Rabies Background and General Virus Information

This individual chapter is part of the Rabies Prevention and Control in Florida guidance documents. The purpose of this compendium is to provide recommended policies and procedures for rabies prevention and control in Florida. It is intended primarily for use by county health department (CHD) staff, animal control specialists, veterinarians, health care providers and others with related responsibilities or interests. This publication, while produced and distributed by the Florida Department of Health (DOH) Division of Disease Control and Health Protection, has been developed by a multidisciplinary Florida Rabies Advisory Committee that represents the major agencies, institutions and organizations involved with rabies prevention and control in the state. The individual chapters and associated resources are routinely updated and posted on the following website: *www.floridahealth.gov/diseases-and-conditions/rabies/professionals.html.*

A. Background—United States

Human exposure to rabies most frequently involves the bite of a rabid animal. Exact figures are not available, but bites from some type of domestic or wild animal to Florida residents and visitors (especially children) are common each year. Dogs are the major source of animal bites in Florida, followed by cats, rodents, raccoons, bats, and other species. The threat of rabies transmission from animals to humans warrants the maintenance of a statewide surveillance system with thorough investigation and follow-up of all humans exposed to a suspected rabid animal. Successful control of this disease in any community ultimately depends upon a coordinated effort to: 1) immunize a large proportion of all dogs, cats, and ferrets kept as pets; 2) manage domestic and wild nuisance and stray animals; 3) implement an effective public information campaign; and 4) provide continuous education and training for health care providers, animal control workers, and employees of other allied agencies and organizations.

Human rabies is a rare disease in the United States, with two to three cases reported on average annually. A significant number of cases are due to exposures that occur outside the U.S. and often occur in countries where canine rabies variant is still endemic such as Haiti, Mexico, India, and the Philippines.1 Most of the human rabies cases with exposure in the U.S. since 2003 involved bat rabies variants; three involved eastern U.S. raccoon variant (one exposure via organ transplant); one involved Puerto Rican dog/mongoose variant. Specific bat variants identified in the U.S.-acquired cases were strains associated with either silver-haired (*Lasionycteris noctivagans*), eastern pipistrelle (*Perimyotis subflavus*), or Brazilian free-tailed (*Tadarida brasiliensis*) bats.2,3

Four fatal rabies infections occurred as a result of organ transplantations (liver, kidney, and blood vessel) in 2004 and one in 2013 (kidney); the donors were later found to be infected with rabies virus.4 The first human case associated with the raccoon rabies variant was diagnosed in Virginia in 2003, although the actual exposure history was not determined.5 In 2011, a North Carolina resident who became ill and died while in Florida was later determined to have

5 CDC. First human death associated with raccoon rabies - - Virginia, 2003. MMWR 2003; 52(45); 1102-1103.
died from raccoon rabies variant when a Maryland organ recipient developed rabies and died in 2013. Both cases were found to have the same rabies variant. The North Carolina case reportedly had a history of at least two raccoon bites and extensive contact with raccoons during his lifetime, but never sought medical attention or rabies post-exposure prophylaxis (PEP).\(^6\)

The first human case to survive symptomatic rabies without PEP treatment was reported in 2004 when a 14-year-old Wisconsin girl survived symptomatic rabies acquired from a bat bite.\(^7\) In 2011, an 8-year-old California girl with encephalitis who was treated using the Wisconsin protocol also survived apparent rabies infection; exposure likely occurred through feral cat contact.\(^8\) In 2008, a Brazilian boy who became symptomatic after receiving partial rabies PEP (no rabies immunoglobulin) recovered using a similar treatment protocol. However, the same treatment protocol has failed when used on numerous other occasions. In 2009, a 17-year-old girl in Texas with exposure to bats two months prior appeared to have survived an abortive case of rabies with only minimal to moderate medical intervention.\(^9\) Scientists conducting a serostudy in the Peruvian Amazon reported serologic evidence of rabies titers in persons with no history of rabies PEP and likely vampire bat contact.\(^10\) In spite of these unusual cases, rabies continues to remain a nearly universally fatal disease once patients become symptomatic.

