



Common Misperceptions About Rabies Can Lead to Tragic Consequences

Misperception #1. Rabies is eradicated from the US.

It might be easy to think that rabies has been eradicated from the United States (US). Following the large-scale implementation of rabies vaccination programs targeted at dogs in the middle of the 20th century, the transmission of canine-variant rabies virus within this species has been eliminated.¹

However, in 2016 the US Centers for Disease Control and Prevention (CDC) reported 4910 cases of rabies in a variety of wild and domestic animals. The majority (91.4%) of cases were among wildlife, predominantly bats, raccoons, and skunks. The remainder (8.6%) occurred among domesticated animals, such as cats (257 cases), cattle (70 cases), and dogs (58 cases). This information highlights that rabies continues to circulate among wild and domesticated animals. Humans are also at risk as there have been 40 confirmed cases of rabies among humans in the US and Puerto Rico from 2003 through October 2017.²



Misperception #2. Nobody has died from rabies in the US for several decades.

The CDC has reported that over the course of the 20th century, the number of deaths due to rabies in the US declined from 100 cases per year to only 1 to 2 cases per year.³ Given this steep decline in human mortality from rabies, it is perhaps not surprising that many people may overlook the news reporting that rabies continues to inflict humans.

All but 3 of the 40 human cases of rabies reported in the US and Puerto Rico from 2003 through October 2017 resulted in death.² Two cases of human rabies were reported in

2017.² The first case was a 65-year-old woman from Virginia who traveled to India, was bitten by a dog in March 2017, but did not receive treatment with rabies postexposure prophylaxis (PEP). The second case was a 56-year-old woman from Florida who reported that she had been bitten on the hand by a bat but waited approximately 2 months before seeking medical care for symptomatic rabies. Early in 2018, a 6-year-old boy in Florida was reported to have died after exposure to a bat.⁴

Misperception #3. Rabies is not a problem in my area.

In 2016, with the exception of Hawaii, all states in the US (including Puerto Rico) reported at least several cases of rabies among samples from wildlife or domestic animals. However, there is a geographic variation across the US of the prevalence of rabies virus and the type of rabies virus variant among animals. States such as Delaware, Louisiana, Mississippi, and New Mexico reported fewer than 10 cases of rabies among tested animals. However, 11 other states reported hundreds of rabies cases, ranging from 146 cases in Massachusetts to 751 cases in Texas.²

Misperception #4. Individuals with rabies virus exposure always seek medical care.

Case reports and investigations by the CDC suggest that the public in the US does not often adequately appreciate the risk of rabies transmission, or the steps required to prevent rabies infection after a potential exposure.²⁻⁵ Reports of 3 human deaths in 2017 and 2018 highlight that exposed individuals often do not understand the extent of their injuries or the consequences of becoming ill with the virus. In each of these cases, the victims did not seek medical help immediately after the exposure and delayed seeking care until appearance of symptoms. Unfortunately, once a patient exhibits signs and symptoms of the disease, rabies is virtually 100% fatal and there is no consistently proven effective treatment.^{6,7}

Misperception #5. Rabid dogs are a thing of the past, so I do not have to worry about rabies.

Nationwide implementation of rabies vaccination programs targeted at dogs starting in the middle of the 20th century effectively eliminated canine-variant rabies virus transmission within this species by 2007.^{1,6}

However, dogs can still get infected with other variants of rabies virus through exposure to infected wildlife.^{1,6} Therefore, it is imperative that owners of dogs maintain the recommend rabies virus vaccination schedules.¹ Additionally, the adoption of dogs from countries in which rabies is endemic and rabies vaccination programs and appropriate quarantine periods are not properly implemented pose the risk of importing an infected dog into the US.^{1,6}

Individuals traveling abroad also need to be mindful that dogs continue to serve as the single most important rabies virus reservoir among animals in developing countries.^{2,7} The death of a 65-year-old woman from Virginia who was bitten by a rabid dog in India and died after returning to the US² serves as an important reminder of the potential dangers such animals can pose to travelers.

Misperception #6. Bats may carry rabies virus, but nobody comes into contact with them.

According to the CDC, in 2016, rabid bats were reported in 46 of the 48 contiguous states and were the leading species for rabies positivity across the US.² This reservoir of rabies virus among bats poses a risk of transmission of the virus to humans from an exposure.

Exposures to bats may be unintentional, as was the case of a 77-year-old woman from Wyoming in 2015 who was asleep but awoke to find a bat on her neck. The woman was evidently either not aware that this incident may have exposed her to rabies virus or did not know how to respond, since she did not receive rabies PEP and subsequently died of confirmed rabies infection.⁸

The possibility of exposure to bats during sleep led to the largest military investigation of rabies virus exposure in the US.⁹ A colony of approximately 400 to 600 bats was found to be nesting inside the walls of dormitory buildings at a US Air Force training center in San Antonio, Texas. Of the 922 trainees evaluated for potential exposure to bats, 200 were deemed to be at a sufficiently high risk and required rabies PEP. Fortunately, no human rabies infections were reported in this investigation. This case reinforces that humans, while sleeping, can be unknowingly exposed to bats, potentially allowing for transmission of the rabies virus from bat to human.

