



Animal Bites and Rabies Risk

a guide for health professionals



For Consultation on Animal Bites and Rabies Risk in Humans

MINNESOTA DEPARTMENT OF HEALTH

Zoonotic Diseases Unit
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St. Paul, MN 55155

Telephone: 651-201-5414 or toll free: 1-877-676-5414

24/7 telephone consultation on potential rabies exposure is available to healthcare providers, veterinarians, public health professionals, and law enforcement at: 651-201-5414. Rabies consultations are available to the public at the same number Monday – Friday, 8:30 a.m. to 4:30 p.m.

For Consultation on Rabies Exposure of Animals

MINNESOTA BOARD OF ANIMAL HEALTH

625 North Robert Street
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Telephone: 651-201-6808

For Specimen Submission for Rabies Testing During Regular Business Hours

VETERINARY DIAGNOSTIC LABORATORY

University of Minnesota
1333 Gortner Avenue
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For Specimen Submission for Rabies Testing on Holidays, Weekends, and After Business Hours

UNIVERSITY OF MINNESOTA VETERINARY MEDICAL CENTER

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ANIMAL BITES AND RABIES RISK: A GUIDE FOR HEALTH PROFESSIONALS

Table of Contents

I. INTRODUCTION	1
II. MANAGEMENT OF ANIMAL BITES TO HUMANS	1
Consultations on animal bites and rabies risk.....	1
Evaluation of the patient following an animal bite	1
Assessment of the need for rabies post-exposure prophylaxis.....	1
Table 1: Human Rabies Risk Evaluation: Species of the Biting Animal.....	2
Table 2: Guidelines for Managing Animal Bites and Bat Encounters in Humans.....	3
Figure 1: Evaluation of Potential Rabies Exposures Flowchart	4
Factors to consider when determining need for PEP	5
Type of exposure	5
Location and severity of the bite	5
Circumstances of the bite incident.....	5
Vaccination status of the biting animal.....	5
Species of the animal and requirements of the 10-day confinement and observation period.....	6
Rationale for a 10-day confinement and observation period.....	6
III. MANAGEMENT OF HUMAN-BAT ENCOUNTERS.....	6
Bat encounters and bat bites	6
When should a bat be submitted for rabies testing?	6
How to capture a bat and submit it for testing.....	7
Assessment of the need for rabies PEP following a bat encounter	7
IV. RABIES POST-EXPOSURE PROPHYLAXIS (PEP) REGIMEN	8
Rabies PEP overview	8
Human rabies immune globulin (HRIG)	8
Interference of HRIG with live virus vaccine administration.....	8
Rabies vaccine	9
Previously vaccinated persons	9
Deviations from recommended PEP vaccination schedule.....	9
Table 3: Rabies Post-Exposure Prophylaxis for Healthy, Immunocompetent Persons, Including Pregnant Women	10
Table 4: Rabies Post-Exposure Prophylaxis for Immunocompromised Persons	11
Human rabies biologics	12
Human rabies immune globulin (HRIG) products	12
Human rabies vaccines	12
Patient assistance programs	12
Adverse reactions	13

V. RABIES PRE-EXPOSURE PROPHYLAXIS (PEP) REGIMEN	13
Who should receive rabies pre-exposure prophylaxis?	13
Pre-exposure rabies vaccination series	14
Antibody titers and booster vaccination	14
Table 5: Rabies recommendations for pre-exposure vaccinated persons	15
Commercial laboratories offering RFFIT rabies antibody titer testing	15
VI. MANAGEMENT OF ANIMALS EXPOSED TO A RABID ANIMAL	16
VII. MINNESOTA’S RABIES RULES.....	16
VIII. RABIES TESTING	17
Background	17
Guidelines for submitting suspect animals for rabies testing	17
Laboratory testing, result reporting, and positive result follow-up	18
Rabies testing in humans	18
IX. REFERENCES.....	18
X. MAP	19
University of Minnesota Veterinary Diagnostic Laboratory and Veterinary Medical Center, St. Paul Campus of the University of Minnesota	
XI. FREQUENTLY ASKED QUESTIONS	20
XII. RABIES SPECIMEN SUBMISSION FORM.....	22

I. INTRODUCTION

Rabies is a fatal neurologic illness transmitted to people by direct contact with the saliva of a rabid animal, normally through a bite; however, transmission through saliva contact with mucous membranes or a fresh wound is possible. The virus cannot penetrate intact skin. Rabies virus is inactivated rapidly by ultraviolet light and desiccation and does not persist in the environment; therefore, contact with the environment around a rabid animal such as with bedding or water bowls does not present a risk. In Minnesota, rabies is found mainly in skunks and bats. Livestock and pets generally develop the disease following a bite from a rabid skunk. People in turn, are generally exposed to rabies by bats, livestock, and unvaccinated pets. Bites from wild carnivores and large rodents such as muskrats, groundhogs, and beavers are also of concern (see Table 1 for species of concern). Species that are not a rabies risk in Minnesota include mice, hamsters, guinea pigs, gerbils, squirrels, chipmunks, rats, voles, and rabbits. For more general information and current statistics on rabies in Minnesota see: www.health.state.mn.us; search: rabies.

II. MANAGEMENT OF ANIMAL BITES TO HUMANS

Consultations on animal bites and rabies risk

- Available 24/7 at (651) 201-5414 for healthcare providers, veterinarians, public health professionals, and law enforcement.
- Available to the public Monday-Friday, 8:30 a.m. to 4:30 p.m. at (651) 201-5414.
- Please do not call the MDH Public Health Laboratory.
- For questions regarding animals that have been bitten by a suspect rabid animal in which there is no human exposure, please contact the Board of Animal Health (BAH) at (651) 201-6808.

Evaluation of the patient following an animal bite

- Wash the wound well with soap and running water.
- Assess the need for tetanus vaccination booster.
- Assess the need for antibiotics.
- Assess the need for rabies post-exposure prophylaxis (PEP).

