

Human Rabies

Signs and symptoms	<ul style="list-style-type: none"> • Encephalomyelitis with initial headache, fever, malaise • Later in illness – seizures, hypersalivation, hydrophobia, delirium, paralysis, coma • Death from cardiac arrest or respiratory paralysis around day 10 from onset
Incubation	Usually 3-8 weeks, range 9 days to several years
Case classification	Clinical definition: Acute encephalomyelitis almost always progressing to coma or death within 10 days of onset
	Confirmed: Consistent clinical illness and reference laboratory confirmation
Differential diagnosis	Any infectious encephalitis, transverse myelitis, stroke, psychosis, brain tumor, atropine poisoning, prion disease (CJD), tetanus
Treatment	A small number of cases survive with intensive and aggressive ICU treatment
Exposure	Bats in Washington; foxes, skunks, and raccoons elsewhere in the United States; dogs and other canids and carnivores in other countries
Laboratory testing	<p>Local Health Jurisdiction (LHJ) should contact Communicable Disease Epidemiology (CDE) to arrange testing (206-418-5500 or 877-539-4344)</p> <ul style="list-style-type: none"> • Complete CDC form: http://www.cdc.gov/rabies/pdf/RORform.pdf • Healthcare provider should use proper PPE during specimen collection • Best specimens (amounts given are minimum, obtain all first four specimens): <ol style="list-style-type: none"> 1) saliva ~5 cc in sterile sealed plastic tube; 2) nape of neck biopsy 5-6 mm diameter full thickness biopsy on sterile gauze in sterile sealed plastic container; 3) serum 0.5 ml in sterile sealed plastic tube; 4) CSF 0.5 ml in sterile sealed plastic tube; 5) if available, brain biopsy in sterile sealed plastic tube; 6) if available, fresh frozen brain stem, cerebellum, and hippocampus specimens from autopsy <p><i>Specimen shipping (Section 4):</i></p> <ul style="list-style-type: none"> • Keep all specimens cold, ship cold with Virology form http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf • Specimen Collection and Submission Instructions https://www.cdc.gov/rabies/specific_groups/doctors/ante_mortem.html
Public Health Actions	<p>LHJ should immediately contact CDE for diagnosis or testing (206-418-5500 or 877-539-4344)</p> <ul style="list-style-type: none"> • Identify contacts sharing exposure with the patient • Identify contacts exposed to the patient’s saliva • Recommend post-exposure prophylaxis for contacts as indicated
EMERGENCY	<p><i>Infection Control:</i></p> <ul style="list-style-type: none"> • Limit healthcare personnel involved and recommend PPE: gowns, goggles, masks, and gloves, particularly during intubation and suctioning (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5913a3.htm). • For autopsy recommend PPE: N95 or higher respirator, full face shield, goggles, gloves, complete body coverage by protective wear, and heavy or chain mail gloves to help prevent injury. Minimize aerosols by using a handsaw rather than an oscillating saw and avoid contact of the saw blade with brain tissue. Use a 10% solution of sodium hypochlorite for disinfection. • If exposure occurs during health care, provide rabies post-exposure prophylaxis

Human Rabies

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To assist in the diagnosis of human cases of rabies.
2. To identify persons potentially exposed to a human rabies patient and provide counseling about post-exposure prophylaxis (PEP).
3. To offer PEP to others who may have been exposed to the same source as the patient.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction.**
2. Health care facilities: **immediately notifiable to local health jurisdiction.**
3. Laboratories: Rabies virus **immediately notifiable to local health jurisdiction;** specimen submission required – clinical specimen associated with positive result (2 business days).
4. Veterinarians: **Suspected human or animal cases notifiable immediately to the local health jurisdiction;** animal cases notifiable to Washington State Department of Agriculture (see: <http://app.leg.wa.gov/WAC/default.aspx?cite=16-70>).
5. Local health jurisdictions: **suspected and confirmed cases are immediately notifiable** to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) (206-418-5500 or 1-877-539-4344).

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin investigation immediately.
2. Provide infection control recommendations if a patient is seeking health care.
3. Facilitate transport of specimens to the Centers for Disease Control and Prevention. Please call CDE prior to submitting specimens (206-418-5500 or 877-539-4344).
4. Identify potentially exposed persons and make post-exposure prophylaxis (PEP) recommendations.
5. Report all *confirmed* cases to CDE (see definitions below). Complete the rabies case report form (<http://www.doh.wa.gov/Portals/1/Documents/5100/210-060-ReportForm-Rabies.pdf>) and enter the data into the Public Health Issues Management System (PHIMS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

The disease is caused by the rabies virus (Family *Rhabdoviridae*, genus *Lyssavirus*), a single stranded RNA virus. In the United States, there are several rabies virus variants (strains) circulating among reservoir hosts including raccoon, fox, skunk, and bat variants.

