

# RABIES PREVENTION IN TEXAS



[Texas Department of State Health Services](#)  
[Zoonosis Control](#)

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This document can be accessed at:

<http://www.dshs.state.tx.us/idcu/disease/rabies/information/prevention/pamphlet/>

**Texas Department of State Health Services  
RABIES PREVENTION IN TEXAS**

For assistance on problems or questions regarding rabies prevention, call your local health department, a Zoonosis Control regional office (contact information listed on pages 26-29 of this document) of the Texas Department of State Health Services (DSHS), the DSHS Zoonosis Control Branch (512-776-7255), or the DSHS Infectious Disease Control Unit (512-776-7455) during working hours. For emergency consultations on nights, weekends, and holidays, contact the DSHS Health Service Region (HSR) for your area:

<b>HSR</b>	<b>HSR EMERGENCY HOTLINE</b>
1	806-744-3577
2/3	817-825-9230
4/5N	866-310-9698
6/5S	800-270-3128 or 713-767-3000
7	254-778-6744
8	210-949-2121
9/10	888-847-6892
11	956-421-5559

**INTRODUCTION**

Although rabies rarely affects humans in the United States, every year many people receive rabies postexposure prophylaxis (PEP). Appropriate management of those who may have been exposed to rabies infection depends on the evaluation of the risk of infection (type of exposure, type of animal, availability and rabies vaccination status of the animal involved in the exposure, etc.) and the efficacy and risk of prophylactic treatment. All available methods of systemic prophylactic treatment possibly can be complicated by instances of adverse reactions. These are rarely severe. Decisions on management must be made promptly; the longer treatment is postponed, the less likely it is to be effective. The urgency for treatment must be tempered by recognition that human rabies is an extremely rare event in Texas and that hasty decisions have led to the inappropriate vaccination of people who were not at risk for infection.

Data on the efficacy of active and passive immunization after rabies exposure have come from both human and animal studies. Evidence from laboratory and field experience in many areas of the world indicates that PEP (combining wound cleansing, vaccine, and rabies immune globulin) is uniformly effective when appropriately used. Rabies has not occurred in persons who have received prompt PEP following the guidelines found in this manual.

Since the mid-1900s, the number of human rabies cases has declined significantly in the United States. This is probably due to several factors. Improved domestic animal control (including effective leash laws, domestic animal rabies vaccination programs, and stray animal collection) has been a major factor. Before the implementation of improved animal control measures, rabid domestic animals were the most common source of human rabies in the United States. They remain the leading source of human rabies in many other parts of the world.

The control of two recent major rabies epizootics in Texas has also contributed to the low incidence of rabies in domestic animals. The aggressive use of oral rabies vaccination programs for coyotes and gray foxes, which began in selected strategic areas of Texas

during 1995, has greatly decreased the risk of domestic animals and humans becoming infected with the rabies virus via these wildlife species.

Rabies continues to be enzootic in skunks in Texas. The number and percentage of skunks that are positive for rabies varies cyclically. Field studies are being conducted on oral rabies vaccination efforts for skunks.

Rabies is also enzootic in bats in Texas. In the United States, the vast majority of recent human rabies cases have been identified as being due to a bat strain of rabies virus, often with the victim not remembering or disclosing an animal bite of any kind. This has resulted in a more liberal interpretation of rabies exposure by this mammal:

*“...in situations in which a bat is physically present and the person(s) cannot reasonably exclude the possibility of a bite exposure, post exposure prophylaxis should be given unless prompt capture and testing of the bat has excluded rabies virus infection.”*  
(MMWR 1996; 45:209)

## **RABIES BIOLOGICALS**

There are two types of rabies immunizing products for use in humans: 1) vaccines that induce an active immune response, which requires about 7-10 days to develop but may persist for as long as a year or more; and 2) immune globulins that provide rapid passive immune protection for a short period of time (half-life of approximately 21 days). Both types of products should be used concurrently for PEP in those persons who have never received prior vaccination against rabies.

### **Vaccines for Use in Texas**

This section contains some pertinent information on some of the rabies biologicals that may be available in Texas. The package insert should be consulted before the use of any of these products.

#### **HDCV**

Human diploid-cell vaccine (HDCV): HDCV is prepared using a rabies virus grown in human diploid cell culture, which is then inactivated. Vaccine is supplied as 1 ml, single-dose vials of freeze-dried vaccine with accompanying diluent for intramuscular (IM) injection for pre- and postexposure administration. It must be used immediately after reconstitution.

#### **PCECV**

Purified chick embryo cell vaccine (PCECV): PCECV contains a freeze-dried inactivated rabies virus grown on cultures of chicken fibroblasts. This vaccine is licensed in the United States for IM use in both pre- and postexposure immunization. The schedules and dosage for PCECV vaccine are the same as for HDCV.

