

Rabies Revisited: From Pathogenesis to One Health Solutions for Elimination

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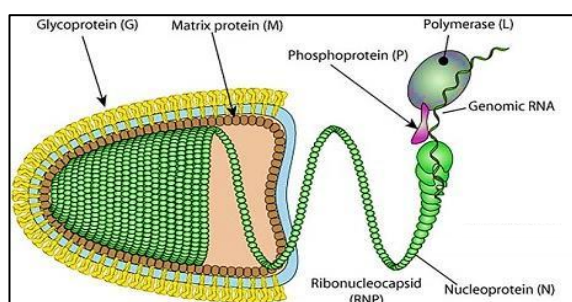
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Abstract

Rabies is a zoonotic disease, transmitted to humans mostly through transmission of *Lyssavirus* by bites of infected dogs. The 2025 World Rabies Day theme, "Act Now: You, Me, Community," underscores the collective responsibility in combating rabies. This theme emphasizes the importance of individual actions, community engagement, and collaborative efforts across sectors to eliminate rabies. By vaccinating dogs, educating the public, and ensuring access to post-exposure prophylaxis, we can significantly reduce and eventually eliminate rabies as a public health threat. This manuscript delves into the pathogenesis of rabies, its clinical manifestations, diagnostic methods, and, most importantly, the strategies for its prevention and control, aligning with the global call to action for a rabies-free world.

1. Introduction

Rabies is an ancient zoonotic disease of viral origin that has been recognized since antiquity for its devastating impact on both humans and animals. It is characterized as an acute, progressive, and invariably fatal encephalomyelitis caused by viruses of the *Lyssavirus* genus. Human infection occurs most commonly through the bites of rabid dogs, which remain the principal reservoir in many endemic regions. Despite the availability of effective vaccines and preventive measures, rabies continues to cause tens of thousands of deaths globally each year, with the majority of cases concentrated in Asia and Africa. The disease not only represents a persistent public health challenge but also reflects gaps in animal vaccination, public awareness, and timely access to post-exposure prophylaxis. With its continued presence in domestic and wild animal populations, rabies remains a priority zoonosis requiring sustained surveillance, prevention, and control under a One Health framework.

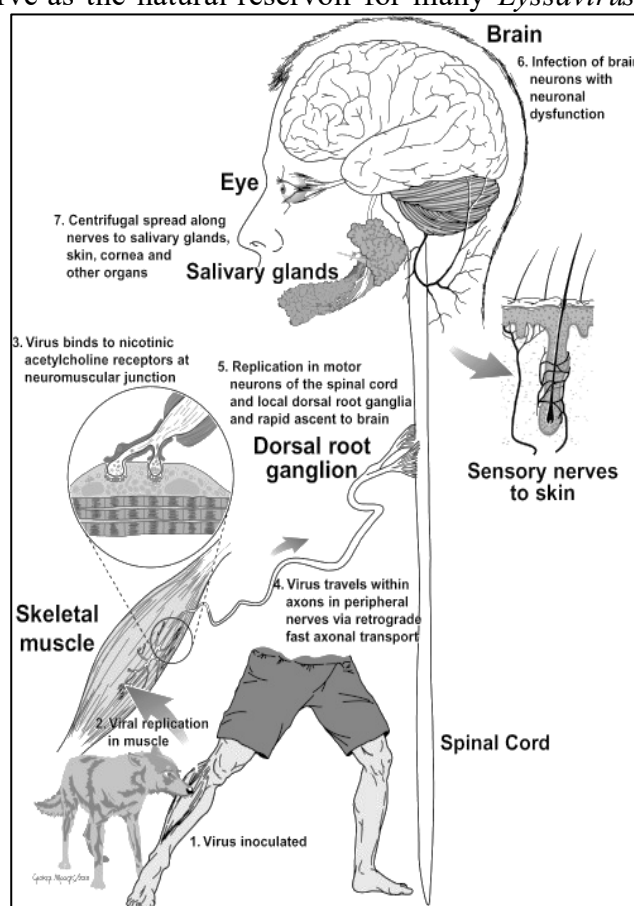


2. Epidemiology

2.1 Causative Agent: Rabies is attributed to viruses of the *Lyssavirus* genus within the *Rhabdoviridae* family, order *Mononegavirales*. Among these, the rabies virus (RABV), which serves as the prototype member of the genus, is the primary agent responsible for the disease. Structurally, lyssaviruses are bullet-shaped particles, typically about 180 nm in length (ranging from 130–250 nm) and 75 nm in diameter (ranging from 60–110 nm). The virus is composed of two main components: a nucleocapsid core and an outer lipoprotein envelope. The core contains a tightly packed ribonucleoprotein (RNP) complex that houses the viral nucleic acid essential for replication and transcription. Surrounding this, the lipid envelope is embedded with spiky glycoprotein projections that facilitate binding of the virus to host cell receptors. The genome is a negative-sense, single-stranded RNA molecule of approximately 12 kb, which encodes five key proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and the large RNA-dependent RNA polymerase protein (L).

