

# RABIES

## Report Immediately

### ✓ DISEASE AND EPIDEMIOLOGY

#### Clinical Description

##### Animal Rabies

Rabies is primarily a disease of the central nervous system. Animals with rabies can appear aggressive (“furious rabies”), or normal or meek (“dumb rabies”). Animals with furious rabies often exhibit aggressive or unusually excited behavior; they may excessively salivate and may attack other animals or humans. Dumb rabies may be more difficult to detect; animals may seem tame, wounded, or dazed. The behavior of an animal, however, is not a reliable indicator of whether or not it has rabies.

##### Human Rabies

Human rabies presents as a rapidly progressing illness, with a duration of 2–21 days. A prodromal phase, lasting about 2–10 days, is characterized by pain and numbness/tingling at the site of the bite (present in 50–80% of cases) and by nonspecific complaints such as fatigue, headache, and fever. Behavioral changes may also be apparent, including apprehension, anxiety, agitation, irritability, insomnia, and depression.

The prodromal phase is followed by the neurologic phase, during which the following can occur: disorientation and hallucinations, paralysis, episodes of terror and excitement, hydrophobia (fear of swallowing liquids), hyperventilation, hypersalivation, and seizures. These symptoms are invariably followed by coma and death. Once symptoms begin, drugs or treatments typically do not improve the patient’s condition.

#### Causative Agent

The rabies virus is a rhabdovirus of the genus *Lyssavirus*. All members of the genus are antigenically related, but use of the nucleotide sequencing and monoclonal antibodies can show differences according to animal species or geographic location.

#### Differential Diagnosis

The differential diagnosis for rabies includes: delirium tremens, reaction to illicit drugs, strychnine poisoning, acute psychosis, tetanus, bacterial meningitis, cerebral abscess, viral encephalitis, cerebral malaria, post rabies vaccine encephalitis, and snake bite.

## **Laboratory Identification**

### **Animal Testing**

The UPHL performs rabies testing on animal specimens. Local health departments, animal control officers, and the public must make arrangements for testing and transport of specimens to the UPHL. Animal control officers and veterinarians need to be familiar with the proper way to euthanize, preserve, and ship the animal specimens to the laboratory. Except for whole bats and other very small animals, only heads will be accepted.

### **Human Testing**

Human rabies testing requires consultation between LHD, UDOH and CDC. All clinical samples from suspect cases of human rabies should be sent to the UPHL for forwarding to the CDC for testing. Contact the UDOH Epidemiology or UPHL Virology Section for specific instructions regarding types of specimens to submit and the proper methods for submission.

## **Treatment**

### **Human**

Specific immunological protection in humans is provided by administration of human rabies immune globulin (HRIG) at the site of the bite as soon as possible after exposure to neutralize the virus, then giving the vaccine at a different site to elicit active immunity. As much of the HRIG should be infiltrated into and around the bite wound and the rest, if any, should be given IM. Vaccine should be given as soon as possible after exposure and, once initiated; the last dose should be given within 14 days. Vaccine should be given IM on days 0, 3, 7, and 14. Once symptoms develop, rabies is typically fatal. Therefore, treatment needs to be initiated as soon as possible following exposure.

### **Animal**

Regularly vaccinating animals is the best way to prevent rabies. If animals are current on vaccines and are exposed to rabid animals, they may only require booster vaccinations. Depending on vaccine status of the animal exposed to a rabid animal, quarantine may be put into place. Quarantine periods (up to six months) exist for domestic animals exposed to a rabid or potentially rabid animal. (See Isolation and Quarantine Requirement Section)

For additional information, please see the National Association of State Public Health Veterinarians Inc. (NASPHV) Compendium of Animal Rabies Prevention and Control 2011. <http://www.nasphv.org/Documents/RabiesCompendium.pdf>

### **Case Fatality**

Rabies is nearly always fatal in humans. Recently, there have been documented cases that have survived rabies without prior post-exposure prophylaxis, but this treatment regimen is rarely successful.

## **Reservoir**

Although all species of mammals are susceptible to rabies virus infection, only a few species are important for maintaining the disease in nature. In the U.S., raccoons, skunks, foxes, and coyotes are the major reservoirs in ground animals, and bats are the major non-ground animal reservoir. The most prevalent strain in Utah is the bat strain. In developing countries, dogs are the principal problem. Any rabies strain can be passed to other animals and humans through exposure to infectious saliva. Small rodents (e.g., squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (rabbits and hares) have not been known to transmit rabies to humans and are almost never found to be infected with rabies. Rodents and lagomorphs which are caged outdoors are sometimes exceptions because the cages may allow exposure to rabid animals, but may also provide enough protection for the caged animal to survive and later develop rabies.