### B. Background—Florida

In Florida, 77 fatal cases of human rabies have been reported between 1881 and 2015. Most of these involved children exposed to rabid dogs and cats. The first known human case of rabies in Florida was recorded as “hydrophobia” on the death certificate of a 38-year-old man from Key West in 1881. Historical documents indicate that rabies was considered rare in 1894 but was becoming more common in northern Florida counties. In 1895, despite legislation giving authority to the state health officer to prevent rabies among dogs, the disease continued to increase. By the turn of the century, severe outbreaks of canine rabies were occurring in most major cities resulting in 14 human cases reported between 1911 and 1913. The last case of human rabies acquired in Florida was reported in 1948 when a 35-year-old man from Tampa was bitten by a neighbor’s dog and refused treatment. Four additional cases have been reported in adult males in 1994, 1996, 2004, and 2011. Three were found to have been bitten by dogs in either Haiti (1994, 2004) or Mexico (1996). The most recent case (2011) was most likely due to a bite or other exposure to a rabid raccoon in North Carolina. Rabies was not the initial diagnosis in this case and patient organs (kidneys, liver, and heart) were transplanted in four other recipients. Diagnosis of rabies in the donor was made after one of the kidney recipients developed clinical rabies in February 2013. Once the rabies diagnosis was made, the three other recipients including one Florida resident immediately received rabies post-exposure prophylaxis and survived.\(^11\)

---


The DOH Bureau of Public Health Laboratories (BPHL), then the State Board of Health Laboratory, first documented animal rabies in Florida in 1905. During the first quarter of the 20th century, rabies in dogs was a major problem. The disease in dogs was finally brought under control in the early 1950s as public concern stimulated passage of rabies vaccination and animal control ordinances in many Florida cities and counties. Since 1960, only sporadic canine cases have been reported, averaging three per year. Still, since the late 1980s, the number of cases in cats has been increasing while the trend in dogs has remained the same. Cats were not included in many of the rabies vaccination and animal control ordinances of the 1940s, but attention is now being focused on including them in prevention programs. A state law enacted in 1994 requires that dogs and cats be vaccinated against rabies. In 1998, the legislation was modified to require ferret vaccination.

Rabies in raccoons and other wildlife is considered endemic throughout the state with four to six epizootics occurring sporadically each year. There was a dramatic rise in cases of animal rabies during 1996 and 1997 with over 250 cases reported each year. According to BPHL, 83 confirmed rabid animals were reported in 2015. Raccoons, foxes, and bats represent the greatest number of cases in wildlife. Among domestic animals reported, rabid cats outnumber any other domestic species and in recent years are similar in number to rabid foxes. The proportion of rabid cats has ranged from 8-16% in the past five years, the highest proportion by far of any domestic animal. Urban and suburban epizootics of raccoon rabies that spill over into foxes, bobcats, otters, and unvaccinated cats, dogs, horses, and livestock present unique control problems for local authorities.

Among wildlife in Florida, raccoons, bats, and foxes are the animals most frequently diagnosed with rabies. The first reported case of rabies in raccoons occurred in 1947 in Brevard County. Raccoons are now the main rabies reservoir species in Florida. The widespread distribution of this species, its ability to thrive near high-density human populations, its gregarious behavior, and the lack of consistently recognizable signs of disease in the raccoon make it a constant public health hazard. The other rabies reservoir in Florida are bats. Rabies in insectivorous bats in the United States was first recognized in 1953 in a yellow bat from Hillsborough County. Signs of the disease in these species may not initially be visible. Although foxes are not considered rabies reservoirs in Florida, they are highly sensitive to the virus and infections are common in these species due to spillover from raccoons. In the 1950s, outbreaks of fox rabies in the Panhandle were common, but in the 1960s, cases in foxes declined in this area. Since then, only sporadic cases in foxes associated with spillover during raccoon epizootics have been reported. However, since 1993, cases of rabies in gray foxes increased throughout the state and on average now account for approximately 10-15% of rabies cases.