#### **HRIG**

Human rabies immune globulin (HRIG): HRIG is concentrated rabies antibodies collected from the plasma of immunized human donors. Rabies neutralizing antibody content is standardized to contain 150 international units (IU) per ml.

## **RATIONALE OF TREATMENT**

The physician must evaluate each possible rabies exposure. Local or state public health officials should be consulted if questions arise about the need for prophylaxis.

Additionally, a helpful guide entitled *Human Rabies Postexposure Prophylaxis (PEP) in Texas – Guide (Table 1)* can be found in the **RABIES POSTEXPOSURE PROPHYLAXIS (PEP) FOR HUMANS** section of this manual.

## **MANAGEMENT OF BITING ANIMALS**

A healthy dog, cat, or domestic ferret that has potentially exposed a person to rabies should be quarantined in a licensed facility or a veterinary clinic (under specific conditions defined in law, home confinement may be allowed by the local rabies control authority), observed for 10 days from the time of the exposure, and evaluated by a veterinarian at the first sign of illness during the observation period. Any illness in the animal should be reported immediately to the local rabies control authority. If signs suggestive of rabies develop, the animal should be euthanized in a manner that preserves the head in an undamaged state and its head removed and shipped at 32 to 45 degrees Fahrenheit for examination by a qualified laboratory designated by the DSHS. Any unowned dog, cat, or domestic ferret that potentially exposes a person to rabies may be humanely killed and the head submitted for rabies examination.

Signs of rabies in wild animals cannot be interpreted reliably; therefore, any free-roaming high-risk animal\* that potentially exposes a person to rabies must be euthanized at once (without damage to the head) and the brain submitted for examination for rabies. A low-risk animal that the local rabies control authority has cause to believe may be rabid must likewise be tested. (Refer to Table 1. for a list of high- and low-risk animals.) If the brain is negative by fluorescent-antibody examination for rabies, the saliva can be assumed to contain no virus and the exposed person need not be treated. Exotic animals, such as lions, tigers, or monkeys, that have been kept in captivity for extended periods of time are unlikely to be infected with rabies; they can be confined and observed for thirty days rather than euthanized and tested for rabies. Livestock can also be confined and observed for 30 days in lieu of testing.

\* Refer to Texas Administrative Code, Sections 169.27(e) and (h) or consult with the Local Rabies Control Authority for your area pertaining to exemptions to mandatory euthanasia for certain high-risk animals that meet captivity parameters as specified in state law:

[http://texreg.sos.state.tx.us/public/readtac\\$ext.ViewTAC?tac\\_view=5&ti=25&pt=1&ch=169&sch=A&rl=Y](http://texreg.sos.state.tx.us/public/readtac$ext.ViewTAC?tac_view=5&ti=25&pt=1&ch=169&sch=A&rl=Y)

## **COLLECTION AND SUBMISSION OF ANIMAL SPECIMENS FOR RABIES TESTING AT THE DSHS LABORATORY IN AUSTIN**

When packing specimens for rabies diagnosis, some basic information, as mandated in Texas Administrative Code, Section 169.33, is provided below. For details on packing, labeling, shipping, and Code of Federal Regulations requirements, plus laboratory hours and standard procedures, please refer to the website of the DSHS Laboratory Services Section at

[http://www.dshs.state.tx.us/lab/rab\\_prep-ship.shtm](http://www.dshs.state.tx.us/lab/rab_prep-ship.shtm)

- Damage to the brain by shooting or other trauma shall be avoided.

- The head of the suspect animal shall be separated from the body by a qualified person wearing personal protective equipment as soon as possible after the death of the animal. Only the head shall be submitted with the exception that whole bats and small rodents may be submitted. If only the brain is submitted rather than the entire head, the minimum tissue requirements for rabies testing are a complete transverse cross section of the brain stem and tissue from one of the following: cerebellum and/or hippocampus. Submissions that do not meet these tissue requirements will be considered unsatisfactory due to a lack of sufficient material.

- The specimen shall be immediately chilled to between 32 degrees Fahrenheit and 45 degrees Fahrenheit either in a refrigerator or by packing for shipping with sufficient amounts of refrigerants in the container; the specimen should not be frozen. When shipping, sufficient refrigerant shall be added so the specimen will remain chilled for a minimum of 48 hours. Do not use dry ice. Gel packs or similar refrigerants are recommended. Ice is not recommended.

- If specimens are shipped, containment in compliance with requirements in the Code of Federal Regulations (CFR), Title 49, shall be used for packing. Packing methods shall prevent leakage and provide for proper identification (such as an identification number) of the specimen.