Assessment of the need for rabies post-exposure prophylaxis

- Is this a species that we are concerned about? (Table 1)
- Was there a bite or saliva exposure to a mucous membrane? (Table 2; Figure 1)
- Is the animal available for 10 days of observation or testing? (Table 2; Figure 1)

Table 1: Human Rabies Risk Evaluation: Species of the Biting Animal

Species of Concern		
Domestic Animals	Cat Dog Ferret Alpaca Cow Donkey	Goat Horse Llama Mule Pig Sheep
Wild Animals, Captive Wild or Hybrid Animals Please consult with MDH about bites from these wild animals. 24/7 consultation is available to health care providers and veterinarians at: (651) 201-5414	Badger Bat Bear Beaver Bison Bobcat Coyote Deer Elk Ermine Fisher Fox Lynx Marten Mink	Monkey Moose Mountain lion Muskrat Opossum Otter Porcupine Puma/Cougar Raccoon Skunk Weasel Wolf Wolf/dog hybrid Wolverine Woodchuck
Bites From These Species are Not a Rabies Concern in Minnesota*		
All amphibians All birds All reptiles Chipmunk Gerbil	Gopher Guinea pig Hamster Hare Hedgehog Mole	Mouse Rabbit Rat Shrew Squirrel Vole

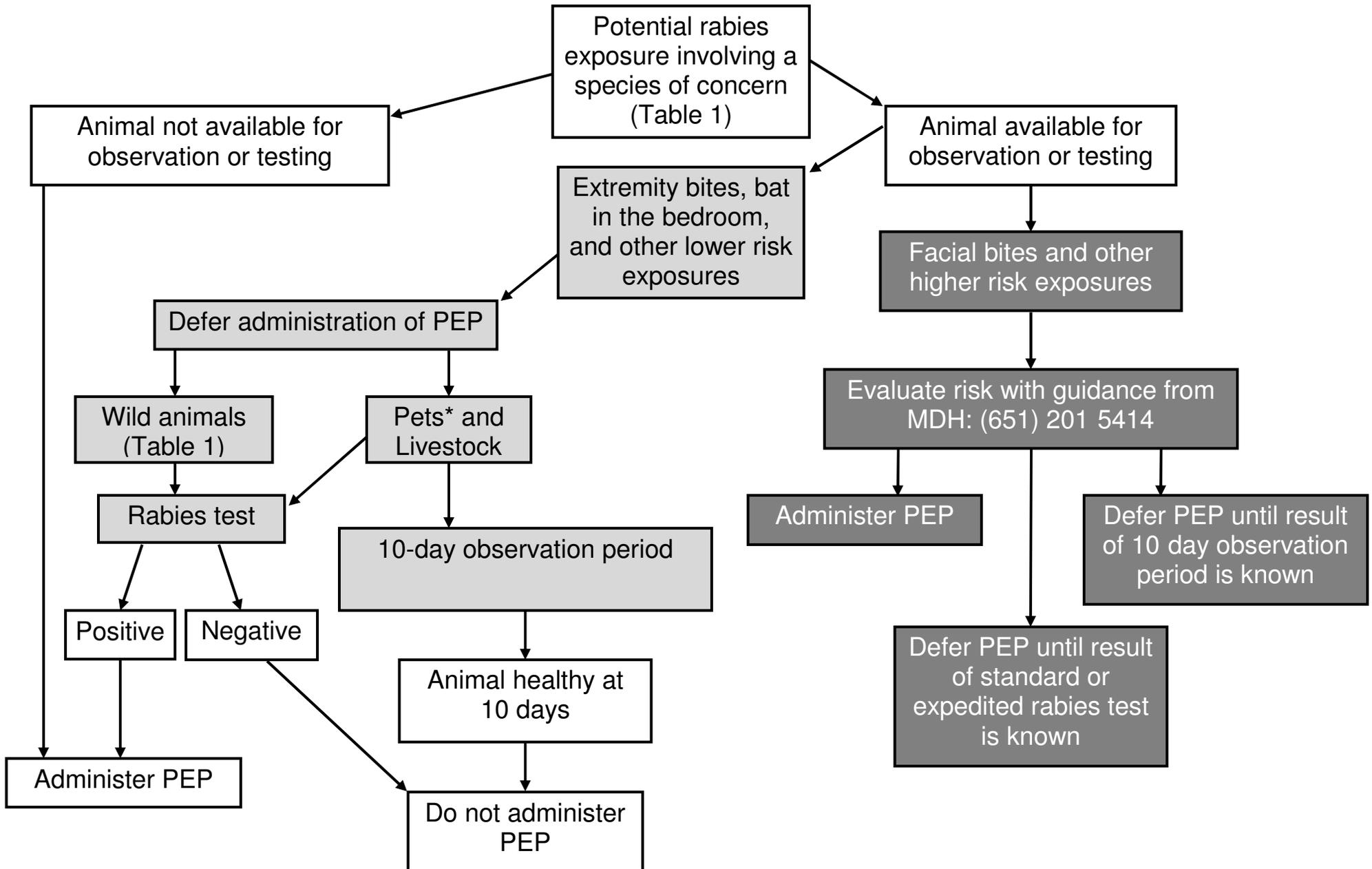
*MDH strongly discourages testing small rodents or rabbits for rabies, but unique situations do occur in which testing may be justified. Please do not submit these species without first consulting with MDH at (651) 201-5414.

**Table 2: Guidelines for Managing Animal Bites
and Bat Encounters in Humans**

Animal species	Situation	Location of bite (or non-bite) exposure	Rabies post exposure prophylaxis (PEP) recommendations
Dogs, Cats, Ferrets	Animal available to be confined and observed for 10 days or tested for rabies	Extremities	Defer administration of PEP until outcome of 10 day observation period or rabies testing is known
		Face or head	Consult with MDH epidemiologists
	Animal unavailable	Anywhere on body	Administer PEP regimen
Horses and other Livestock (ex. cow, sheep, goat, pig, llama)	Animal available to be confined and observed for 10 days	Extremities	Defer administration of PEP until outcome of 10 day observation period is known
		Face or head	Consult with MDH epidemiologists
	Animal unavailable	Anywhere on body	Consult with MDH epidemiologists
Bats, Skunks, Raccoons, Foxes, and other Wild Animals (see Table 1)	Wild animal available for euthanasia and testing	Anywhere on body	Consult with MDH epidemiologists. In most cases, PEP can be deferred until rabies test results are known
	Wild animal unavailable	Anywhere on body	Administer PEP regimen

MDH epidemiologists are available 24/7 to healthcare providers at (651) 201-5414 to discuss management of possible rabies exposure in humans.

Figure 1: Evaluation of Potential Rabies Exposures Flowchart



* Dogs, cats, and ferrets

Factors to consider when determining need for PEP

Type of exposure

- **Bite exposures:** Consultation with a healthcare provider is recommended anytime a bite wound breaks the skin. Considerations include wound cleaning, tetanus vaccination, the need for antibiotics, and whether or not rabies post-exposure prophylaxis (PEP) is indicated.
- **Non-bite exposures:** Non-bite exposures include saliva contact to mucous membranes, saliva contact to fresh, non-scabbed skin wounds, and scratches. In general, the risk of rabies is very low following non-bite exposures; however, there are rare reports of rabies transmission by these routes suggesting that they constitute sufficient risk to consider administration of PEP on a case-by-case basis.

Location and severity of the bite

When a bite is to an extremity, there is adequate time and it is safe for the patient to wait for completion of a 10-day observation and confinement period of the animal, or for rabies test results on the animal to determine whether or not PEP is necessary. Bites to the face and head are more urgent, and consultation with MDH on these cases is recommended (Table 2; Figure 1). Regardless of location, the deeper and more serious the bite wound(s), the greater the urgency for PEP. Normal laboratory turn-around time for rabies testing in Minnesota is 1 to 2 business days. In urgent situations, expedited rabies testing can be arranged by calling MDH at (651) 201-5414.

