DATE
June 4, 2020

SUBJECT Rabies Post Exposure Prophylaxis Administration

INSTRUCTIONS

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Categories of Health Alert Messages:

Health Alert: conveys the highest level of importance; warrants immediate action or attention.

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hhshan@mt.gov

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Rabies Post Exposure Prophylaxis (rPEP) Regimen Administration for Vaccinated and Unvaccinated Patients

BACKGROUND

Potential rabies exposures tend to increase in incidence during the spring and summer months due to an increased likelihood for contact between humans and animals. Exposure to a human by a species susceptible to rabies infection is a reportable condition to local health departments. Local health officers and their designated staff are tasked with making a recommendation for rPEP based on the circumstance of the exposure and animal species.

In the US, there are two ACIP recommended rPEP regimens. Patients who are not previously vaccinated are recommended to receive both Human Rabies Immunoglobulin (HRIG) and a four-dose rabies vaccination series (five doses for those with certain types of immunosuppression) for known or potential exposures to rabies. HRIG should always be administered for unvaccinated patients regardless of exposure type. Withholding HRIG from a rPEP series may result in an rPEP failure. Patients who have been previously vaccinated should receive a two-dose vaccine series without the administration of HRIG. The regimens as outlined below are nearly 100% efficacious when administered as recommended.

Additionally, these regimens are the only treatment available for exposures and should be administered once it has been determined with local public health departments that a rabies exposure occurred or cannot be ruled out even if there has been a delay in identification. These recommendations are outlined in more detail in the following sections.

INFORMATION FOR HEALTHCARE PROVIDERS

The need for rPEP is determined based on a number of factors. Rabies is a slow-moving virus, and some time may be taken for public health investigation to avoid unnecessary rPEP. Below is information regarding exposures that occur in Montana. Out of state and international exposures may need further assessment by public health.

Exposure Assessment

Valid exposures to rabies are considered one of the following:

1. Bite exposures that break the skin from a species capable of transmitting the rabies virus.
2. Non-bite exposures involving contamination of open wounds or mucous membranes with saliva or other potentially infectious material, such as brain matter.
3. Bat exposures either through direct contact with the bat (i.e., flying into the person or handling the bat) or bats in rooms with people who may be unaware a bite or contact occurred, such as those who are sleeping, intoxicated. In addition, this may also include those unable to recall contact with the bat such as young children or those with impaired cognition. Bite wounds from bats may become indiscernible very quickly.
Exposures Due to Cats, Dogs, and Ferrets

Exposures to a cat, dog, or ferret that appeared healthy at the time of the exposure can be confined for 10 days and observed in a location deemed appropriate by the local health officer or designee. No rPEP is needed during the observation period. Per CDC, no person in the United States has ever contracted rabies from a dog, cat, or ferret held in confinement for 10 days. If the animal is healthy at the end of the confinement, rPEP is unnecessary. In Montana, it is the responsibility of the local health officer to oversee monitoring of the animal. If the animal cannot be found for observation, then a recommendation can be made based on circumstances of the exposure and local epidemiology by the local health officer or designee.

If a dog, cat, or ferret appears ill at the time it bit the patient or becomes ill with symptoms suggestive of rabies during the 10-day observation, the local health officer will refer the animal for evaluation by a veterinarian and may elect to test for rabies. Owned cats, dogs, and ferrets are considered low-risk animals for rabies transmission in Montana, and feral animals are considered medium-risk.

Exposures to Bats and Skunks

Bats and skunks are considered high risk animals in Montana as they have rabies endemic in their population. Rabid bats are found statewide. The skunk rabies variant is found in populations east of the continental divide, though rabid skunks have been found west of the divide infected with bat variants. If the animal is readily available for testing, contact your local public health office to arrange rabies testing. If the animal is positive for rabies, unsuitable for testing, or unavailable for testing after an exposure has occurred, administer rPEP.

Bat exposures constitute the most common reason for rPEP to be administered. In 2019, rPEP was administered or recommended to be administered to 210 individuals. Of those exposures, 83 were due to bats. CDEpi has already received reports of exposures to bats in May. Bat activity tends to peak in July and end in September or October. In 2019, 83% of bats tested negative, 8% were unsuitable for testing, and 9% were positive at the Montana Veterinary Diagnostic Laboratory (196 total bats tested).

Exposures to All Other Mammalians

Refer to the DPHHS Rabies Webpage (https://dphhs.mt.gov/publichealth/cdepi/diseases/rabies) for information on the species and management of exposures to these animals.