There are also instances when a bat exposure is known, but people fail to take appropriate action and seek medical care. In January 2018, a 6-year-old boy in Florida was described as intentionally touching and being scratched by a captured bat and subsequently dying of rabies after his parents failed to bring the boy for medical evaluation and care.⁴

Misperception #7. The clinical manifestations of rabies infection in animals are unique and easily discoverable.

While animals do show signs and symptoms of rabies infection, many of these clinical manifestations are not specific enough to provide a clear warning. The earliest clinical manifestations of rabies infection, such as fever, vomiting, and anorexia,¹⁰ can also be seen with many other illnesses and are not very helpful in aiding in the diagnosis of rabies infection in animals.

As rabies infection progresses, other features of infection, such as weakness, paralysis, seizures, difficulty breathing, difficulty swallowing, and excessive salivation, may manifest. Abnormal behaviors involving aggression, self-mutilation, and encephalitis may also become evident with disease progression.¹⁰

Misperception #8. A bite injury from a potentially rabid animal is easy to recognize.

An unprovoked attack and a bite from a dog or cat and any bite from a wild animal should be interpreted as potential rabies virus exposures. These scenarios are clear indications for seeking medical attention and evaluation for possible rabies infection. Additionally, other forms of exposure, such as a scratch or exposure of an open wound on a person's skin to saliva or neural tissue from a rabid animal, have the potential of transmitting the rabies virus.⁶

Unfortunately, bite injuries from smaller animals, such as bats, are sometimes difficult to detect. In this regard, any direct contact between a person and a bat should be considered a potential rabies virus exposure and an indication for rabies PEP unless the bat is captured and tests negative for rabies virus infection, or the person is reasonably certain that there was no bite, scratch, or mucous membrane exposure to saliva or neural tissue.⁶

If needed, healthcare professionals can contact their local or state public health officials for further assistance in evaluating individual cases for potential rabies virus exposure.

Misperception #9. The indications for administering rabies PEP are always clear to healthcare providers.

The CDC has published recommendations for evaluation of potentially rabid animals and administration of rabies PEP to humans exposed to those animals.⁶ The recommendations also cite that some situations may require consulting local or state public health officials. Those officials may, in turn, need to contact the CDC directly for guidance in rare or difficult situations. This guidance underscores the reality that frontline clinicians may not always know immediately how to handle potential rabies virus exposures and may need to consult other colleagues and experts to determine an appropriate course of action in individual cases.

CDC Guide for Evaluating the Need for Rabies PEP⁶

Animal type	Evaluation	Prophylaxis
Dogs, cats, and ferrets	Healthy; available for observation	No ^a
	Rabid or suspected rabid	Yes
	Unknown	Consult public health officials
Bats, most carnivorous wild mammals	Regard as rabid ^b	Yes
Livestock, large rodents (eg, groundhogs), small rodents, lagomorphs (eg, rabbits, hares), other mammals	Consider individually	Consult public health officials Bites from small rodents, rabbits, and hares almost never require PEP

^a Unless animal develops clinical signs of rabies during the 10-day observation period.

^b Unless animal tests negative for rabies.

Misperception #10. Wound care and rabies vaccination are usually enough to manage the risk of rabies infection.

People who have come in contact with a potentially rabid animal may be unaware of the risk of rabies transmission and simply disregard the incident and not seek medical care.²⁻⁵ Healthcare professionals may also not be very familiar with how to handle such situations. Care of such patients involves evaluation of the wound and determination of the patient's rabies vaccination history before planning further care.¹¹

Wound care includes cleansing with soap and water. If available, a virucidal agent, such as povidine-iodine solution, can also be used to irrigate the wound.^{11,12}

Subsequent management depends on the patient's rabies vaccination history¹¹:

1. Patients who have not been previously vaccinated against rabies should receive rabies PEP that includes four 1-mL doses of a rabies vaccine, with the first dose given as soon as possible after the exposure incident (the date of the first dose is defined as day 0 of the rabies PEP regimen). The vaccine doses should be administered intramuscularly into the deltoid area in adults and in the anterolateral aspect of the thigh in children. The remaining 3 subsequent vaccine doses should be administered on days 3, 7, and 14.

These patients should also receive a dose of human rabies immune globulin (HRIG) on day 0. The HRIG dose should be injected into and around all wound areas, with any remaining HRIG volume injected intramuscularly at a site away from the rabies vaccine administration site to avoid interaction with the vaccine.

2. Patients who have previously been vaccinated with the rabies vaccine should not receive HRIG but should receive additional doses of vaccine. Specifically, these patients should receive two 1-mL doses of vaccine on days 0 (day of first vaccine dose) and 3.

