BATS AND RABIES
WHAT RABIES PROPHYLAXIS IS NEEDED AND WHEN?

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There currently is no effective treatment for rabies, an almost always fatal disease. Bats are increasingly being implicated as the principal wildlife reservoir for rabies transmission to humans. The best we can do is to aim for prevention by reducing the possibility of exposure and to apply prophylactic measures if exposure occurs.

Rabies is a lethal disease caused by ribonucleic acid (RNA) viruses of the family Rhabdoviridae and genus Lyssavirus.¹ This worldwide zoonosis may infect all mammals, including humans. Eleven rabies species have been identified, with all but 1 genotype being found in bats.²

Over the past 2 decades, bats have been reported as the most frequent carriers of human rabies infections in the United States.¹

Among a notable number of human rabies patients, a history of prior contact with bats was not elicited. As a result, postexposure prophylaxis for such patients was not provided.³⁴

Exposure to the clinically ill mammal carrier occurs most often through a bite or scratch. The incubation period of lyssaviruses may range from days to several years but is most frequently between 2 and 12 weeks.⁵⁶ The virus then enters the central nervous system and causes acute encephalomyelitis, which is almost always fatal (Figure 1).⁶⁷

Reliably effective treatment of rabies is not currently available. As a result, the primary means for averting deaths attributed to rabies is through prophylactic measures.

Prevention of the disease in man is possible by reducing the probability of exposure to the virus from potentially rabid animals, as well as through the application of preexposure and postexposure strategies.⁸

Annually, 16,000 to 39,000 people in the United States are potentially exposed to rabies and receive effective postexposure prophylaxis (PEP) to deter the development of rabies.¹⁸

The direct cost of PEP is estimated to be around $2,500, and treatment is often administered unnecessarily.⁹¹⁰

After the effective prevention of canine rabies...
in the United States, the primary maintenance of rabies virus has been among wildlife species. Over the past 2 decades, the majority of naturally acquired, indigenous human rabies cases in the United States were primarily associated with exposure to rabid bats.

Bats and rabies

Bats constitute the sole mammalian species with the ability to fly. In excess of 1,100 species of bats have been documented globally. More than 30 rabies-infected bat species have been reported in the United States, with multiple viral lineages associated with different bat species. Rabid bats are increasingly implicated as the principal wildlife reservoir for rabies transmission to humans. Subclinical rabies infections have been described among several bat species worldwide. Viral RNA has been detected in the saliva, blood, and various organs of healthy bats captured in field colonies; however, most cases detected so far have been in either diseased or deceased animals.

Moreover, experimental infection of bats with rabies most often leads to short excretion and rapid death. The rabies virus is inactivated by desiccation and ultraviolet irradiation, and it does not persist outside the infected animal.

Bat rabies virus variants associated with silver-haired bats (Lasionycteris noctivagans) and eastern pipistrelles (Pipistrellus subflavus) have biologic characteristics that might allow for an elevated likelihood of infection after superficial inoculation, including infection of epidermal cells.

Although bats described as having aggression, ataxia, disorientation, or lethargy are significantly more likely to have rabies than those with none of these signs, bats found dead are no more likely to have rabies than those reported alive before submission for examination.

Rabies is reported in less than 1% of free-ranging bats and is diagnosed in 5% to 15% of bats submitted for public health evaluation.

**Epidemiology of bat rabies**

From 1990 to 2007, 34 human rabies cases associated with bats were reported in the United States. Bite or contact with a bat was reported in the minority of cases (6 and 2, respectively), whereas no bite but possible physical contact was reported in 15 cases (presence of a bat in home or workplace or in the room where the person had been sleeping).

In 11 cases, no encounter with a bat was reported. In these cases, after matching the genetic sequences of the human rabies viruses with those of bats, the most plausible hypothesis is that an unreported or undetected bat bite had occurred.

Clustering of human cases associated with bat exposures within the same family, group, or community has
BATS AND RABIES

never been reported in the United States.1,19,20

A decrease in the absolute number of reported rabid bats was noted during 2009.14 The proportion of bats submitted for testing that were rabid decreased from 5.9% in 2008 to 5.8% in 2009. Rabid bats were reported in all 48 contiguous states. Eight states (Idaho, Illinois, Indiana, Mississippi, Nevada, Oregon, Utah, and Washington) reported rabies only in bats.

A 50% or higher increase in the number of rabid bats was reported in 8 states (Arkansas, Indiana, Maryland, North Carolina, New Hampshire, New Mexico, Oklahoma, and West Virginia). No human rabies cases were reported during the first 7 months of 2010.14,21

Most states have a rabies hotline to get information about exposures and treatment. Contact details for state and local consultation offices are available online (www.cdc.gov/rabies/resources/contacts.html).

Who needs postexposure prophylaxis after bat contact?
The necessity of postexposure prophylaxis for rabies after bat contact poses special challenges. Exposures could occur in circumstances considered otherwise negligible because of the limited injury inflicted by the bat.

