

# Rabies Exposure in Humans & Pets

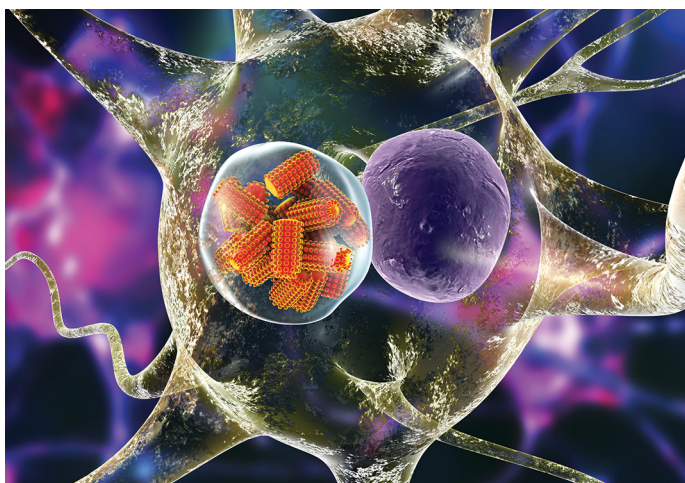
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Rabies virus infections in humans are nearly always fatal but are almost completely preventable with appropriate postexposure prophylaxis (PEP). Proper management of rabies exposure is therefore critical.

Rabies virus is a zoonotic *Lyssavirus* and accounts for substantial mortality rates internationally in both humans and animals. Rabies is estimated to kill 50 000 humans per year,<sup>1</sup> although this is concentrated in developing countries with endemic canine rabies and often inadequate public education and health systems. Canine variant rabies is not present in the United States, but some risk is still present because of spillover of other rabies virus variants from wildlife reservoirs (eg, skunks, bats, raccoons, foxes) into domestic animals. (See **Resource**, page 39.)

Rabies is rarely identified in domestic dogs in the United States, with only 67 cases reported in 2015.<sup>2</sup> The disease incidence is higher in cats, with 244 US cases reported in 2015.<sup>2</sup> However, because rabies virus is endemic in wildlife reservoirs throughout North America and much of the world, some potential for rabies exposure in humans and domestic animals always is present.



**FIGURE 1** Illustration of rabies virus in a neuron

## Key Communication Points

- Rabies vaccination of dogs, cats, and ferrets does not impact quarantine of an animal that has bitten a human but can have a major influence on the approach to an animal that has been bitten.
- The potentially significant consequences of rabies exposure to an unvaccinated animal must not be ignored; in the author's experience, euthanasia of unvaccinated dogs in lieu of quarantine presumably kills many more dogs in North America than rabies.

## What Constitutes Rabies Exposure?

Confusion often exists when responding to a potential rabies exposure case. Understanding what constitutes exposure and the ideal protocol when managing exposure is critical to facilitating an appropriate response and calming concerns.

Rabies virus must be inoculated into the body for infection to occur. Inoculation typically occurs via bites from animals in late stages of rabies infection, when they are shedding large amounts of rabies virus in saliva. Scratches are a potential exposure risk if rabies virus has been previously deposited on the skin via saliva and the scratch inoculates the wound, or if saliva is on the paw and the animal then scratches a human or another animal. The approach to managing scratch cases varies by region and should be decided on a case-by-case basis. Direct contact of rabies virus with mucous membranes (eg, saliva or neurologic tissue contact with the nose, mouth, or eyes) also poses a transmission risk.

Rabies virus is shed in the late stages of infection, as infected patients capable of transmitting rabies virus develop clinical signs and die within a short period of time. This results in a relatively short observation period (ie, usually 10 days) to determine whether an animal that has bitten another individual may have been shedding rabies virus at the time of the bite.

Any potential rabies exposure should be assessed by healthcare and public health professionals to determine the best response.

## Rabies Exposure in a Pet

Management of potential rabies exposure in a pet is designed to reduce the risk to both animals and humans. The 2 priorities to address first are the vaccination status of the bitten animal and whether the biting animal is available for observation or testing. Appropriate response is determined based on the regulations in the jurisdiction where the bite occurred and the specific scenario of each incident. Responses can include vaccination, observation, quarantine, and, in some cases, euthanasia.

In some areas, risk assessment can determine the appropriate response to rabies exposure in an unvaccinated domestic animal, depending on the likelihood of exposure based on the nature of the bite and rabies virus patterns and epidemiology in the area. In regions where the canine rabies virus variant is not present (eg, United States, Canada), dog-to-dog transmission of rabies is rare and most rabid domestic animals are infected by wildlife. For example, a bite to a pet dog from another pet dog that cannot be traced (eg, a roaming dog that bites another dog in a dog park), with no evidence of abnormal behavior, in a region with a very low incidence of rabies in domestic animals and wildlife, may be deemed a low enough risk that specific measures are not taken.

Guidelines for rabies exposure are not absolute, and specific responses may vary between or even within regions. Recommended observation or quarantine periods may vary. For example, in Ontario, Canada, observation periods are no longer recommended for vaccinated animals that are exposed but receive a booster vaccine within 7 days.<sup>3</sup> In Texas, exposed and unvaccinated animals must be vaccinated immediately, confined for 90 days, and given booster vaccines on weeks 3 and 8.<sup>4</sup> Familiarity with the regulations and recommendations related to rabies exposure in the specific practice area is important.

