Bats Are Unique and Dangerous Sources of Rabies:
An Illustrative Case of Human Fatality

The most common virus variants responsible for rabies in humans are bat-related.\textsuperscript{1,2} Of the 26 cases of rabies acquired in the United States or Puerto Rico since 2003, a bat was implicated as the source of infection in 65% (ie, 17 cases), including 7 cases with a reported bat bite, 6 cases without a reported bite but with known bat exposure, and 4 cases without a known exposure to bats.\textsuperscript{2} Injuries associated with bat encounters can be difficult to determine, as bat bites or even scratches are much less obvious than those associated with raccoons or foxes.\textsuperscript{1,2} Furthermore, some bat-related rabies viruses may be more likely than other rabies viruses to result in infection after inoculation into relatively superficial wounds of the epidermal layers.\textsuperscript{1,3} Because of the uniqueness of bat exposures, these situations must be considered high risk\textsuperscript{4} and postexposure prophylaxis (PEP) should be considered in any situation where there may have been human contact with a bat.\textsuperscript{1,2} (See box on next page.)

Rabies Fatality Reported in Missouri in 2014

A recently reported case of a 52-year-old Missouri man with known bat exposure but no known bites who died from rabies 2 weeks after he first visited an emergency department underscores the threat of delayed recognition of rabies exposure in general, and bat exposure more specifically.\textsuperscript{2,4} The patient initially presented to an emergency department on September 12 with an acute, unexplained encephalitis manifesting as neck pain, paresthesia, and tremors and progressing over several days to the point of requiring intubation and other life support efforts (See Figure. Timeline of Events in Reported Fatal Case of Rabies in 52-Year-Old Missouri Man).\textsuperscript{4} A broad set of evaluations including a drug screen, an arbovirus panel, tricyclic antidepressant levels, and testing for Rocky Mountain spotted fever, ehrlichiosis, syphilis, and herpes simplex virus were uniformly negative, leading to a consideration of rabies as the underlying cause. Rabies testing was initiated on September 18 and rabies was confirmed on September 24, 12 days after the patient’s initial emergency department visit. The patient died shortly after life support was removed on September 26.

The virus variant identified from the patient was ultimately found to be from a tricolored bat. Although this variant can infect species other than bats, a public health investigation determined

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that a bat was the most likely source of rabies infection in this patient. Among other notable factors, the patient, who lived in a rural, deeply wooded area, had reported seeing a bat in his home in late August or early September 2014 and worked in a warehouse where bats were occasionally seen. Heightened concern for the appearance of a bat in his home may have led to PEP for this patient; clearly, the need for education about potential sources of rabies in the US and the urgency of promptly seeking medical attention after any potential rabies exposure remains high.4

### Bats and Rabies: Implications for Emergency Departments, Public Health Departments, and the Public

- **Bats should be kept out of houses and public buildings**
- **Contact with a bat is a high-risk exposure that deserves special assessment**: any direct contact between a person and a bat should be evaluated as a potential exposure.
- **If possible, bats involved in potential human exposures should be safely collected and submitted for rabies diagnosis**.
- **PEP, which includes thorough wound washing and the administration of both the rabies vaccine and human rabies immune globulin (HRIG), should be considered for any direct human contact with a bat unless**:
  - There is absolute certainty that a bite, scratch, or mucous membrane exposure did not occur or
  - The bat can be captured and tests negative for rabies
- **PEP should also be considered in situations where the level of contact with a bat is uncertain**, such as:
  - If a bat is discovered in a room with a sleeping person, or if a person awakens to find a bat in the room
  - If a bat is found in a room with an unattended child, intellectually impaired person, or a person who is intoxicated

HRIG is made from human plasma. Plasma products carry a risk of transmitting infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.

Soreness at the site of injection and mild temperature elevations may be observed at times. Sensitization to repeated injections has occurred occasionally in immunoglobulin-deficient patients. Angioneurotic edema, skin rash, nephrotic syndrome, and anaphylactic shock have rarely been reported after intramuscular injection so that a causal relationship between immunoglobulin and these reactions is not clear.

