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Popular Article

# Rabies: A Comprehensive Review

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**Abstract**

Rabies is a viral disease of dogs which affects the central nervous system of most mammals including humans and is invariably fatal. Despite medical advancements, rabies continues to be a prominent global health issue as a zoonotic disease. This review aims to provide a comprehensive understanding of rabies by covering various aspects including its epidemiology, pathogenesis, clinical features, diagnosis, prevention and control. The persistence of rabies throughout history emphasizes the need for a multidisciplinary approach in order to effectively control its impact. By synthesizing current knowledge, this article aims to offer valuable insights for healthcare professionals, policymakers, and stakeholders worldwide, highlighting key areas to focus on for improved prevention and control strategies.
Keywords: Rabies, dog bite, vaccine, Negri body, hydrophobia.

## Introduction

Rabies is a lethal disease which is distributed worldwide and is caused by rabies virus which gets transmitted by the bite of affected animals. The spread of urban rabies is mainly due to unvaccinated domestic street dogs and cats. Street virus is the natural virus present in rabid animals. Most human rabies cases are found in developing nations where canine rabies is endemic. Sylvatic rabies is spread by animals such as wolves, foxes, skunks, raccoons and jackals, which act as the main reservoirs and transmitters of the disease. These animals maintain a cycle among themselves and transmit the virus to dogs and other domestic animals. Humans can contact rabies by encountering the wildlife cycle of the disease. In certain countries, bat rabies is prevalent, with vampire bats serving as important hosts and vectors for the virus. Insectivorous bats and frugivorous (fruit-eating) bats are currently significant vectors. There are several countries that have achieved canine rabies elimination

or are close to achieving it include: Australia, New Zealand, Japan, Taiwan, Hong Kong, Singapore, Fiji, the United Kingdom, Ireland, Norway, Sweden, Jamaica, and Barbados. In India, the islands of Andaman and Lakshadweep are also free from rabies.

**Aetiology**

Rabies is caused by a neurotropic, bullet shaped, enveloped, negative sense single stranded RNA virus.

*Lyssavirus* genus belonging to *Rhabdoviridae* family includes seven genotypes:

- Rabies virus (genotype 1)
- Lagos bat virus (genotype 2)
- Mokola virus (genotype 3)
- Duvenhage virus (genotype 4)
- European bat lyssavirus 1 (genotype 5)
- European bat lyssavirus 2 (genotype 6)
- Australian bat lyssavirus (genotype 7)

Most clinical cases are due to infection with Rabies virus (RABV) (genotype 1) and other genotypes produce clinical signs indistinguishable from rabies.

**Epidemiology**

Rabies is prevalent throughout the world except in Islands. Many of the countries are endemic for rabies, except Australia and Antarctica. Two epidemiologically important infectious cycles are recognized, urban rabies in dogs and sylvatic rabies in wildlife. More than 95% of human cases are the result of bites from rabid dogs. Racoons, skunks, foxes and bats are important reservoirs in sylvatic rabies **(*Quinn et al, 2011*)**.

**Transmission**

It usually occurs through bites. Infected animals excrete virus in their saliva before the onset of clinical signs. Non-bite transmission methods are inhaling RABV particles, organ and corneal transplants, and infection of open wounds, abrasions and mucous membranes with saliva and brain tissue from a rabid animal containing RABV **(*Singh et al, 2017*).**

**Pathogenesis**

Following entry of virus in the body and incubation, there is local replication in the myocytes. The virus enters peripheral nerve endings by binding to receptors like nicotinic acetylcholine at the motor end plate. RABV travels towards the central nervous system (CNS) by utilizing sensory and motor axons through a rapid axonal retrograde transport mechanism. Replication in the brain and



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spinal cord results in degeneration of ganglion cells, as well as the infiltration of mononuclear cells and neuronophagia. Additionally, there is perineural and perivascular infiltration. It is important to note that the dysfunction of neurons occurs due to neuronal degeneration, rather than the death of the neurons. It shows centrifugal spread and is released at axon terminals where it infects many non-nervous tissues including the salivary glands.

**Clinical signs and symptoms**

After exposure, incubation period can last up to a few days or a year depending upon the site of bite and concentration of the virus. There are two forms of rabies:

- **Furious (Excitative) form**: Results in hyperexcitability, aggressiveness and irrational behaviour. Biting and barking at inanimate objects, flaccidity or in-coordination, pica and spasms are observed.
- **Paralytic (Dumb) form:** Results in paralysis of muscles, difficulty in swallowing, profuse salivation and dropping of the jaw.

Hydrophobia is seen in humans which is due to the inability to swallow water because of pharyngeal paralysis **(*Quinn et al, 2011*)**.