C. Virus Characteristics

Rabies is caused by a neurotropic (special affinity for nervous tissue) virus of the genus *Lyssavirus* in the family Rhabdoviridae that occurs in most countries throughout the world. The bullet-shaped rabies virion consists of a helical ribonucleoprotein capsid enclosed within a lipoprotein envelope covered with glycoprotein projections. The virus is sensitive to ether, sunlight, heat, strong acids/bases, and formalin and is not persistent in the environment. Rabies virus strains present in the different geographic locations in the U.S. include raccoon, fox, skunk, bat, and mongoose (Puerto Rico) variants.
The virus is usually transmitted to people when they are bitten or have an open wound or mucous membrane exposed to the infectious saliva of a rabies vector. The virus initially replicates in muscle, connective tissue, or nerves at the site of inoculation with subsequent entry into nerve endings and then travels via nerves to the spinal cord and brain. The virus then spreads from the brain to the salivary glands and other organs. Infection of the salivary glands produces large volumes of virus in the saliva that, in turn, promotes opportunities for continued virus transmission. Infected animals can transmit rabies virus not only while clinically ill but also for a number of days prior to onset of symptoms. Incubation periods are variable in all species. The majority of cases develop clinical disease 20-60 days after exposure and almost all cases occur within six months of exposure, although more prolonged incubation periods have been reported in both animals and humans. The incubation period was 17 months for the 2013 Maryland organ transplant recipient who died from a raccoon rabies virus infection after having been on immunosuppressive medication since the time of the transplant surgery. It is not clear why prolonged incubation occurs in some cases, although host immune status, virus dose, and virus strain likely play some role.

Morbidity (illness) periods in most animal species are typically short, lasting only a few days to about two weeks. Studies have shown that some animals can survive natural infection and antibodies to rabies virus have been isolated from the blood of asymptomatic raccoons captured during urban epizootics in Florida.

Other rabies-related viruses in two phylogroups (I and II) have been isolated in Africa, Europe, Australia, and Eurasia. Bats appear to act as the primary reservoir for these viruses except for Mokolo virus, which may be maintained in shrews. Rare human deaths have been associated with several of these viruses. Rabies vaccine and immunoglobulin will cross-protect against other Lyssavirus members in phylogroup I, but do not appear to neutralize viruses in phylogroup II. Currently, there is no commercially available post-exposure treatment for phylogroup II lyssaviruses.

D. Florida Rabies Virus Variants

In July 1998, BPHL-Jacksonville began monoclonal antibody (MAB) testing of rabies-positive specimens from terrestrial mammals. MAB tests identify the strain of rabies virus, an important tool in describing the epidemiology of rabies. MAB testing confirms that the dominant rabies virus line in terrestrial animals in Florida is the raccoon strain. In more recent years, the CDC and Kansas State Rabies Laboratory have provided molecular typing for many of the Florida samples.

Analysis of DOH bat rabies data collected from 1953-1973 compared with similar data collected from 1994-2006 demonstrated changing bat rabies epidemiology in Florida. Historically, over 75% of bats testing positive for rabies in Florida were Lasius intermedius, the northern yellow bat. Current DOH BPHL data suggest that Tadarida brasiliensis, the Brazilian free-tailed bat, is now the bat species most likely to be involved in human and domestic pet rabies exposures. There are insufficient data to conclusively determine whether the increasing number of T. brasiliensis rabies cases are due to increased human contacts or increased rabies prevalence within the species. However, in a rapidly developing state such as Florida, this colonial species’ ability to utilize roost sites in man-made structures compared to the less adaptable, solitary, tree-roosting L. intermedius suggests habitat availability may be favoring T. brasiliensis, increasing chances of bat-to-human contact and possible rabies exposure. Data analyses also demonstrated that although bat rabies cases still typically peak
in August, cases have become more common in the winter, likely because the Brazilian free-tailed bat is more active in winter than the northern yellow bat.

Rabies viruses from 27 bats collected in Florida between 2005-2007 and gene sequenced by CDC were found to fall into six different clades, including four *L. borealis* (red bat) clades, one *L. cinereus* (hoary bat) clade, and an apparently emerging *T. brasiliensis* virus clade. Per CDC data, human cases of rabies in other states have been associated with *T. brasiliensis* variants. Sequencing of specimens from rabid bats submitted to Kansas State University Rabies Laboratory identified *T. brasiliensis* variant, *L. intermedius* variant, *Lasiurus* variant, and *Eptesicus* (big brown bat) variant.