- A completed DSHS Form G-9, Rabies Submission Form, which is available at the department's Laboratory Services Section, DSHS, 1100 West 49th Street, Austin, Texas 78756, or at [http://www.dshs.state.tx.us/lab/rab\\_testing.shtm](http://www.dshs.state.tx.us/lab/rab_testing.shtm), is required for each specimen submitted to the DSHS Laboratory Services Section. Each form must contain the same identification information provided with the specimen. Submission form(s) shall be contained in a water-proof bag.

- Labeling on the outside of the shipping container shall be legible and include:

1. name, address, and telephone number of the laboratory;
2. name, return address, and telephone number of the shipper;
3. language in compliance with requirements in the CFR, Title 49, pertaining to the shipment of infectious substances for diagnostic purposes; and
4. the following information: "RABIES IDENTIFICATION TEAM, LABORATORY SERVICES SECTION - REFRIGERATE ON ARRIVAL."

- The following procedures are required for shipment:

1. shipment shall be by bus or other reliable carrier; the department does not recommend the United States Postal Service. If an overnight carrier (other than bus) is used, ship the specimen such that it will arrive by Friday or delay shipment until Monday. Do not ship via overnight carrier on Friday or the day before a holiday. These services do not deliver to the department on the weekend or on holidays;
2. a shipping receipt will be obtained and retained by the shipper;

3. at the time of the shipment, the shipper shall notify laboratory personnel of the shipment via telephone or laboratory-approved electronic format; and
4. the shipper shall provide the return postage (in the form of stamps, not money) if return of the shipping container is desired.

### **LIST OF DSHS-DESIGNATED LABORATORIES**

Contact information is provided to allow submitters to check with a specific laboratory for information on submission and testing procedures, **plus any possible charges for testing**, prior to submitting the specimen.

Austin - Laboratory Services Section, Department of State Health Services, 1100 West 49th Street, Austin, Texas 78756. Telephone the rabies shipment notification hotline at 1-800-252-8163 or the local telephone at: (512) 776-7595, (512) 776-7515, or (512) 776-7491. Email: [Letha.Zuckero@dshs.state.tx.us](mailto:Letha.Zuckero@dshs.state.tx.us)  
Website: [http://www.dshs.state.tx.us/lab/rab\\_prep-ship.shtm](http://www.dshs.state.tx.us/lab/rab_prep-ship.shtm)

Houston Department of Health and Human Services, Bureau of Laboratory Services, 2250 Holcombe Blvd, Houston, Texas 77030. Telephone: 832-393-3912 Email: [Cynthia.turner@houstontx.gov](mailto:Cynthia.turner@houstontx.gov)  
Website: <http://www.houstontx.gov/health/Lab/rabies.html>

San Antonio Metro Health Laboratory, 332 W. Commerce St., Room 201, San Antonio, Texas 78205. Telephone: (210) 207-8820 or (210) 207-8787. Email: [ralph.pruett@sanantonio.gov](mailto:ralph.pruett@sanantonio.gov), [mark.wade@sanantonio.gov](mailto:mark.wade@sanantonio.gov) or [mireya.huizar@sanantonio.gov](mailto:mireya.huizar@sanantonio.gov)

Tillman Health Center-Laboratory, 222 South Campbell, El Paso, Texas 79901. Telephone: (915) 212-0240. Email: [Carlos.fierro@elpasotexas.gov](mailto:Carlos.fierro@elpasotexas.gov)  
Website: <http://www.elpasotexas.gov/health/laboratory.asp>

### **MANAGEMENT OF DOMESTIC ANIMALS EXPOSED TO RABID ANIMALS**

ANY DOMESTIC ANIMAL THAT IS BITTEN BY, DIRECTLY EXPOSED BY PHYSICAL CONTACT WITH, OR DIRECTLY EXPOSED TO FRESH TISSUES OF A RABID ANIMAL IS REGARDED AS HAVING BEEN EXPOSED TO RABIES.

(The following paragraphs paraphrase portions of the Texas Administrative Code, Sections 169.21 – 169.34, Rabies Control and Eradication).

An animal should be considered not currently vaccinated if documentation of vaccination within the appropriate timeframe is not available or if the initial immunization was given less than 30 days previously.

Not currently vaccinated domestic animals considered to have been exposed to rabies must be euthanized **or** vaccinated against rabies immediately, placed in confinement for 90 days, and given booster vaccinations during the third and eighth weeks of isolation. For young animals, additional vaccinations may be necessary to ensure that the animal

receives at least two doses at or after the age prescribed by the USDA for the vaccine administered.

