



RABIES

Rabies as a disease was described and recorded by Democritus as early as 500 B.C.

The rabies virus is a lyssavirus in the genus *Rhabdovirus*. “Lyssa” is the Greek word for madness, and for most of antiquity, rabies has been associated with “mad dogs” and the potential encephalopathy (brain disease) that could ensue in a person if bitten by a rabid dog.

Globally, rabies is considered the tenth most common cause of death. Rabies kills an estimated 30,000 to 70,000 humans worldwide every year, and 100 million people are treated with rabies post-exposure vaccine prophylaxis. In developing countries, rabies is transmitted to humans primarily by domesticated dogs and cats.

Although it still remains a zoonotic (illness transmitted from animal to man) threat in the United States today, rabies in domesticated animals and humans has fallen to a very low level; from 1990 to 2005, there was an average of 3 human cases of rabies reported annually in the U.S. compared to an average of 22 cases in 1950. This is due to widespread vaccination of domesticated animals, animal control efforts to reduce stray animal numbers, and effective post-exposure treatments for humans. Pet vaccination programs have had a tremendous impact on human rabies in the United States; begun in the 1940s and 1950s, these programs have reduced the number of U.S. dog rabies cases from thousands every year to a few hundred per year. In 1938, there were 8,452 canine and 47 human rabies cases in the U.S. and in 1946, there were 8,384 canine and 33 human rabies cases, while in 1994, there were only 153 canine and 6 human cases in the United States.

Wildlife is the major reservoir of rabies in the U.S. Confirmed cases of rabies in animals in this country have been increasing over the last decade. There are 7,000 to 9,000 cases of animal rabies every year in the U.S., with 90% or more of these occurring in wildlife. Rabies became established in raccoons in the mid-Atlantic states in 1977, then migrated slowly north and east until 1994, when it eventually moved into Maine and bordering Canada. In addition, a strain of rabies affecting foxes has been spread into the northern New England states since 1994. Bat rabies is enzootic in all contiguous 48 U.S. states.

There have been six known cases where a human recovered from a rabies infection. Five of these recoveries were individuals either previously vaccinated against rabies or received some form of post-exposure prophylaxis before the onset of symptoms, and only one person recovered without neurologic sequelae (side effects). There has been one recent, December 2004, rabies survivor in the U.S., and she was neither previously vaccinated against rabies nor treated with rabies post-exposure prophylaxis. Not one of these

cases should be used to minimize the lethality of human rabies or the importance of rabies vaccination protocols.

The rabies virus is an RNA virus and a rhabdovirus of the genus *Lyssavirus*. A lipoprotein envelope surrounds the helical-shaped core of the virion. Spike-like projections of G proteins are imbedded into a lipid (fat molecules) envelope. Monoclonal antibody typing and PCR techniques can differentiate between the different strains of the virus associated with the different animal reservoirs and geographical regions.

The most likely mode of transmission of the rabies virus is by introduction of saliva containing rabies particles into a bite wound. Rabies transmission can also occur if saliva or central nervous system fluid or tissue from a rabid animal contacts a fresh wound or mucus membrane lining (eye, nose, mouth, genitalia, or anus). In the past, aerosol transmission of rabies is thought to have occurred under unusual circumstances in bat caves or laboratories where high concentrations of aerosolized virus were present in a confined area. A small number of human infections have also resulted from surgical corneal (outer layer of the eye) and organ transplants, both in the U.S. and internationally.

When rabies virus has been introduced into a wound or onto a mucus membrane, it first multiplies at the site of inoculation. The virus must then gain access to the peripheral nervous system

Exposure to rabies can occur from:

1. A visible bite or significant scratch penetrating the skin from a confirmed, suspected, or potentially rabid animal.
2. A non-bite exposure is direct contact of a wound (one that has been bleeding within the previous 24 hours) or mucus membrane with potentially infectious material such as saliva or central nervous system tissue (i.e. brain or spinal cord tissue) from a confirmed, suspected, or potentially rabid animal.
3. Eating any part of a confirmed or suspected rabid animal.
4. Physical contact with a bat where a bite cannot be positively ruled out is considered an exposure, as are certain situations where a bat is discovered in the presence of a person who cannot positively determine or communicate that a bite occurred (the person was sleeping, a child, or a person debilitated in some manner).
5. Aerosolized rabies virus is thought to have caused disease and is considered exposure in rare circumstances (i.e. in a research lab or possibly a bat cave).

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(nerve tracts) to migrate and ascend (“climb up”) to the central nervous system and the brain.

All mammals are capable of being infected with rabies, but there are varying degrees of susceptibility between different types of animals. For example, foxes, coyotes, wolves, raccoons, skunks, bats, cats, dogs, and cattle are considered highly susceptible to rabies. However, some animals are very resistant to infection with the virus, and these mammals are considered low risk for the infection. Although opossums can contract rabies, laboratory research has demonstrated the dose of rabies virus required to cause disease in these creatures is 50,000 times that needed to infect a fox! The incidence of clinical rabies among rodents (except woodchuck) and rabbits is extremely rare due to these animals’ decreased chance of surviving an attack by a rabid animal, but it has been known to happen.

