NEW YORK STATE DEPARTMENT OF HEALTH
Rabies Policies and Procedures
(518) 473-4439
(866) 881-2809 (after hours)

Updated September 13, 2024

SUBJECT: Guidance Regarding Human Exposure to Rabies and Postexposure Prophylaxis Decisions

I. Human exposure to rabies

Human exposures to rabies can generally be categorized as bite, open wound, mucous membrane, or other types of exposure:

Bite exposure: Any penetration of the skin of a person by the teeth of a rabid or potentially rabid animal.

Open wound exposure: Introduction of saliva or other potentially infectious material (cerebrospinal fluid, spinal cord, or brain tissue) from a rabid or potentially rabid animal into an open wound (e.g., broken skin that bled within the past 24 hours).

Mucous membrane exposure: Introduction of saliva or other potentially infectious material (cerebrospinal fluid, spinal cord, or brain tissue) from a rabid or potentially rabid animal onto any mucous membrane (eyes, nose, mouth).

Other exposure: Any interaction with a rabid or potentially rabid animal where a bite, open wound, or mucous membrane exposure cannot be definitively ruled out. This includes situations where a bat is found in a room with a sleeping person, unattended child, intoxicated or mentally compromised person.

Situations that **DO NOT MEET** the criteria for potential human exposure to rabies include the following:

- Wounds of unknown origin where no animal was ever witnessed by any person at the scene.
- Petting a rabid or potentially rabid animal with no saliva contact.
- Direct contact with a bat where the person exposed is reasonably certain a bite did not occur.
- Exposure situations of any type involving **wild/free-roaming** rabbits or small rodents (e.g., squirrels, chipmunks, rats, mice).
- Exposure situations of any type involving pet rabbits or small pet rodents (e.g., rats, mice) **housed exclusively indoors**.
- Contact with the blood, urine, feces (e.g., guano), milk, or spray (e.g., from a skunk) of a rabid or potentially rabid animal.
- Secondary exposure scenarios (i.e., contact with an animal, surface, or object that has had contact with a rabid or potentially rabid animal) that do not meet the definition of open wound or mucous membrane exposure.

Human exposures to bats in multiple person dwellings

Group homes, long term care facilities, dormitories, and camps are examples of dwellings where many persons could be potentially exposed ("other exposure" category, above) to bats. It is absolutely imperative in these multiple person exposure situations to make every attempt to capture the bat for testing, make a list of all persons with possible contact, and thoroughly review each individual's potential exposure. Generally, all persons exposed in these settings should be evaluated as any exposed individual would be evaluated.

Potential exposure scenarios not covered in this guidance document should be discussed as needed on a case by case basis for determination of human exposure criteria by contacting the New York State Department of Health (NYSDOH) Bureau of Communicable Disease Control (BCDC) at (518) 473-4439 and after hours at (866) 881-2809.

II. Determining rabies status of the animal

To assist in rabies postexposure prophylaxis (RPEP) decisions, any potentially rabid animal that comes into contact with a human, causing them to be potentially exposed to rabies, should be evaluated for rabies either by confinement/observation (domesticated animals only, see below) or by laboratory testing.

For bat and other non-domesticated animal exposures, every attempt should be made to safely capture the animal to be submitted for laboratory testing. For domesticated[1] animal exposures, decisions about whether to evaluate by confinement/observation versus laboratory testing should take into consideration the risk of rabies in the exposing animal based upon species, behavior, clinical presentation, and exposure circumstances. Table 1 describes various factors that can be used to aid in this assessment; however, often there is no single factor alone that places the risk of rabies clearly into the high or low risk categories. All factors should be considered and contribute to the overall risk assessment.

