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Objective—To determine whether postexposure rabies prophylaxis (PEP) in domestic animals, as mandated in Texas, has continued to be effective and to evaluate preexposure or postexposure vaccination failures from 2000 through 2009.

Design—Retrospective case series.

Animals—1,014 unvaccinated domestic animals (769 dogs, 126 cats, 72 horses, 39 cattle, 3 sheep, 4 goats, and 1 llama) that received PEP and 12 vaccinated domestic animals (7 dogs and 5 cats) with possible failure of protection.

Procedures—Zoonotic incident reports from 2000 through 2009 were reviewed for information regarding unvaccinated domestic animals that received PEP in accordance with the state protocol after exposure to a laboratory-confirmed rabid animal; reports also were reviewed for any preexposure or postexposure vaccination failures. The state-required PEP protocol was as follows: 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.

Results—From 2000 through 2009, 1,014 animals received PEP; no failures were recorded. One preexposure vaccination failure was recorded.

Conclusions and Clinical Relevance—The Texas PEP protocol was used during the 10-year period. Results indicated that an effective PEP protocol for unvaccinated domestic animals exposed to rabies was 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. (J Am Vet Med Assoc 2010;237:1395–1401)

Any considerations need to be addressed when deciding on the disposition of an unvaccinated domestic animal that has been exposed to a rabid animal.1,2 This situation poses a dilemma for the attending veterinarian, the animal’s owner, animal control officials, and public health authorities. Although concern for public health is a prime consideration, the emotional and monetary value of a domestic animal cannot be overlooked.

The NASPHV recommends the following protocol for currently vaccinated animals that have been exposed to rabies: revaccinate the animal immediately, keep it under the owner’s control, and observe it for 45 days. Texas law provides a similar protocol as an option for a currently vaccinated rabies-exposed animal, which includes an immediate revaccination and a 45-day confinement that restricts the animal to an area, in isolation from other animals and people, except for contact necessary for its care. Alternatively, the animal may be euthanatized.4 The NASPHV recommends that rabies-exposed dogs, cats, and ferrets that have been previously vaccinated against rabies but that are not current with regard to rabies vaccination at the time of exposure be given a postexposure prophyaxis (PEP).
exposure be evaluated on a case-by-case basis. In the past, the NASPHV had recommended that unvaccinated (ie, no history of previous vaccination) dogs, cats, and ferrets 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. However, in 2005, those recommendations were modified to an unvaccinated, rabies-exposed animal being euthanatized or kept in strict isolation for 6 months and vaccinated at entry into isolation or 1 month prior to release. Immediate slaughter or a 6-month period of close observation with no vaccination during or after the observation period has been and continues to be recommended by the NASPHV for unvaccinated livestock. However, Texas has developed and evaluated additional options for PEP that involve alterations from the national recommendations. Those alterations include a required immediate vaccination against rabies, additional subsequent vaccinations against rabies, and an abbreviated isolation period.

Currently, there are no USDA-licensed rabies vaccines specifically for use in PEP of previously unvaccinated animals. Still, questions arise as to why PEP is accepted and considered effective in humans but not in domestic animals. The standard PEP for humans includes immediate administration of rabies immune globulin and a series of 4 (or 5) doses (depending on the immunocompetence or other special health circumstances of the exposed person) of rabies vaccine over a 1-month period administered on days 0, 3, 7, and 14 (and potentially 28). The recommendation to reduce the number of postexposure vaccinations by making the fifth dose optional (based on the individual’s health circumstances) was adopted in Texas in 2010 in accordance with recommendations from the Advisory Committee on Immunization Practices and the CDC.