**Diagnosis**

Since rabies is a serious zoonotic disease, precise and rapid detection of suspected cases is necessary to provide timely treatment and effective preventive measures. By observing common clinical symptoms in dogs and other animal species, a preliminary diagnosis can be reached. Animals exhibiting unusual behavior must be isolated to ensure they do not harm others for a period of 10 days. The detection of Negri bodies by Sellar's staining is a traditional method for diagnosis of rabies. Negri bodies are eosinophilic intracytoplasmic inclusion bodies present in hippocampus in dogs and Purkinje cells of cerebellum in cattle. Babes nodules are also observed in histopathological examination. The fluorescent antibody test (FAT) on acetone-fixed brain tissue smears is considered the gold standard for diagnosing rabies due to its brief duration, cost-effectiveness, and superior sensitivity.

The cultivation of the rabies virus can be carried out in neuroblastoma cells or baby hamster kidney cells. The viral culture is particularly useful in cases where the results of the Fluorescent Antibody Test (FAT) are uncertain. The rabies virus, which does not cause any damage to the cells, can be identified in tissue cultures by using conjugated antisera.

**Prevention and control**

A comprehensive and efficient approach to effectively manage and eliminate the disease



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includes the implementation of the following strategies:

- Thorough examination and analysis of the RABV at regional reference laboratories, as well as national and international levels.
- Identification and regulation of the source through which the virus enters.
- Increasing the rate of vaccination among animals to combat rabies.
- Imposing restrictions on the movement of animals.
- Providing public and professional outreach programs and educational initiatives **(*Singh et al, 2017*).**

The timetable for pre-exposure and post-exposure rabies vaccination for humans is outlined as follows:

1. **Pre-exposure Vaccination:**
   - Pre-exposure vaccination is advised for individuals at high risk of rabies exposure, such as veterinarians, laboratory workers, and travelers to rabies-endemic regions.
   - The standard pre-exposure vaccination schedule comprises three doses of rabies vaccine given on days 0, 7, and 21 or 28. A booster dose may be administered at one year, followed by subsequent doses every 2-3 years for ongoing protection (***Hankins et al, 2004)***.
2. **Post-exposure Vaccination:**
   - Post-exposure vaccination is provided following a potential rabies exposure, like a bite or scratch from a rabid or potentially rabid animal.
   - The post-exposure vaccination schedule typically involves immediate wound care, followed by a series of rabies vaccine doses. The regimen may vary depending on the individual's vaccination status and the severity of the exposure.
   - The recommended post-exposure vaccination regimen for individuals not previously vaccinated against rabies includes four doses of rabies vaccine: one dose on day 0 (as soon as possible after exposure), followed by doses on days 3, 7, 14 and 28. Additionally, rabies immune globulin (RIG) may be administered at the wound site on day 0 for added protection (***Hankins et al, 2004*).**
   - For individuals who have received pre-exposure vaccination (i.e., completed the series), the post-exposure regimen typically involves two doses of rabies vaccine: one on day 0 and another on day 3. RIG is generally unnecessary unless the individual has a compromised immune response.
   - It is crucial to recognize that these vaccination schedules may differ based on regional



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protocols, individual risk factors, and healthcare provider advice. In the event of potential rabies exposure, individuals should promptly seek medical attention for assessment and appropriate care, including wound management and vaccination, to prevent rabies development.

**Vaccination schedule for dogs:**

1. **Pre-exposure Vaccination:**

| Age of Dog | Vaccination Schedule |
|---|---|
| 12-16 weeks | Initial vaccination |
| 1 year after initial | Booster shot |
| Every 1-3 years | Subsequent booster shots |

2. **Post-exposure Vaccination:**

| Situation | Vaccination Schedule |
|---|---|
| Previously vaccinated dog | Two doses of rabies vaccine, 3 days apart. |
| Unvaccinated dog bitten by a suspect animal | It is recommended to administer the rabies vaccine promptly. If there has been no previous vaccination, the veterinarian may recommend taking extra precautions such as rabies immune globulin (RIG). The veterinarian will provide guidance on when to administer subsequent doses. |

**Conclusion**

Rabies continues to be a major global public health issue, posing severe consequences for both human and animal communities. Vaccination is a crucial aspect of rabies control efforts, which includes the immunization of domestic animals and wildlife reservoirs, as well as raising public awareness and promoting responsible pet ownership. While rabies poses intricate challenges, it is a condition that can be successfully managed and eventually eradicated through continuous endeavors, governmental dedication, and worldwide collaboration. By giving importance to rabies prevention and control initiatives and executing strategies based on evidence, a future can be constructed where rabies no longer threatens the well-being of both humans and animals.

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