Table 1: Factors to aid in the assessment for the risk of rabies in the exposing animal

High-suspect for rabies	**Low-suspect for rabies**
Behavior abnormal for the species or changes in behavior of a known animal	Normal animal behavior
Clinical signs compatible with rabies	No clinical signs of rabies
Unprovoked attack*	Provoked attack*
Rabies vector species (bat, raccoon, fox, skunk)	Owned domesticated species[1]; wild or outdoor housed rabbits and small rodents
Actual or possible contact with a known rabid animal	No neurologic signs (stumbling, seizures, tremors, reduced or heightened excitability)

*Note: Provoking behaviors by a person can include taking food, surprising, inflicting pain, moving suddenly, making loud noises, touching, making eye contact, running, biking, invading territory, approaching a mother animal with a litter, or getting near an old or ill/injured animal.

Confinement/observation

Confinement/observation is considered only for domesticated animals (dog, cat, ferret, sheep, goat, cattle, horse, donkey, mule, or swine). If a domesticated animal has exposed a human and is a low-suspect for rabies, it may be held in confinement and observed daily for signs of rabies for 10 days commencing from the day the exposure occurred. RPEP of exposed persons should not be automatically initiated when pursuing 10-day confinement/observation. Note that animals under rabies observation should not be vaccinated until the conclusion of the 10-day period to avoid potential vaccine reactions that may mimic early rabies signs.

If an animal dies or becomes clinically ill during the 10-day observation period, and the county health authority and consulting veterinarian find the presentation compatible with rabies, then the animal shall be humanely euthanized and submitted for rabies testing immediately. RPEP of exposed persons should then be initiated only if rabies is not ruled out.

Laboratory testing

Pursuant to the New York State (NYS) Sanitary Code, human exposure from bat and other non-domesticated animal species generally requires euthanasia and testing of the animal to determine rabies status and the necessity of RPEP.

1 Domesticated animals include dogs, cats, ferrets, horses, donkeys, mules, cattle, sheep, goats, and pigs.

Any animal (domesticated or non-domesticated) that is a high-suspect for rabies (see Table 1) and/or exhibiting clinical signs compatible with rabies and has exposed a human should not be confined and observed but shall immediately humanely euthanized and submitted for rabies testing.

Obtaining laboratory testing
Laboratory testing of animals that have potentially exposed a human or animal to rabies is available free of charge at the NYSDOH Wadsworth Center Rabies Laboratory. Testing is performed during routine business hours but can be performed on an emergency basis if the situation warrants, such as when an animal that is strongly suspected to be rabid has bitten a human and treatment is being withheld pending test results.

Detailed submission guidelines (including submission policies for animal species and human specimens) are available at: www.wadsworth.org/rabies or by phone at (518) 485-6464. After hours, please contact (518) 527-7369 or (518) 527-7370.

III. RPEP for exposed persons never previously vaccinated for rabies

For all persons who have never been previously vaccinated for rabies, RPEP includes:

- wound management
- administration of Human Rabies Immune Globulin (HRIG)
- administration of four doses of rabies vaccine on days 0, 3, 7, and 14
- administration of a fifth dose of rabies vaccine on day 28 for persons with immunosuppression

The schedule for all vaccine doses should be adhered to as closely as possible.

This guidance document covers detailed information about timeliness, wound management, HRIG administration, vaccine administration, scheduling variations, and discontinuation of RPEP. Situations falling outside the general recommendations in this guidance document should be discussed on a case by case basis by contacting the NYSDOH BCDC at (518) 473-4439 and after hours at (866) 881-2809.

Timeliness
RPEP should be authorized and provided as soon as possible after exposure to an animal that is known to be rabid or is a high-suspect for rabies. In general, RPEP should only be delayed when a suspect animal's rabies status can be determined with confinement/observation or when laboratory test results will be available in a timely manner. For incidents involving bite, mucous membrane, open wound, or other exposures from an animal known to be rabid or is a high-suspect for rabies but is not available for testing, RPEP should be authorized and initiated regardless of the length of time since the exposure occurred.

For bite, mucous membrane, open wound, or other exposures to animals that are low-suspect for rabies, RPEP for exposures that occurred more than 3 months previously should be discussed on a case-by-case basis through consultation with the NYSDOH prior to authorizing and initiating RPEP. Exposures involving a bat found in a room where exposure cannot be definitively ruled out (as defined in Section I) and that occurred more than 3 months prior should not be authorized.