## **Transmission**

Transmission of rabies virus usually begins when infected saliva of a host is passed to an uninfected animal. The most common mode of rabies virus transmission is through the bite and virus-containing saliva of an infected host. Though transmission has been rarely documented via other routes such as contamination of mucous membranes (i.e., eyes, nose, mouth), aerosol transmission, and corneal and organ transplantations.

## **Incubation Period**

### **Animal Rabies**

Depending on a number of factors, including the animal species, the virus strain and the anatomical site of exposure, the incubation period may vary from a few days to several years, but is typically 1–3 months. Some animals, such as dogs and cats, have been studied extensively, and the incubation period for these animals rarely exceeds six months.

### **Human Rabies**

The incubation period for human rabies is usually 3–8 weeks, but can be as short as 9 days (although 9-day incubation periods have not been documented in the U.S. with native strains) or as long as 7 years. Less than 1% of human cases have an incubation period longer than 6 months. The incubation period is typically related to the site of exposure; for example, the incubation period is usually shorter if the virus is inoculated closer to the central nervous system (brain) or in an area that is more highly innervated (such as the hand). The incubation period also depends on the severity of exposure (a larger dose of virus results in a shorter incubation period), the age of the exposed person (younger age generally results in a shorter incubation period), and the strain of the virus.

## **Period of Communicability**

### **Animal Rabies**

Animals are not infectious until virus appears in their saliva, generally toward the end of the incubation period. Dogs, cats, and ferrets may shed virus for about 3–7 days before the onset of clinical signs and may continue shedding throughout the course of their illness. The shedding/communicability period for most wild animals has not been determined, although skunks may shed virus for up to 18 days before death. Carcasses of animals with rabies may contain infectious virus, depending on temperature and environmental conditions. Rabies virus may persist in a frozen carcass for many weeks. Drying and sunlight rapidly deactivate rabies virus. Dried saliva or a dried animal carcass would not contain live rabies virus.

### **Human Rabies**

Rabies virus in humans may be transmissible beginning up to one week before symptom onset and will remain infectious until death. Saliva is considered potentially infectious, as are other bodily tissues and fluids. It should be noted, however, that with the exception of corneal and solid organ transplants from infected persons, there have been no documented cases of person-to-person transmission of rabies at this time.

## **Epidemiology**

### **Human**

In the U.S. over the past century, the number of human deaths attributed to rabies has declined from 100 or more each year to an average of 1–2 each year. The decline is due to pet vaccination and animal control programs, begun in the 1940s, that have essentially eliminated the domestic dog as a reservoir of rabies, and to the development of effective human rabies vaccine and immune globulin. Since 1995, 46 human rabies deaths in the U.S. have been reported to the Centers for Disease Control and Prevention (CDC), with 35 of those associated with bat variants. Eleven of these deaths are believed to have been caused by contact with rabid animals (mostly dogs) outside the U.S. In 2004, a case of rabies in an organ donor and four cases of rabies in organ recipients were identified. Worldwide, an estimated 55,000–65,000 human rabies deaths occur each year. The vast majority of these deaths occur in developing countries.

### **Animal**

Animal rabies exists in most parts of the world. In the U.S., Hawaii is the only state that has never reported an indigenously-acquired rabies case in humans or animals. Wild animals accounted for 92% of reported cases of rabies in 2010. Raccoons continued to be the most frequently reported rabid wildlife species (36.5% of all animal cases during 2010), followed by skunks (23.5%), bats (23.2%), foxes (7.0%), and other wild animals, including rodents and lagomorphs (1.8%). Reported cases decreased among all wild animals during 2010. Most of

the continental U.S. has endemic rabies in terrestrial mammals; bat rabies is endemic in Alaska, as well as throughout the continental U.S. Dogs are a primary reservoir for human rabies in Mexico and much of Central and South America, Asia, and Africa. In the U.S., children are exposed to rabid and potentially rabid animals more often than are adults. Utah averages 12-15 positive rabid bats per year. In 2006, Utah had its first non-bat mammal since 1995, a fox. The last human case of rabies in Utah was in 1944.

