

Rabies virus infection in a pet guinea pig and seven pet rabbits

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- ▶ To prevent rabies virus infection, domestic rabbits and pet rodents should be protected from contact with wild animals by, for example, using double-cage housing when housed outside.
- ▶ Pet rabbits or rodents with any possible contact with a wild animal, particularly if the rabbit or rodent has wounds of unknown origin, should be quarantined for 6 months to allow observation, to prevent escape, and to avoid contact with humans who will require treatment if the rabbit or rodent develops rabies.
- ▶ Bites and scratches to humans from rodents and lagomorphs should be evaluated for potential rabies virus exposure on an individual basis, with consideration of whether the animal was caged outside or permitted outdoors unsupervised.

In October 2003 in Madison County, New York, a normally docile 6-year-old long-haired male guinea pig (*Cavia porcellus*) bit its owner in the area of the clavicle when it was hugged by the owner. At the time, the owner believed that the bite occurred because the guinea pig was squeezed too hard. After several days, the owner recalled an incident 26 days prior to being bitten in which a raccoon was seen in the yard when the guinea pig was outside. The owner heard the guinea pig squeal and saw a raccoon running and climbing a tree. The guinea pig had burrowed beneath a doghouse; no wounds were visible, although the owner later recalled that the guinea pig had hind limb lameness for 3 days. The raccoon was not captured for rabies virus testing; however, a neighbor later reported seeing a dead raccoon on the side of the road around the same time.

Six days after the owner was bitten, the owner contacted local health authorities, who recommended

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that the guinea pig be tested for rabies virus. The following day, the owner took the guinea pig to a veterinary clinic to be euthanized. The veterinary technician reported a poor coat, weepy eyes, and a thin body condition. Because of a lack of neurologic signs or any limb weakness, the need for euthanasia was questioned. However, to reassure the owner, the guinea pig was euthanized and submitted for testing 7 days after biting the owner.

The guinea pig was shipped to the New York State (NYS) Department of Health Wadsworth Center Rabies Laboratory for diagnostic testing; results of the direct fluorescent antibody test¹ were positive for rabies virus. The rabies virus variant was identified by monoclonal antibody typing at the NYS Rabies Laboratory as the variant associated with the raccoon rabies epizootic in the eastern United States. Laboratory analysis of the distribution of rabies antigen in the guinea pig's body was also performed. Cryostat-cut tissue sections were analyzed by use of the direct fluorescent antibody test. Rabies antigen was widely distributed in a sublingual salivary gland (Figure 1). Evidence of virus was also detected in the tongue and buccal tissues. This was the first small rodent with positive results for rabies virus reported in NYS since the advent of modern diagnostic methods. The owner began postexposure treatment 8 days after being bitten, receiving 5 doses of rabies virus vaccine (administered over 1 month) and 1 dose of immune globulin.

Between 1992 and 2001, the Wadsworth Center Rabies Laboratory also diagnosed rabies in 7 lago-

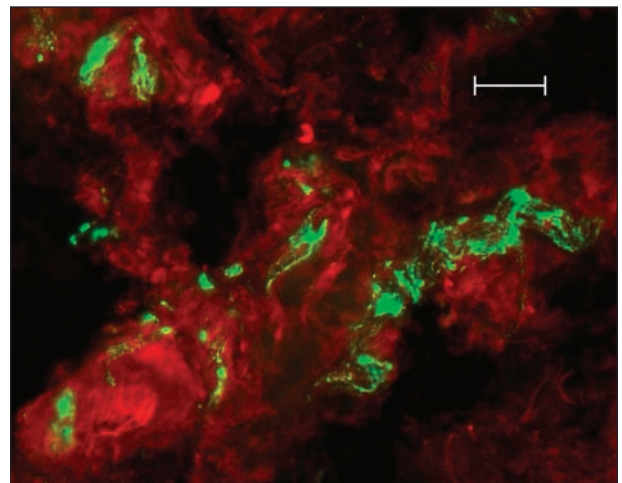


Figure 1—Photomicrograph of a sublingual salivary gland of a guinea pig after direct fluorescent antibody testing. Rabies viral antigen appears as apple-green fluorescence. Notice antigen in secreting cells of serous alveoli. Frozen section; bar = 50 μ m.