Transmission of bat rabies virus can occur from minor and/or underappreciated or unrecognized bites or lesions. In human rabies cases thought to be of bat origin in the United States, 60% of cases in the 1990s and 17% of cases after 2000 did not report a bat bite.14 This may be attributed to the limited bite size inflicted, lack of realization of previous bat exposure, and/or a recall bias secondary to the manifestation of rabies.22 For these reasons, any direct exposure to a bat should be evaluated for a potential exposure to rabies.

If it is feasible, bats involved in potential human exposures should be submitted for rabies diagnosis to specialized laboratories in a timely and secure manner. If it is deemed that the bat is not rabid, as in most cases of surveyed bats (approximately 94%), there is no need for further investigations or postexposure prophylaxis.1,11

The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention has made recommendations regarding rabies exposure evaluation of persons with direct contact with bats, as well as persons who may have had an unacknowledged contact with bats.1,7

Direct contact is defined as bite, scratch, and/or mucous membrane exposure (abrasions, open wounds) with a bat.

Indirect contact includes those situations in which a deeply sleeping person awakens to find a bat in the room, an adult witnesses an unattended child sleeping in a room with a bat, or a mentally disabled or intoxicated person finds a bat in a room.

If a person can be reasonably certain that a bite, a scratch, or mucous membrane contact did not occur, or the bat is available for testing and is negative for the presence of rabies virus after laboratory evaluation, PEP is not necessary (Table 1).1 In more complex situations in which there is doubt about the type of exposure, consultation with either an infectious diseases specialist or local health department professional should be sought.

Table 1 When to give prophylaxis after bat exposure

<table>
<thead>
<tr>
<th>Give prophylaxis</th>
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</thead>
<tbody>
<tr>
<td>Bat is not available and there is</td>
</tr>
<tr>
<td>• Certain contact</td>
</tr>
<tr>
<td>- Bite</td>
</tr>
<tr>
<td>- Scratch</td>
</tr>
<tr>
<td>- Mucous membrane contact</td>
</tr>
<tr>
<td>• Possible contact</td>
</tr>
<tr>
<td>- Deeply sleeping person awakens to find a bat in the room</td>
</tr>
<tr>
<td>- Adult witnesses a bat in the room of a previously unattended child or a mentally disabled or intoxicated person</td>
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<table>
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<tr>
<th>Do not give prophylaxis</th>
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</thead>
<tbody>
<tr>
<td>• Bat testing is negative for rabies</td>
</tr>
<tr>
<td>• Reasonable certainty from an aware person of no possible contact</td>
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</tbody>
</table>

Information from Manning SE, et al.1
What type of postexposure prophylaxis is appropriate?

Postexposure prophylaxis for the prevention of rabies in humans exposed to the rabies virus should be given as soon as possible and includes 3 steps: 1) prompt and thorough wound cleansing, 2) passive vaccination with human rabies immune globulin (HRIG), and 3) vaccination with cell culture rabies vaccines (Table 2; Figure 2). This combined prophylaxis has been found uniformly effective when appropriately administered.

When a documented or likely bat exposure has occurred, postexposure prophylaxis should be administered regardless of the length of the delay because the incubation period may extend over several years. In a person who already has clinical signs compatible with rabies, the administration of postexposure prophylaxis has been demonstrated to be consistently ineffective.

The combination of HRIG and vaccine is recommended for both bite and nonbite exposures reported by persons who have never been previously vaccinated for rabies, regardless of the interval between exposure and initiation of prophylaxis. If postexposure prophylaxis has been initiated and appropriate laboratory diagnostic testing (ie, the direct fluorescent antibody test) indicates that the exposing animal is not rabid, postexposure prophylaxis may be discontinued.

Because of the potential consequences of inadequately managed rabies exposure, pregnancy is not considered a contraindication to postexposure prophylaxis.

TREATMENT OF WOUNDS

Wound cleansing is especially important in rabies prevention because thorough wound cleansing alone without other postexposure prophylaxis had been shown to reduce the likelihood of rabies in animal studies.

Immediate gentle irrigation with water or a dilute water-povidone-iodine solution should be performed with special care so as not to damage skin or tissues (Table 2).

RABIES IMMUNE GLOBULIN

Use of rabies immune globulin (RIG) provides a rapid, passive immunity that extends over a limited time period because the RIG half-life approximates 21 days. Two antirabies immune globulin (IgG) formulations prepared from hyperimmunized human donors have been licensed and are currently available in the United States (Table 3). It is recommended that HRIG should be administered concurrently with the

<table>
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<th>TABLE 2</th>
<th>Rabies postexposure prophylaxis schedule—United States 2010</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>Regimen</td>
</tr>
<tr>
<td>Wound cleansing</td>
<td>Immediate, thorough cleansing of all wounds with soap and water. If available, a virucidal agent (eg, povidone-iodine solution) should be used to irrigate the wounds.</td>
</tr>
<tr>
<td>HRIG</td>
<td>Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (IM) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.</td>
</tr>
<tr>
<td>Vaccine</td>
<td>Human diploid cell vaccine or purified chick embryo cell vaccine 1.0 mL, IM (deltoid area), for immunocompetent persons. 4 doses (1 each on days 0, 3, 7 and 14) for immunocompetent persons.</td>
</tr>
</tbody>
</table>

Abbreviations: HRIG, human rabies immune globulin; IM, intramuscular; RIG, rabies immune globulin.

a. The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.

b. For persons with immunosuppression, rabies postexposure prophylaxis should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

Information from Rupprecht CE, et, and Committee on Infectious Diseases.
first vaccine dose in all postexposure prophylaxis regimens with the exception of previously vaccinated individuals.

