures were recorded from 1995 through 1999 (**Table 3**); these included a 1-year-old horse and 3 dogs ranging in age from 11 months to 6 years (the ages cited here reflect the animals' ages on the rabies incident date). These animals had been vaccinated from 7 to 11.5 months (mean, 9 months) prior to the rabies incident date. The dogs had been given vaccines approved for triennial use; 1 dog (dog 7) may have been < 3 months of age at the time of its only rabies vaccination. The vaccine administered to the horse was licensed for annual use in horses. One dog (dog 5) was given a booster 11 months after the initial vaccination with the same type of vaccine that it had received previously. The booster was administered 2 days after the dog fought with a coyote that had escaped and was not tested; the dog had been reported to be healthy on both vaccination dates. This dog was infected with the Texas fox-domestic dog/coyote variant of rabies virus (as confirmed by use of monoclonal antibody testing). Clinical signs in this dog were observed by its owner 15 days after the booster was administered.

Clinical signs of rabies in the other animals were observed by the owners 2 to 3 days prior to the date the

Table 2—Data from unvaccinated domestic animals that developed rabies after PEP

Dog No.	Age	No. of PEP vaccinations	Date of		
			Exposure	PEP	Rabies incident
1	8 months	1	02-06-95 (suspected)	02-15-95	03-02-95
2	1 year	1	03-24-96	03-29-96	04-09-96
3	8 weeks	1	04-17-96 (suspected)	04-25-96	05-09-96
4	5 weeks	1	06-17-97	06-20-97	07-07-97

Table 3—Data from domestic animals that developed rabies after preexposure rabies vaccination

Animal No.	Age	Vaccination data			Date of rabies incident
		No. of previous	Date of last	Recommended booster interval	
Dog 5	15 months	1	03-03-94	3 y	02-24-95
Dog 6	5–6 years	multiple	06-08-95	3 y	03-27-96
Horse 1	1 year	1	06-20-98	1 y	01-30-99
Dog 7	11 months	1	04-04-99	3 y	12-08-99

animals died or were euthanatized. One dog (dog 7) had been in a fight with a skunk within a month prior to the rabies incident date, but the skunk was not submitted to be tested for rabies. Two dogs (dogs 6 and 7) were infected with the Texas fox variant of rabies virus (confirmed by use of polymerase chain reaction). The horse was infected with the south central skunk variant of rabies virus (confirmed by use of monoclonal antibody testing). An additional 6 dogs and 1 cat that had been previously vaccinated developed rabies, but they only received one vaccination < 30 days prior to the rabies incident date and thus were not considered true rabies vaccination failures.

Discussion

Reporting of possible PEP failures by attending veterinarians and owners has been considered an acceptable active surveillance system, because at the time of the initial rabies investigation, the attending veterinarian and the exposed animal's owner were instructed to report any evidence of rabies during the animal's life. Additionally, according to Texas' Rabies Control Act,[8] veterinarians and owners must report an animal that they know or suspect is rabid, and, during rabies case investigations, zoonosis control personnel report any PEP failures. However, it is possible that an owner may not submit an animal for testing because of fear of legal implications if the animal did not receive a preexposure rabies vaccination according to state law, the mandated PEP protocol was not followed, or because of the aesthetically negative image of removing the pet's head for testing. However, given the life-threatening nature of this disease, underreporting is highly unlikely and, therefore, would not have altered the findings of this study substantially.

Recommendations for the application of PEP protocol in domestic animals are based on the likelihood that they were exposed to a rabid animal. Exposures include being bitten by a rabid animal, nonbite exposure (ie, saliva contacting an open wound or mucous membrane), or being in an area (ie, in a stable in which a rabid animal was found) or scenario (ie, in a fight with a high risk animal that escaped) in which exposure could potentially have occurred.

In the previously cited Texas PEP study,[1] the interval between the first postexposure vaccination and the rabies incident date was 14 to 23 days (mean, 16.8 days). In the PEP failures between 1995 and 1999, the interval between the first postexposure vaccination and the rabies incident date was 11 to 17 days (mean, 14.5 days); the incubation period ranged from 15 to 25 days (mean, 19.5 days). The typical incubation period for rabies in dogs reportedly ranges from 21 to 56 days.[12] In one study of Texas rabies cases in canines, the incubation period ranged from 12 to 60 days (mean, 23 days).[5]

Although Texas state law allows for PEP in animals < 3 months of age, if vaccines that are approved by the USDA for use in animals 3 months of age or older are administered to younger animals, there is an increased chance that the vaccine will be ineffective. Successful PEP in dogs < 3 months of age has been difficult to achieve because of the lack of age-appropriate vaccine, the immature immune systems of puppies, or both.[10] It is possible that, with the advent of vaccines approved for use in dogs and cats 8 weeks of age or older,[2] some of the obstacles associated with PEP in young animals will be eliminated.

Data obtained from this study provide a basis for justifying the possibility of decreasing the isolation period from 90 to 60 days for unvaccinated animals that are exposed to a rabid animal. Prompt administration of the first rabies vaccine and adherence to the booster schedule are necessary factors if this is to become a workable and effective option. Extended delays in the administration of the initial postexposure vaccination appear to adversely affect the effectiveness of the PEP. Technically, dogs 1 and 3 of this study would not necessarily be classified as true PEP failures by definition, because the protocol states that, after exposure, the animal must be vaccinated immediately. Therefore, with the exclusion of these 2 failures, the PEP recommendations for the 1995 through 1999 study period would be considered 99.8% effective.

Results derived from this study indicate that an effective PEP protocol for unvaccinated domestic animals exposed to rabies includes immediate rabies vaccination, a strict isolation period of 90 days, and booster vaccinations during the third and eighth weeks of the isolation period. However, the importance of preexposure rabies vaccination in domestic animals must not be ignored. Preexposure rabies vaccination protects animals from unknown or undetected rabies exposures; therefore, it is strongly advocated from a public health and safety perspective as well as from a legal standpoint.

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