morphs, all pet domestic rabbits (*Oryctolagus cuniculus*) in NYS (excluding New York City). Three rabbits had been exposed to raccoons (*Procyon lotor*), and 1 rabbit had been exposed to a skunk (*Mephitis mephitis*). Exposures in the remaining 3 domestic rabbits were not known. Raccoon-variant rabies virus was confirmed in all 7 rabbits by use of the same methods as for the guinea pig. A description of each of these 7 cases follows.

In October 1992, an adult domestic rabbit in Cattaraugus County was euthanatized after developing neurologic signs including paralysis and mild hypersalivation. In addition, the rabbit was noticed biting the air and clamping onto the bars of the cage with its mouth. The rabbit had been permitted out of its cage outdoors for a short time, but contact with wild animals was not observed. After rabies was diagnosed in the rabbit, 3 staff members at the veterinary clinic and 2 children received postexposure treatment, although information on their exposures and justification for postexposure treatment were not available.

In July 1994, a domestic Lop rabbit in Cayuga County became lethargic, stopped eating, and died. The owner notified the local health department, which recommended that the rabbit be submitted for rabies virus testing. Other than the rabbit's death, the reason for health department notification and the recommendation for rabies virus testing were not reported. The rabbit had a positive test result for raccoon-variant rabies virus, although no known exposure to a raccoon or other animal was reported. The rabbit had been housed outside in a cage. Four family members and 1 additional person received postexposure treatment because of concerns about direct contact with the rabbit's saliva.

In September 1996, an adult domestic rabbit in Dutchess County was tethered outside and was attacked at night by a skunk. A dog chased the skunk away from the rabbit, and the skunk was shot, taken to a veterinary clinic, and submitted for rabies virus testing; results were positive for rabies virus. Thus, the dog, which had been vaccinated for rabies virus, received a rabies virus vaccine, and the rabbit was quarantined. During the quarantine period, approximately 46 days after the skunk attack, the rabbit developed neurologic signs including paralysis. Raccoon-variant rabies virus was confirmed in the rabbit and skunk. Two veterinary hospital staff each received 2 postexposure rabies virus vaccinations because contact with the skunk likely occurred when it was being prepared for laboratory submission, although details of exposure were not reported.

In September 1997, a 2-year-old female rabbit in Columbia County was euthanatized and submitted for rabies virus testing after paralysis of the hind limbs was detected. Test results were positive for rabies virus; however, exposure to another animal had not been observed. The rabbit had been housed in a cage that was positioned under an overhang in an open barn. Three family members and 1 additional person received postexposure treatment because direct contact with the rabbit's saliva was a concern, and 3 veterinary office staff members who had received preexposure

vaccinations for rabies virus each received 2 postexposure vaccinations for rabies virus after handling the rabbit and having direct contact with its saliva.

In May 2001, 1 of 7 pet rabbits in Schuylar County was found lying on its back and moving its limbs rapidly before it died. A raccoon had been seen on top of the rabbit cage and had been shot 21 days earlier. At that time, a wound was detected on the rabbit's ear, and a 12-year-old girl cleaned the rabbit's ear. The rabbit's owner cleaned the rabbit cage and disposed of the raccoon while wearing latex gloves. The raccoon was submitted for rabies virus testing, and results were positive. One adult and 3 children (ages 12, 8, and 5 years) in the family began postexposure treatment because of the possibility of direct contact with the rabid raccoon's saliva. The county health department recommended quarantine of all 7 rabbits and advised having only 1 older child who had received postexposure treatment care for them. However, the family was not strict with the quarantine, and after rabies was diagnosed in the rabbit, 3 additional children (2 children that were 2 and 3 years old in the same family and a 9-year-old child from another family) began postexposure treatment because direct contact with the rabbit's saliva was a concern. In addition, the remaining 6 rabbits were euthanatized and cremated.

