

Assessing the Need for PEP

Administration of rabies PEP is a medical urgency, not a medical emergency. Persons who have been bitten by animals suspected or proven to be rabid should begin PEP as soon as possible. However, very long incubation periods (up to 1 year) have been reported in humans. Thus, when a documented or likely exposure has occurred, PEP is indicated regardless of the length of the delay, provided the clinical signs of rabies are not present. Under most circumstances, PEP should not be initiated if the bite was from a healthy dog/cat/ferret that is available for a 10-day quarantine. However, if during the 10-day quarantine period, the animal begins to show signs of rabies, the PEP should be started immediately and the animal tested as soon as possible.

Health care providers should evaluate each possible exposure to rabies and when necessary consult with the Alabama Department of Public Health regarding the need for rabies PEP.

In the US, the following factors should be considered in the rabies risk assessment before PEP is initiated:

- Type of exposure (bite vs. non-bite)
- The geographic location of the incident
- The type of animal that was involved
- Circumstances of the exposure (provoked or unprovoked)
- The vaccination status of the animal
- Whether the animal can be safely captured and tested for rabies

In general, the highest risk of rabies transmission is associated with bite exposure from terrestrial wild carnivores or bats (see **Rabies Treatment Decision Flow Chart**). Raccoons, skunks, foxes, and coyotes are the terrestrial animals most often infected with rabies. All bites by such wildlife must be considered possible exposures to the rabies virus. PEP should be initiated as soon as possible after patients are exposed to wildlife unless the animal has already been tested and shown not to be rabid. In addition, bats are increasingly implicated as important wildlife reservoirs for variants of rabies virus transmitted to humans. In all instances of potential human exposures involving bats, the bat in question should be safely collected, if possible, and submitted for rabies diagnosis. Rabies PEP is recommended for all persons with a bite, scratch, or mucous membrane exposure to a bat, unless the bat is available for testing and is negative for evidence of rabies. PEP might also be appropriate even if a bite, scratch, or mucous membrane exposure is not apparent when there is reasonable probability that such exposure might have occurred.

The likelihood of rabies in a domestic animal varies by region; hence, the need for PEP also varies. In the continental US, rabies among dogs is reported most commonly along the US-Mexico border and sporadically in area of the US with enzootic wildlife rabies. During most of

the 1990s, more cats than dogs were reported rabid in the US. The majority of these cases were caused by the raccoon variant in the eastern US. The large number of rabies-infected cats might be attributed to fewer cat vaccination laws, fewer leash laws, and the roaming habits of cats. In many developing countries, dogs are the major vector of rabies; exposures to dogs in such countries represent an increased risk of rabies transmission. In the United States, a currently vaccinated dog, cat, or ferret is unlikely to become infected with rabies. Although all species of livestock are susceptible to rabies, they are infrequently found to be infected. Small rodents (i.e., squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (including rabbits and hares) are almost never found to be infected with rabies and have not been known to transmit rabies to humans.

An unprovoked attack by an animal is more likely than a provoked attack to indicate that the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as provoked.

Refer to the chart below and to the Rabies Treatment Decision Flow Chart on the proceeding pages for specific guidelines.

Table 1. Rabies Post-Exposure Prophylaxis Schedule – US, 2008

Animal Type	Evaluation and Disposition of Animal	Exposure Prophylaxis Recommendations
Dogs, Cats, and Ferrets	<ul style="list-style-type: none"> • Healthy and available for 10 day quarantine • Rabid or suspected rabid • Unknown (i.e., escaped) 	<ul style="list-style-type: none"> • Persons should not begin PEP unless animal develops clinical signs of rabies.* • Immediate PEP. • Consult local rabies officer or Alabama Department of Public Health officials
Skunks, raccoons, bobcats, foxes, and most other carnivores; bats	Regarded as rabid unless animal proven negative by laboratory tests. **	Consider immediate PEP
Livestock, small rodents, lagomorphs (rabbits and hares), large rodents (woodchucks and beavers), and other mammals	Consider individually.	Consult local rabies officer or Alabama Department of Public Health officials. Bites of squirrels, hamsters, mice, and rats, most other rodents, and rabbits almost never require PEP. Large rodents may be a risk.

* During the 10-day quarantine period, begin PEP at the first sign of rabies in a dog, cat, or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.

** The animal should be euthanized and tested as soon as possible. Discontinue vaccine if rabies test results are negative.

Definitions
Exposure is any contact with saliva or brain/nervous tissue through open cuts in the skin, scratches, or mucous membrane (mouth or eyes).

PEP is postexposure prophylaxis or treatment, which usually includes HRIG and 4-doses of rabies vaccine.