Cats are more commonly involved in exposures than dogs because cats interact more with wildlife, and cat control and rabies immunization regulations are more difficult to enforce, if not entirely different. According to the Centers for Disease Control, inconsistent use of vaccination in cats over the past years has been responsible for an increased incidence of feline rabies in recent years. The frequency of human rabies exposures attributable to cats is increasing at a greater rate than those associated with dogs. Some reports state that rabid cats are more likely than dogs to stalk and attack humans and other animals.

Humans are relatively resistant to clinical disease. The risk of developing rabies following the bite by a **proven** rabid dog is estimated to be about 15% without post-exposure treatment.

The incubation period is the time interval between exposure to the virus and onset of the first clinical signs or symptoms of the disease. The length of the incubation period is determined by several factors including viral strain, dose of virus, site of virus inoculation (bite site), age of animal, and many other host factors including immune system status. The spread of the virus in the central nervous system is relatively rapid (48 to 120 hours).

The incubation period for rabies in wild animals is unknown and extremely variable. Animals can acquire the virus not only through bites from a rabid animal, but also transplacentally (through placental tissues prior to birth), transmammary (through the mother’s milk), and/or from eating tissues of a dead rabid animal. Once a wild animal gets rabies, it may incubate the disease for a long time without showing signs and may even shed the virus without ever becoming ill. Because of this, wild animals can-

Major stages of rabies infection:

1. Prodromal stage
 - may last 2-3 days
 - subtle temperament changes
 - mild fever
 - self mutilation at bite site
 - slow blink reflexes

2. Furious stage
 - animal increasingly restless and irritable
 - visual and auditory stimuli may trigger episodes of aggression and vocalizing
 - may roam long distances
 - may attack inanimate objects and eat odd substances
 - later muscular incoordination, disorientation, generalized (grand mal) seizures
 - cats especially tend to show furious signs and aggression in common

3. Paralytic stage
 - usually appears 2 to 4 days after onset of clinical signs
 - laryngeal/pharyngeal paralysis leads to drooling, changes in vocalization, and difficulty eating, drinking, and breathing
 - final stage includes coma and respiratory paralysis leading to death
 - the longest recorded survival time in the paralytic stage was 7 days (average)
 - duration of clinical signs is 3-5 days)

not be considered to be free of rabies even if purchased from a pet shop, acquired as a baby, or held for a long period of time.

When a susceptible animal is exposed to rabies, the virus travels up peripheral nerves to the spinal cord (taking 9 days to 1 year), then spreads throughout the spinal cord and brain (taking another 2 to 6 days), and then spreads from the brain to other tissues, most importantly – the salivary glands.

Clinical signs appear when the rabies virus reaches the brain, usually 15 to 25 days after exposure but sometimes taking as long as one year. This is the reason for the long quarantine period for animals bitten by an unknown attacker.

Rabies infection has classically been divided into 3 major stages: prodromal, furious, and paralytic or “dumb” rabies. Classical descriptions may be misleading however, as rabies can be quite variable in its presentation. Not all animals pass through all of the clinical stages and the animals may vacillate between the stages.

In human beings, the early signs of rabies are often headache, fever, malaise, and apprehension. Numbness or sensory irritation is often experienced at the site of inoculation. Excitability and aerophobia (fear of flying) are also frequent symptoms. The disease then progresses to paresis (weakness, incoordination) or paralysis, delirium, seizures, and coma. Death is generally the result of respiratory paralysis. Once the symptoms of rabies appear, there is no effective treatment or cure.

The infectious period is **NOT** the same as the incubation period. The infectious period is the time during which a rabid animal is shedding virus in its saliva and is capable of transmitting rabies to

Typical Rabies Incubation Range by Species

1. Cats 2 weeks to 6 months
2. Dogs 2 weeks to 6 months
3. Ferrets 3 to 10 weeks
4. Skunks 5 to 20 weeks
5. Raccoons 4 weeks to 6 months
6. Cattle 2 to 12 weeks
7. Horses 3 to 8 weeks
8. Humans 9 days to 7 years

another animal or person. Rabies virus must have reached the brain before it can be excreted in the saliva; thus most rabid animals are infectious just a few days before the onset of noticeable symptoms and during the course of the disease. In dogs, cats, and ferrets, communicability is usually 3 to 7 days before the onset of symptoms (rarely over 4 days) and until the death of the animal – this is the basis for the 10-day quarantine for these animals. In studies with skunks, some skunks shed the virus up to 18 days prior to observable signs; there is also research demonstrating that skunks, and some other species, may be able to survive a rabies infection.

Although humans or animals that have just come into contact with a potentially rabid animal are at risk for acquiring rabies, they are not themselves immediately contagious to others.