Exceptions to these general guidelines about timeliness should only be made on a case-by-case basis and through consultation with the NYSDOH prior to authorizing and initiating RPEP.

Delay of RPEP while attempting to locate the exposing animal
For exposures to domesticated animals, all efforts should be made to capture and test (or observe) domesticated animals when there has been a human exposure.

Historically, 3 days has been used as a general guideline for how long one might reasonably wait before deciding that the animal is not likely to be found and so prophylaxis should be started. This "3 day rule" is not intended as an absolute cutoff for starting treatment. The length of time to wait (if any)

before starting treatment ultimately depends on the circumstances of an individual exposure. In general, due to risk of side effects and resource/cost issues, it is preferable to wait to start treatment when steps are underway to determine the animal's rabies status. Additional guidelines to help determine when to start treatment include:

- Domesticated animals, where the bite victim cannot be 100% sure of what the animal looked like should not have treatment delayed if rabies prophylaxis is indicated.
- Domesticated animals with a collar and seen around the area may be worth looking for longer than 3 days, in hopes that the animal and its owner reappear in the area. This decision should be made in the context of the bite circumstance and behavior of the animal, for example:
    - The animal was owned, but had an abrupt behavior change, bit someone, and is now gone: treatment should be considered if the animal is not found in three days.
- The animal was a recognized stray, bite was provoked, animal observed to act normally before and after the bite: delaying treatment beyond three days should be considered if steps are actively underway to capture or at least observe the animal (even if not captured) as healthy.
- For an animal which is clearly owned and the owner is identified but cannot be reached, consideration may be given to trying to locate the owner and animal for the full 10 days.

These decisions should be made on a case-by-case basis through consultation with the NYSDOH and depending on the likelihood of the animal being rabid and the likelihood of an exposure.

For wildlife exposures where the animal has escaped or been released, unless there is something very remarkable about the animal and/or the circumstances, positive identification cannot be assured, so treatment should not be delayed.

Wound management
All RPEP should begin with immediate thorough wound cleansing with soap and water and irrigation of the wound with a virucidal agent such as povidone-iodine solution when available.

Dose and site for administration of HRIG
A single 20 IU/kg body weight dose of HRIG, **infiltrated into and around the wound(s)**, should be given when RPEP is initiated (day 0). If it is not possible to infiltrate the entire dose at the site of the wound(s), the remainder should be administered intramuscularly (IM) at a site distant from the site of rabies vaccination. **However, every effort should be made to administer at least some HRIG into the site(s) where the exposure occurred**. HRIG should never be administered in the same syringe or at the same site as vaccine.

HRIG administration considerations:

- Medical personnel should ensure that the correct concentration of rabies antibodies per milliliter contained in the HRIG formulation is used when calculating the volume of HRIG for the recommended dose of 20 IU/kg. Currently there are three HRIG products approved by the U.S. Food and Drug Administration (FDA) available for use in the United States. Imogam® and KEDRAB have a potency value of 150 IU/ml, and HyperRab™ has a potency value of 300 IU/ml. The volume HRIG required for the recommended dose of 20 IU/kg using a product with a concentration of 300 IU/ml is approximately one half of that required for products with a concentration of 150 IU/ml.
- The full dose of HRIG should be infiltrated in the area around the wound. HyperRab™. with a potency value of 300 IU/ml may be diluted with dextrose, 5% (D5W) if additional volume is needed to infiltrate the entire wound. Do not dilute with normal saline.
- If the wound has healed, or there is no obvious wound at the anatomic site of exposure, HRIG must still be administered at the site where contact or wound occurred.
- For mucous membrane exposures the entire dose of HRIG must be administered IM at a site distant from the site of rabies vaccination.
- If a patient was administered a full dose of HRIG without having the wound(s) or exposure site

infiltrated appropriately, administration of additional HRIG into and around the wound(s) within 7 days after the first dose of vaccine may be indicated especially for exposure to animals that are high-suspect for rabies. Re-administration of HRIG should include only the volume sufficient to infiltrate into and around the wound(s) (even if completely healed) up to a maximum volume of a full repeat dose. This is important even if only part of the HRIG can be infiltrated into the wound. Do **not** re-administer any of the remaining calculated dose IM if it was previously provided IM.