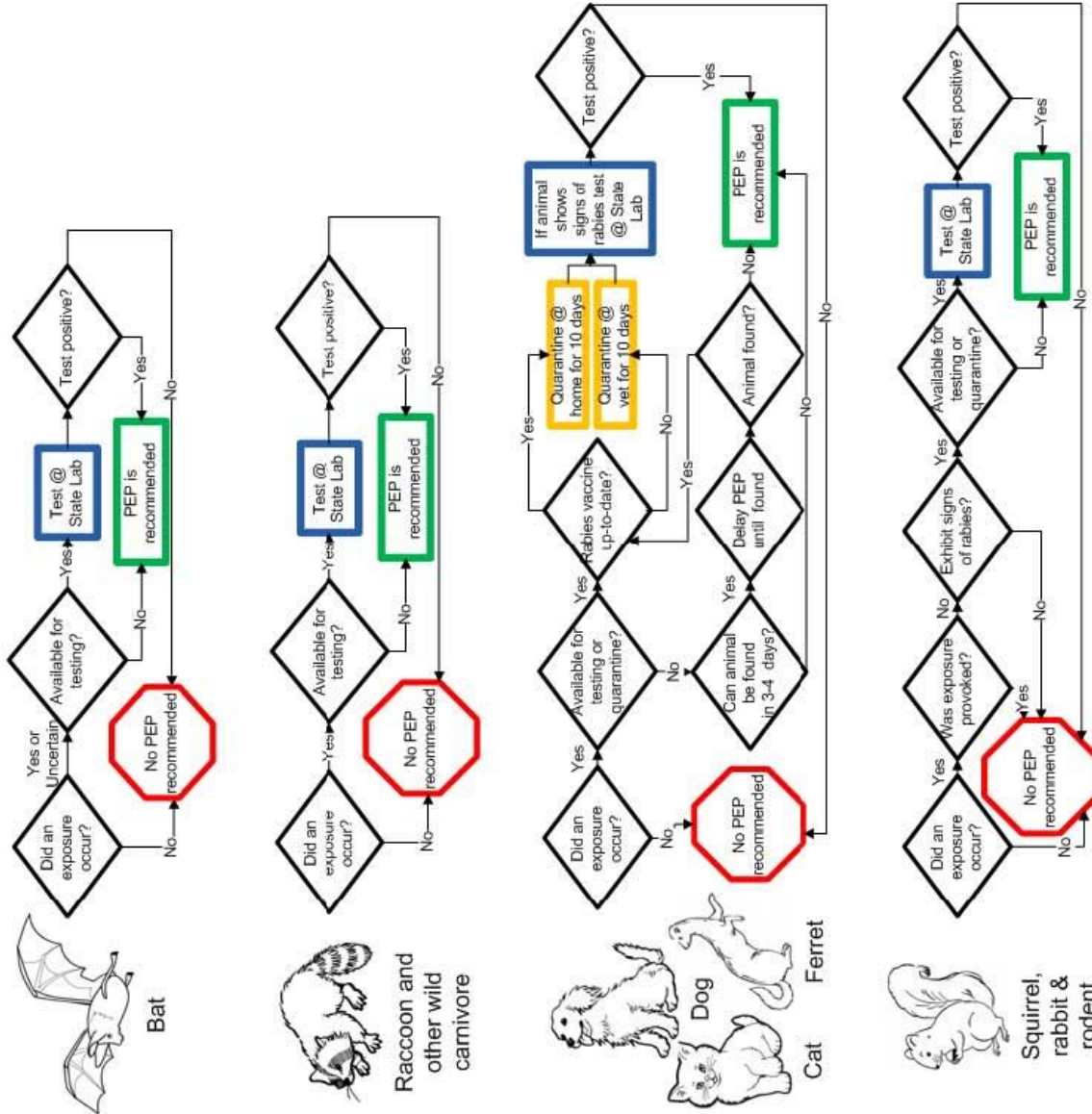
Provoked is an intentional act that causes the animal to react in a hostile manner.

Quarantine is separating suspected animal from other animals and people.

Signs of rabies include obvious changes in normal behavior, like aggression, attack without reason, foaming at mouth, no interest in food or water, stagger, tired, or paralysis. In wild animals, they may act very tame.

Uncertain exposure can occur with bats because they have small teeth and may leave marks that are not easily seen.

For more information, go to www.adph.org/epi. Rabies to review the Rabies Bite Manual, Alabama Rabies Law, Rabies data, and CDC Rabies links. For questions, please call the Epidemiology Division, Zoonotic Branch at 1-800-338-8374.



For large animals, like cows and horses, please contact Epidemiology Division, Zoonotic Branch, 1-800-338-8374.