Currently vaccinated domestic animals considered to have been exposed to rabies must be euthanized **or** vaccinated immediately and placed in confinement for 45 days.

These periods of confinement for domestic animals possibly exposed to the rabies virus should not be confused with the 10-day observation period for a dog, cat, or domestic ferret that has potentially exposed a human to rabies as described in the **RABIES POSTEXPOSURE PROPHYLAXIS (PEP) FOR HUMANS** section. A dog, cat, or domestic ferret exposed to a rabid animal may develop rabies long after the exposure since the incubation period for rabies can be more than one year (average incubation is 3-8 weeks). A prolonged confinement is necessary to exclude the possibility of subsequent development of rabies in a dog, cat, or domestic ferret exposed to a rabid animal.

The above recommendations apply only to animals for which there is a USDA-licensed vaccine. For all other animals, refer to the latest edition of the publication titled *The Compendium of Animal Rabies Prevention and Control* by the National Association of State Health Veterinarians. No licensed vaccine is currently available for wild animals or hybrids of wild and domestic animals. The administration of a rabies vaccine in a species for which no licensed vaccine is available is at the discretion of the veterinarian; however, an animal receiving a rabies vaccine under these conditions will not be considered to be vaccinated against rabies virus in potential rabies exposure situations.

## **RABIES POSTEXPOSURE PROPHYLAXIS (PEP) FOR HUMANS**

The essential components of animal bite wound management are prompt, thorough cleansing of wounds and immunization, including administration, in most instances, of both rabies immune globulin and vaccine.

### **Cleansing of Wounds**

Wound cleansing cannot be overemphasized. Immediate and thorough washing of all bite wounds and scratches with soap and water (and an iodine-based antiseptic, if available and the person is not allergic) is a critical measure for preventing rabies. In experimental animals, simple local wound cleansing has been shown to markedly reduce the likelihood of rabies. Tetanus vaccination and measures to control bacterial infection should be provided as indicated.

### **Decision to Provide PEP**

The decision to treat or not to treat must be based on all available information about the circumstances surrounding the exposure incident. The *Human Rabies Postexposure Prophylaxis (PEP) in Texas - Guide (Table 1)* found in this section is helpful in evaluating a possible rabies exposure and determining whether PEP is needed. Local or state health departments may be consulted to clarify the guide and to provide information concerning the prevalence of animal rabies in the geographic locale where the possible exposure occurred. Information on the number of cases of laboratory-confirmed rabies in Texas by county and species of animal is available at:

<http://www.dshs.state.tx.us/idcu/disease/rabies/cases/statistics/>

A 10-day observation period from the time of the bite is necessary for a dog, cat, or domestic ferret that has bitten or otherwise potentially exposed a person to rabies; the animal is placed in quarantine until the end of this period. Generally, rabies-infected dogs, cats, or domestic ferrets will survive no more than 3-5 days once the rabies virus becomes present in the saliva. A dog, cat, or domestic ferret that develops clinical signs of rabies more than ten days after having bitten a person is considered not to have had rabies virus present in its saliva at the time the bite occurred. Since exposure to rabies virus did not occur at the time of the bite, PEP is not necessary.

## PEP Regimen

The PEP should include administration of both rabies immune globulin (HRIG) and vaccine (such as HDCV or PCECV). An exception is made for exposed persons who have been previously immunized with the recommended pre- or postexposure regimens of HDCV or PCECV (or who have been immunized with other types of rabies vaccines and have documented rabies antibody production). In these cases, HRIG should not be given and a dose of vaccine should be given on day 0 and day 3 (**Table 2**).

The combination of rabies immune globulin and rabies vaccine is recommended for both bite exposures and nonbite exposures, regardless of the interval between exposure and treatment. **The sooner treatment is begun after exposure, the better the chance of effectiveness.** In most cases, it is acceptable to withhold PEP for up to 72 hours while awaiting rabies test results or making efforts to locate the biting animal for testing or quarantine/observation; however, if the animal was displaying clinical signs of rabies, the exposed individual should begin treatment without awaiting test results (treatment can be discontinued if test results are negative). If there was a delay in recognizing a rabies exposure, treatment should be started even if months have lapsed since that exposure.

**Table 1. Human Rabies Postexposure Prophylaxis (PEP) in Texas – Guide**

These guidelines can help determine if PEP is needed after a potential rabies exposure. An exposure is defined as 1) an animal bite (or scratch) that breaks the skin or 2) exposure of broken skin (bled or had serous drainage within the past 24 hours) or mucous membranes to saliva or cerebrospinal fluid. Stool, blood, urine, and skunk spray do not contain rabies virus.