The need to provide alternatives for postexposure management of exposed, unvaccinated domestic animals has been recognized in Texas. For instance, southern Texas has had a rabies epizootic in canids that began in 1988. Rabies involving the domestic dog–coyote variant of rabies virus is readily transmitted from coyotes to domestic dogs and from one domestic dog to another; rabies in a domestic animal population increases the chances for human exposure. San Antonio, a heavily populated city whose inhabitants are once threatened because of its proximity to the rabies epizootic in canids in southern Texas, had a high proportion of rabies-susceptible domestic animals (as indicated by an estimated vaccination coverage of only 25% of its pet population) despite a Texas law that stated that owners were required to vaccinate their dogs and cats against rabies. According to reports from the Texas DHS (formerly the Texas Department of Health), for all animals tested for rabies that have nonnegative results (ie, determined by a laboratory to have a positive result or had no result because samples were unsuitable for testing because of decomposition or destruction of required tissue), more people were exposed to rabies via a domestic animal than via a wild animal. In 1 published report, approximately 86% of humans in the United States that receive PEP do so because of exposure to rabid or potentially rabid dogs and cats; this high percentage is reflective of the close relationship between humans and dogs and cats.

The Rabies Control Act of the Texas Health and Safety Code6 was enacted in 1979. The accompanying rule (Rabies Control and Eradication) in the TAC7 created under this statute included the aforementioned PEP for animals current with regard to rabies vaccination that were exposed to a rabid animal as well as a PEP protocol for exposed animals that were not current with regard to vaccination against rabies or were unvaccinated. The group of unvaccinated animals that received PEP was included in the study reported here. The TAC provisions applied to animals for which a USDA-licensed (approved) vaccine was available. The TAC requirements from 1979 through 1987 were to euthanatize the animal exposed to rabies or to immediately vaccinate the animal against rabies, keep it in strict isolation for 6 months, and administer an additional dose of vaccine to the animal 1 month prior to its release from isolation. Immediate vaccination was mandated on the basis of field experiences in Texas involving rabies epizootics in canids in the 1970s in which an event similar to the early death phenomenon associated with vaccinations in relation to incubation periods was observed. During these rabies epizootics, it was determined that vaccination may hasten the onset of clinical signs of rabies in dogs that are in the incubation stages of the disease. Additionally, historical literature had indicated that although the incubation period for naturally exposed dogs typically ranged from 21 to 60 days, an animal exposed to rabies prior to vaccination would develop rabies within 1 month after vaccination. A dose of rabies immune globulin was not included in these recommendations because of limited availability for domestic animals plus the concern about possible adverse reactions. In a retrospective study of the ZIRs prepared during each rabies case investigation performed by the Texas Department of Health (now the DSHS), this protocol was found to be 99.7% effective (711/713 unvaccinated animals that received PEP did not develop rabies). When the NASPHV modified their recommendations in 2005, vaccination at the time of entry into isolation was added as an option.

In 1988, the TAC regarding PEP was amended, and rabies-exposed, unvaccinated domestic animals (for which a USDA-licensed vaccine was available) were euthanatized or received a vaccination against rabies immediately and were kept in strict isolation for 90 days with booster vaccinations administered during the third and eighth weeks of the isolation period. (In December 2007, the TAC was amended to 90 days of confinement, but the intent was that the confinement should remain in the form of strict isolation.) The modification to include a booster vaccination at the third week of isolation was based on the possibility of a poor titer response after the first vaccination, as detected in specimens voluntarily submitted by veterinarians and evaluated by use of a rapid fluorescent focus inhibition test for the detection of antibodies against rabies. The vaccination booster at the eighth week of isolation was included as a safety measure. 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 administered vaccine. In retrospective studies of the ZIRs of the Texas Department of Health (and subsequently the DSHS) during 1988 through 1994, this protocol was determined to be 99.5% effective (629/632 unvaccinated animals that received PEP did not develop rabies). From 1995 through 1999, use of this protocol was found to be 99.5% effective (826/830 unvaccinated animals that received PEP did not develop rabies). Two of the 4 animals that developed rabies would not be classified technically as true PEP failures by definition because they did not receive (as indicated in the protocol) immediate vaccination after the rabies exposure (there were delays in initial vaccine administration of 8 and 9 days, respectively). Therefore, with the exclusion of these 2 animals, the PEP recommendations for the 1995–1999 study period would be considered 99.8% effective.