B. Description of Illness

Rabies is a rapidly progressive, acute viral encephalomyelitis. Initial symptoms may include headache, fever, and malaise. Initial neurologic symptoms may include paresthesias or pain often affecting the limb or site where the inoculation occurred and subtle changes in personality. Later neurologic symptoms can include seizures, hypersalivation, hydrophobia, delirium, agitation, and paralysis. Neurological deterioration is rapid; death is often due to cardiac arrest or respiratory paralysis. Death occurs an average of 10 days after the onset of symptoms. A small number of rabies cases survived with intensive treatment and a case of presumptive abortive rabies has been described in a person not receiving intensive care treatment:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5907a1.htm>

For information on animal rabies and exposure assessment, please see the Surveillance and Reporting Guidelines for Suspected Rabies Exposure found at:

<http://www.doh.wa.gov/Portals/1/Documents/5100/420-073-Guideline-RabiesSuspectedExposure.pdf>.

C. Human Rabies in Washington State

Two human cases of rabies have been reported in Washington State in the past 50 years, one in 1995 and one in 1997 (MMWR 1997;46(33):770–4), both due to bat rabies variants.

D. Reservoirs

Bats are the only known reservoir for rabies in Washington State and rabid bats are found throughout the state. The percentage of bats in the wild that are infected with rabies is very low (less than 1%), however 3–10% of the sick and injured bats submitted for testing in Washington are rabid (see Table 1). Rabies has also occurred recently in Washington in animals other than bats (Table 2).

Bats are also the primary reservoir for rabies in Oregon, Idaho, and British Columbia. However, rabid non-bat animals have been detected in these states and province. Oregon identified 25 rabid foxes with bat-variant rabies out of 154 tests during 2000–2014 and one coyote out of 563 tests, almost from counties in the southwest part of that state. In 2015 a rabid cat was identified in southwestern Oregon. Idaho detected a rabid bobcat in 2001 and a rabid skunk in 2004 (both bat-variant rabies) as well as a rabid skunk in 2014 with no variant type given. British Columbia found 4 skunks in a park in Vancouver in 2004 and a cat in 2007 with bat-variant rabies. This shows that bat rabies spills over to other wild and domestic animals.

In other parts of the United States, skunks, raccoons and foxes are important rabies reservoirs (along with bats). Elsewhere, dogs and other carnivores are important reservoirs.

Table 1: Rabid Bats Detected in WA, 2000–2015

Year	Rabid bats / Total bats tested (%)
2015	9/305 (3)
2014	15/276 (5)
2013	12/284 (4)
2012	9/221 (4)
2011	11/204 (5)
2010	14/200 (7)
2009	14/311 (5)
2008	17/337 (5)
2007	22/315 (7)
2006	15/273 (5)
2005	15/245 (6)
2000-4	100/1319 (8)

Table 2: Rabid Non-Bat Animals and Rabies Strain Type in WA, 1986–2015

Year	Animal type (County)	Rabies Strain
2015	Cat (Jefferson)	Bat-variant
2002	Cat (Walla Walla)	Bat-variant
1994	Llama (King)	Bat-variant
1992	Horse (Franklin)	Unknown
1987	Dog (Pierce)*	Unknown: history of bat exposure

* infection was not confirmed at CDC

E. Modes of Transmission

Rabies may be transmitted when saliva or other potentially infectious material (central nervous system tissue) penetrates the skin or contaminates the mucosa of a susceptible mammal. Although person-to-person transmission of rabies has been confirmed only via corneal and organ transplantation, transmission through bites or other mucous membrane exposure is theoretically possible. In addition, four cases of rabies may have occurred as the result of exposure to large amounts of aerosolized rabies virus (e.g., exposure to millions of bats in a cave or through handling laboratory specimens). Rabies is not transmitted by contact with blood, urine or feces, by touching fur, or by being sprayed by a skunk. The virus becomes inactive with drying.

F. Incubation Period of Human Rabies

The incubation period of rabies in humans is typically 3 to 8 weeks but can range from 5 days to several years.