Risk Category of Biting Animal	Laboratory Testing Result	Quarantine/ Observation or Testing	Human Postexposure Prophylaxis
<b>Low</b> (rabbits, opossums, and armadillos, plus mice, rats, squirrels, nutria, shrews, prairie dogs, beavers, gophers, and other rodents)	Testing is not required unless the Local Rabies Control Authority (LRCA) or physician has cause to believe the animal is rabid.	Not applicable	Testing or PEP is not required unless the LRCA or physician has cause to believe the biting animal is rabid.
<b>High<sup>1</sup></b> (Bats <sup>2</sup> , coyotes, foxes, raccoons, skunks) or type of biting animal is unknown	Positive or non-negative <sup>3</sup>	Animal tested	Administer PEP (usually acceptable to wait up to 72 hours for test results or efforts to locate the animal before beginning PEP unless animal displayed signs compatible with rabies).
	Negative	Animal tested	PEP not administered.
	Animal not available	Not possible	Administer PEP.
<b>Dog, Cat, Domestic Ferret<sup>4</sup></b>	Positive	Animal tested	Administer PEP (usually acceptable to wait up to 72 hours for test results or efforts to locate the animal before beginning PEP unless animal displayed signs compatible with rabies).
	Negative	Animal tested	PEP not administered.
	Not tested pending outcome of quarantine (animal placed in quarantine or home confinement until end of a 10-day observation period).	Animal placed in quarantine or home confinement until end of a 10-day observation period. If animal shows clinical signs of rabies, it should be immediately euthanized and tested.	PEP not administered if animal is available for 10-day observation. If animal shows clinical signs of rabies, it should be immediately euthanized and tested; PEP could be started immediately without waiting for test results and discontinued if test is negative.
	Animal not available or non-negative <sup>3</sup>	Not possible	Consult public health professional.
<b>All Other Warm-Blooded Animals</b>	Positive	Animal tested	Administer PEP.
	Negative	Animal tested	PEP not administered.
	Non-negative <sup>3</sup>	Animal tested	Consult public health professional.
	Not tested	30-day observation <sup>5</sup>	Consult public health professional.
	Animal not available	Not possible	Consult public health professional.

1. Refer to Texas Administrative Code, Sections 169.27(e) and (h) or consult with the Local Rabies Control Authority for your area pertaining to exemptions to mandatory euthanasia for certain high-risk animals that meet captivity parameters as specified in state law: [http://texreg.sos.state.tx.us/public/readtac\\$ext.ViewTAC?tac\\_view=5&ti=25&pt=1&ch=169&sch=A&rl=Y](http://texreg.sos.state.tx.us/public/readtac$ext.ViewTAC?tac_view=5&ti=25&pt=1&ch=169&sch=A&rl=Y)

2. In incidents involving bats, PEP may be appropriate even in the absence of demonstrable bite, scratch, or mucous membrane exposure in situations in which there is reasonable probability that such exposure may have occurred (e.g., sleeping individual awakes to find a bat in the room, a person witnesses a bat in the room with a previously unattended child, mentally challenged person, intoxicated individual, etc.).

3. "Non-negative" includes all specimens not suitable for testing (destroyed, decomposed, etc.).

4. The decision whether a dog, cat, or domestic ferret should be euthanized and tested or quarantined rests with the Local Rabies Control Authority.

5. The Local Rabies Control Authority may authorize a 30-day observation period in lieu of testing.

## Table 2. Rabies postexposure prophylaxis (PEP) schedule, United States

From 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 (ACIP)*. *MMWR* 2010;59 (No. RR-2): 6.

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm>

Vaccination Status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	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 (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because HRIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area <sup>†</sup> ), 1 each on days 0, <sup>§</sup> 3, 7 and 14. <sup>¶</sup>
Previously vaccinated**	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area <sup>†</sup> ), 1 each on days 0 <sup>§</sup> and 3.

\* These regimens are applicable for persons in all age groups, including children.

<sup>†</sup> 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.

<sup>§</sup> Day 0 is the day dose 1 of vaccine is administered.

<sup>¶</sup> For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

\*\* Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

For immunocompetent patients, four 1.0 ml doses of HDCV or PCECV should be given intramuscularly (in the deltoid region) in adults or the anterolateral thigh in infants. Although it is recommended that the same product be used for all doses, there is no evidence of a decrease in effectiveness should a different product need to be used to complete a treatment regimen. The first dose should be given **as soon as possible after exposure**; the first day of administration is considered to be day "0." Additional doses should be given on days 3, 7, and 14 after the first dose. The spacing between doses represents the minimum interval to produce an effective antibody level as quickly as possible. The intervals should not be shortened or lengthened. If weekends or holidays preclude adhering to the schedule, lengthen an interval, but do not shorten it; it is important to obtain the first three injections within the first 14 days, but without reducing the stated interval between injections. Antibody response following the recommended vaccination regimen has been uniformly satisfactory; therefore, routine postvaccination serologic testing is not recommended by, nor available from, the DSHS.