From 1979 through 1987 (the period in a study that included the first version of the Texas PEP protocol), there were 6,568 laboratory-confirmed cases of rabies in animals in Texas, which included 856 domestic animals. From 1988 through 1994 (the second period in the study that included the current PEP protocol), there were 3,150 confirmed cases of rabies in animals in Texas, which included 618 domestic animals. From 1995 through 1999 (a period in another study that also included the current PEP protocol), there were 1,910 confirmed cases of rabies in animals in Texas, which included 286 domestic animals. This trend for high numbers of rabies cases, and thus the opportunity for exposure to rabid animals, continues to be prevalent in Texas. From 2000 through 2009, there were 9,188 laboratory-confirmed cases of rabies in animals in Texas, which included 523 domestic animals. Therefore, the objectives of the study reported here were to determine whether the effectiveness of the PEP protocol, as mandated by the state of Texas, was continued from 2000 through 2009 and to investigate any PEP and pre-exposure vaccination failures during this period.

Materials and Methods

Selection criteria—The ZIRs from the DSHS filed from 2000 through 2009 were reviewed. Each of the 9,188 reports corresponded with an investigation of a laboratory-confirmed case of rabies in an animal. Reports of unvaccinated (no history of vaccination against rabies) domestic animals that received PEP in accordance with the TAC after exposure to a rabid animal were included in the analysis.

Medical records review—Records were examined for any PEP failures in which an exposed, unvaccinated animal began PEP and subsequently developed rabies. To be classified as a true PEP failure, the rabies vaccine had to be one licensed by the USDA and had to have been administered in accordance with the Texas PEP protocol. Reports in which pre-exposure vaccination failure in a domestic animal was documented also were evaluated. For a pre-exposure vaccination failure, the disease had to have developed in an animal that had been previously vaccinated against rabies with a USDA-licensed product at least 30 days before onset of the clinical signs of rabies and within the time frame of the duration of immunity of the product.

Procedures—Testing of submitted specimens to detect rabies was performed by laboratories associated with the Texas DSHS in Austin, the El Paso City-County Health Department, the Houston Department of Health and Human Services, the San Antonio Metropolitan Health District, or the Department of Defense Veterinary Food Analysis and Diagnostic Laboratory at Fort Sam Houston. Submitted specimens were tested for rabies virus antigen by means of direct immunofluorescence microscopic examination of brain tissue impressions. Antigenic analysis of specimens with positive results for rabies virus was performed with monoclonal antibodies against the viral nucleoprotein to identify rabies virus variants. To verify certain variants (ie, domestic dog–coyote vs Texas fox) or resolve atypical or unexpected results, a genetic analysis of the nucleoprotein sequence (ie, amplification with a reverse transcription PCR assay followed by sequence analysis) was conducted. In addition, the direct rapid immunohistologic test was used to accomplish field testing; all positive results were verified in the DSHS laboratory via direct immunofluorescence examination.

Each laboratory-confirmed case of rabies was investigated by personnel from the DSHS Regional Zoonosis Control, local health departments, or local rabies control authorities, and the standardized ZIR was then 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; vaccine information (if applicable); any person or persons or domestic animals or animals that were exposed to the rabid animal; the disposition of the animal or PEP status; and the attending veterinarian’s contact information. Vaccination status of the exposed animal or animals was also included in the report.

Data from the ZIRs were evaluated by additional Zoonosis Control staff to differentiate among levels of exposure of unvaccinated domestic animals to rabid animals. Three categories of exposure were classified as follows: category 1, considered a direct exposure; category 2, considered a probable exposure; and category 3, considered a low-probability exposure (Appendix). Because the study involved field observations and the focus was on animals exposed to rabies that received PEP in accordance with the Texas protocol, control animals were not available for comparison.