G. Period of Communicability

Rabies virus is present in saliva, cerebrospinal fluid (CSF), and neurologic tissues of infected patients who are in the final (clinical) stage of disease.

Rabid dogs, cats and ferrets are considered communicable no more than 10 days prior to symptom onset. Little or nothing is known about how early communicability starts in other species, including humans.

H. Treatment

There is no proven effective treatment for rabies once clinical signs develop. “When a definitive diagnosis is obtained, primary health considerations should focus, at a minimum, on comfort care and adequate sedation of the patient in an appropriate medical

facility. As new potential treatments become available, medical staff at specialized tertiary care hospitals might consider institution of an aggressive approach to experimental therapies, especially in confirmed cases in young healthy persons at an early stage of clinical disease, after in depth discussions and informed consent by the patient, family or legal representatives (<http://www.mcw.edu/Pediatrics/InfectiousDiseases/PatientCare/Rabies.htm>). Parties authorized to give permission for such treatment also should be aware of the high probability for treatment failure, the anticipated expenses, and that in the rare instances of patient survival, the recovery might be associated with a variety of neurologic deficits requiring a lengthy period of rehabilitation.” See: (MMWR 2008;57:RR-3 <http://www.cdc.gov/mmwr/PDF/rr/rr5703.pdf>).

For information regarding management of human rabies, please see: http://www.cdc.gov/rabies/specific_groups/doctors/index.html.

3. CASE DEFINITIONS

A. Clinical description

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

B. Laboratory criteria for diagnosis

1. Detection by direct fluorescent antibody of Lyssavirus antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck), or
2. Isolation (in cell culture or in a laboratory animal) of Lyssavirus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue, or
3. 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,
4. 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
5. Detection of Lyssavirus viral RNA (using reverse transcriptase-polymerase chain reaction [RT-PCR]) in saliva, CSF, or tissue.

C. Case classification (2011)

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

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

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Rabies should be considered in patients with signs or symptoms of encephalitis or myelitis. The course of the illness, additional history such as potential exposures, and laboratory tests for other more common etiologies can determine if samples specific for rabies should be collected. All human rabies diagnostic testing will be performed at

Centers for Disease Control and Prevention (CDC). **Health care providers who wish to test a patient for rabies should contact their local health jurisdictions who in turn will contact DOH Office of Communicable Disease Epidemiology (1-877-539-4344).**

For information regarding specimen collection and tests performed at CDC see “Specimen Collection” section below.

B. Tests Available at Washington State Public Health Laboratories (PHL)

All human rabies diagnostic testing will be performed at CDC. Please call Office of Communicable Disease Epidemiology (CDE) at (206) 418-5500 to arrange for testing.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

See Suspected Rabies Exposure guideline for information about testing animals for rabies (<http://www.doh.wa.gov/Portals/1/Documents/5100/420-073-Guideline-RabiesSuspectedExposure.pdf>).

C. Specimen Collection

(Note: the following information was accessed on March 25, 2016, from the CDC web site: http://www.cdc.gov/rabies/specific_groups/doctors/ante_mortem.html.)

1. Patient History

The health care provider submitting specimens for human rabies testing should complete the CDC Patient Information Form (<http://www.cdc.gov/rabies/pdf/RORform.pdf>). This form must accompany any samples sent to the Rabies Laboratory at the CDC.

2. Antemortem Samples

All samples should be considered as potentially infectious. Test tubes and other sample containers must be securely sealed (tape around the cap will insure that the containers do not open during transit). If immediate shipment is not possible, samples should be stored frozen at -20°C or below. Samples should be shipped frozen on dry ice by an overnight courier in water-tight primary containers and leak-proof secondary containers that meet the guidelines of the International Air Transport Association. The rabies laboratory at CDC should be telephoned (404-639-1050) at the time of shipment and given information on the mode of shipment, expected arrival time, and courier tracking number.