### E. Clinical Signs in Animals

Initial symptoms of clinical rabies are often vague and non-descriptive. As the disease progresses, rabid animals exhibit certain clinical signs that are typical of rabies, with variations peculiar to carnivores, ruminants, and bats. It is extremely rare to observe all signs in a single infected animal. This chapter presents information regarding the animal species that elicit most rabies-associated questions. Persons requiring more detailed information on these and other species are referred to "Rabies in Florida". The incubation periods provided are general ranges and may occasionally extend beyond ranges provided in this chapter. It is also important to consider that noticeable signs of rabies (i.e., a morbidity period) in wild animals may be lacking. Following the general rule that all warm-blooded animals are potentially susceptible to the disease should lead to consideration of rabies in all such cases. Any clinical suspicion of rabies must be confirmed by laboratory examination.

1. **Dogs**
   - Virus excretion can begin 4 days before onset of illness.
   - The incubation period (time from infection to clinical signs) for dogs generally ranges from 9 to 182 days, with most cases showing clinical disease (morbidity) within 21 to 56 days.
   - The morbidity period (time from onset of clinical signs to death) is usually 1 to 7 days.
     - The “prodromal phase” of the morbidity period is generally 2 to 3 days duration. The dog may exhibit a subtle change in temperament with a slight rise in temperature, dilation of pupils, and a sluggish corneal reflex.
     - The “excitatory phase” of the morbidity period is 1 to 7 days duration. The dog becomes increasingly irritable, restless, or nervous. Photophobia (avoids light), hyperesthesia (increased sensitivity to stimulation), and pica (eats unusual items) may be present. At this time, the dog is very dangerous because of its tendency to bite anything that is encountered.
     - Signs of the impending “paralytic phase” soon become apparent with a change in bark (due to paralysis of laryngeal muscles) and difficulty in swallowing (due to spasms and eventual paralysis of pharyngeal muscles).

---

leading to drooling of saliva. Toward the end of this phase, convulsive seizures and muscular incoordination develop, as well as a "far-off" look in the eyes. The paralytic phase of the morbidity period is usually from 1 to 7 days. Most dogs have a predominant excitatory phase ("furious rabies") but some will seemingly progress rapidly into the paralytic phase ("dumb rabies"). Paralysis rapidly becomes generalized, and the animal slips into a coma and soon dies from respiratory arrest.

- Because there is no readily available test to determine if a dog is the product of a wolf cross, owners who represent their animals as "part wolf" will be subjected to managing the animal differently than dogs. No information is available on the incubation and morbidity periods of rabies in wolf-dog crosses.

2. Cats

- Virus excretion can begin 4 days before onset of illness.
- The incubation period for cats typically ranges from 9 to 51 days, with most cases showing clinical disease within 14 to 21 days.
- The morbidity period is generally from 1 to 8 days.
  - The "prodromal phase" of the morbidity period is 1 day in duration. Low-grade fever and a pronounced change in behavior characterize this phase; the cat may also become unusually affectionate or withdrawn.
  - The "excitatory phase" of the morbidity period is 2 to 4 days duration. It may begin with increased accumulation of saliva, slight incoordination or muscular tremors, often accompanied by nervousness, aggressiveness, and irritability. At this time, the cat may be particularly dangerous, often attempting to bite and scratch anything encountered.
  - The "paralytic phase" of the morbidity period is 3 to 4 days duration. Difficulty in swallowing develops, causing the animal to drool saliva; convulsions may occur at this point. The cat develops ascending and generalized paralysis; coma and death soon follow.