## ✓ PUBLIC HEALTH CONTROL MEASURES

### Public Health Responsibility

*Note: Due to the rarity and potential severity of human rabies, a confirmed human rabies diagnosis will be made with extensive involvement from the UDOH and the CDC.*

- Immediately notify the UDOH Division of Epidemiology to report any suspect or confirmed case(s) of human rabies.
- Assist UDOH with obtaining clinical specimens needed for laboratory confirmation, if necessary.
- Identify potentially exposed persons.
  - Institute isolation and quarantine requirements as they apply to a particular case.

Provide education and guidance as requested from the public and/or providers. Educational components are listed below. For further questions, guidance can be provided by UDOH and/or CDC.

### Prevention

Prevention of human rabies relies upon controlling rabies in the animal population. Therefore, animal quarantine regulations and animal vaccination regulations must be enforced.

### Personal Preventive Measures/Education

- Provide the public with the following guidance in order to help prevent rabies and/or potential exposures: Vaccinate pets; cats, dogs, and ferrets are required by law. Although not required by law, livestock vaccinations are encouraged.
- Do not feed or handle wild or stray animals. Avoid sick animals or animals that are acting strangely.
- Do not touch or handle dead animals.
- If there are questions regarding capture of an animal or handling of a carcass, contact the local animal control officer.
- Cover your garbage cans and keep pet food indoors so wild animals are not attracted to it.
- Do not keep wild animals as pets. This is illegal as well as dangerous.
- Never handle bats. A bat bite or scratch may be so small as to go unnoticed. Persons who awaken to find a bat in their room and others

who are unable to provide clear details of whether an exposure occurred, such as young children, or people with disabilities alone with a bat in a room, may require post exposure prophylaxis. Consult with the UDOH or a health care provider.

When a person calls about a secondhand or indirect exposure (usually contact with a pet that was previously bitten by a wild or potentially rabid animal), make sure that the person does not touch the pet's bite wound. Suggest gloves, soap, and water to clean the wound to avoid human exposure to the attacking animal's saliva.

## **Vaccine**

Two types of rabies vaccines are available for use in the United States. They include human diploid cell vaccine (HDCV, Imovax<sup>®</sup> Rabies, sanofi pasteur), and purified chick embryo cell vaccine (PCECV, RabAvert<sup>®</sup>, Novartis Vaccines and Diagnostics). Ideally an immunization series should be initiated and completed with one vaccine product. No clinical studies have been conducted that document a change in efficacy or the frequency of adverse reactions when the series is completed with a second vaccine product. Pre- or post exposure prophylaxis should not be withheld or delayed due to unavailability of same vaccine product, if a second vaccine product is available

Pre-exposure vaccination should be offered to persons in high-risk groups, such as veterinarians, animal handlers, and certain laboratory workers. Pre-exposure vaccination also should be considered for other persons whose activities bring them into frequent contact with rabies virus or potentially rabid bats, raccoons, skunks, cats, dogs, or other species at risk for having rabies. In addition, international travelers might be candidates for pre-exposure vaccination if they are likely to come in contact with animals in areas where dog rabies is enzootic and immediate access to appropriate medical care, including biologics, might be limited.

Pre-exposure prophylaxis is administered for several reasons. First, pre-exposure vaccination does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for RIG and decreasing the number of doses of vaccine needed -- a point of particular importance for persons at high risk for being exposed to rabies in areas where immunizing products might not be available or where they might be at high risk for adverse reactions. Second, pre-exposure prophylaxis might protect persons whose post-exposure therapy is delayed. Finally, it might provide protection to persons at risk for unapparent exposures to rabies.

Pre-exposure prophylaxis should be given in three 1.0-mL injections of HDCV, or PCECV and should be administered IM (intra-muscularly) in the deltoid region -- one injection per day on days 0, 7, and 21 or 28.

## Chemoprophylaxis

**Post-exposure prophylaxis:** Specific immunological protection in humans is provided by administration of human rabies immune globulin (HRIG) at the site of the bite as soon as possible after exposure to neutralize the virus, then giving the vaccine at a different site to elicit active immunity. As much of the HRIG should be infiltrated into and around the bite wound and the rest, if any, should be given IM. Vaccine should be given as soon as possible after exposure and once it is initiated, the last dose should be given within 28 days. Vaccine should be given IM on days 0, 3, 7, and 14.