All four samples listed below are required to provide an antemortem rule out of rabies. Rabies cannot be ruled out unless all samples are submitted for testing.

a. Saliva

Using a sterile eyedropper pipette, collect saliva and place in a small sterile container which can be sealed securely. No preservatives or additional material should be added. Laboratory tests to be performed include detection of rabies RNA (by reverse transcription and polymerase chain reaction, RT/PCR, of extracted nucleic acids) and isolation of infectious virus in cell culture. Tracheal aspirates and sputum are not suitable for rabies tests.

b. Neck Biopsy

A section of skin 5 to 6 mm in diameter should be taken from the posterior region of the neck at the hairline. The biopsy specimen should contain a minimum of 10 hair follicles and be of sufficient depth to include the cutaneous nerves at the base of the follicle (full thickness biopsy). Place the specimen on a piece of sterile gauze moistened with sterile water and place in a sealed container. Do not add preservatives or additional fluids. Laboratory tests to be performed include RT/PCR and immunofluorescent staining for viral antigen in frozen sections of the biopsy.

c. Serum and cerebral spinal fluid (CSF)

At least 0.5 ml each of serum and CSF should be collected in sterile sealable tubes; no preservatives should be added. Do not send whole blood. If no rabies vaccine or rabies immune serum has been given, the presence of antibody to rabies virus in the serum is diagnostic and tests of CSF are unnecessary. Antibody to rabies virus in the CSF, regardless of the immunization history, suggests a rabies virus infection. Laboratory tests for antibody to rabies include indirect immunofluorescence and virus neutralization.

d. Brain biopsy

The rarity of rabies and the lack of an effective treatment make the collection of a brain biopsy for antemortem testing unwarranted; however, biopsy samples negative for herpes encephalitis should be tested for evidence of rabies infection if there is no other diagnosis. The biopsy is placed in a sterile sealed container; do not add preservatives or additional fluids. Laboratory tests to be performed include RT-PCR and immunofluorescent staining for viral antigen in touch impressions.

3. Postmortem Samples

In certain cases, human samples may need to be tested for rabies postmortem. See Section 6A for infection control recommendations. Consult with CDE before shipping any samples to the Rabies Laboratory at the CDC. Fresh tissue samples from the central nervous system (brain) should be submitted.

Postmortem diagnosis of rabies is made by immunofluorescent staining of viral antigen in touch impressions of brain tissue. Portions of the medulla (brain stem), the cerebellum, and the hippocampus should be frozen and shipped on dry ice to a public health laboratory or the CDC laboratory. Preservation of tissues by fixation in formalin is not recommended if rabies diagnosis is desired.

5. ROUTINE CASE INVESTIGATION

Interview the case and others who might provide pertinent information.

A. Evaluate the Diagnosis

Interview the health care provider and/or family member to collect clinical information. Review laboratory testing to date. Since testing at the CDC is always recommended, facilitate the collection and shipping of appropriate specimens to CDC.

CDC has resources for management of rabies:

http://www.cdc.gov/rabies/specific_groups/doctors/human_rabies.html

B. Identify Source of Infection

Ask about animal bites and exposure history during the exposure period (years). If the animal is still available for testing, arrange to send it to the Washington State Public Health Laboratories (see Suspected Rabies Exposure guideline for details at: <http://www.doh.wa.gov/Portals/1/Documents/5100/420-073-Guideline-RabiesSuspectedExposure.pdf>).

C. Identify Potentially Exposed Persons

Identify persons who may have been exposed to the patient and others who may have been exposed to the same source as the patient. It may be appropriate for these people to begin post-exposure prophylaxis even without a definitive diagnosis.

Although person-to-person transmission of rabies by bite has never been confirmed, rabies post-exposure prophylaxis (PEP) is recommended for certain persons who have exposure to a human with rabies. “Postexposure prophylaxis is indicated only when the patient has bitten another person or when the patient's saliva or other potentially infectious material such as neural tissue has contaminated an open wound or mucous membrane (MMWR 2008;57:RR-3).” Consult with Office of Communicable Disease Epidemiology regarding PEP of persons exposed to a human with rabies. PEP should also be recommended to persons who have been exposed to the same source as the patient (e.g., handled the same bat).

For more information on post-exposure prophylaxis, please see the Suspected Rabies Exposure guideline found at: <http://www.doh.wa.gov/Portals/1/Documents/5100/420-073-Guideline-RabiesSuspectedExposure.pdf>.

D. Infection Control Recommendations

Person-to-person transmission of rabies has never been documented in a healthcare setting. However, staff providing patient care should wear gowns, goggles, masks, and gloves, particularly during intubation and suctioning (MMWR 2008;57:RR-3).

Aerosol transmission of rabies has occurred only in laboratory settings. To avoid risk at autopsy of a suspected rabies case, limit the healthcare personnel involved and require appropriate personal equipment including an N95 or higher respirator, full face shield, goggles, gloves, complete body coverage by protective wear, and heavy or chain mail gloves to help prevent injury from instruments or bone fragments. Minimize aerosols by using a handsaw rather than an oscillating saw when cutting bone, and by avoiding contact of the saw blade with brain tissue. Use a 10% solution of sodium hypochlorite for disinfection of all exposed surfaces and equipment during and after the autopsy. Rabies vaccination is not required to perform such autopsies. If injury or mucous membrane contamination occurs during an autopsy, provide rabies post-exposure prophylaxis.