RECOMMENDATIONS

Administration of rPEP has a number of considerations for clinicians. Wound cleansing is especially important in rabies prevention because thorough wound cleansing alone without other postexposure prophylaxis markedly reduced the likelihood of rabies in animal studies. When a patient presents a healthcare setting with an animal bite, wash the wound well with soap and water:

- Irrigation with a virucidal agent, such as diluted povidone-iodine, is also recommended by CDC.
  - Quaternary ammonium compounds are not considered superior to soap and water.
- Wound cleansing can greatly reduce the risk of contracting rabies.
- Assess tetanus vaccination and booster, if indicated.

For rPEP regimens recommended in the US, one or two products are used depending on the rabies vaccination status of the patient:

1. **Human Rabies Immune Globulin (HRIG)** – confers immediate protection with antibodies for rabies virus
2. **Rabies Vaccine** - patient develops antibodies over a 2 to 4-week period
CDC Recommended PEP Schedule*

The schedule for rabies vaccine and HRIG administration is timed with day 0 being the day the regimen was started.

<table>
<thead>
<tr>
<th>Previously unvaccinated individuals</th>
<th>Previously vaccinated individuals</th>
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<tbody>
<tr>
<td>Vaccine</td>
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<td>day 14</td>
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<tr>
<td>HRIG</td>
<td>No HRIG needed</td>
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* Reduced dose regimen was recommended in 2010. Five dose series still used for those with immunosuppression from disease, corticosteroid, and other immunosuppressive agents with doses on days 0, 3, 7, 14, and 28. Hold immunosuppressive agents, if possible, while receiving rPEP and check a titer 2 weeks after administration is complete to ensure the patient has protective titer level.

Key Points for the Administration of HRIG

- HRIG should be infiltrated around or inside wound if one is present (mucous membrane or bat exposures may lack a wound)
- Remaining volume IM at site distant from vaccine such as the anterolateral thigh
- Administer 20 IU/kg body weight
- Depending on the product, concentrations may be 300 IU/1 mL of solution or 150 IU/1 ml of solution
- Never use same syringe as rabies vaccine
- Do not administer more than necessary
- If HRIG is not immediately available, it may be administered up to day 7 after starting the vaccine regimen
- Do not administer after day 7 or dose 3 of vaccine or in previously vaccinated patients
- In cases of exposures without a wound (i.e., mucosal exposures to fluids), inject away from vaccination site
- **When initiating rPEP for unvaccinated patients, always administer HRIG regardless of species of exposing animal or whether or not a bite wound is present – withholding HRIG for bat exposures may result in rPEP failure as immediate protection from rabies will not be provided**

Key Points for the Administration of Rabies Vaccine

- The deltoid is the only acceptable site for adults and older children
- In younger children, the anterolateral thigh is acceptable
- Never administer vaccine at same site of HRIG
- Never administer in gluteal area due to poor absorption; doses given here will have to be re-administered
- Dose is not decreased for children
Use of Rabies Antibody Titers with rPEP Administration

Antibody titers alone do not always directly correlate with absolute protection because of other important immunologic factors. A theoretical protective level of 0.5 IU/mL (used by the World Health Organization) as an indicator of an adequate adaptive immune response or complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test (RFFIT) are considered adequate. However, for previously vaccinated patients who experience an exposure, the two-dose post exposure prophylaxis regimen should still be administered regardless of a known antibody titer level because this protective level is only theoretical. Do not delay rPEP to await a titer level as these laboratory results may require 2-3 weeks to obtain.

Postvaccination antibody levels are indicated with those who are immunosuppressed or experienced major deviations from the rPEP schedule to document seroconversion. Consult with local health departments if the titer is not within adequate range. RFFIT testing for human sera is available through Kansas State University Veterinary Diagnostic Laboratory (http://www.ksvdl.org/rabies-laboratory/rffit-test/rffit-submission-forms.html). For a fee, testing can be expedited in cases where serologic response rPEP needs to be ascertained.

Recommendations for serologic monitoring of antibody levels for those who are at frequent to continuous risk of inadvertent rabies exposure can be found on page 19 of the 2008 Human Rabies Prevention MMWR from CDC (https://www.cdc.gov/mmwr/pdf/rr/rr57e507.pdf).

REPORTING

Report potential rabies exposures to humans to the local health department and indicate whether or not rPEP was administered. In many instances, local public health can assist with observation and/or testing of the exposing animal so rPEP can be avoided. Please refer to your facility’s reporting protocol to the local health department. If you are unable to reach the local health department and require immediate consultation, you may contact CDEpi at 406-444-0273.

RESOURCES