Misperception #11. Rabies PEP requires multiple, painful, intra-abdominal injections over a 1-month period.

Current CDC guidance for rabies PEP does not require any intra-abdominal injections. Instead, intramuscular injections of rabies vaccine plus injection of HRIG into and around the wound areas are recommended for patients who have not been previously vaccinated against rabies. In total, these patients would receive four 1-mL doses of vaccine, starting on day 0 (the day of the first vaccine dose) followed by 3 more vaccine doses on days 3, 7, and 14, plus HRIG on day 0.¹¹

Patients who have been previously vaccinated only require two 1-mL intramuscular injections of the rabies vaccine on days 0 and 3.¹¹

Misperception #12. During HRIG administration, 50% of the dose should be injected into and around the wound, and the remaining 50% should be administered elsewhere at distant sites.

Neither the CDC nor the World Health Organization (WHO) recommend this 50/50 split of the HRIG dose as a component of rabies PEP.^{11,13}

Existing CDC guidelines recommend that HRIG be administered at a dose of 20 IU/kg body weight, with the full dose infiltrated around and into the wound(s), if anatomically feasible. Any remaining volume from the HRIG dose should be administered by intramuscular injection at an anatomical site distant from the site of vaccine administration.¹¹

The latest guidance from the WHO reinforces the efficacy of infiltrating the HRIG dose, calculated according to body weight, into and around the wound.¹³

Clinicians face a critical challenge when deciding how to administer HRIG to patients of varying body sizes and wound sizes. Small patients with large wounds need to be handled differently from large patients with small wounds. For a low-body-mass patient with a large wound, the clinician needs to determine how a relatively small HRIG dose can be extended to provide adequate coverage of the affected area.¹⁴ At the other extreme, the clinician will need to take a different approach when treating a small wound in a large-body-mass patient; the challenge here is to administer a sufficient volume of HRIG into that small area without risking creation of a compartment syndrome.¹⁴ A

higher-concentration HRIG formulation (300 IU/mL) may be an option in these cases. A higher-concentration product delivers more antibodies per milliliter into and around the wound sites.

Misperception #13. HRIG should be administered only for severe bite injuries.

The CDC recommends that previously unvaccinated people who may have been exposed to rabies virus through bite or nonbite exposures should receive rabies PEP with HRIG and rabies vaccine.¹¹ If at any time lab testing of the suspected source shows that the animal was not rabid, then rabies PEP may be stopped.¹¹ Administration of rabies biologics is not dependent on the severity of the bite as scratch and minor bite injuries can also be a source of infection.⁶

Rabies vaccine and HRIG should be given to all persons suspected of exposure to rabies virus with the exception of individuals who have previously been immunized with rabies vaccine.¹¹ HRIG should be administered as soon as possible after exposure, preferably at the same time as the first dose of the rabies vaccine is administered.¹¹ HRIG should be administered no later than day 7 after the first dose of the rabies vaccine is administered (counted as day 0).¹⁵ Beyond day 7 after administering rabies vaccine, HRIG is not indicated since an antibody response to vaccine is presumed to have occurred.¹⁵

Indication and Usage

HYPERRAB[®] (rabies immune globulin [human]) is indicated for postexposure prophylaxis, along with rabies vaccine, for all persons suspected of exposure to rabies.

Limitations of Use

Persons who have been previously immunized with rabies vaccine and have a confirmed adequate rabies antibody titer should receive only vaccine.

For unvaccinated persons, the combination of HYPERRAB and vaccine is recommended for both bite and nonbite exposures regardless of the time interval between exposure and initiation of postexposure prophylaxis.

Beyond 7 days (after the first vaccine dose), HYPERRAB is not indicated since an antibody response to vaccine is presumed to have occurred.

Important Safety Information

For infiltration and intramuscular use only.

Severe hypersensitivity reactions may occur with HYPERRAB. Patients with a history of prior systemic allergic reactions to human immunoglobulin preparations are at a greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available for treatment of acute allergic symptoms, should they occur.

HYPERRAB is made from human blood and may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

The most common adverse reactions in >5% of subjects during clinical trials were injection-site pain, headache, injection-site nodule, abdominal pain, diarrhea, flatulence, nasal congestion, and oropharyngeal pain.

Do not administer repeated doses of HYPERRAB once vaccine treatment has been initiated as this could prevent the full expression of active immunity expected from the rabies vaccine.

Other antibodies in the HYPERRAB preparation may interfere with the response to live vaccines such as measles, mumps, polio, or rubella. Defer immunization with live vaccines for 4 months after HYPERRAB administration.

Please see accompanying full Prescribing Information for HYPERRAB.

**You are encouraged to report negative side effects
of prescription drugs to the FDA. Visit www.fda.gov/medwatch,
or call 1-800-FDA-1088.**

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