The ability of the rabies virus to survive depends on the surrounding environment. Normally, the rabies virus cannot live long in a warm, putrefied tissue, and survives in the body less than 24 hours after death. The rabies virus is immediately inactivated when dried and does not survive for any appreciable time in the environment. A few minutes in direct sunlight will inactivate the rabies virus. However, under cool conditions (as in refrigeration) it may live for many days, and if the virus is frozen at **-70 degrees centigrade, it can live for years!** Rabies virus is no longer active in dried saliva and is killed by bleach, ethyl alcohol (rubbing alcohol), soap, detergent, and quaternary ammonium compounds.

Rabies infection is often suspected because of neurological signs that are present in an animal. However, due to the atypical nature of the disease, rabies should be considered in any animal that suddenly develops profound behavioral changes, or features of limb paralysis, or both.

If a potential rabies exposure occurs, the direct fluorescent antibody (DFA) test is the only acceptable method of determining that the suspect animal does NOT have rabies; the ten-day quarantine only determines if an animal was shedding virus at the time of the bite or exposure. The DFA test is a rapid, sensitive, and reproducible laboratory method for detecting rabies antigen in animal tissue. Fresh brain samples are required. Tissue should be stored under refrigeration and should be maintained on wet ice for transport to the state laboratory.

If you witness a wild animal attacking a human or pet, the creature should be captured for rabies testing. All states have rabies testing facilities. **REMEMBER** fresh brain samples are needed for testing! **DO NOT** shoot the wild animal in the head or strike it on the skull. Damage to the head will cause too much brain trauma and testing will not be able to be performed. The animal should be shot in the trunk to dispatch it.

It is not necessary that animals show neurological signs at the time of examination, and all animals excreting virus in their saliva should have virus in their brain detectable by the DFA testing.

There are many diseases and conditions found in both wildlife and domestic animal species that clinically resemble rabies, including canine distemper, toxoplasmosis, larval migrans, lead poisoning, antifreeze poisoning, herpes virus infection, listeriosis, Eastern, Western, and Venezuelan equine encephalomyelitis, and bovine spongiform encephalitis.

Always contact your veterinarian if you suspect a pet has had an exposure to the rabies virus. Rabies vaccinations are mandatory

within the United States and Canada. Rabies vaccines are very inexpensive and after the original inoculation, Rabies boosters are currently protective for 3 years.

- 1. Canine distemper:** virus similar to human measles; affects dogs, raccoons, coyotes, foxes, skunks, mink and ferrets; causes abnormal behavior, aggressiveness, disorientation, twitching, convulsions, paralysis, and death; no danger to humans.
- 2. Toxoplasmosis:** caused by a protozoan *Toxoplasma gondii*; infects cats and many herbivorous and carnivorous wildlife species; causes muscle incoordination, tremors, twitching, ataxia, and seizures; may be a danger to humans through improper handling of infected cat litter or soil containing cat feces.
- 3. Visceral Larval Migrans:** caused by the aberrant migration of nematode (roundworm) larvae in unnatural, co-incident hosts; affects humans, chickens, groundhogs, rabbits, and rodents. Results in cysts or granuloma formation in the brain, eye, and other internal organs; worm migration may result in circling, head tilt, blindness, or paralysis; serious illness in humans.
- 4. Toxin ingestion:** several elements and chemicals may produce toxicological symptoms mimicking rabies – i.e. lead, mercury, antifreeze (ethylene glycol), organophosphates; all can cause tremors, blindness, organ failure, and paralysis. Even natural toxins in some toads and lizards can mimic the symptoms of rabies.
- 5. Herpes Virus infection:** species-specific herpes viruses occur in many species of domesticated and wild animals; each causes circling, incoordination, tremors, and paralysis.
- 6. Listeriosis:** caused by the bacteria *Listeria monocytogenes*; an important cause of human food-borne illness; usually a non-contagious disease of farm animals (primarily cattle) that can infect other mammals like humans and the red fox; causes circling, head tilt, stupor, and paresis.
- 7. Arboviral encephalitis:** most arboviral encephalitis infections of man and mammals can be expected to present clinically as a suspected rabies case; Eastern Equine Encephalitis (EEE) is being diagnosed more commonly in pets and exotic species; this fatal disease of the horse often referred to as “sleeping sickness” is extremely difficult to differentiate clinically from rabies.
- 8. Neuropathies of uncertain etiology:** several other conditions can mimic rabies – feline vestibular syndrome, canine idiopathic trigeminal neuropathy, bovine spongiform encephalopathy (“mad cow disease”), transmissible mink encephalopathy, and chronic wasting disease of deer and elk – all show signs very similar to rabies.
- 9. Localized Lesions and Obstructions:** viral and fungal infections of the mouth (drooling); foreign objects in mouth or throat (drooling); cancers or tumors in the central nervous system (behavior changes, head tilt, circling); and kidney or liver failure (toxin accumulation – stupor, seizures).