For immunocompromised patients, five 1.0 ml doses of HDCV or PCECV should be given intramuscularly (in the deltoid region) in adults or the anterolateral thigh in infants on days 0, 3, 7, 14, and 28.

Every attempt should be made to adhere to the recommended vaccination schedules. Once vaccination is initiated, delays of a few days for individual doses are unimportant, but the effect of longer lapses of weeks or more is unknown. Most interruptions in the vaccine schedule do not require reinitiation of the entire series. For most minor deviations from the schedule, vaccination can be resumed as though the patient were on schedule. For example, if a patient misses the dose scheduled for day 7 and presents for vaccination on day 10, the day 7 dose should be administered that day and the schedule resumed, maintaining the same interval between doses. In this scenario, the remaining dose would be administered on day 17 (or days 17 and 31 for immunocompromised patients receiving a 5<sup>th</sup> dose).

The selection of sites for intramuscular injections appears to be critical for vaccine efficacy. Again, in adults and larger children, HDCV or PCECV should be given in the deltoid area. In infants and small children, the anterolateral thigh may be used. In the two laboratory-confirmed human cases of rabies following PEP with HDCV and HRIG within 24 hours, HDCV was administered in the gluteal area. Presumably, subcutaneous fat in the gluteal area may interfere with the immunogenicity of the vaccine.

The HRIG is administered only once, at the beginning of PEP, to provide passive immunity until the patient responds to the vaccine by active production of antibodies. Complete prophylaxis, including HRIG in a non-immunized person, should still be administered even if months have lapsed between the possible exposure and its recognition. If HRIG was not given when rabies vaccination was begun, it can be given up to the eighth day after the first dose of vaccine was given. From the eighth day (Day 7 of the formal treatment regimen) on, HRIG is not indicated because an antibody response to the vaccine is presumed to have occurred. For example, if the Day 0 rabies vaccine dose was given on March 10<sup>th</sup>, HRIG should not be given after March 17<sup>th</sup>.

The recommended dose of HRIG is 20 IU/kg or 0.06 ml/lb of body weight. As much as possible of the full dose of HRIG should be thoroughly infiltrated into and around the wound(s). Any remaining volume of HRIG should be administered IM in the closest muscle mass of suitable size to accommodate the remaining volume, with the caveat that it

should not be administered in the same site as the first vaccine dose. Anterior lateral thigh muscles are frequently used as HRIG injection sites when the complete amount, due to anatomic limitations, cannot be administered around the wound(s). The HRIG should be injected into muscle, not adipose tissue. Particular care should be taken when administering HRIG in the gluteal area due to the increased risk of injection into adipose tissue. The HRIG may partially suppress the active production of antibodies; therefore, no more than the recommended dose of HRIG should be given. (Note: human immune globulin used to treat hepatitis cannot be substituted for HRIG.)

Additional guidelines on vaccine administration are in the *ACIP General Recommendations on Immunization* (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm>).

For dealing with more significant deviations to the PEP regimen, contact the DSHS Zoonosis Control Branch (refer to contact information at the end of this document) or the Centers for Disease Control and Prevention (<http://www.cdc.gov/vaccines/vpd-vac/rabies/default.htm>).

In unusual instances, such as when the patient is immunodeficient or immunosuppressed, serologic testing (Rapid Fluorescent Focus Inhibition Test - RFFIT) is indicated 2 to 4 weeks after completing the rabies postexposure vaccination series.

#### **These are laboratories that provide the rabies RFFIT:**

The Rabies Laboratory  
Kansas State University  
2005 Research Park Circle  
Manhattan, KS 66502  
Phone: 785-532-4483  
Email: [rabies@vet.k-state.edu](mailto:rabies@vet.k-state.edu)  
[www.vet.ksu.edu/rabies](http://www.vet.ksu.edu/rabies)

Atlanta Health Associates  
309 Pirkle Ferry Rd. Suite D300  
Cumming, GA 30040  
Phone: 800-717-5612  
Email: [info@atlantahealth.net](mailto:info@atlantahealth.net)  
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Maryland Department of Health and Mental Hygiene Laboratories Administration  
ATTENTION: ACCESSIONING RABIES/RFFIT TITER TESTING  
201 W. Preston St.  
Baltimore, MD 21201  
Phone: 410-767-6177  
410-767-6120 (to request RFFIT collection kit)  
410-767-6177 (additional information from Rabies-Zoonotic Diseases Program)  
<http://dhmh.maryland.gov/laboratories/SitePages/Rabies.aspx>

### **TREATMENT OUTSIDE THE UNITED STATES**

If PEP is begun outside the United States with locally produced biologicals, it may be desirable to provide additional treatment, including restarting PEP with products licensed for use in the US, when the patient reaches the US. For specific advice in such cases, contact the Regional Zoonosis Control office for your area (refer to the Zoonosis Control contact section at the end of this document). You may also refer to the World Health Organization (<http://www.who.int/topics/rabies/en/>) or the Centers for Disease Control and Prevention (<http://www.cdc.gov/vaccines/vpd-vac/rabies/default.htm>).