For more information see:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5913a3.htm>.

6. MANAGING SPECIAL SITUATIONS

Not applicable.

7. ROUTINE PREVENTION

A. Human Pre-exposure Immunization

Rabies pre-exposure vaccinations are administered to individuals such as laboratory workers testing for rabies virus, veterinarians and their staff, wildlife biologists, rehabilitators, animal control officers who routinely have contact with stray domestic, exotic, and/or wild animals, and travelers having exposure risk for prolonged periods in rabies enzootic areas where medical care may be difficult to obtain. Pre-exposure immunization consists of three cell culture rabies vaccinations given on days 0, 7, and either 21 or 28. For information regarding checking rabies titers following vaccination, see the current ACIP recommendations (MMWR 2008;57:RR-3 <http://www.cdc.gov/mmwr/PDF/rr/rr5703.pdf>. and MMWR 2010;59:RR-2 <http://www.cdc.gov/mmwr/PDF/rr/rr5902.pdf>).

B. Prevention Recommendations

1. Be a responsible pet owner:

- Keep vaccinations up-to-date for all dogs, cats and ferrets. This is important not only to keep your pets from getting rabies, but also to provide a barrier of protection to you, if your animal is bitten by a rabid wild animal.
- Keep your pets under direct supervision so they do not come in contact with wild animals. If your pet is bitten by a wild animal, seek veterinary assistance for the pet immediately.
- Call your local animal control agency to remove any stray pets from your neighborhood. Such animals may be unvaccinated and could be infected by the disease through contact with wild animals.
- Spay or neuter your pets to help reduce the number of unwanted pets that may not be properly cared for or regularly vaccinated.

2. Avoid direct contact with unfamiliar animals

- Enjoy wild animals (raccoons, skunks, foxes) from afar. **Do not** handle, feed, or unintentionally attract wild animals with open garbage cans or litter.
- **Never** adopt wild animals or bring them into your home. **Do not** try to nurse sick wild animals. Call animal control or a wildlife rescue agency for assistance. In Washington it is illegal to own certain species of wild animals (bat, skunk, fox, raccoon, coyote).
- Teach children **never** to handle unfamiliar animals, wild or domestic, even if they appear friendly. “Love your own, leave other animals alone” is a good principle for children to learn.
- Prevent bats from entering living quarters or occupied spaces in homes, churches, schools, or other similar areas, where they might come in contact with people or pets.
- When traveling abroad, avoid direct contact with wild animals and be especially careful around dogs in developing countries. Rabies is common in developing countries in Asia, Africa, and Latin America where dogs are the major reservoir of

rabies. Before traveling abroad, consult with a health care provider, travel clinic, or your health department about the risk of exposure to rabies, appropriateness of pre-exposure prophylaxis, and how you should handle an exposure, should it arise.

3. Keep bats out of your home

Some bats live in buildings, and there may be no reason to evict them if there is little chance for contact with people. However, bats should always be prevented from entering rooms of your home. For assistance with "bat-proofing" your home, contact an animal-control or wildlife conservation agency. If you choose to do the "bat-proofing" yourself, here are some suggestions.

- Carefully examine your home for holes that might allow bats entry into your living quarters. Any openings larger than a quarter-inch by a half-inch should be caulked.
- Use window screens, chimney caps, and draft-guards beneath doors to attics, fill electrical and plumbing holes with stainless steel wool or caulking, and ensure that all doors to the outside close tightly.
- Additional "bat-proofing" can prevent bats from roosting in attics or buildings by covering outside entry points. Observe where the bats exit at dusk and exclude them by loosely hanging clear plastic sheeting or bird netting over these areas. Bats can crawl out and leave, but cannot re-enter due to the barrier. After the bats have been excluded, the openings can be permanently sealed.

ACKNOWLEDGEMENTS

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UPDATES

July 2008: Additional details were added to Sections 2H, 6A and 6B based on information in the most recent ACIP recommendations (MMWR 2008;57:RR-3).

March 2010: Updated case definition

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. There is an updated case definition for 2011 and in Section 6A additional infection control measures for autopsies.

November 2013: Reviewed and later sections reorganized.

December 2016: Front page added, tables updated through 2015