Circumstances of the bite incident

Factors surrounding the circumstances of the bite relevant to rabies risk include the species of the animal, whether the bite occurred in an urban or rural setting, if the animal runs loose/unmonitored when outdoors, if there was a history of a skunk on the premises within the past few months, whether the pet has a previous history of aggressive behavior, and whether the bite was provoked or unprovoked.

Vaccination status of the biting animal

In the United States, rabies vaccine is licensed for dogs, cats, ferrets, sheep, cattle and horses. An animal is currently vaccinated and can be considered immunized if the primary vaccination was given at least 28 days before the biting incident, or if the animal has received a primary vaccine and a booster vaccination within the timeframe recommended by the manufacturer. Typically, dogs and cats are vaccinated for rabies as puppies or kittens, and the vaccination is boosted at one year of age. After that, dogs are generally vaccinated for rabies every 3 years, and cats are generally vaccinated annually or every 3 years, depending on the vaccine used.

Even though rabies rarely occurs among currently vaccinated animals, out of an abundance of caution, all dogs, cats and ferrets are confined and observed for 10 days, or euthanized and tested for rabies following a bite to a human. This is the law in Minnesota and it applies regardless of the animal's vaccination status.

Species of the animal and requirements of the 10-day confinement and observation period

Dogs, cats, ferrets, and livestock such as horses, cattle, goats and sheep should be confined and observed for 10 days following a bite, to rule out rabies risk. There is no such option for wild animals that bite humans; these bites are handled on a case-by-case basis following consultation with MDH (Table 2; Figure 1).

Following a bite, a dog, cat, or ferret that is currently vaccinated for rabies may be confined in the home or as directed by local authorities. A dog, cat, or ferret that is not currently vaccinated for rabies may be required by local authorities to be confined at a veterinary clinic or other secure location at the owner's expense. Any illness in an animal under confinement must be reported to MDH. If, during the 10-day confinement period, an animal shows signs suggestive of rabies, or dies naturally or is euthanized, it must be tested for rabies.

Rationale for a 10-day confinement and observation period

Animals cannot transmit the rabies virus to humans until the virus is present in the animal's salivary glands and saliva. Once the disease has progressed to this stage in domestic animals, they will begin to show obvious clinical signs of rabies. The time period between the onset of viral shedding and onset of clinical signs of rabies is known to be at maximum 3 to 4 days in dogs, cats and ferrets. Thus, if a dog, cat or ferret had rabies virus in its saliva at the time of a bite (and could have transmitted the disease to the victim), it will be sick or dead within 3 to 4 days. The 10-day confinement period includes a safety factor.

III. MANAGEMENT OF HUMAN-BAT ENCOUNTERS

Bat encounters and bat bites

Most people who have been bitten by a bat report a stinging or needle prick sensation. However, bat bites may not be noticed, especially if someone is asleep, and bat bites may leave little or no evidence of a wound or puncture. Therefore, if there is any chance that there was physical contact with a bat, the bat should be tested for rabies. If the bat is not available for testing, then rabies post-exposure prophylaxis (PEP) should be administered.

When should a bat be submitted for rabies testing?

- A person has been bitten or has had any physical contact with a bat.
- A person wakes up to find a bat in the bedroom.
- A bat is found in a room with an unattended child.
- A bat is found in a room with anyone who cannot reliably communicate whether or not there was physical contact.

How to capture a bat and submit it for testing

- Use a container with a lid. Do not use pillowcases, blankets or towels, as bats may bite through fabric.
- Wear leather gloves.
- Approach the bat slowly and place the container over the bat. Then slide the lid (or a piece of cardboard) underneath the bat and flip the container over, trapping the bat inside.
- Secure the lid with tape.
- There is no need to kill the bat; the bat may be hand delivered alive to the Minnesota Veterinary Diagnostic Laboratory during normal business hours for testing or it may be euthanized by a veterinarian prior to submission. The brain must remain intact for the bat to be tested for rabies.
- If the bat is dead, keep it cool, but avoid freezing. If the bat has been inadvertently frozen, it is still worthwhile to submit it as many will still be testable.
- Whenever possible, deliver the bat in person to the Veterinary Diagnostic Laboratory, keeping it cool during transport. Hand delivery reduces the time to testing, which can be important for maintaining sample quality, especially during summer months.
- For more information on rabies specimen submission, including after-hours submissions, see pages 17-18.

Veterinary Diagnostic Laboratory
University of Minnesota
1333 Gortner Ave
St. Paul, MN 55108
Phone: 1-800-605-8787; (612) 625-8787
(See map for directions, page 19)

- If hand delivery is not possible, you may contact a local veterinary clinic to euthanize the bat (if necessary), package it, and arrange for overnight shipment to the Veterinary Diagnostic Laboratory.
- In some Minnesota communities, an animal control officer or pest-control professional may be called to capture a bat and submit it for rabies testing.

Assessment of the need for rabies PEP following a bat encounter

- Administration of rabies PEP should generally be deferred until the results of a rabies test are known. Test results are available within 1 to 2 business days and only 3% to 4% of bats test positive for rabies.
- PEP should be initiated when there is a human/bat encounter during which physical contact occurred or may have occurred, and the bat is not available for testing.
- 24/7 telephone consultation on potential rabies exposure is available to healthcare providers, veterinarians, public health professionals, and law enforcement at: (651) 201-5414. Rabies consultations are available to the public at the same number Monday – Friday, 8:30 a.m. to 4:30 p.m.

IV. RABIES POST-EXPOSURE PROPHYLAXIS (PEP) REGIMEN

Rabies PEP overview

The rabies PEP regimen involves administration of human rabies immune globulin (HRIG), which is given only once, and a series of four 1.0 mL rabies vaccinations (Table 3). HRIG and the first vaccination are given on the first day of treatment (designated day 0) and three additional rabies vaccinations are given on days 3, 7, and 14.

Immunocompromised persons receive a fifth vaccination on day 28, and should be tested for seroconversion 7 to 14 days following completion of the PEP regimen (Table 4).

Patients who have previously received either pre or post-exposure rabies prophylaxis should receive only two rabies vaccine boosters following an exposure, given on days 0 and 3. Patients who have been previously vaccinated SHOULD NOT receive HRIG, even if the pre- or post-exposure rabies prophylaxis regimen was given many years prior (Table 3; Table 4).

Human rabies immune globulin (HRIG)

Human rabies immune globulin (HRIG) is infiltrated around the site of the bite(s), and provides rapid passive immune protection with a half-life of approximately 21 days. It is administered only once, on the first day of the PEP regimen (designated day 0). No more than the recommended dosage of HRIG should be given because excessive HRIG can partially suppress active production of antibody. If the HRIG was not administered on day 0, it may be administered up to and including day 7 of the PEP regimen. Beyond day 7, HRIG is not indicated, as the patient's antibody response to the vaccine occurs in that timeframe.