Rabies Post-Exposure Vaccination for Humans

In general, post-exposure prophylaxis (PEP) is indicated for persons exposed to a rabid animal in order to prevent infection with rabies virus. The ADPH follows the most recent recommendations from ACIP in the *Morbidity and Mortality Weekly Report (MMWR)* “Use of a Reduced (4 Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies.” These recommendations reduce the number of vaccine doses to four. The reduction in doses recommended for PEP was based in part on evidence from rabies virus pathogenesis data experimental animal work, clinical studies, and epidemiologic surveillance. These studies indicated that 4 vaccine doses in combination with rabies immune globulin (RIG) elicited adequate immune responses and that a fifth dose of vaccine did not contribute to more favorable outcomes. For persons previously vaccinated with rabies vaccine, the reduced regimen of 4 1-mL doses of HDCV or PCECV should be administered intramuscularly. The first dose of the 4-dose course should be administered as soon as possible after exposure (day 0). Additional doses then should be administered on days 3, 7, and 14 after the first vaccination. ACIP recommendations for the use of RIG remain unchanged. For persons who previously received a complete vaccination series (pre-or postexposure prophylaxis) with a cell-culture vaccine or who previously had a documented adequate rabies virus-neutralizing antibody titer following vaccination with non cell-culture vaccine, the recommendation for a 2-dose PEP vaccination series has not changed. Similarly, the number of doses recommended for persons with altered immunocompetence has not changed; for such persons, PEP should continue to comprise a 5-dose vaccination regimen with 1 dose of RIG. Recommendations for pre-exposure prophylaxis also remain unchanged with 3 doses of vaccine administered on days 0, 7, and 21 or 28. Prompt rabies PEP combining wound care, infiltration of RIG into and around the wound, and multiple doses of rabies cell-culture vaccine continue to be highly effective in preventing human rabies. See Table 2 on page 19 for specific schedule and administration instructions.

Rabies Post-exposure Prophylaxis (PEP) for Non-immunized People

Treatment	Regimen
Wound Cleansing	Clean immediately with soap and water. If possible, irrigate wound with a anti-virus agent, like povidine-iodine
HRIG	If possible, full dose infiltrated around the wound. Any remaining should be administered intramuscularly (IM), at site distant from the vaccine.
Rabies Vaccine	4 doses, 1 ml, IM, upper arm area, days 0, 3, 7, and 14

Immunosuppression

Recommendations for rabies pre- and postexposure prophylaxis for persons with immunosuppression have not changed. General recommendations for active and passive immunization in persons with altered immunocompetence have been summarized previously ([27,28](#)). This updated report discusses specific recommendations for patients with altered immunocompetence who require rabies pre- and postexposure prophylaxis. All rabies vaccines licensed in the United States are inactivated cell-culture vaccines that can be administered safely to persons with altered immunocompetence. Because corticosteroids, other immunosuppressive

agents, antimalarials, and immunosuppressive illnesses might reduce immune responses to rabies vaccines substantially, for persons with immunosuppression, rabies PEP should be administered using a 5-dose vaccine regimen (i.e., 1 dose of vaccine on days 0, 3, 7, 14, and 28), with the understanding that the immune response still might be inadequate. Immunosuppressive agents should not be administered during rabies PEP unless essential for the treatment of other conditions. If possible, immunosuppressed patients should postpone rabies preexposure prophylaxis until the immunocompromising condition is resolved. When postponement is not possible, immunosuppressed persons who are at risk for rabies should have their virus-neutralizing antibody responses checked after completing the preexposure series. Post vaccination rabies virus-neutralizing antibody values might be less than adequate among immunosuppressed persons with HIV or other infections (29,30). When rabies pre- or postexposure prophylaxis is administered to an immunosuppressed person, one or more serum samples should be tested for rabies virus-neutralizing antibody by the RFFIT to ensure that an acceptable antibody response has developed after completing the series. If no acceptable antibody response is detected after the final dose in the pre- or postexposure prophylaxis series, the patient should be managed in consultation with their physician and appropriate public health officials.

Variation from Human Rabies Vaccine Package Inserts

These new ACIP recommendations differ from current rabies vaccine label instructions, which still list the 5-dose series for PEP. Historically, ACIP review and subsequent public health recommendations for the use of various biologics have occurred after vaccine licensure and generally are in agreement with product labels. However, differences between ACIP recommendations and product labels are not unprecedented. For example, during the early 1980s, ACIP review and recommendations concerning the intradermal use of rabies vaccines occurred well in advance of actual label claims and licensing (9). On the basis of discussions with industry representatives, alterations of current product labels for HDCV and PCEC are not anticipated by the producers of human rabies vaccines licensed for use in the United States.