

General Information

- The classical rabies virus belongs to serotype 1 of the genus *Lyssavirus* in the family Rhabdoviridae.
- It is a bullet-shaped, enveloped, single-stranded RNA virus that survives very poorly in the environment.
- Rabies virus infections have highly variable incubation periods and clinical signs in all susceptible species.
- The virus can infect any mammal, but only carnivores and bats maintain the infection naturally. Herbivores, rodents, rabbits and other non-biting animals are not epidemiologically significant in the propagation of the disease, but they are variably susceptible to infection. Birds cannot transmit rabies virus.
- The importance of this disease is based on the near 100% mortality rate in all species once clinical signs appear, and the high cost of post-exposure prophylactic treatment for humans and control programs in animals.

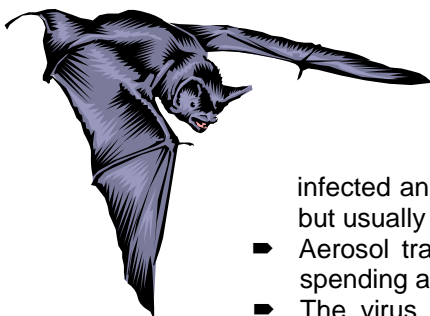
Prevalence and Risk Factors

- Rabies occurs worldwide, although there are some areas in Europe and some island nations that are rabies-free. Every year there are over 50 000 human deaths worldwide due to rabies, mostly in India and areas where canine rabies is still common, and mostly associated with transmission from dogs.
- In Canada, the USA and western Europe, canine rabies has been eradicated, and the disease is maintained by certain species of local wildlife. However, dogs (and cats) can still become infected and transmit wildlife strains of rabies virus, which are infective to all mammals. Transmission from wildlife to humans is considerably less common as there is much less direct contact compared with dogs.
- From 2000 to 2006, there were 15 reported cases of human rabies in the USA, nine of which were the result of exposure to bats, and four of which were the result of exposure to rabid dogs. In the same period, only two cases of human rabies were reported in Canada, which were associated with exposure to bats.

The wildlife reservoir hosts of rabies are different in various regions of North America, but include foxes, skunks, raccoons, coyotes and various species of bats. Infections in domestic species and humans are the result of spill-over from these reservoir populations. Of the nearly 7000 cases of animal rabies reported in the USA in 2004, 92% were in wildlife species, of which over 2500 cases were in raccoons. Many kinds of bats, including fruitivorous and insectivorous species, are capable of transmitting rabies. Rabies in rodents and lagomorphs (rabbits and hares) is uncommon, and the potential for transmission to humans is low, but the risk should be assessed on a case-by-case basis. In the USA, but not Canada, rabies is now more commonly reported in cats than in dogs.



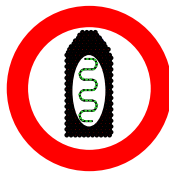
Transmission



- Rabies can only be transmitted by exposure of a mucous membrane or wound (broken skin) to the saliva of an infected animal or infected tissue (such as brain, spinal cord).
 - The most common source of rabies in human cases worldwide is dogs, but in the United States and Canada it is bats.
 - Depending on the strain of virus and the host species involved, an infected animal may shed virus in its saliva for up to 14 days before clinical signs develop, but usually for less than 10 days (hence biting animals are usually isolated for 10 days).
 - Aerosol transmission has been reported in two scientists who contracted the virus after spending a few hours in a heavily populated bat cave, supposedly without being bitten.
 - The virus has never reportedly been spread to a human by ingestion, although such transmission has been shown experimentally in animals, and may occur in wildlife as well.
- Rabies can also be transmitted by solid organ and corneal transplants.

Clinical Course and Signs

The incubation period of rabies depends on the amount of virus transmitted, and the severity and location of the bite wound (the more distal the bite to the brain and spine, the longer the incubation period). It is typically 2-3 months in humans, but it can last anywhere from 7 days to six years. The virus first replicates at the site of



inoculation, and then travels through peripheral nerves from this site to the spinal cord and brain where it causes nonsuppurative encephalomyeloradiculitis. From there it can spread via other nerves to virtually any tissue, but particularly to the salivary glands, at which point it can also be transmitted to another host. Rabies is almost invariably fatal once clinical signs appear. Only a handful of human patients have ever been reported to survive following the onset of clinical disease. In 2004, a teenager bitten by a rabid bat in Wisconsin (USA) was the first person reported to have recovered from rabies infection following experimental treatment, without the use of biologicals. There are two major forms of clinical rabies: paralytic (or dumb) rabies, and furious rabies.



- The initial clinical signs of rabies include neuropathic pain at the site of the original wound, and a non-specific prodrome with mild behavioural changes.
 - Patients often go through a phase of excitation and hyperaesthesia, but remain aware of their condition. Classically patients develop dysphagia and are unable to swallow liquids or saliva, or they may experience laryngeal spasm on inspiration, resulting in respiratory difficulty.
 - Signs progress to paralysis and ultimately death within 2-6 days without intensive treatment. With treatment patients can be kept alive for weeks, but rabies is always progressive – static or improving clinical signs make rabies a very unlikely diagnosis.
- Atypical cases are becoming more common, therefore one cannot rely on clinical signs alone for diagnosis.