## Isolation and Quarantine Requirements

### Isolation

**Human:** Typically, persons with human rabies require hospitalization for severe illness. Standard body fluid precautions should always be followed. As stated previously, person-to-person transmission of rabies has not been documented, but may be possible.

**Animal:** Isolations may range from 10 days to 6 months depending on the vaccination status of the animal (see quarantine requirements).

**Hospital:** Standard body substance precautions.

### Quarantine

**Animal:** Quarantines may range from 10 days to 6 months, depending on the vaccination status of the animal (see below). Euthanasia may sometimes be recommended.

**DOGS, CATS, AND FERRETS:** Rabies virus may be excreted in the saliva of infected dogs, cats, and ferrets during illness and/or for only a few days prior to illness or death. A healthy dog, cat, or ferret that bites a person should be confined and observed daily for 10 days; administration of rabies vaccine to the animal is not recommended during the observation period to avoid confusing signs of rabies with possible side effects of vaccine administration. Such animals should be evaluated by a veterinarian at the first sign of illness during confinement.

Animals with up-to-date vaccine that are exposed to a confirmed rabid animal should be given a booster and observed for 45 days.

Any unvaccinated animal that is exposed to a confirmed rabid animal should be in strict quarantine for 6 months or euthanized. Any illness in the animal should be reported immediately to the

local health department. If signs suggestive of rabies develop, the animal should be euthanized and the head shipped for testing. Any stray or unwanted dog, cat, or ferret that bites a person may be euthanized immediately and the head submitted for rabies examination.

For more detailed information on isolation and quarantine, please see the NASPHV Compendium of Animal Rabies Prevention and Control, 2011.

**OTHER BITING ANIMALS:** Other biting animals which might have exposed a person to rabies should be reported immediately to the local health department. Management of animals other than dogs, cats, and ferrets depends on the species, the circumstances of the bite, epidemiology of rabies in the area, biting animal's history, current health status, and potential for exposure to rabies. Prior vaccination of these animals may not preclude the necessity for euthanasia and testing.

## ✓ CASE INVESTIGATION

### Reporting

- Report all suspect and confirmed cases of rabies.
- Animal bites are not reportable to the UDOH. However, an epidemiologist is available 24/7 (1-888-EPI-UTAH) for consultation on animal bite management regarding rabies exposures

### Case Definition

#### Rabies (2011)

##### Clinical Description

Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom.

##### Laboratory Criteria for Diagnosis

###### Animal

- A positive direct fluorescent antibody test (preferably performed on central nervous system tissue)
- Isolation of rabies virus (in cell culture or in a laboratory animal)

###### Human

- Detection of Lyssavirus antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck) by direct fluorescent antibody test, or
- Isolation (in cell culture or in a laboratory animal) of a Lyssavirus from saliva or central nervous system tissue, or



- Identification of Lyssavirus specific antibody (i.e., by indirect fluorescent antibody (IFA) test or complete rabies virus neutralization at 1:5 dilution) in the CSF, or
- Identification of Lyssavirus specific antibody (i.e. by indirect fluorescent antibody (IFA) test or complete rabies virus neutralization at 1:5 dilution) in the serum of an unvaccinated person, or
- Detection of Lyssavirus viral RNA (using reverse transcriptase-polymerase chain reaction [RT-PCR]) in saliva, CSF, or tissue.

Comment: Laboratory confirmation by all of the above methods is strongly recommended.

**Case Classification**

**Animal**

*Confirmed:* a case that is laboratory confirmed.

**Human**

*Confirmed:* a clinically compatible case that is laboratory confirmed by testing at a state or federal public health laboratory.

