

Approach with an Abundance of Caution— Increasing Awareness of Rabies Risk

Advances in rabies vaccines—such as routine vaccination of domestic animals and accessibility to modern postexposure prophylaxis (PEP)—have greatly reduced exposure incidents and raised the efficacy of PEP to essentially 100%.¹ The number of rabies-related human deaths in the United States (US) declined from more than 100 annually at the turn of the 20th century to one or two per year in the 1990s.¹

This reduction may contribute to a general lack of awareness and the failure of patients and healthcare professionals to consider the risk of rabies following possible exposures.¹ In the US, two recent cases of rabies failed to be identified by healthcare professionals when patients presented to urgent care and emergency department (ED) environments, resulting in the patients' deaths.^{2,3}

In November 2018, a 55-year-old Utah man died from rabies following contact with a bat. When he first presented to his local ED with neck and back pain, he was sent home with steroids and other pain management treatment intended for a potential pulled muscle. Following his death, the Utah Department of Health as well as this man's family released statements hoping to elevate public awareness.^{3,4} Bats are the most common source of rabies in Utah, according to Utah Department of Health epidemiologist Dallin Peterson. Peterson also noted that a bite or scratch from a bat may not be felt by the receiver because a bat's teeth and claws are very small.⁴



Gary Gilles, 55-year-old Utah man, with his granddaughter.
The family wants others to be aware of risk.

Likewise, in May 2017, a 65-year-old Virginia woman died from rabies following contact with a dog while visiting a yoga retreat in India.² After returning to the US and seeking help at an urgent care facility for arm pain, she was diagnosed with carpal tunnel syndrome and discharged with a nonsteroidal anti-inflammatory drug and hydrocodone. The next day she was evaluated at a regional hospital with shortness of breath, anxiety, insomnia, and difficulty swallowing water. The patient expressed concern about the possibility of having been exposed to a toxic substance. She was given lorazepam for a presumed panic attack and discharged. On the following day, she was transported to the ED of another hospital with chest discomfort, shortness of breath, and increased anxiety. She died two weeks later.

Regarding the latter case, the Virginia health district of the two hospitals and urgent care facility that were involved initiated a local public health investigation to assess exposure risk and assist in the implementation of the Advisory Committee on Immunization Practices (ACIP) recommendation for PEP.² Delayed or missed diagnosis puts everyone at risk. Of the 258 employees identified for rabies exposure risk, 250 were located and assessed, and PEP was recommended for approximately one-third (figure 1). At one point during the care of the patient, enhanced contact precautions were implemented due to the development of an antibiotic-resistant urinary tract infection in the patient. This provided an opportunity to assess reported exposures before and after implementation of these precautions. The rate of daily PEP recommendations decreased significantly after diagnosis of rabies but not after implementation of enhanced contact precautions.

“I had no clue. We would wake up in the night and they [bats] would be walking on our bed.”