3. Raccoons

- The incubation period generally ranges from 10 to 107 days.
- The morbidity period is usually 1-13 days. The most common type of abnormal behavior observed in raccoons is aggressiveness. Other clinical abnormalities noted in rabid raccoons include incoordination leading to an inability to walk, or unusual behavior such as wandering aimlessly in daylight, and showing no fear of dogs or humans. Although many raccoons die of rabies, serologic testing of healthy raccoons indicates some develop immunity to the virus and survive the infection.
- It is possible raccoons, like other animals, shed virus before developing symptoms of the disease. On several occasions, raccoons virus has been isolated from the brain and salivary glands of normal-acting free-roaming raccoons trapped during urban outbreaks.

4. Bats

- The incubation period generally ranges from 16 to 209 days.
• The morbidity period is usually 4 to 17 days. Infected bats may die from rabies with or without evidence of neurologic disease (i.e., may show no signs of illness at all before death).
  ° Behavioral changes associated with rabies may differ markedly between colonial and non-colonial species of bats. Solitary non-colonial species typically become furious and may attack without provocation, whereas most colonial species, especially the highly colonial free-tailed bats, do not usually become aggressive.
  ° While bats commonly transmit rabies virus by biting, the bite wounds may be small and difficult to recognize. Rare airborne transmission of rabies virus has occurred in two Texas caves heavily populated by infected bats.

5. Foxes and Coyotes

• Foxes are extremely sensitive to rabies virus and the incubation period in both gray and red foxes generally ranges from 9 to 109 days.

• The morbidity period in foxes is usually 1 to 15 days. The behavior of rabid foxes usually conforms to either a pattern of aggression or confusion and their normal caution toward humans is lost. The persistence and success of the attack of an aggressive fox is determined by its condition, since in many cases the animal is too weak or uncoordinated to effectively attack. The fox that exhibits confusion as a predominant sign bites people and other animals only when approached by them.

• No information is available on the incubation and morbidity periods of rabies in Florida coyotes. In 1994, an outbreak of rabies in fox-hunting dogs was reported from Alachua County. These animals were diagnosed with the coyote strain of rabies, presumably from coyotes illegally translocated from south Texas. Since then, no other rabid animals have been reported with this rabies strain in Florida.

6. Ferrets, Skunks, and Otters

• The family of Mustelidae includes skunks, otters, minks, weasels, and ferrets. In Florida, wild skunks and otters become involved in outbreaks of raccoon rabies as incidental hosts and vectors. Mustelids in general are considered to be highly susceptible to, and capable of, transmitting rabies if infected.

• Ferrets sold as pets in the United States are derived from European stock, which have been domesticated for centuries and selectively bred for productivity and behavior traits. The popularity of the ferret as a personal pet has led to increased biting incidents. This is a cause of concern because owners in some circumstances allow animals to either escape or free range in their yards or neighborhoods. As a result of their exposure to wildlife, several have been diagnosed with rabies in the United States including one case from Brevard County, Florida in 1996. The CDC conducted a series of infection experiments using several strains of rabies virus to evaluate incubation periods, viral shedding, and transmission in the domestic ferret. Based upon the results of this research and the availability of an approved vaccine*, it is required by Florida

---

law that ferrets be vaccinated against rabies, and are managed in the same way as dogs and cats.

- Virus excretion can begin 2 days before onset of illness.
- The incubation period for ferrets generally ranges from 10 to 96 days.
- The mean morbidity period for ferrets ranges from 1 to 10 days. Clinical signs included ataxia, lethargy, fever, tremors, bladder atony, paresis, weight loss, and aggression.
- The incubation period for skunks generally ranges from 12 to 177 days\(^{16}\).
- The morbidity period for skunks is usually from 1 to 18 days. Anorexia is one of the most reliable indicators of the onset of clinical rabies in this species. The virus does not infect the scent glands of skunks and, consequently, rabies is not transmitted via their musk spray. Rabid skunks often become extremely aggressive, reacting violently to external stimuli such as sound or movement. During such reactions, skunks will bite and hold on to their victims tenaciously. Paralysis and coma commonly follow these furious signs before death. A small proportion of rabid skunks will show neither furious nor paralytic signs of rabies, but may be just found dead.
- No information is available on the incubation or morbidity periods for rabies in Florida otters.