- Physicians are often concerned about pain, potential scarring, or potential tissue damage that might be caused by attempting to infiltrate HRIG into fingers, face, joint areas, etc. However, it must be made clear that treatment failures have been documented in other countries when HRIG was not administered at the site of the actual wound. Even if only a small amount of HRIG can be infiltrated, an attempt should be made to instill HRIG at the site of a rabies exposure. This includes RPEPs provided due to bat-skin contact in the absence of a visible wound, but where there is concern because of the possibility of a bat bite. The only exceptions are mucous membrane exposures or bat exposures in which there is no information about the site of exposure; therefore, HRIG should be administered IM at a site distant from the site of rabies vaccination.
- If administration of HRIG was not done at the time RPEP was initiated (e.g., because insufficient quantity was available to treat the patient), it may be given up to the 7th day after the first dose of vaccine. HRIG should not be administered more than 7 days after the first dose of vaccine due to concern that the HRIG could interfere with an individual's active immune response to the vaccines.

Dose and site for administration of human rabies vaccine

RPEP consists of **four** doses of rabies vaccine, 1 ml administered IM in the deltoid area or, for small children, in the anterolateral aspect of the thigh. The first vaccine dose is given when RPEP is initiated on day 0 (the same day as HRIG is administered) and three additional doses are given 3, 7, and 14 days after the first vaccination. Currently there are two human rabies vaccines licensed by the FDA available in the U.S., Imovax® and RabAvert®.

Rabies vaccine administration considerations:

- Rabies vaccine should **never** be given in the gluteal area. This is a specific warning on the product label because of concern for administering the vaccine into adipose (fatty) tissue rather than muscle, which may result in lower neutralizing antibody titers.
- If a dose of vaccine has erroneously been given in the gluteal area, the provider should be advised of the administration error. The necessary follow-up action (e.g., whether to repeat the vaccine dose or not) is generally left to clinician's judgment; however, the NYSDOH recommends that such vaccine doses be treated as though they did not happen unless the provider is certain, due to the body type of the patient, that they did not inject the vaccine into adipose (fat) tissue.
- Rabies vaccine should never be given in the same muscle as HRIG. If HRIG and vaccine were erroneously administered into the same muscle, that vaccine dose should be treated as if it were not given. If within the first 2 days of HRIG initiation, the vaccine dose should be given as soon as possible in an appropriate body site and that dose now considered to be "day 0." If subsequent vaccine doses have already been given, the "day 3" dose should be treated as "day 0" and the schedule adjusted accordingly.
- It is acceptable to give HRIG in the same limb as the vaccine, as long as they are administered in different muscles (e.g., HRIG in a bite wound on the hand, vaccine in the deltoid muscle of that same arm).

Immunosuppressed patients

Immunosuppression (either due to illness, medication, or therapy for an illness or condition) is a clinical diagnosis determined by the patient's physician. Those who are immunosuppressed should receive a 5th dose of rabies vaccine on day 28. In addition, these patients should have their response to treatment assessed with serum antibody titers 1–2 weeks after finishing the postexposure treatment course. Information on specific conditions that may cause immunosuppression can be found in the Advisory

Committee on Immunization Practices (ACIP) General Best Practices for Immunization, available at: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html.

A patient who fails to seroconvert with an acceptable antibody response after the fifth and last dose should be managed in consultation with their physician and appropriate public health officials. Information on titer testing at the NYSDOH Wadsworth Center Rabies Laboratory is available at: http://www.wadsworth.org/rabies/prof/SerologyGuidelines.htm.