Diagnosis

- There is no antemortem test by which to diagnose rabies that is sensitive enough to reliably rule out the disease. The diagnosis is usually made by direct immunofluorescence of neural tissue post-mortem, which has very high sensitivity and specificity. It can also be used on various samples from live human patients with excellent specificity, but its sensitivity in these cases is limited.
- Reverse-transcriptase PCR can also be used to detect virus in the saliva infected humans.
- Histological examination of cerebral tissue for Negri bodies has reasonable specificity if the examiner is experienced with their identification, but this test is not used for rabies diagnosis in Canada because the fluorescent antibody test is vastly superior.
- Strains can be typed to help determine the source of rabies virus, if needed.
- Antemortem testing is not performed in animals. Suspect animals are euthanized and tested post-mortem.
- Serology is primarily used to determine host response to pre- or post-exposure vaccination in humans. It cannot be used reliably for diagnosis of infection, particularly in previously immunized patients.

One cannot rule out rabies based solely on a lack of definitive exposure. People can unknowingly be bitten by bats while sleeping, and the fur or hair of animals can make it very difficult to detect small bite wounds. There are no characteristic serum biochemical or haematological abnormalities. However, if clinical signs fail to progress or if clinical signs improve at all over 7-10 days, then rabies is extremely unlikely.

In humans, samples that should be collected antemortem for rabies testing include saliva, a skin biopsy from the neck at the base of the skull, serum and cerebrospinal fluid. Samples should be handled with level 2 biosafety precautions. If a brain biopsy is collected for testing of other neuropathogens and the results are negative, the tissue should then be tested for rabies, but it is not recommended that such a sample be collected solely for the purpose of rabies testing, as testing of saliva by RT-PCR is considered as accurate in clinical cases.

Biting Animals and Suspected Rabid Animals

- **Rabies is a reportable disease in Canada and the USA**, therefore suspect cases must be brought to the attention of a federal veterinary inspector or state authorities, who can also provide further assistance.
- All animal bites should be reported to the provincial ministry of health. Any dog, cat or ferret that has bitten a human should be isolated for at least ten days (or longer) and monitored for development of clinical signs of rabies. If an animal under such isolation, or any animal with known exposure to another rabid animal, develops clinical signs compatible with rabies, the animal will be euthanized immediately and tested for rabies. Stray/feral animals or wild animals that bite a human may be euthanized and tested for rabies without undergoing the period of isolation. Unvaccinated animals with known exposure will also be euthanized, or else isolated for at least six months and monitored for development of clinical signs.



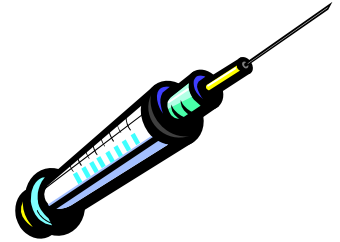


- If a person has close contact with a feral animal that cannot be captured for testing, the decision to administer post-exposure treatment must be made on a case-by-case basis, depending on the species involved, type of contact, patient's condition and the local epidemiological disease patterns.

Treatment

There is NO effective treatment for rabies. Once clinical signs appear, the mortality rate is virtually 100%.

- Initial bite wound care is very important if rabies transmission is at all possible. The bite should be cleaned vigorously with soap and water for at least 15 minutes and then disinfected with alcohol, povidone iodine or a quaternary ammonium compound. Avoid primary closure of the wound.
- Humans who have been exposed to the virus can be given prophylactic immunization in order to help the body eliminate the virus before it invades local peripheral nerves and travels to the central nervous system. It is important to bear in mind that such treatment can be quite expensive and is not without its own risks, but also that any delay in obtaining treatment can significantly decrease its efficacy. If the biting animal is isolated and remains healthy for 10-14 days, or if the animal is euthanized and testing shows it was negative for rabies, further post-exposure treatments should be stopped.
- Post-exposure prophylaxis consists of active immunization with rabies vaccine, and in the acute period passive immunization with rabies immunoglobulin (RIG). As much of the RIG dose as possible is injected locally around the wound, and the remainder is given intramuscularly (usually in the gluteal muscle). In Canada and the USA, vaccine is administered intramuscularly on days 0 (along with RIG), 3, 7, 14 and 21.



Infection Control

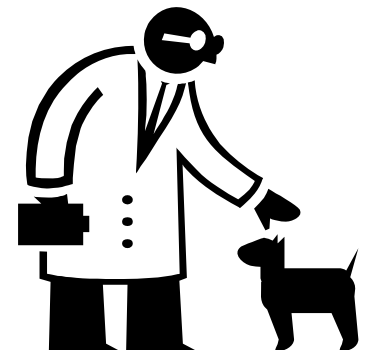


Control of rabies in people depends on control of rabies in animals. Companion animals have the highest degree of human contact and therefore pose the most significant risk to people if they become infected. Immunization of pets, particularly those that venture outside, and control of feral, non-immunized populations is of primary importance. In wild carnivores, control efforts are now being focused on immunization in combination with reduction of population density. A key component of rabies control programs is public education, which should be promoted by health care, public health and veterinary professionals alike.