7. **Horses and Mules**

- The incubation period is generally short, although periods up to six weeks have been recorded.
- The morbidity period is usually 5 to 8 days.
  - “Prodromal” signs of the morbidity period include low-grade fever, behavioral changes, and rubbing or biting at the site of exposure.
  - Rabid horses usually show a marked “excitatory phase” lasting from 1 to 4 days. They may become restless, have muzzle tremors, grind their teeth, foam at the mouth, whinny as if in great pain, strain at the bowels, and show signs of severe colic. They may lash out with incredible fury at any perceived threat or restraint and may exhibit an increase in sexual excitement. In some horses, the “excitatory phase” may be absent or very transient. These animals often exhibit a paralytic clinical syndrome akin to dumb rabies in dogs and very similar to that seen in arboviral equine encephalitis.
    - The “paralytic phase” of the morbidity period is 1 to 4 days. As paralysis develops, rabid horses fall down repeatedly, finally remaining down and thrashing their legs prior to death.
- It is highly recommended that horses be immunized by a licensed veterinarian against rabies annually with an approved vaccine\(^*\), both for the protection of the animal and to allow free movement of the horse into Florida. The American Association of Equine Practitioners (AAEP) now categorizes rabies as a core

equine vaccine. If a horse is unvaccinated and exposed to a rabid animal while out of state, it must complete a 6-month quarantine before it is allowed transport into Florida.

8. Rodents and Rabbits

- Rabies is uncommon in most rodents, although they are susceptible to the disease. Infection is seen most often in large rodents such as woodchucks. Small rodents such as mice, rats, and squirrels rarely survive attacks from rabid animals. Prior to 1938, five cases of rabies had been reported in rodents in Florida. From 1957 through 1983, 17,487 squirrels, rats, and mice were examined for rabies in Florida; only one was found to be rabid. The positive case was a flying squirrel collected from Pinellas County in 1961. In 2001, the first rabid beaver was reported in Florida.

- Rabies is a very uncommon disease in pet rodents. However, it is important to avoid contact between pet rodents and wildlife. In 2004, raccoon-variant rabies was found in pet rabbits (seven cases) and a guinea pig in New York State; all rodents had contacts with raccoons while caged outdoors.\(^{17}\)

- The response of rodents to rabies virus has been investigated in five species and it was found that the majority (55-100%) of animals inoculated with the virus died of rabies, with incubation periods ranging from 10-86 days.\(^ {18}\)

- The clinical signs of rabies were markedly different between squirrels and the other rodents in a study conducted by Winkler et al. About half of the squirrels died without demonstrable clinical illness. The other half died after exhibiting signs of furious rabies for approximately 1 day. In contrast, the rats and mice exhibited progressive ascending paralysis of 3-6 days duration without any signs of aggressive behavior.

9. Monkeys and Other Non-Human Primates (NHPs):

Monkeys and other NHPs are believed to be relatively resistant to rabies infection similar to humans and captive-borne vaccinated NHPs with limited exposure are considered low risk. Between 1957 and 1975, 636 monkeys and four chimpanzees were tested at Florida health laboratories and all were found to be negative for rabies.\(^ {19}\) However, a rabies variant has been identified in marmosets in Brazil, demonstrating that this group of animals is not entirely without risk for rabies infection.\(^ {20}\) Bites should be evaluated on a case-by-case basis. Herpes B virus prophylaxis, ideally initiated within hours of a bite, scratch or mucous membrane exposure, should be considered for all bites caused by macaque (Macaca spp.) monkeys or other NHPs in close contact with macaques (www.cdc.gov/herpesbvirus/index.html). Immediate, thorough wound care is imperative and follow-up serologic evaluation is also recommended. Health status of the animal should be determined by the animal’s regular veterinarian.

---


or another veterinarian familiar with NHPs. All bites from free-ranging monkeys should be reported to CHDs; all bites from captive monkeys should also be reported to the appropriate regional Florida Fish and Wildlife Conservation Commission Captive Wildlife Law Enforcement Investigator, as they are the permitting entity and can also verify animal species and origin (captive bred vs. wild caught).

F. Additional Resources*

Additional rabies guidance, information, and resource documents can be found at the following website: www.floridahealth.gov/diseases-and-conditions/rabies/professionals.html.