All PEP vaccine administrations (ie, rabies vaccination administered immediately and booster vaccinations administered during the third and eighth weeks of the 90-day isolation period) involved a vaccine licensed by the USDA because USDA-licensed vaccines are required by Texas law. Rabies vaccines used for the PEP protocol were administered via the route prescribed by the USDA. The vaccinations were administered by or under the direct supervision of a licensed veterinarian (in accordance with state law), except that an individual with an established veterinarian-client-patient relationship may have obtained rabies vaccine from a veterinarian to administer to that individual’s livestock.
some instances, rabies vaccines approved for use in animals ≥ 12 weeks old were administered to animals < 12 weeks old as allowed for in the Texas PEP protocol. For any animal that received PEP, the attending veterinarian and owner were instructed to report to the DSHS if the animal developed rabies or clinical signs indicative of rabies. To assess the interval between administration of preexposure rabies vaccination and the development of rabies, the period that included 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.

Texas law was taken into consideration when determining preexposure vaccination failures. On February 21, 1996, the TAC mandated that vaccines with a 3-year duration of immunity be administered to dogs and cats on an annual basis. On July 12, 1998, the law was amended to allow the annual administration of vaccines licensed for 1 or 3 years in cats. The law was amended again on March 19, 2003, to allow dogs and cats that received vaccines with a 3-year duration of immunity to be vaccinated every 3 years. On December 20, 2007, this scope was broadened to allow veterinarians to administer rabies vaccines in accordance with the vaccination schedule for the length of immunity as licensed by the USDA for a particular vaccine. During all these time frames, manufacturers of rabies vaccines recommended a booster vaccination be administered 1 year after the initial vaccination, regardless of the duration of immunity for the vaccine.

Results

From 2000 through 2009, the PEP protocol that had been amended in 1988 was in effect and being implemented (ie, 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 10-year period, 769 unvaccinated dogs and 126 unvaccinated cats received PEP. For livestock, there were 119 animals that had not been vaccinated against rabies previously and that received PEP, including 72 horses, 39 cattle, and 3 sheep. Additionally, 4 goats and 1 llama also received PEP; however, USDA-licensed rabies vaccines for goats and llamas do not exist. The TAC does state that administration of a rabies vaccine in a species for which there is no USDA-licensed vaccine can be performed at the discretion of the attending veterinarian; however, the animal would not be considered to be current with regard to vaccination against the rabies virus in potential rabies exposure situations.

During this 10-year period, none of the 1,014 animals that received PEP developed rabies. Of the 1,014 animals that received PEP, 295 (29%) were in category 1 (considered a direct exposure), 388 (38%) were in category 2 (considered a probable exposure), and 331 (33%) were in category 3 (considered a low-probability exposure). These categories were designed to address concerns about whether an animal receiving PEP was truly exposed.

One preexposure rabies vaccination failure was recorded from 2000 through 2009. It involved a 15.5-month-old cat (the age of the cat on the rabies incident date). This cat had been vaccinated once 10.5 months prior to the rabies incident date. It had been given a vaccine with a 3-year duration of immunity; it was not yet due for the booster vaccination 1 year after the initial vaccination. A clinical sign of rabies (difficulty walking) was observed by the owner on the same date that the animal was euthanatized; attending veterinary staff also observed signs such as aggressive behavior (the cat lunged at staff members) and seizures before the cat was euthanatized, and a specimen was submitted to test for rabies. The cat was infected with the Texas fox variant of the rabies virus (confirmed via PCR assay).