Also in May 2001, a 2-year-old male rabbit bred for meat in Dutchess County developed neurologic signs compatible with rabies 3 weeks after a raccoon was seen on top of its cage. After the incident, a scratch was noticed around the rabbit's eye. The owner called local health authorities immediately and was advised about the requirements for 6-month quarantine. Because of appropriate precautions taken during quarantine, no human required postexposure treatment for contact with the rabbit.

In September 2001, a 2-year-old female Jersey Wooley rabbit from Rensselaer County was chased out of its cage by a raccoon and into a bucket of diesel fuel. The raccoon ran away and was not tested for rabies virus. The owner took the rabbit to a veterinary clinic to clean off the fuel. A veterinarian examined the rabbit and found no evidence of bite or injury. The veterinarian recommended that the owner quarantine the rabbit that was attacked and a rabbit that had been in an adjoining cage. Three weeks after the attack, the rabbit that had been chased developed clinical signs compatible with rabies, including lethargy and inappetence. One week later, the rabbit died. The rabbit was taken to a veterinary clinic; the head was removed and submitted for rabies virus testing. Results of testing performed on brain tissue were positive for rabies virus. The rabbit in the adjoining cage with no observed contact with the raccoon but possible contact with the rabid rabbit remained in quarantine. It did not develop rabies throughout the 6-month quarantine period. The adult owner received postexposure treatment because direct contact with the rabbit's saliva was a concern.

Rabies in domestic rodents and lagomorphs is not common. Although they can clearly act as "spillover species," occasionally contracting strains of the virus usually hosted by various carnivores, rodents and lago-

morphs have not been found to be natural reservoirs for rabies virus.² Results of a study³ in Florida in the 1950s and early 1960s indicated that only 1 of 10,000 rodents was infected with rabies virus. In the United States from 1992 to 2002, of the 87,700 cases of rabies in animals that were reported, 621 were in rodents and lagomorphs.⁴⁻¹⁴ Rabid groundhogs (sometimes referred to as woodchucks or marmots [*Marmota monax*]) represent most of those cases (n = 559), but there were also 25 rabid rabbits.⁴⁻¹⁴ Rabid guinea pigs were not reported. Prior to 1992, the CDC reported 3 rabid guinea pigs in the United States, 2 between 1971 and 1973,¹⁵ and 1 between 1953 and 1970.¹⁶ In NYS from 1992 to 2002, among the 14,025 cases of rabies in animals reported, 133 were in rodents and lagomorphs.¹⁷ Similar to that reported in the United States, groundhogs (n = 118) represented most of the cases.

Since the 1970s, raccoon-variant rabies virus has spread from the southeastern United States north along the Atlantic coastal region.¹⁸ As the raccoon rabies outbreak spread northward, an increase in the number of rabid rodents and lagomorphs followed. Except for 2 rabid groundhogs in Iowa, all of the cases of rabies in groundhogs were in states in which raccoon rabies is epizootic.⁴⁻¹⁴ Similarly, for rabid rabbits from 1992 to 2002, all of the cases (except for 1 in Texas) have been in states with raccoon-variant rabies virus (7 in NYS; 4 in New Jersey; 3 in Delaware; 2 each in Maryland, North Carolina, and New Hampshire; and 1 each in Connecticut, Massachusetts, Pennsylvania, and Virginia).⁴⁻¹⁴ In the report described here, variant testing in NYS confirmed that the 7 rabbits and 1 guinea pig had raccoon-variant rabies. It has been suggested that groundhogs, being large rodents, can survive contact with rabid raccoons better than small rodents.^{15,16} In addition, groundhogs compete with raccoons for den sites, increasing their potential for contact with rabid raccoons.¹⁵ Most of the domestic rabbits of this report were partially protected by single-cage housing, which permitted wild vectors of rabies virus to injure and infect but not kill them.