**Case Investigation Process**

Please refer to following chart for post-exposure prophylaxis guidelines:

**GUIDE TO RABIES POST-EXPOSURE EVALUATION AND MANAGEMENT**

Animal Type	Evaluation and Disposition of Animal	Post-exposure Prophylaxis (PEP) Recommendation
Dogs, cats, ferrets, cattle, horses and sheep	<b>Healthy</b> and available for 10 day observation, <b>quarantine</b> regardless of vaccination status <sup>1</sup>	Should not begin PEP unless animal develops rabies
	Rabid	Immediate PEP
	Suspected Rabid Available for testing	Await testing results; begin PEP immediately if the animal is positive for rabies.
	Unavailable for testing	Immediate PEP
	Unknown (escaped)	Immediate PEP
Skunks, raccoons, bats, <sup>2</sup> foxes, and most other carnivores, including dog/wolf hybrids <sup>3</sup> ; woodchucks and livestock for which there is NO USDA- approved rabies vaccine	Regard as rabid until animal proven negative by laboratory tests. <sup>4</sup> (Animal available for testing.)	Await testing results; begin PEP immediately if the animal is positive for rabies.
	Animal unavailable for testing	Immediate PEP
Rodents (except woodchucks), and lagomorphs (rabbits and hares) and other small mammals except bats	Consider individually <sup>5</sup>	Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require PEP. However, testing and/or PEP is indicated in some circumstances.

Footnotes

1. If a dog, cat, ferret, cattle, horse or sheep being held for the 10-day quarantine develops signs of rabies or signs of any illness, it should be euthanized and tested immediately. If the results are positive, the exposed person should begin PEP immediately.
2. It may be difficult to recognize that an exposure to a bat has occurred since the size of bites or scratches by bats may be very small. Therefore, bat bites may go unnoticed or be mistaken for an insect bite or sting. Post-exposure treatment should be given in any situation where a bat is physically present and a bite, or any other exposure/contact, cannot be ruled out. When children are involved, and/or there are no witnesses to rule out a potential exposure, this is particularly important.
3. Dog/wolf hybrids, regardless of vaccination history, should be considered as wild, unvaccinated animals.
4. The animal should be humanely killed and tested as soon as possible. Holding for observation is not recommended. Do not give post-exposure prophylaxis if immunofluorescence test results of the animal are negative.
5. Rodents (except woodchucks), lagomorphs (rabbits, hare), and other small mammals except bats:
  - Small mammals caged outdoors: Outdoor cages may allow exposure to rabid animals, and several rabies cases have been reported from animals caged in this manner. If the animal is not available for testing, post-exposure prophylaxis is recommended.
  - Small mammals caged indoors: Healthy hamsters, gerbils, rats, mice, and rabbits, etc., which have been caged exclusively indoors for the past 6 months and which have no history of receiving a modified live rabies vaccine, pose no risk. Treatment would not be recommended for the exposed person.
  - Wild rodents, lagomorphs and other small mammals except bats: These animals are unlikely to have rabies. Each exposure needs to be evaluated as outlined below.
    - Provoked bite: If the bite was provoked (such as through feeding, petting, or playing with the animal) and the animal appeared healthy, it is unlikely that the animal was rabid at the time of the bite and most experts would not recommend post-exposure prophylaxis.
    - Unprovoked bite or unhealthy animal: If the bite was unprovoked or the animal appeared unhealthy, it should be submitted to the Utah Public Health Laboratory for testing. If the animal is unavailable for testing, PEP should be considered.

**NOTE:** Birds, reptiles, amphibians, and fish do not get rabies.

(Adapted from: CDC, MMWR. January 8, 1999 / Vol. 48 / No. RR-1. and Massachusetts Department of Public Health.)

- UPHL will notify UDOH immediately of all positive results.
  - If human rabies is suspected, contact UDOH for specimen collection and coordination between UDOH and UPHL for shipment to CDC.
- UDOH will notify LHD.
- Identify victim; note date, time and location of incident.
- Ascertain immunization status of person and/or animal.
- Note the location of the wound.
- Reinforce proper wound care. Wash with soap and water for 10 minutes.
- LHD will contact Animal Control; bite victim, etc. to determine if anyone is in need of post-exposure prophylaxis.
  - If there is a need for post-exposure prophylaxis, LHD may call UDOH to assist in coordinating with hospital.

*The UPHL is the only facility in Utah that tests for rabies. Human rabies tests are only performed by the CDC.*

### **Outbreaks**

More than one related case of rabies in a domestic animal such as dogs, cats, or ferrets in a year will constitute an outbreak.

### **Identification of Case Contacts**

Rabies exposures are often identified on a case-by-case basis. If you are unsure whether an exposure occurred, contact UDOH for consultation.

### **Case Contact Management**

Rabies is transmissible from person to person through secretions. All individuals who came into contact with secretions during the infectious period are considered contacts. These contacts should receive vaccine prophylaxis as appropriate.

## ✓ REFERENCES

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