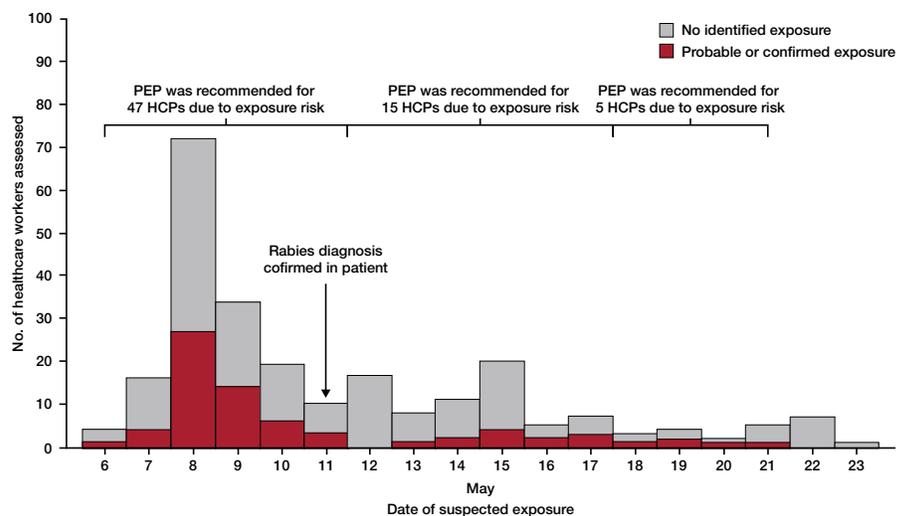
—Juanita Gilles

Since rabies is nearly always fatal once symptoms develop, all potential exposures must be taken seriously and awareness is key. Anyone who is bitten by or has bare-skin contact with a bat, or any other potential contact with a bat (such as waking up in a room with a bat) *should be considered as having been exposed to rabies and treated accordingly*. The rabies virus carried by dogs has all but been eliminated from the US, but remains widespread in many developing countries and is one of the leading global causes of human death.⁵ Still, all dog bites—especially when vaccination history is uncertain (eg, unfamiliar or wild dogs)—carry a risk of infection and assessment for need of PEP care is an essential step in the appropriate management.⁶

ACIP Recommendations

In the event of a suspected rabies exposure, ACIP recommends PEP as soon as possible.⁷ PEP has been shown to be highly effective at preventing rabies if administered prior to symptom onset. Persons with a history of vaccination should receive a 2-dose booster vaccination series if exposed, while persons with no history of vaccination require a 4-dose vaccination series with rabies immune globulin administered at the site of exposure.

Figure 1. Delayed or Missed Diagnosis Puts Everyone at Risk. Number of Healthcare Professionals (HCPs) at Risk Before and After Confirmed Rabies Diagnosis and Implementation of Enhanced Precautions—Virginia, 2017^{2*}

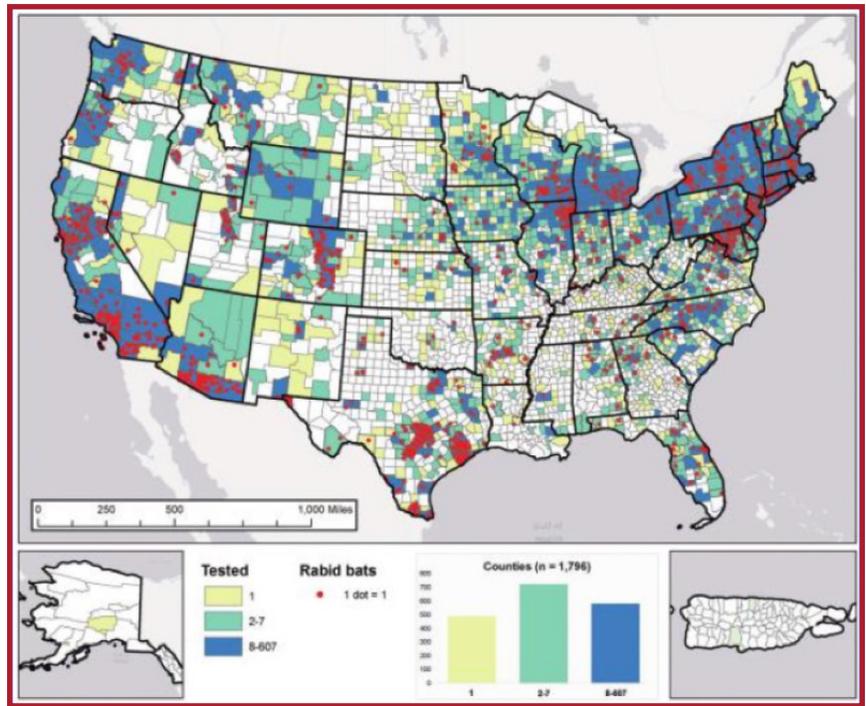


*Guidelines for precautions are available online at <https://www.cdc.gov/infectioncontrol/guidelines/isolation/appendix/standard-precautions.html>. “Enhanced precautions” were implemented in response to the patient’s urinary tract infection.

Bottom Line: Rabies Is Still a Threat

The overall conclusion is that, despite great progress against rabies, the risk to humans still remains and awareness of that risk is important for the general public and for HCPs. Bats are the leading rabid species and the most common mode of transmission in the US.^{8,9} Forty-seven jurisdictions reported rabid bats in 2017 with five (Arkansas, Delaware, New Hampshire, New Mexico, and the District of Columbia) reporting a $\geq 50\%$ increase from the previous year (figure 2).⁸ Feral cats and wild dogs also remain a public health concern.¹⁰

Figure 2. Bats Tested For Rabies (2017)



Adapted from Ma 2018

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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.**