Rabies is a disease with nearly a 100% mortality rate in humans and other mammals. The virus infects the nervous system, causing behavioral signs that are frequently classified as the furious form (aggression, biting, vocalizations, self-mutilation, and gnawing on objects) or the paralytic form (lethargy, flaccid muscle weakness, and paralysis).^{19,20} Rabbits infected with the virus usually develop paralytic rabies,¹⁹ but some rodents and lagomorphs develop the furious form of rabies.³ In addition, some rodents have died of rabies without having clinical signs. In the report described here, the rabid guinea pig was euthanatized before clear clinical signs associated with rabies were detected. In a study²⁰ of experimental rabies virus infection in wild rodents in 1972, clinical signs were not detected in approximately half of infected squirrels that died of rabies. Cases of reportedly subclinical or paralytic rabies raise the question of whether rabies in rodents and lagomorphs is sometimes undiagnosed because clinical signs are not detected or are not recognized as rabies; thus, animals are not tested. However, even with concern that rabies in pet rodents and lagoon-

morphs may be underdiagnosed, they are disproportionately represented among tested animals. In 1984, 10% of animals tested for rabies virus in the United States were rodents; however, rodents accounted for only 0.5% of rabies cases.¹⁵

Rabies virus infection in small domestic rodents and lagomorphs represents a small but preventable problem. In all of the cases of rabies in NYS described herein, the animals may have been exposed to rabies virus because they had been permitted to run in outdoor areas or had been housed in cages accessible to raccoons or skunks. Because there is no approved vaccine to prevent rabies in rodents and lagomorphs, the best preventative measures are to closely supervise pet rodents and rabbits when in open outdoor areas and, if rabbits are to be housed outside, to house them in double cages impenetrable to rabid wild animals. Extralabel administration of rabies virus vaccines is permitted by veterinarians in animals in which the risk of rabies virus infection is high, particularly if animals will be used in situations in which public contact is encouraged, such as petting zoos.²¹ In addition, owners must be educated on the need for euthanasia or appropriate 6-month quarantine procedures for domestic animals after rabies virus exposure.²² If appropriate quarantine procedures are not followed and the animal develops rabies, human exposure can occur and lead to costly postexposure treatment.

In the United States, the first human death from raccoon-variant rabies virus was reported in Virginia in 2003.²³ Fortunately, no human in the United States has reportedly developed rabies after exposure to a rabid rodent or lagomorph.² Postexposure treatment is generally not recommended for all bites, scratches, or other contacts of concern from rodents and lagomorphs; however, these incidents are evaluated on an individual basis.²⁴ Pet rodents and lagomorphs frequently die of unknown causes, and diagnostic testing for rabies virus may not be sought. With no bites reported from the 7 rabbits with rabies in NYS and no details of the reported salivary contacts, we cannot determine the likelihood of humans dying from rabies if the rabbits had not been tested or if humans in contact with those rabbits had not received postexposure treatment. The guinea pig did bite its owner, and biting behavior is often associated with rabies virus infection. In addition, the guinea pig had other nonspecific clinical signs compatible with some type of illness; however, none of those clinical signs would have been clearly recognized as rabies. The wide distribution of rabies virus in the salivary glands strongly suggests the presence of infectious rabies virus in the saliva when the guinea pig died. However, we cannot be certain whether the guinea pig was shedding virus when it bit its owner.

The cases of rabies reported herein do not provide sufficient evidence to suggest that all pet rodents and lagomorphs should be euthanatized and tested for rabies virus if a human is bitten or exposed to saliva or nervous tissue. If the person potentially exposed has concerns that an animal has clinical signs of illness or an animal has potentially been exposed to rabies virus through contact with another animal, then consideration should be given to definitively determining the

rabies status through euthanasia and testing. In dogs, cats, and ferrets, the rabies status at the time of a bite can be established if they remain healthy during a subsequent 10-day confinement and observation period.²⁴ In pet rodents and lagomorphs, research on clinical signs and shedding periods is required to determine whether such observation periods would provide complete assurance of rabies status at the time of a bite. In the interim, animal and human health will be best protected by housing and maintenance of pet rodents and lagomorphs that prevent exposure to rabies virus and appropriate investigation, rabies virus testing, and provision of postexposure treatment to potentially exposed humans, depending on the species, clinical signs, history of exposure to other animals, and circumstances of human exposure.