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Figure. Timeline of Events in Reported Fatal Case of Rabies in 52-Year-Old Missouri Man

Sept 12: Initial ED Visit
• Acute onset of severe neck pain radiating down left arm to hand
• Initial dx: cervical muscle strain and radiculopathy

Sept 13: Second ED Visit
• Numbness/tingling in left arm
• Severe bilateral upper body tremors
• Sweating
• Continued neck pain
• Dx: herniated disc

Sept 14: Transferred to Tertiary Care Hospital for Neurological Evaluation
• Condition progressively worsens
• Rigidly and action tremors in upper extremities
• At admission to tertiary care: febrile, tachycardic, tachypneic, and hypertensive with bilateral upper extremity tremors and whole body myoclonic jerks

Sept 15: Third ED Visit
• Symptoms progress
• Patient becomes anxious and fearful
• Visual hallucinations
• Admitted with suspicion of serotonin syndrome secondary to cyclobenzaprine prescribed Sept 12

Sept 16: Transferred to Tertiary Care Hospital for Neurological Evaluation
• Condition progressively worsens
• Rigidity and action tremors in upper extremities
• At admission to tertiary care: febrile, tachycardic, tachypneic, and hypertensive with bilateral upper extremity tremors and whole body myoclonic jerks

Sept 18: RABIES TESTING INITIATED
• MO Dept of Health and Senior Services notified of potential case

Sept 19-Sept 26
• Traumatic lumbar puncture yields hemorrhagic CSF with elevated glucose, protein, and white blood cells (Sept 19)
• EEG studies show minimal generalized slowing of brain activity
• Patient requires cardiovascular support, continuous mechanical ventilation, and hemodialysis

Sept 24: RABIES CONFIRMED
• Rabies virus antigen in skin biopsy
• Rabies virus detected in saliva and skin by RT-PCR
• Virus variant associated with tricolor bat

Sept 26: PATIENT DEATH
• Life support withdrawn given advanced stage of illness and worsening prognosis

CSF, cerebrospinal fluid; dx, diagnosis; ED, emergency department; EEG, electroencephalogram; MO, Missouri; RT-PCR, reverse transcription polymerase chain reaction.

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IMPORTANT SAFETY INFORMATION

Rabies vaccine and HyperRAB® S/D (rabies immune globulin [human]) should be given to all persons suspected of exposure to rabies with one exception: persons who have been previously immunized with rabies vaccine and have a confirmed adequate rabies antibody titer should receive only vaccine. HyperRAB S/D should be administered as promptly as possible after exposure, but can be administered up to the eighth day after the first dose of vaccine is given.

HyperRAB S/D should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations.

The attending physician who wishes to administer HyperRAB S/D to persons with isolated immunoglobulin A (IgA) deficiency must weigh the benefits of immunization against the potential risks of hypersensitivity reactions. Such persons have increased potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA.

As with all preparations administered by the intramuscular route, bleeding complications may be encountered in patients with thrombocytopenia or other bleeding disorders.

Soreness at the site of injection and mild temperature elevations may be observed at times. Sensitization to repeated injections has occurred occasionally in immunoglobulin-deficient patients. Angioneurotic edema, skin rash, nephrotic syndrome, and anaphylactic shock have rarely been reported after intramuscular injection so that a causal relationship between immunoglobulin and these reactions is not clear.

Administration of live virus vaccines (e.g., MMR) should be deferred for approximately 3 months after rabies immune globulin (human) administration.

HyperRAB S/D is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent that can cause disease. There is also the possibility that unknown infectious agents may be present in such products.

Please see HyperRAB S/D full Prescribing Information for complete prescribing details.

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.
REFERENCES

Please see Important Safety Information at the end of this article and HyperRAB® S/D [rabies immune globulin (human)] full Prescribing Information for complete prescribing details.

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