- The recommended dosage of HRIG is 20 IU/kg body weight for all ages including children.
- Infiltrate as much of the HRIG as possible into and around the bite wound.
- Administer the remaining HRIG intramuscularly (IM) at a site distant from the first vaccination site, generally in the quadriceps or deltoids.
- If there is no wound, such as following a bat-in-the-bedroom exposure, then administer the entire dose of HRIG in the quadriceps or deltoids.

Interference of HRIG with live virus vaccine administration

HRIG can interfere with live virus vaccines. Therefore the recommended interval between HRIG and measles- or varicella-containing vaccines is four months. See CDC chart:

http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/A/mmr_ig.pdf.

Rabies vaccine

A 1.0 mL dose of rabies vaccine is given IM in the deltoid area of adults or the anterolateral thigh of young children on days 0, 3, 7, and 14 of the rabies PEP regimen (Table 3). The first vaccination is given concurrently with the HRIG at a site distant from the HRIG. An additional fifth dose of rabies vaccine is given on day 28 to immunocompromised patients (Table 4). Rabies vaccine must **NOT** be given in the gluteals due to the possibility of poor absorption from that site and lower neutralizing antibody titers.

Two inactivated, cell culture rabies vaccines are currently available in the United States: human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC). Both are considered equally safe and efficacious. It is recommended that a vaccine series be initiated and completed with the same vaccine product; however, decreased efficacy or increased frequency of adverse reactions have not been documented when the series is initiated with one vaccine product and completed with another. The rabies vaccine series induces an active immune response that requires 7 to 10 days to develop and persists for many years. A rabies vaccine information statement (VIS) is available from CDC at: <http://www.cdc.gov/vaccines/hcp/vis/vis-statements/rabies.html>

Previously vaccinated persons

Previously vaccinated individuals are those who have completed a pre-exposure or post-exposure regimen of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC), or who have received a different vaccine outside of the U.S. and have a documented serum titer corresponding to complete neutralization at $\geq 1:5$ serum dilution (or its equivalent, approximately 0.1-0.2 IU/mL) by the rapid fluorescent focus inhibition test (RFFIT) (Reference 7). Following an exposure, previously vaccinated persons are given two 1.0 mL doses of vaccine intramuscularly in the deltoid area on days 0 and 3. **No HRIG is administered.** Please consult with MDH epidemiologists if the patient's previous pre- or post-exposure vaccination regimen was administered more than 20 years prior to the current exposure.

Deviations from recommended PEP vaccination schedule

Once the decision to initiate rabies PEP has been made, the PEP regimen should be started as soon as possible. Every effort should be made to adhere to the recommended PEP regimen schedule, especially the first two days of treatment, days 0 and 3. After day 3 of the regimen, deviations of a few days are acceptable. For most minor delays or interruptions, the vaccination schedule can be shifted and 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 final dose given one week later on day 17. Please consult MDH epidemiologists for advice when substantial deviations from the recommended schedule have occurred.

Table 3: Rabies Post-Exposure Prophylaxis for Healthy, Immunocompetent Persons, Including Pregnant Women

Vaccination Status	Treatment	Dosage/Administration Guidelines for All Ages	Day of Regimen
Not Previously Vaccinated	<ul style="list-style-type: none"> • Wound cleansing • Tetanus toxoid booster* • Human rabies immune globulin (HRIG) 	<ul style="list-style-type: none"> • 20 IU/kg body weight • Infiltrate HRIG into and around the wound • Remaining HRIG given IM at a site distant from the vaccination site 	Day 0 (HRIG can be given up to day 7)
	<ul style="list-style-type: none"> • Rabies vaccine 	<ul style="list-style-type: none"> • Four 1.0 mL doses, given IM <ul style="list-style-type: none"> ▪ Adults/older children: deltoid area ▪ Young children: anterolateral thigh ▪ Never in gluteals 	Days 0, 3, 7, 14
Previously Vaccinated†	<ul style="list-style-type: none"> • Wound cleansing • Tetanus toxoid booster* • Rabies vaccine 	<ul style="list-style-type: none"> • Do not give HRIG • Two 1.0 mL doses, given IM <ul style="list-style-type: none"> ▪ Adults/older children: deltoid area ▪ Young children: anterolateral thigh ▪ Never in gluteals 	Days 0, 3

* Indicated if last tetanus vaccine was more than 5 years prior to exposure

† Completed pre- or post-exposure regimen of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC) within the past 20 years, or received another vaccine with documented serum titer corresponding to complete neutralization at $\geq 1:5$ serum dilution (or its equivalent, approximately 0.1-0.2 IU/mL) by the rapid fluorescent focus inhibition test (RFFIT).

Table 4: Rabies Post-Exposure Prophylaxis for Immunocompromised Persons

Vaccination Status	Treatment/Testing	Dosage/Administration Guidelines for All Ages	Day of Regimen
Immunocompromised, Unvaccinated Persons	<ul style="list-style-type: none"> Wound cleansing Tetanus toxoid booster* Human rabies immune globulin (HRIG) 	<ul style="list-style-type: none"> 20 IU/kg body weight Infiltrate HRIG into and around wound Remaining HRIG given IM at a site distant from the vaccination site 	Day 0 (can be given up to day 7)
	<ul style="list-style-type: none"> Rabies vaccine 	<ul style="list-style-type: none"> Five 1.0 mL doses, given IM <ul style="list-style-type: none"> Adults/older children: deltoid area Young children: anterolateral thigh Never in gluteals 	Days 0, 3, 7, 14, 28
	<ul style="list-style-type: none"> Post vaccination serologic testing 	<ul style="list-style-type: none"> Submit serum (2cc) for rabies antibody titer by RFFIT‡ Adequate antibody titer: complete neutralization at $\geq 1:5$ dilution (or its equivalent, 0.1-0.2 IU/mL) by the RFFIT method 	7-14 days following PEP completion
Immunocompromised, Previously Vaccinated Persons†	<ul style="list-style-type: none"> Wound cleansing Tetanus toxoid booster* Rabies vaccine 	<ul style="list-style-type: none"> DO NOT give HRIG Two 1.0 mL doses, given IM <ul style="list-style-type: none"> Adults/older children: deltoid area Young children: anterolateral thigh Never in gluteals 	Days 0, 3
	<ul style="list-style-type: none"> Post vaccination serologic testing 	<ul style="list-style-type: none"> Submit serum (2cc) for rabies antibody titer by RFFIT‡ Adequate antibody titer: complete neutralization at $\geq 1:5$ dilution (or its equivalent, 0.1-0.2 IU/mL) by the RFFIT method 	7-14 days following PEP completion

* Indicated if last tetanus vaccine was more than 5 years prior to exposure

† Completed pre- or post-exposure regimen of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC) within the past 20 years, or received another vaccine with documented serum titer corresponding to complete neutralization at $\geq 1:5$ serum dilution (or its equivalent, approximately 0.1-0.2 IU/mL) by the rapid fluorescent focus inhibition test (RFFIT).