Two animals with rabies (1 dog and 1 cat) were not considered current with regard to vaccination under Texas law at the time (> 1 year had elapsed since the rabies vaccine was administered), but they were within the 3-year duration of immunity for the vaccine used. However, neither animal had received the booster vaccination at 1 year after the initial vaccination, as recommended by the vaccine manufacturer. The dog had been vaccinated (with a vaccine licensed with a 3-year duration of immunity) 2 years and 9 months prior to the rabies incident date. Twelve days after the dog had suspected exposure to a skunk, it was administered a booster vaccination. However, the dog developed rabies and died 8 days after it received the booster vaccination. The cat was vaccinated (with a vaccine licensed with a 3-year duration of immunity) against rabies 2 years and 3 months prior to the rabies incident date. A PCR assay was used to confirm the variants of rabies virus to be south-central skunk for the dog and Texas fox for the cat.

During the 10-year period of the study, an additional 6 dogs and 3 cats that had been previously vaccinated developed rabies; however, either the licensed duration of immunity for the administered vaccine had lapsed or the only vaccination that the animal had received had been administered < 30 days prior to the rabies incident date. Thus, none of these were considered true rabies vaccination failures.

Discussion

Reporting of possible PEP failure by attending veterinarians and owners has been considered an acceptable system because at the time of the initial rabies investigation, the attending veterinarian and the owner of the exposed animal are instructed to report any evidence of clinical signs of rabies in the animal. Additionally, according to the Texas Rabies Control Act, veterinarians and owners must report an animal that they know or suspect is rabid. Furthermore, during rabies case investigations, DSHS Zoonosis Control personnel would detect and 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 had not received a preexposure rabies vaccination in accordance with state law or the mandated PEP protocol was not adhered to or because of the aesthetically negative image of removing the pet’s head for testing. Additionally, the determination that animals receiving PEP did not develop rabies is based on subjective observation by the animal’s owner and the attending vet-
Texas law allows for PEP in animals < 3 months old. However, if vaccines that are licensed by the USDA for use in animals ≥ 3 months old are administered to animals < 3 months old, there is an increased chance that the vaccine will be ineffective (ie, PEP was initiated, but the animal still developed rabies). One explanation for failure to achieve successful PEP in dogs < 3 months old is the lack of age-appropriate vaccines.6 Of the 10 animals with PEP failure previously recorded in Texas from 1983 to 1997,12 7 of the dogs involved were ≤ 1 year old. It is possible that with the further development of vaccines licensed for use in younger animals,3 some of the obstacles associated with PEP in these animals will be eliminated.

On the basis of the aforementioned Texas studies,12 extended delays in the administration of the initial postexposure rabies vaccination appear to adversely affect the effectiveness of PEP. Prompt administration of the first rabies vaccine and adherence to the booster schedule are important components for successful PEP. However, future considerations may include whether the booster vaccination on the eighth week is necessary and whether modification to a shorter isolation period is warranted.

The Oklahoma State Department of Health has incorporated aspects of the Texas PEP protocol into their requirements. The Oklahoma Administrative Code31 adheres to the Texas PEP 3-vaccination schedule for dogs, cats, and ferrets that are not current with regard to vaccination against rabies (which includes animals that have never been vaccinated against rabies). However, a 6-month quarantine period is required in Oklahoma. During the first 3 months of this 6-month period, the animal must be kept in strict quarantine under veterinary supervision at a veterinary facility or a recognized animal control facility; during the last 3 months, an owner with appropriate accommodations (such as an enclosed kennel, fenced yard, or indoor confinement) can quarantine the animal on the owner's premises.4 Animals < 16 weeks old at the time of entry into quarantine may be required to receive a booster vaccination in addition to the ones in the aforementioned protocol. Similar to the situation in Texas, the option to euthanize the animal is also available in Oklahoma. For exposed livestock or equids that are not current with regard to vaccination against rabies, Oklahoma adheres to any applicable NASPHV or State Department of Agriculture guidelines.

In reviewing data provided from the Oklahoma State Department of Health,6 63 unvaccinated animals (58 dogs and 5 cats) that were exposed to a laboratory-confirmed rabid animal received PEP in accordance with the Oklahoma postexposure protocol from 2003 through 2008. On the basis of the categories designed for the study reported here, 40 animals were in category 1 (considered a direct exposure), 23 animals were in category 2 (considered a probable exposure), and no animals were in category 3 (considered a low-probability exposure). There have been no failures of PEP in these 63 animals.