- People should avoid direct contact with bats and all wildlife rabies hosts, particularly if the animals are behaving abnormally (i.e. nocturnal animals such as bats seen during the day or found on the ground).
- It is also important to prevent bats from gaining access to dwellings, and to try to prevent pets and other domestic animals from being bitten by bats.

Vaccines

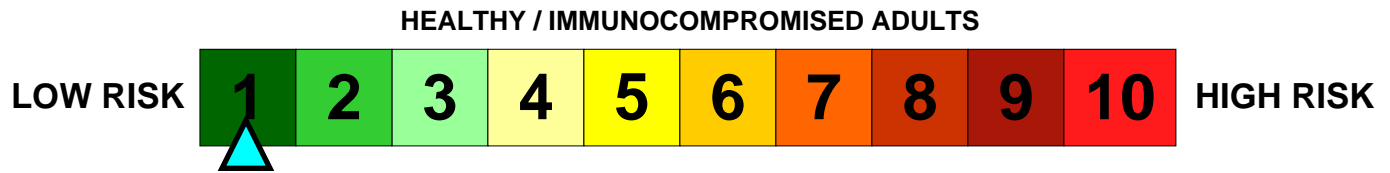
- Human vaccination is limited to those at increased risk of exposure, including veterinarians, animal handlers and animal control personnel. All people in a veterinary practice that may have contact with animals should be vaccinated (this may also include front-office staff in some practices). These individuals should have their antibody titre checked every two years, and booster vaccination should be considered if the titre is less than 0.5 IU/mL. Laboratory workers who may be exposed to the virus are considered the highest risk, and should have their titre checked every six months.
- In humans, the current vaccine of choice is the human diploid cell vaccine (HDCV) – an inactivated cell-cultured vaccine that is administered in three doses by intramuscular injection in the deltoid region. The site of vaccination is important, as absorption from vaccine administered in the gluteal muscles has been shown to be suboptimal. The vaccine is highly immunogenic, and 99% of those treated seroconvert.
- Companion animals should be vaccinated at 3 months of age and then annually or every three years, depending on the product used. Such vaccination is required by law in some areas of Canada and the USA.





Zoonotic Disease Risk

In adults, the risk of rabies *exposure* from pets is:



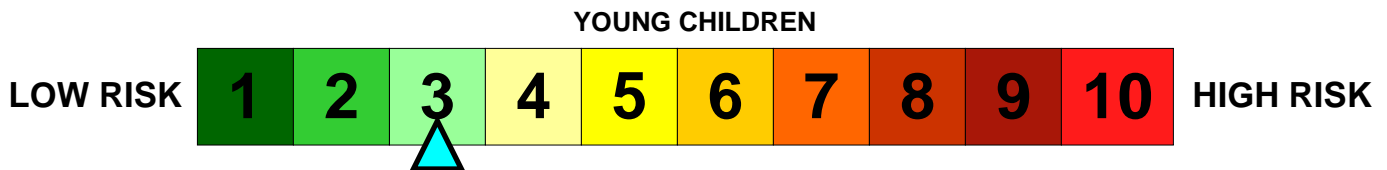
Individuals with Compromised Immune Systems:

- Because both pre-exposure and post-exposure rabies prophylaxis may be significantly less effective in individuals who are immunocompromised, these individuals are at slightly *increased risk of becoming ill* and succumbing to the disease if they are exposed to rabies. They should therefore avoid situations and occupations which entail any increased risk of exposure to rabies. If it cannot be avoided, their antibody titres must be monitored very carefully to ensure that their response to immunization is adequate and protective.

Young Children:

- When it comes to animals, young children are more likely than adults to try to touch or pick up an unfamiliar animal, and they are also more likely to, either intentionally or unintentionally, provoke or frighten an animal and thus be bitten.
- Young children should always be supervised when playing with animals, and they should be taught never to approach or touch any unfamiliar animal, even if it seems very friendly or if it looks sick or unconscious.

Overall, for children the risk of rabies *exposure* from pets is likely:



Additional Information

Centers for Disease Control and Prevention (CDC). Rabies website - <http://www.cdc.gov/rabies/healthcare.html>

Jackson AC, Warrell MJ, Rupprecht CE, et al. Management of rabies in humans. Clin Infect Dis. 2003;36:60-63.

Wilde H. Failures of post-exposure rabies prophylaxis. Vaccine. 2007;25:7605-7609.

Centers for Disease Control and Prevention (CDC). Public health response to a rabid kitten – four states, 2007. MMWR Morb Mortal Wkly Rep. 2008;56:1337-1340.