# Rabies Exposure in a Human

## Exposure by a Pet Dog, Cat, or Ferret

Management of potential rabies exposure in humans focuses on determining if there is a reasonable concern that the biting animal was shedding rabies virus.<sup>5</sup> Although rabies vaccination is highly effective in animals, there is no guarantee that a vaccinated animal does not have rabies. Therefore, the animal's vaccination status has no impact on the response to an animal biting a person.

The focus of response is instead on determining whether the animal might be rabid. The pet dog, cat, or ferret is ideally observed for 10 days because, if the animal is still alive and neurologically normal at the end of this period, he or she could not have been shedding rabies virus at the time of the bite. (See **Table 1.**)

The alternate approach involves testing (ie, euthanasia and brain analysis) that is typically undesirable. This alternative is best reserved for situations in which it is unsafe or inhumane to keep a biting animal alive for the observation period, when observation is otherwise difficult to perform, or if the animal shows signs of rabies at the time of the bite.

## Resource

- Compendium of animal rabies prevention and control, 2016. Brown CM, Slavinski S, Ettestad P, et al. *J Am Vet Med Assoc.* 2016; 248(5):505-517. doi:10.2460/javma.248.5.505

TABLE 1  
**Common Responses to Rabies Exposure in Humans<sup>a</sup>**

Scenario	Common Response
Person is bitten by a dog, cat, or ferret that is available for testing or observation	<ul style="list-style-type: none"><li>• Quarantine the biting animal for 10 days. If no evidence of rabies is seen after quarantine, no further action is needed.</li><li>• With severe bites to the head or neck, PEP is sometimes started immediately and then stopped if rabies is ruled out.</li></ul>
Person is bitten by a dog, cat, or ferret that is not available for testing or observation	<ul style="list-style-type: none"><li>• Perform a risk assessment based on the epidemiology of rabies in the area and the circumstances of the bite to determine whether PEP is indicated.</li></ul>
Person is bitten by a rabies reservoir species that is available for testing	<ul style="list-style-type: none"><li>• Await test results.</li><li>• With severe bites to the head or neck, PEP is sometimes started immediately and then stopped if rabies is ruled out.</li></ul>
Person is bitten by a rabies reservoir species that is not available for testing	<ul style="list-style-type: none"><li>• Perform a risk assessment based on the epidemiology of rabies in the area and the circumstances of the bite, with PEP most often recommended.</li></ul>

<sup>a</sup> Decisions should be made on a case-by-case basis by local public health or medical personnel.

## TAKE ACTION

- 1 Communicate the effectiveness of rabies vaccination and the legal implications of vaccinating and not vaccinating, and strongly recommend vaccination for all pets.
- 2 To facilitate a prompt, effective response to potential rabies exposure, ensure clear communication with relevant public health and animal health authorities and an understanding of current recommendations.

# Heartgard<sup>®</sup> Plus

(ivermectin/pyrantel)

## CHEWABLES

**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATIONS:** For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of ascarids (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

**DOSAGE:** HEARTGARD<sup>®</sup> Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	Cheewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older.

For dogs over 100 lb use the appropriate combination of these chewables.

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

**EFFICACY:** HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D. immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*).

**ACCEPTABILITY:** In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

**PRECAUTIONS:** All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus.

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

**Keep this and all drugs out of the reach of children.**

In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

**ADVERSE REACTIONS:** In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

**SAFETY:** HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

**HOW SUPPLIED:** HEARTGARD Plus is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251.



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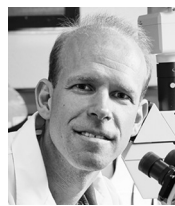
## Exposure by Wildlife

In situations in which the biting animal is a rabies-reservoir species (eg, fox, skunk, bat, raccoon, mon-goose), the bitten individual should seek medical and public health consultation and receive PEP. If the biting wildlife is available for testing, PEP can usually be delayed pending results. If the wildlife is unavailable, the individual should receive PEP right away.

Bites from non-rabies-reservoir species (eg, rats, squirrels, otters) should be assessed on a case-by-case basis (see **Table 1**, page 39), considering the circumstances of the bite (eg, the animal's behavior preceding the bite) and the epidemiology of rabies in that species and geographic region. ■

## References

1. Rabies. World Health Organization. <http://www.who.int/biologicals/areas/vaccines/rabies/en>. Published 2016. Accessed 2017.
2. Birhane MG, Cleaton JM, Monroe BP, et al. Rabies surveillance in the United States during 2015. *J Am Vet Med Assoc*. 2017;250(10):1117-1130.
3. Rabies in Ontario: post-exposure management. Ontario Ministry of Agriculture Food and Rural Affairs. <http://www.omafra.gov.on.ca/english/food/inspection/ahw/rabies.htm#22>. Updated April 26, 2017. Accessed June 5, 2017.
4. Rabies prevention in Texas. Texas Department of State Health Services. <https://www.dshs.texas.gov/idcu/disease/rabies/information>. Published 2016. Accessed 2017.
5. Weese JS, Fulford MB. *Companion Animal Zoonoses*. Ames, IA: Wiley Blackwell; 2011.



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**FUN FACT:** Dr. Weese's main "job" is coaching girls hockey. Also, a chinchilla was recently added to his family's menagerie, which already includes cats, alpacas, fish, a dog, and a llama.