## PREEXPOSURE VACCINATION

Preexposure vaccinations are given for several reasons. First, it may provide protection to people with inapparent exposures to rabies. Second, it may protect persons whose postexposure therapy might be delayed. This is of particular importance for persons at high risk of being exposed in countries where the rabies biologicals may be difficult to obtain. Finally, although it does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for HRIG and decreasing the number of doses of rabies vaccine needed. The guidelines for evaluating the need for preexposure immunization are found in **Table 3**. The schedule for preexposure vaccinations is located in **Table 4**.

**Table 3. Rabies preexposure vaccination guide**

<b>Risk category</b>	<b>Nature of risk</b>	<b>Typical populations</b>	<b>Preexposure recommendations</b>
Continuous	Virus present continuously, often in high concentrations. Aerosol, mucous membrane, bite, or nonbite exposure. Specific exposures may go unrecognized.	Rabies research lab worker,* rabies biologics production workers.	Primary course. Serologic testing every 6 months; booster vaccination if antibody titer falls below acceptable level.**
Frequent	Exposure usually episodic, with source recognized, but exposure may also be unrecognized. Aerosol, mucous membrane, bite, or nonbite exposure.	Rabies diagnostic lab workers,* spelunkers, veterinarians and staff, veterinary students, and animal control and wildlife workers in rabies-enzootic areas.***	Primary course. Serologic testing every 2 years; booster vaccination if antibody titer falls below acceptable level.**
Infrequent (greater than population at large)	Exposure nearly always episodic with source recognized. Mucous membrane, bite, or nonbite exposure.	Veterinarians and staff, veterinary students, and animal-control and wildlife workers in areas of low-rabies occurrence. Travelers visiting foreign areas of enzootic rabies for more than 30 days.	Primary course; no serologic testing or booster vaccination.
Rare (population at large)	Exposures always episodic. Mucous membrane or bite with source recognized.	US population at large, including persons in rabies enzootic areas.	No vaccination necessary.

\* Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor.

\*\* Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by RFFIT. Booster dose should be administered if the titer falls below this level.

\*\*\* Texas is considered to be a rabies-enzootic area.

Again, preexposure vaccinations do not eliminate the need for prompt PEP following an exposure; it only reduces the extent of the postexposure regimen.

## Vaccination Schedule

For preexposure immunization, three 1.0 ml injections of HDCV or PCECV should be given intramuscularly (IM) in the deltoid area, one on each day: 0, 7, and either 21 or 28 (the first day of administration is considered to be day “0”) (**Table 4**). The antibody response following the recommended vaccination regimen with HDCV or PCECV has been uniformly satisfactory; therefore, routine postvaccination serology is not necessary.

If possible, immunosuppressed patients should postpone rabies preexposure prophylaxis until the immunocompromising condition is resolved. When postponement is not possible, immunosuppressed persons who are at risk for rabies should have their virus-neutralizing antibody responses checked 2 to 4 weeks after completing the preexposure series.

## Booster Doses of Vaccine

The recommended schedules for booster doses for persons at risk of rabies exposures are outlined in **Table 3**. The addresses and phone numbers of laboratories offering rabies serologic testing can be found in the **RABIES POSTEXPOSURE PROPHYLAXIS (PEP) FOR HUMANS** section.

## Postexposure Therapy of Previously Immunized Persons

When an immunized person who was vaccinated according to the recommended preexposure or postexposure regimen with HDCV or PCECV, or who has previously demonstrated rabies antibody, is exposed to rabies, that person should receive two IM doses (1.0 ml each) of HDCV or PCECV, one immediately and one 3 days later (**Table 2**). The HRIG should **not** be given in these cases. If the immune status of a previously vaccinated person who did not receive the recommended HDCV or PCECV regimen is not known, full primary PEP (HRIG plus five doses of HDCV or PCECV) may be necessary.