‡ Refer to page 15 for laboratories that offer the RFFIT

Human rabies biologics

Rabies products are commercially available through pharmaceutical distributors or may be obtained directly from the manufacturers using the toll-free numbers listed below. The Minnesota Department of Health does not provide rabies biologics. Check with your pharmacy to determine availability.

Human rabies immune globulin (HRIG) products

Imogam[®] Rabies-HT
Sanofi Pasteur
www.vaccineshoppe.com
1-800-822-2463

HyperRab[™] S/D
Grifols Therapeutics
Bayer Biological Products
<http://www.hypermunes.com>
1-800-243-4153

Human rabies vaccines

Human Diploid Cell Vaccine (HDCV)
Imovax IM[®] (pre- and post-exposure)
Sanofi Pasteur
www.vaccineshoppe.com
1-800-822-2463

Purified Chick Embryo Cell Vaccine (PCEC)
RabAvert[®] (pre- and post-exposure)
GlaxoSmithKline
www.gsksource.com
1-888-825-5249

Patient assistance programs

Both rabies vaccine manufacturers have patient assistance programs that provide biologics to qualifying underinsured or uninsured patients.

An application form and information about Sanofi Pasteur's Patient Assistance Program (providing Imogam[®] Rabies HT and Imovax[®] IM) can be found at: www.needymeds.org/brand-drug/name or by telephone at 1-888-847-4877.

Information on the GlaxoSmithKline Patient Assistance Program (providing RabAvert[®]) is available at: www.gsk-vap.com or by telephone at 1-800-589-0837.

Adverse reactions

In general, there is a very low frequency of serious adverse reactions to the rabies PEP regimen. Local pain, headache and low-grade fever may follow administration of HRIG. Pain, erythema, swelling, itching, and other mild local reactions are reported among 11-90% of vaccinees. Rabies PEP should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Non-steroidal anti-inflammatory drugs and antipyretic agents, such as ibuprofen or acetaminophen, may be used to control mild adverse reactions.

An immune-complex-like reaction (generalized urticaria, sometimes accompanied by arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise) occurs in approximately 6% of pre-exposure vaccinated individuals receiving a booster dose of rabies vaccine after primary vaccination. Although it is rare, this reaction can occur in persons receiving their primary vaccination regimen. No deaths resulting from these reactions have been reported.

When a person with a history of serious hypersensitivity to rabies vaccine must be revaccinated, antihistamines may be administered concomitant with vaccine, and the patient should be observed for development of anaphylaxis immediately following vaccination. The Zoonotic Diseases Unit is available at (651) 201-5414 for consultation about the management of possible rabies exposure and PEP in patients with a history of serious adverse reactions to rabies vaccine.

For more information regarding the safety of rabies biologics, please consult Manning, SE., et al., *Human rabies prevention--United States, 2008: Recommendations of the Advisory Committee on Immunization Practices*. MMWR Recomm Rep, 2008. 57(RR-3): p.9-10.

V. RABIES PRE-EXPOSURE PROPHYLAXIS (PEP) REGIMEN

Pre-exposure vaccination against rabies simplifies the rabies post-exposure treatment, and it may protect in cases of unrecognized rabies exposure or when post-exposure treatment is delayed. It does not eliminate the need for appropriate treatment following a known rabies virus exposure.

Who should receive rabies pre-exposure prophylaxis?

- Veterinarians, veterinary technicians, animal control officers, wildlife rehabilitators, zoo employees, certain laboratory workers, and others who have regular contact with potentially rabid animal species.
- International travelers to areas with endemic canine rabies who are likely to come into contact with dogs or wild animals and where access to medical care and appropriate biologics may be limited.

Pre-exposure rabies vaccination series

- Three 1.0 mL doses of rabies vaccine are given IM, one injection per day, on days 0, 7, and 21 or 28, in the deltoid area of adults or in the anterolateral thigh of young children.
- Human diploid cell vaccine (HDVC) or purified chick embryo cell vaccine (PCEC) may be used, although it is recommended that the vaccine series be initiated and completed with the same vaccine product.
- No HRIG should be given.

Antibody titers and booster vaccination

- Following their initial rabies vaccination series, persons in high-risk occupations should have their virus neutralizing rabies antibody titers checked periodically (Table 5).
 - Every 6 months in persons in the continuous-risk category.
 - Every 2 years for persons in the frequent-risk category.
- The RFFIT (Reference 7) is the only recommended test for determining virus neutralizing antibody levels against the rabies virus. Other available titer tests (including the ELISA test) are not recommended for this purpose.
- There are currently two working guidelines (or recommended “cut-offs”) for antibody titer levels below which a rabies-vaccinated person should receive a booster vaccination.
 - The ACIP (Reference 1, pg. 18) recommends that a single booster rabies vaccination be given when the titer falls below that corresponding to complete neutralization at a serum dilution $\geq 1:5$ by the rapid fluorescent focus inhibition test (RFFIT), a virus neutralization test. Complete viral neutralization at a 1:5 dilution is approximately equal to a titer of 0.1-0.2 IU/mL, depending on the reporting laboratory.
 - MDH generally recommends that the ACIP guideline be used.
 - WHO recommends that a single booster rabies vaccination be given when the titer drops below 0.5 IU/mL by the RFFIT.
 - Healthcare providers should take into consideration their patient’s risk of exposure, time until the next titer test, previous rabies titer results, health status, and accessibility to healthcare should a potential exposure occur, when determining when to administer a rabies vaccine booster to a patient.

Table 5: Rabies recommendations for pre- exposure vaccinated persons

Pre-exposure rabies prophylaxis	Serologic testing	Rabies booster	Post-exposure rabies prophylaxis for pre-exposure vaccinated persons
Three 1.0 mL IM rabies vaccinations are given. One injection per day on days 0, 7, and either 21 or 28	<p><u>Continuous Risk</u>[†] Rabies titers performed every 6 months using the RFFIT* method</p> <p><u>Frequent Risk</u>[‡] Rabies titers performed every 2 years using the RFFIT* method</p>	A single booster rabies vaccination is given when the rabies titer drops below that corresponding to complete neutralization at ≥1:5, approximately 0.1-0.2 IU/mL ¹ by the RFFIT* method	<ul style="list-style-type: none"> • Following a rabies exposure, two 1.0 mL rabies vaccinations are given on days 0 and 3 • No human rabies immune globulin (HRIG) is given • No serum titer test is performed

† Rabies research laboratory workers; rabies biologics production workers

* RFFIT = rapid fluorescent focus inhibition test

‡ Veterinarians and staff; animal control and wildlife workers; rabies diagnostic laboratory worker

¹ The ACIP recommendation for an adequate titer, i.e. complete viral neutralization at ≥1:5 serum dilution, is equivalent to approximately 0.1-0.2 IU/mL depending on the reporting laboratory

Commercial laboratories offering RFFIT rabies antibody titer testing

Both require 2.0 mL serum

Rabies Laboratory
 Kansas State University
 2005 Research Park Circle
 Manhattan, KS 66502
 (785) 532-4483
www.ksvdl.org/rabies-laboratory

Atlanta Health Associates
 309 Pirkle Rd, Suite D-300
 Cumming, GA 30040
 1-800-717-5612
www.atlantahealth.net

Testing at KSU may also be requested through Quest Labs as Rabies Vaccine Response End Point Titer (order # 5789)

VI. MANAGEMENT OF ANIMALS EXPOSED TO A RABID ANIMAL

Rabies is a reportable disease in Minnesota. Anyone who has reason to believe that an animal is infected with rabies or has been exposed to rabies should call the Minnesota Board of Animal Health (BAH) at (651) 201-6808. BAH investigates all cases in which a domestic animal has been exposed to rabies under BAH Rules 1721.0570.