References

1. Trimarchi CV, Smith JS. Diagnostic evaluation. In: Jackson A, Wunner W, eds. *Rabies*. London: Academic Press Inc, 2002;307–349.
2. Childs JE, Colby L, Krebs JW, et al. Surveillance and spatiotemporal associations of rabies in rodents and lagomorphs in the United States, 1985–1994. *J Wildl Dis* 1997;33:20–27.
3. Winkler WG. Rodent rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla: CRC Press Inc, 1991; 405–410.
4. Krebs JW, Strine TW, Childs JE. Rabies surveillance in the United States during 1992. *J Am Vet Med Assoc* 1993;203:1718–1731.
5. Krebs JW, Strine TW, Smith JS, et al. Rabies surveillance in the United States during 1993. *J Am Vet Med Assoc* 1994;205: 1695–1709.
6. Krebs JW, Strine TW, Smith JS, et al. Rabies surveillance in the United States during 1994. *J Am Vet Med Assoc* 1995;207: 1562–1575.
7. Krebs JW, Strine TW, Smith JS, et al. Rabies surveillance in the United States during 1995. *J Am Vet Med Assoc* 1996;209: 2031–2044.
8. Krebs JW, Smith JS, Rupprecht CE, et al. Rabies surveillance in the United States during 1996. *J Am Vet Med Assoc* 1997;211: 1525–1539.
9. Krebs JW, Smith JS, Rupprecht CE, et al. Rabies surveillance in the United States during 1997. *J Am Vet Med Assoc* 1998;213: 1713–1728.
10. Krebs JW, Smith JS, Rupprecht CE, et al. Rabies surveillance in the United States during 1998. *J Am Vet Med Assoc* 1999;215: 1786–1798.
11. Krebs JW, Rupprecht CE, Childs JE. Rabies surveillance in the United States during 1999. *J Am Vet Med Assoc* 2000;217: 1799–1811.
12. Krebs JW, Mondul AM, Rupprecht CE, et al. Rabies surveillance in the United States during 2000. *J Am Vet Med Assoc* 2001;219: 1687–1699.
13. Krebs JW, Noll HR, Rupprecht CE, et al. Rabies surveillance in the United States during 2001. *J Am Vet Med Assoc* 2002;221: 1690–1701.
14. Krebs JW, Wheeling JT, Childs JE. Rabies surveillance in the United States during 2002. *J Am Vet Med Assoc* 2003;223:1736–1748.
15. Fishbein DB, Belotto AJ, Pacer RE, et al. Rabies in rodents and lagomorphs in the United States, 1971–1984: increased cases in the woodchuck (*Marmota monax*) in mid-Atlantic states. *J Wildl Dis* 1986;22:151–155.
16. Winkler WG. Rodent rabies in the United States. *J Infect Dis* 1972;126:565–567.
17. Wadsworth Center. NYS Department of Health. Available at: www.wadsworth.org/rabies. Accessed Jul 1, 2005.
18. Guerra MA, Curns AT, Rupprecht CE, et al. Skunk and raccoon rabies in the eastern United States: temporal and spatial analysis. *Emerg Infect Dis* 2003;9:1143–1150.
19. Karp BE, Ball NE, Scott CR, et al. Rabies in two privately owned domestic rabbits. *J Am Vet Med Assoc* 1999;215:1824–1827.
20. Winkler WG, Schneider NJ, Jennings WL. Experimental rabies infection in wild rodents. *J Wildl Dis* 1972;8:99–103.
21. National Association of State Public Health Veterinarians (NASPHV). Compendium of measures to prevent disease associated with animals in public settings, 2005. *MMWR Morb Mortal Wkly Rep* 2005;54(RR-4):9.
22. National Association of State Public Health Veterinarians (NASPHV). Compendium of animal rabies prevention and control, 2005. *MMWR Morb Mortal Wkly Rep* 2005;54(RR-3):4.
23. CDC. First human death associated with raccoon rabies—Virginia, 2003. *MMWR Morb Mortal Wkly Rep* 2003;52: 1102–1103.
24. CDC. Human rabies prevention—United States, 1999. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 1999;48(RR-1):7, 10.