**Table 4. Rabies preexposure vaccination schedule**

Type of vaccination	Route	Regimen
Primary	IM	HDCV or PCECV, 1.0 ml (deltoid area), one each on days 0, 7, and 21 or 28
Booster*	IM	HDCV or PCECV, 1.0 ml (deltoid area), day 0 only

\* Administration of a booster dose of vaccine depends on exposure risk category and serologic testing results as noted in Table 3.

HDCV or PCECV can be used for PEP or booster vaccinations even if another vaccine was used for the initial preexposure vaccination.

## **ADVERSE REACTIONS**

Serious adverse reactions associated with rabies vaccines include systemic, anaphylactic, and neuroparalytic reactions. Serious adverse reactions occur at lower rates with the rabies vaccines currently used in the US than with those used previously.

### **HDCV**

Local and systemic reactions may occur with the use of HDCV. In a study using five doses of HDCV, local reactions, such as pain, erythema, and swelling or itching at the injection site, were reported in about 25% of recipients. Mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness, were reported in about 20% of recipients.

Up to 6% of persons receiving booster doses of HDCV may experience "immune complex-like" reactions (type III IgG mediated hypersensitivity reactions). The illness, characterized by onset 2-21 days post-vaccination, presents with generalized urticaria and may also include arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. No life-threatening cases of "immune complex-like" illness have been reported. This phenomenon rarely occurs with primary immunization with HDCV. The origin of these "immune complex-like" reactions has been attributed to sensitization to the beta-propiolactone-treated human serum albumin present in HDCV.

Those persons with a history of "immune complex-like" illness following HDCV and who must receive rabies vaccine boosters may be candidates for other rabies vaccines which do not have beta-propiolactone bound to human serum albumin. If this is not possible and HDCV must be given, the guidelines in the **Management of Adverse Reactions** section should be followed.

### **PCECV**

As with HDCV, local reactions such as swelling, induration, and reddening have been associated with the administration of PCECV. Systemic allergic reactions are also possible and have been reported.

### **HRIG**

Local pain and low-grade fever may follow receipt of HRIG. Although not reported specifically for HRIG, angioneurotic edema, nephrotic syndrome, and anaphylaxis have been reported after injection of other types of immune globulin (IG). These reactions occur so rarely that a causal relationship between IG and these reactions is not clear.

### **Management of Adverse Reactions**

Once initiated, PEP should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Usually such reactions can be successfully managed with anti-inflammatory and antipyretic agents.

When a person with a history of hypersensitivity must be given rabies vaccine, antihistamines may be given. Epinephrine should be readily available to counteract anaphylactic reactions, and the person should be observed for 15 minutes after vaccination.

Serious systemic anaphylactic or neuroparalytic reactions occurring during the administration of rabies vaccine pose a serious dilemma for the attending physician. A patient's risk of developing rabies must be carefully considered before deciding to discontinue vaccination. Moreover, the use of corticosteroids to treat life-threatening neuroparalytic reactions carries the risk of inhibiting the development of active immunity to rabies. It is especially important in these cases that the serum of the patient be tested for rabies antibodies after completion of the PEP course. Advice and assistance on the management of serious adverse reactions in persons receiving rabies vaccines may be sought from the DSHS Infectious Disease Control Unit (512-776-7455 or 512-776-7676).

All serious systemic neuroparalytic or anaphylactic reactions to a rabies vaccine should be immediately reported to the DSHS Immunization Branch (512-776-7284 or 1-800-252-9152). These reactions should also be reported to the Vaccine Adverse Event Reporting System (VAERS); additional information and forms can be obtained at <http://vaers.hhs.gov/>.

## **PRECAUTIONS AND CONTRAINDICATIONS**

### **Immunosuppression**

Corticosteroids, other immunosuppressive agents, and immunosuppressive illnesses (such as HIV infection and cancer) can interfere with the development of active immunity and predispose the patient to developing rabies. Immunosuppressive agents should not be administered during PEP, unless essential for the treatment of other conditions. When PEP is administered to persons receiving corticosteroids or other immunosuppressive therapy, or to persons having an immunosuppressive illness, it is especially important that the person receive a 5<sup>th</sup> dose of vaccine on day 28 (if the person is not previously immunized) and that serum be tested for rabies antibody to ensure that an adequate response has developed. Information on the laboratories that offer rabies serologic testing is found in the **RABIES POSTEXPOSURE PROPHYLAXIS (PEP) FOR HUMANS** section.

### **Pregnancy**

Fetal abnormalities have not been associated with rabies vaccination. Due to the consequences of an inadequately treated rabies exposure, pregnancy is not considered a contraindication to PEP. If a substantial unavoidable risk of exposure to rabies exists, preexposure prophylaxis may also be indicated during pregnancy.

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\* Requests for rabies biologicals from this location must be reviewed and approved by the Zoonosis Control Program in Region 7 Temple.

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