A wild animal that has potentially exposed a domestic animal to rabies should be tested whenever possible. Local animal control officers in some communities may assist with capturing a wild animal for rabies testing. Veterinarians can be contacted to assist with rabies specimen submission.

For questions about rabies in animals or to report suspect or exposed animals, contact:
Minnesota Board of Animal Health (651) 201-6808
For more information on rabies in animals go to: mn.gov/bah

VII. MINNESOTA'S RABIES RULES

RABIES PREVENTION AND CONTROL

1721.0570 RABIES POSTEXPOSURE MANAGEMENT PROCEDURES FOR ANIMALS.

Subpart 1. **Management of animals exposed to a rabid animal.**

- A. An animal that is determined by the board to have been exposed to rabies must be managed as described in items B to D.
- B. An animal that is currently vaccinated for rabies must be kept under confinement and observed for signs of rabies for 45 days and, unless exempted by the board, revaccinated for rabies within three days of the exposure.
- C. An animal for which there is a licensed rabies vaccine, but which has never been vaccinated for rabies, must be euthanized or quarantined for 180 days.
- D. All other animals must be evaluated on a case-by-case basis. The board may require the exposed animal to be euthanized, quarantined, or confined for up to 180 days. The board may also require the animal to be vaccinated for rabies.

Subp. 2. **Quarantine procedures.** Animals must be quarantined in a manner approved by the board so as to minimize contact with persons or other animals. Dogs, cats, and ferrets, unless exempted by the board, must be vaccinated or revaccinated for rabies at the beginning of the quarantine period.

Subp. 3. **Release of quarantine on rabies-exposed animals.** All animals that are quarantined for rabies must be inspected by a veterinarian at the end of the quarantine period. Quarantine established on an animal under this part must not be released until a written report is received by the board from a licensed veterinarian stating the veterinarian inspected the animal at the end of the quarantine period and observed no signs of rabies. No dog, cat, or ferret may be released from quarantine unless it is currently vaccinated for rabies.

Subp. 4. **Reporting.** Any illness in an animal that is under confinement or quarantine established under this part must be reported immediately to the board.

1721.0580 MANAGEMENT OF ANIMALS THAT BITE HUMANS.

Subpart 1. **Dogs, cats, and ferrets.** A dog, cat, or ferret that bites a human must be kept under confinement and observed for signs suggestive of rabies for ten days, or the animal must be euthanized and tested for rabies. If requested by the Department of Health, a stray or impounded dog, cat, or ferret that bites a human may be euthanized and tested for rabies before the required five-day holding period as specified in part 1721.0520, subpart 10, or in Minnesota Statutes, section 346.47.

Subp. 2. **Other animals.** An animal other than a dog, cat, or ferret that bites a human must be managed on a case-by-case basis based on the recommendations of the Department of Health. The animals may

be required to be confined and observed for signs suggestive of rabies. If the Department of Health requests a rabies test, the animal must be euthanized and tested for rabies.

Subp. 3. **Confinement procedures.** An animal under confinement for rabies observation must be restricted in such a way that the animal can always be found and cannot wander away. A dog, cat, or ferret that is currently vaccinated for rabies may be confined in the home or as directed by local authorities. A dog, cat, or ferret that is not currently vaccinated for rabies may be required by local authorities to be confined at a veterinary clinic or other secure location at the owner's expense.

Subp. 4. **Reporting and testing.** Any illness in an animal that is under confinement and observation for rabies established under this part must be reported to the Department of Health. If the animal shows signs suggestive of rabies, it must be euthanized and tested for rabies. An animal that dies or is euthanized during the confinement period must be tested for rabies.

Subp. 5. **Enforcement.** Local animal control and law enforcement officials are responsible for enforcement of this part.

VIII. RABIES TESTING

Background

- In Minnesota, 31,193 suspect animals were tested for rabies from 2003 to 2015 (median, 2,371 samples per year).
- Of these, 743 (2.4%) tested positive for rabies.
- Skunks and bats form the two wildlife rabies reservoirs in Minnesota and were the animals most commonly found to be rabid.
- Skunks had the highest number and the greatest proportion (299/644; 46%) of positive samples from 2003 to 2015.
- Among bats, 307 (3.5%) of 8,772 submissions tested positive.
- There were 982 raccoons tested during the 13-year period, and all were negative for rabies.
- Among domestic farm animals (cattle, horses, goats, and sheep), cattle had the highest number and greatest proportion of positive samples (51/739; 6.9%).
- Dogs and cats had a lower proportion of positive samples (71/17,957; 0.4%), from 2003 to 2015, although they constituted the majority of submissions.

Guidelines for submitting suspect animals for rabies testing

The only test for rabies in animals that may be used to guide human rabies risk analysis is the direct fluorescent antibody (DFA) test. There is no live animal test for rabies. The animal's brain, specifically sections of the medulla, cerebellum, and hippocampus are required to perform the DFA test. The brain must be relatively fresh and in good condition, as the test cannot be done reliably if the different regions of the brain are not discernable. See the Rabies Specimen Submission Form (page 22) for complete instructions on specimen handling and submission.

Laboratory testing, result reporting, and positive result follow-up

- There is a \$26.25 fee payable to the University of Minnesota Veterinary Diagnostic Laboratory (VDL) for rabies testing by the direct fluorescent antibody (DFA) test. Please add 10% for out-of-state specimens.
- Results for specimens received at the VDL before 11:00 a.m. will be available the next business day by 2 p.m. Results for specimens received after 11:00 a.m. will be available in two business days.
- Expedited testing is available in emergency situations. Healthcare providers, veterinarians, public health or law enforcement may contact MDH Epidemiology at (651) 201-5414 to discuss the need for an expedited test.
- Positive rabies reports are telephoned immediately to the veterinarian, healthcare provider, or other submitter listed on the Rabies Specimen Submission Form.
- Positive test results are reported to the Minnesota Board of Animal Health (BAH) and the Minnesota Department of Health (MDH).
- Situations involving laboratory-confirmed rabies positive animals are investigated, evaluated, and managed by MDH epidemiologists and BAH veterinarians.
- Negative rabies reports are mailed or faxed to the submitter within 1 business day of completion of the test.