RPEP schedule variations
If a patient gets off schedule, consult with the NYSDOH BCDC regarding recommendations for schedule adjustment. In general, RPEP schedule considerations include:

- Under no circumstances should the series be re-started.
- HRIG should not be administered more than once, except in certain circumstances as described above.
- Although HRIG should be given on day 0 with the first dose of vaccine, it can be given up to 7 days after starting the vaccine schedule.
- A deviation of 1 day from the recommended schedule should be managed by maintaining vaccine doses as per the original schedule, if possible.
- If deviations of greater than 1 day from the original schedule are necessary or unavoidable, all subsequent doses should be administered on a new schedule maintaining the same interval between doses.
- If there is concern about **significant** (>2 week) deviation from the schedule, antibody titers should be verified on a serum sample collected 1–2 weeks after the final vaccine dose.
- If a patient began RPEP in another country and needs to continue here, consult with the NYSDOH BCDC. In rare circumstances, it may be necessary to re-start treatment.

Discontinuation of RPEP
If RPEP is begun and the animal's rabies status is ultimately determined to be negative by laboratory testing or confinement/observation, RPEP should be discontinued. Those who receive partial RPEP (2 or more doses of vaccine) should be advised to request a serum antibody titer drawn 1–2 months after the last vaccine dose in order to potentially allow use of the shortened treatment course in the event of a future rabies exposure.

IV. RPEP for exposed persons previously vaccinated for rabies

Previously vaccinated persons are those individuals who have received either:

- A complete rabies pre-exposure or postexposure prophylaxis regimen in accordance with ACIP recommendations using a modern, cell culture-derived rabies vaccine (such as Imovax® or RabAvert®); or
- Rabies vaccination following another protocol or with another vaccine with a subsequent documented rabies virus neutralizing antibody titer.

In all other cases, including partial RPEP regimens without a documented virus neutralizing antibody titer, the full RPEP consisting of HRIG plus four doses (or five doses for immunosuppressed persons) of vaccine should be administered.

RPEP for previously vaccinated persons consists of wound management as above and **two** doses of rabies vaccine, 1 ml administered IM in the deltoid area or, for small children, in the anterolateral aspect of the thigh, given on day 0 and day 3. Rabies vaccine should **never** be given in the gluteal area, as this is a specific contraindication on the product label. The schedule for these doses should be adhered to as closely as possible.

HRIG is not given to previously vaccinated persons receiving RPEP. Administration of HRIG to a person who already has immunity to rabies is contraindicated because it may interfere with the anamnestic response to vaccine. It is unclear whether such administration could interfere sufficiently to cause treatment failure. Thus, every effort must be made to assure that HRIG is only given if the person is not previously vaccinated. If HRIG is erroneously given, the patient should receive an extra dose of

vaccine on or after day seven. This recommendation is not part of the national ACIP guidelines but has been suggested by the Centers for Disease Control and Prevention as a precautionary measure.

V. Adverse reactions to RPEP

Treatment with any biological is not completely risk-free and adverse reactions may occur following the administration of human rabies vaccines or HRIG, although no life-threatening reactions have been reported to date. Thus, decisions on the necessity for RPEP in lower-risk exposures should include consideration of the risk of treatment.

Any adverse events related to rabies treatment should be discussed with experts at the NYSDOH BCDC and reported to VAERS at: https://vaers.hhs.gov/.

VI. Additional resources

Additional information regarding human RPEP recommendations can be found in the following ACIP guidance documents. **Note that in cases where NYS law, regulation, or policy differs from ACIP guidelines, the NYS law, regulation, or policy supersedes ACIP guidelines.**

Centers for Disease Control and Prevention. Human Rabies Prevention – United States, 2008. Recommendations of the Advisory Committee on Immunization Practices. MMWR 2008; 57 (RR-3): 1–28, available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5703a1.htm.

Centers for Disease Control and Prevention. Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies – Recommendations of the Advisory Committee on Immunization Practices. MMWR 2010; 59 (RR-2): 1–9, available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm.

Centers for Disease Control and Prevention. Use of a Modified Preexposure Prophylaxis Vaccination Schedule to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022, available at: https://www.cdc.gov/mmwr/volumes/71/wr/mm7118a2.htm.