HRIG is administered only once (ie, at the initiation of antirabies prophylactic treatment) to previously unvaccinated individuals in order to provide immediate, passive, rabies virus-neutralizing antibody coverage until the patient responds to human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) by actively producing antibodies. If not administered concurrently with the vaccine, HRIG may be administered through the seventh day of the postexposure prophylaxis treatments. Beyond this time, the administration of HRIG is not recommended, because an antibody response to the cell culture vaccine is presumed to have occurred. Because HRIG can partially suppress active antibody production, the administered dose should not exceed the recommended dose of HRIG (20 IU/kg for all age groups).

If it is anatomically feasible, the full dose of HRIG should be thoroughly infiltrated in those areas around and into the wounds. Any remaining volume should be injected intramuscularly (IM) at a site distant from that of the vaccine administration. HRIG should never be administered in the same syringe or in the same anatomic site as the first vaccine dose. However, subsequent doses of the vaccine in the 4-dose series can be administered in the same anatomic location where the HRIG dose was administered, should this be the preferable site for vaccine administration (ie, deltoid for adults or anterolateral thigh for infants and young children).

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Postexposure prophylaxis regimen for rabies. Information from Committee on Infectious Diseases.11

![Figure 2](https://example.com-figure2.png)

1. Thorough cleansing of the wound
2. Vaccination (4 doses at 0, 3, 7, and 14 d intramuscularly)
3. Rabies immunoglobulin (time 0): 20 IU/Kg intramuscularly at different site from the vaccine

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**TABLE 3** Rabies biologic products available in the United States

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose</th>
<th>Route</th>
</tr>
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<tbody>
<tr>
<td>Rabies immune globulin*</td>
<td>20 IU/Kg</td>
<td>Local</td>
</tr>
<tr>
<td>Human rabies vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human diploid cell vaccine</td>
<td>1 mL</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Purified chick embryo cell vaccine</td>
<td>1 mL</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

a. As much of the product as is anatomically feasible should be infiltrated into and around the wound. Any remaining product should be administered intramuscularly in the deltoid or quadriceps (at a location other than that used for vaccine inoculation to minimize potential interference). Information from Manning SE, et al.

**VACCINATION**

Initially, guidelines for vaccination schedules recommended 5 doses for immunocompetent patients. However, recently it was recommended that the number of vaccine doses be reduced to 4. This policy was also endorsed by the American Academy of Pediatrics. The first dose of the 4-dose vaccination schedule should be administered as soon as possible after exposure (Table 2, Figure 2). This date is identified as day 0 of the postexposure prophylaxis series. Additional doses should then be administered on days 3, 7, and 14 after the initial vaccination date. For immunosuppressed persons, an additional fifth dose should be administered on day 28. Immunosuppressive agents should not be administered during postexposure prophylaxis unless they are essential for the treatment of other concomitant conditions. Two rabies vaccines are available for use in the United States (Table 3) and can be given in conjunction with HRIG. Once interrupted, rabies prophylaxis should not be administered on schedule. No testing of patients completing preexposure or postexposure prophylaxis is necessary to document seroconversion unless the person is immunosuppressed. Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local or mild systemic adverse reactions to the rabies vaccine. The HDCV used in Canada and the United States has been associated with allergic reactions (11 cases per 10,000 vaccinated persons, 9 of which were type 1 anaphylactic reactions). Usually such reactions can be successfully managed with epinephrine administration. When a person with a history of severe reactions to the rabies vaccine must be revaccinated, empiric intervention, including pretreatment with antihistamines, may be considered.

**Prevention strategy**

Rabies is associated with the highest case-fatality ratio among infectious diseases. Rabies control in bats by conventional methods is not currently feasible. Prevention of human rabies infection from bat rabies virus continues to be dependent on careful assessment of exposed persons and judicial administration of postexposure prophylaxis.

**Points Taken**

- Two rabies vaccines are available for use in the United States and can be given in conjunction with HRIG.
- Once started, rabies prophylaxis should not be interrupted or discontinued.

Dose Route Rabies vaccines induce an active immune response that includes the production of virus-neutralizing antibodies. The active antibody response requires approximately 7 to 10 days to develop, and detectable rabies virus-neutralizing antibodies generally persist for several years thereafter. A vaccination series is usually initiated and completed with 1 vaccine product. Once vaccination has been initiated, delays of a few days longer than the recommended interval are not thought to reduce effectiveness. However, the potential effect of delays in vaccine dose administration extending several weeks remains unknown. For most cases with minor deviations from the original vaccination schedule, vaccine doses may be administered as though the patient were on schedule. No testing of patients completing preexposure or postexposure prophylaxis is necessary to document seroconversion unless the person is immunosuppressed.
REFERENCES


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