Rabies testing in humans

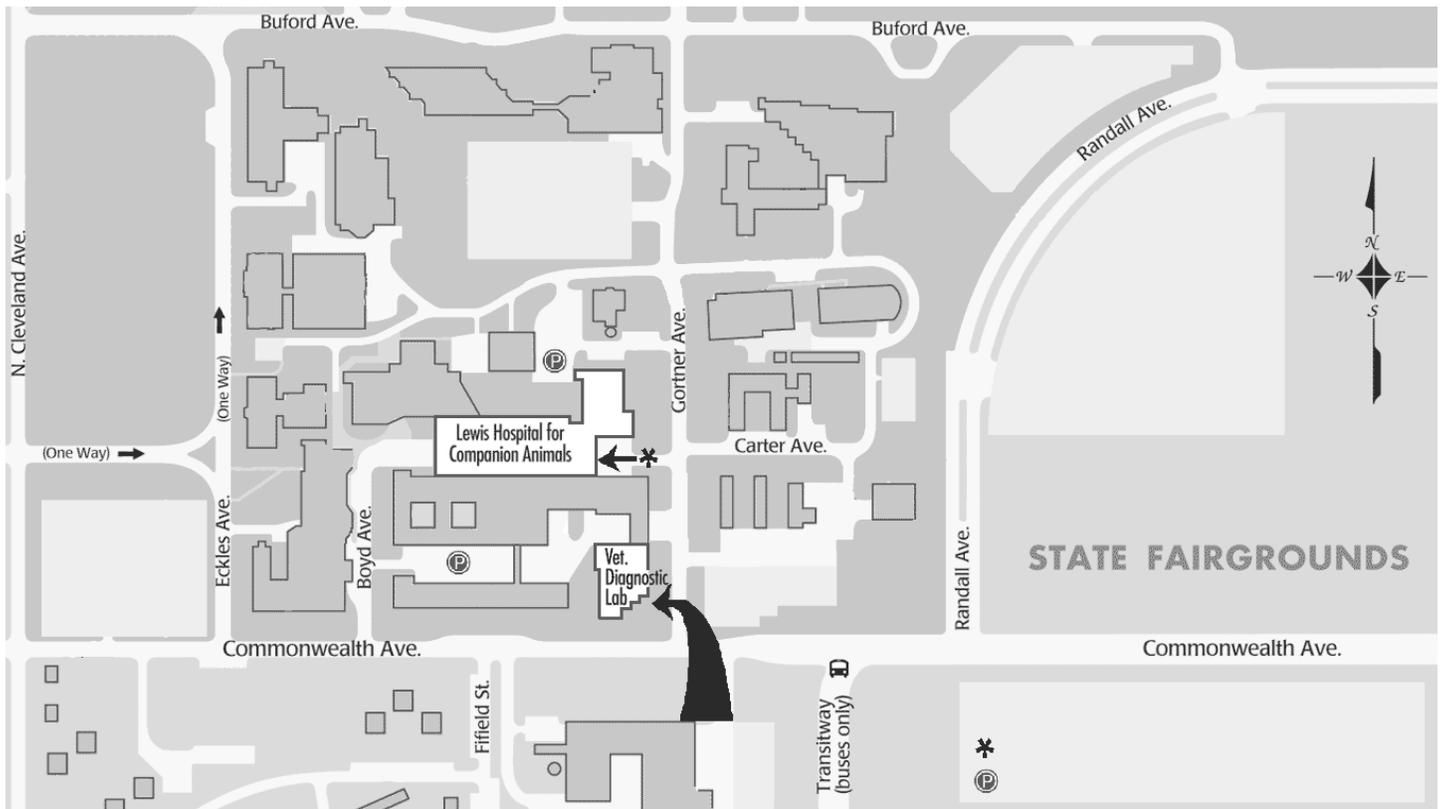
- Testing for diagnosis of rabies in humans is performed at the Centers for Disease Control and Prevention (CDC). Please telephone the MDH Zoonotic Diseases Unit at (651) 201-5414 for assistance with human rabies specimen submission and testing.

IX. REFERENCES

1. Manning, S.E., et al., *Human rabies prevention--United States, 2008: Recommendations of the Advisory Committee on Immunization Practices*. MMWR Recomm Rep, 2008. 57(RR-3): p. 1-28.
2. Rupprecht, C.E., et al., *Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the Advisory Committee on Immunization Practices*. MMWR Recomm Rep, 2010. 59(RR-2): p.1-9.
3. *Compendium of animal rabies prevention and control, 2011:National Association of State Public Health Veterinarians*.JAVMA, 2011. 239(5); p. 609-617.
4. Rabies. In: Heymann D, ed. *Control of Communicable Diseases Manual* 19th Edition. Washington DC: American Public Health Association, 2008; 498-508.
5. Rupprecht, C.E. and R.V. Gibbons, *Clinical practice. Prophylaxis against rabies*. N Engl J Med, 2004. 351(25): p. 2626-2635.
6. Minnesota Board of Animal Health Rules: 1721.0540-1721.0580.
7. College of Veterinary Medicine, Kansas State University. RFFIT-Result interpretation-human. Accessed 05/15/2014. www.ksvdl.org/rabies-laboratory.

X. MAP

Figure 2. University of Minnesota Veterinary Diagnostic Laboratory and Veterinary Medical Center, St. Paul Campus of the University of Minnesota



For directions to St. Paul Campus, visit:
www.vdl.umn.edu/contact-us

XI. FREQUENTLY ASKED QUESTIONS

1. My patient found a bat in her son's bedroom yesterday morning. She opened the window and the bat flew out. She doesn't think the bat bit her son. Do she and her son require rabies post-exposure prophylaxis (PEP)?

Only the son requires rabies PEP because he was asleep in a room with a bat that cannot be tested, and we can't know for certain whether or not the bat bit him while he was asleep. The mother does not need PEP because she wasn't exposed to the bat while asleep and had no physical contact with the bat.

2. My patient started rabies PEP and is scheduled for her 3rd rabies vaccination (day 7) tomorrow. She is currently out of town – is it OK to give the day 7 vaccination 2 or 3 days late? If so, when should her fourth (day 14) vaccination be given?

After the day 0 and 3 vaccinations, minor deviations from the recommended schedule are not important. Give the third vaccination as close to the recommended time as possible, then shift the schedule and resume as though the patient were on schedule, giving the fourth vaccination 7 days later.

3. A neighbor's cat that bit a child on the hand can't be found after one day of searching. How long should I advise the parent to look for the cat before starting the child on rabies PEP?

Because the bite was to an extremity, you can allow the mother to continue searching for the cat for 2 to 3 more days. If the cat has not been found at that point, begin PEP.

4. What are the signs of rabies in cats (or dogs)? My patient is confining a cat that bit her for a 10 day period following the bite. What signs should she be looking for?