In a study,32 investigators evaluated PEP in 29 dogs experimentally infected with rabies. Of those 29 dogs, 18 developed rabies (5/5 that were not treated; 4/4 that
received rabies vaccine alone; 0/5 that received 2 murine anti-rabies glycoprotein monoclonal antibodies and rabies vaccine; 1/5 that received the murine anti-rabies glycoprotein monoclonal antibodies alone; 3/5 that received purified, heat-treated equine rabies immune globulin and rabies vaccine; and 3/5 that received immune globulin alone. For the group that received rabies vaccine alone, boosters were administered on days 3 and 7; all 4 dogs developed signs of rabies and were euthanized on days 9 and 10. Differences in results of vaccine-only intervention between that study (in which it was not successful) and the study reported here (in which it was successful) could be attributable to the fact that the present study involved a large number of field observations (1,014 animals) in which the dose of rabies virus was unknown, whereas that study involved a small number of animals (4 dogs) in which a known amount of rabies virus obtained from a naturally infected dog was injected directly into the highly innervated masseter muscles. Success with the use of monoclonal antibodies (with or without concurrent administration of rabies vaccine) in that study will hopefully initiate more research into use of this option.

Results derived from Texas in the present study support a conclusion that 1 option for an effective PEP protocol for unvaccinated domestic animals exposed to a rabid animal includes immediate rabies vaccination, a strict isolation period of 90 days, and booster vaccinations during the third and eighth weeks of the isolation period. Other protocols also warrant additional study; however, the retrospective case series reported here focused solely on the Texas PEP regimen. Even so, the importance of preexposure rabies vaccination in domestic animals must be emphasized. It should be duly mentioned and stressed that the option of PEP for unvaccinated animals should not serve to supplant the need for preexposure vaccination against rabies. Preexposure rabies vaccination helps protect 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.

References


Appendix

Categories for level of exposure of unvaccinated domestic animals to rabid animals.

<table>
<thead>
<tr>
<th>Category</th>
<th>Exposure</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Considered a direct exposure</td>
<td>Exposed animal was bitten by a rabid animal. Exposed animal attacked a rabid animal (including multiple dogs involved in the attack). Exposed animal killed a rabid animal (including multiple dogs involved in the attack). Exposed animal was attacked by a rabid animal. Exposed animal has injuries indicative of an attack and rabid animal found (dead or alive) nearby. Exposed animal found chewing on or playing with carcass of rabid animal.</td>
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<tr>
<td>2</td>
<td>Considered a probable exposure (ie, would cause a prudent person to seek PEP for the animal)</td>
<td>Rabid animal found dead in pen, stall, small lot, or other enclosure with the exposed animal or animals. Rabid animal found on premises and has injuries indicative of having been attacked by an exposed animal. Rabid animal (typically a skunk) found near a litter of exposed animals (rabid skunks tend to aggressively attack puppies and kittens). Rabid carnivore found alive in yard, pen, small lot, or other enclosure, but no obvious direct contact yet with the exposed animal or animals. Exposed animal rolled on the carcass of the rabid animal.</td>
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<tr>
<td>3</td>
<td>Considered a low-probability exposure but given PEP as a precaution</td>
<td>Rabid herbivore found alive in yard, pen, small lot, or other enclosure, but no obvious direct contact yet with the exposed animal or animals. All exposed animals on the premises (including livestock in a large field or pasture) were vaccinated because they spend time outdoors and may have encountered a rabid animal. Owner expresses uncertainty that there was contact of an exposed animal or animals with a rabid animal. Exposed animal or animals sprayed by a rabid skunk, and owner not certain of additional contact with the rabid skunk. Exposed animal or animals have the odor of a skunk, and a rabid skunk was located on the premises.</td>
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