An animal that had rabies virus in its saliva at the time of biting someone would develop severe illness or die within 3 to 4 days of the bite. (The 10-day observation period includes a safety factor.) Signs to watch for include loss of appetite, depression, lameness, fever, and neurologic signs such as behavior changes, vocalization, circling, or seizures. If the cat develops any of these signs the patient should contact her veterinarian immediately. If the cat is alive and well 10 days following the bite, then there was no risk of rabies at the time of the bite.

5. I have a patient who was bitten by a dog in Mexico two weeks ago. He had a rabies vaccine there and was told that he was protected. Should I restart the entire PEP series?

In situations like this it is best to get as much information as possible about vaccinations given outside the U.S. and then call MDH for a consultation.

6. A patient who was bitten by a bat a few months ago is wondering if it is too late to receive rabies PEP.

There is no time limit regarding the administration of PEP after an exposure. In this case it is still appropriate to initiate PEP. Administration of both human rabies immune globulin (HRIG) and four doses of rabies vaccine is recommended regardless of the time elapsed since the exposure.

7. A 7 year-old boy was bitten by a squirrel he was chasing around a tree. The squirrel is not available for testing. What should be done?

Rabies PEP is not indicated following a squirrel bite in Minnesota. Wash the wound well with soap and water and check that the boy's tetanus vaccination is up to date. Squirrels, chipmunks, mice, rats and other small rodents do not pose a rabies risk in Minnesota.

8. How long does the rabies virus last in the environment?

Rabies virus does not persist in the environment; it is inactivated almost immediately by UV light and desiccation. Rabies is transmitted only through direct contact with a rabid animal through a bite or saliva contact with a mucous membrane. Rabies is not transmitted through environmental contact or through aerosols.



MDH
Use Only

Rabies Specimen Submission Form

Physicians and veterinarians may obtain information on rabies 24/7 from the Minnesota Department of Health at 651-201-5414. Public calls are taken at the same number M-F, 8:00 a.m. to 4:30 p.m.

Submitter

Date: ___/___/___

Name of submitter: _____

(check all that apply): Owner Veterinarian Exposed person
 Other: _____

Clinic/Org. name: _____

Address: _____

City/Zip: _____ County: _____

Phone: _____ Fax: _____

VDL Use Only

Test Animal

Species: _____ Owned Stray Wild Animal name or ID: _____

Date of death: ___/___/___ Tested animal was: Euthanized Killed Found dead

Owner (if different from submitter): _____ Phone: _____

Address/Location of test animal: _____

City/Zip: _____ County: _____

Explain situation: _____

Cremation: Mass (no remains returned)
 Individual (remains returned) Arranged by owner or veterinary clinic. An animal testing positive for rabies cannot be released. If the sample is untestable, remains may be released on a case by case basis.

Exposure

No human exposure Human exposure Date of exposure: ___/___/___

Type of exposure: Bite (where on body): _____ Non-bite

Person(s) exposed: _____ Age(s): _____

Where did exposure occur? _____ County: _____

Phone 1 of exposed person: _____ Phone 2: _____

Laboratory Only

Live Dead: Whole body Head Brain: Hippocampus Cerebellum Brain stem Insufficient Insufficient Insufficient Condition: Good Fair Autolyzed Traumatized Dried No tissue

Date sent to MDH: ___/___/___ Initials: _____ Comments: _____

Species of animal to be tested:

Companion animals should be euthanized by a veterinarian. Live bats will be accepted during normal business hours only; they should be hand delivered and labeled "Live Bat for Rabies Testing." Small rodents (hamsters, gerbils, guinea pigs, squirrels, chipmunks, rats, mice, gophers, etc.), insectivores (moles and shrews), and lagomorphs (hares and rabbits) do not pose a risk for rabies in Minnesota, and should not be submitted for testing. For guidance on unusual situations involving bites from these animals, please call 651-201-5414. Reptiles, amphibians and birds are not susceptible to rabies and will not be tested for it.

Specimen preparation:

Complete, bilateral samples of brain stem, hippocampus and cerebellum are required for rabies testing. If possible, submit the head of large animals and the entire body of small animals. When submitting only the brain, submit the entire brain. Submit fresh, chilled tissues only; do not fix the brain in chemical preservatives. Refrigerate, do not freeze specimens for rabies testing prior to shipping. However, if specimens have been inadvertently frozen, they may yield satisfactory results; do not thaw them prior to shipping.

Packing requirements:

- Chill specimen prior to packing for hand delivery or shipping by overnight carrier. Specimens that have been packed for delivery while still warm may arrive in unsatisfactory condition for rabies testing due to autolysis.
- Double bag and securely seal specimen in heavy, leak-proof plastic bags. Place in a leak-proof container, preferably a Styrofoam box with a cardboard exterior.
- Include leak-proof freezer packs in sufficient number to keep the specimen cold during transit. During the summer months particularly, many samples arrive at the VDL warm and in unsatisfactory condition for rabies testing.
- Fill any remaining space within the container with newspaper or other absorbent packing material to absorb fluids in case of leakage.
- Complete this form, place in a plastic bag and attach to the outside of the specimen container.
- Label the exterior of the box, "Veterinary Diagnostic Specimen."

Delivery instructions:

Whenever possible, specimens should be hand delivered. If hand delivery is not possible, ship by an overnight delivery service (such as FedEx). For next day results, specimens must be received at the VDL by 11:00 am. Specimens should never be sent by mail – even Priority mail. There is a fee of \$26.25 for testing with an additional 10% charge for out-of-state submission. Charges associated with euthanasia, specimen preparation, packaging, shipping and testing are the responsibility of the person requesting the rabies testing. Questions about specimen submission should be directed to the VDL.

Specimens should be delivered to:**Business hours (M-F, 8:00-4:30)**

Veterinary Diagnostic Laboratory (VDL)
University of Minnesota-St. Paul Campus
1333 Gortner Avenue
St. Paul, MN 55108
Phone: 612-625-8787

OR

Non-business hours and holidays*

Veterinary Medical Center
University of Minnesota-St. Paul Campus
1365 Gortner Avenue (adjoining VDL)
St. Paul, MN 55108
Phone: 612-625-9711

*Live bats are not accepted after business hours

Cremation services:

Animal remains will be processed using mass chemical cremation unless arrangements for individual cremation are made by the client or the client's veterinarian. Please indicate individual or mass cremation on the rabies specimen submission form by checking the box. Once the test result is known, an animal testing negative for rabies may be released to a private cremation service. An animal that tests positive for rabies will not be released for cremation due to the risk of human exposure. If an animal is untestable for any reason, remains may be released on a case by case basis.



UNIVERSITY OF MINNESOTA

VETERINARY DIAGNOSTIC LAB



Minnesota
Department
of Health

**Minnesota Department of Health
Infectious Disease Epidemiology, Prevention, and Control Division
Zoonotic Diseases Unit
651-201-5414
www.health.state.mn.us**

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