2.2 Mode of transmission: Rabies can infect any mammal, whether domestic or wild. In fact, domestic dogs are the source of about 99% of human cases. Other animals that can spread the disease include cats, foxes, jackals, wolves, raccoons, mongooses, bears, badgers, monkeys, and bats. Among these, bats serve as the natural reservoir for many *Lyssavirus* species, though the classical rabies virus (RABV) is mainly maintained in mid-sized carnivores such as dogs, foxes, coyotes, raccoon dogs, raccoons, mongooses, and skunks. An exception is seen in the Americas, where several bat species act as the main reservoirs of RABV. These viruses persist in nature through cycles within the same species, occasional spillover between species, and, at times, adaptation to new hosts.

Transmission usually occurs when the saliva of an infected animal enters the body through a bite, scratch, or lick on broken skin or mucous membranes. Less commonly, people may be exposed through aerosols in bat caves, handling of infected carcasses, accidents in laboratories, or even via organ or tissue transplants from infected donors. Once inside, rabies virus shows a strong



preference for the nervous system. It first multiplies at the site of entry, attaches to receptors at nerve endings, and then travels along the nerves to the brain, where it causes acute encephalitis. Unlike many other viral infections, rabies does not produce a detectable level of virus in the blood. After establishing itself in the brain, the virus spreads outward through the nerves to other tissues, which is when clinical symptoms start to appear. Interestingly, although rabies is almost always fatal, there is little visible inflammation in the brain. This suggests that the disease symptoms are likely due to nerve cell dysfunction rather than massive tissue destruction.

3. Clinical Features

Humans: After exposure, the incubation period of rabies generally lasts 20–90 days, although it may be as short as one week or extend beyond a year. The illness typically progresses through four stages: a prodromal phase, followed by an acute neurological stage, then coma, and ultimately death. Two distinct clinical types of rabies are recognized in humans—encephalitic (furious) and paralytic (dumb); which can only be differentiated once neurological symptoms appear.

Animals: In dogs, the incubation period usually ranges between 2–8 weeks, though it can vary from 10 days to 6 months. Clinical signs in affected animals are diverse but often include excessive salivation, paralysis, lethargy, abnormal unprovoked aggression, unusual vocalization, daytime activity in nocturnal species, and loss of normal inhibitions. Unlike humans, hydrophobia is not seen in animals. In dogs, rabies occurs in two clinical forms—furious and paralytic (dumb). The furious form is marked by restlessness, irritability, sudden aggression towards objects, animals, or people, disorientation, and seizures. The paralytic form, on the other hand, is characterized by weakness and paralysis of throat and jaw muscles, foamy salivation, difficulty in breathing, choking, and progressive respiratory failure. Death typically follows within 5–7 days after the onset of symptoms.

4. Laboratory Diagnosis

Diagnosing rabies based only on symptoms is challenging and often unreliable, so laboratory tests are necessary whenever possible. In humans, rabies can be confirmed either before death (ante-mortem) or after death (post-mortem), while in animals, testing is usually done post-mortem. The most reliable method for confirming rabies in both humans and animals is detecting viral antigens in brain tissue after death using the Direct Fluorescent Antibody test (dFAT). Other tests on brain tissue include the Direct Rapid Immunohistochemical Test (dRIT), PCR to detect viral RNA, and examining tissue for Negri

bodies, which are distinctive viral inclusions. For animals in the field, rapid immunochromatographic tests (RIDT) can be used as quick screening tools.

5. Treatment

Presently, there is no effective therapy recognised for rabies. The clinical course is rapid with an invariably fatal outcome. The patient should preferably be managed in a quiet, dark, draft-free room to avoid any stimulation. Treatment is mainly supportive and may include the use of sedative, anti-pyretic, analgesic and anti-convulsant drugs to relieve symptoms.



“IF BITTEN, SEEK MEDICAL HELP IMMEDIATELY!”

6. Prevention and Control

The Ministry of Health and Family Welfare, Government of India, has been running the National Rabies Control Programme since the 12th Five-Year Plan. In 2021, India also launched the National Action Plan for the Elimination of Dog-Mediated Rabies (NAPRE), which provides a comprehensive strategy to fight rabies. Because rabies affects both humans and animals, a ‘One Health’ approach—cooperation between human health, animal health, environmental, and other sectors—is essential to successfully control the disease. Experiences from other countries show that dog-mediated human rabies can be eliminated through mass vaccination of dogs, public education, access to post-exposure prophylaxis (PEP), and strong surveillance of human and animal cases. Although rabies can be prevented with vaccines, thousands of people still die each year, mainly due to lack of awareness. Educating healthcare workers and engaging the public to recognize the disease and seek timely PEP after exposure is crucial to prevent these deaths.

Vaccination:

Mass vaccination of dogs is one of the most effective ways to control and even eliminate rabies. Studies suggest that vaccinating about 70% of dogs in areas where rabies is common can eradicate the disease in dogs and dramatically reduce human cases.

Types of vaccines available:

- **Modified Live Virus (MLV) Vaccines:** These are used in pet dogs and cats and are also widely used for oral vaccination of wildlife, such as foxes in Canada and Europe, or raccoon dogs in Finland. They are derived from the SAD (Street Alabama Dufferin) virus strain and are considered safe.



- **Vectored Recombinant Rabies Vaccines:** These vaccines use harmless viruses (like poxvirus or adenovirus) that carry only the rabies virus glycoprotein G gene, which provides protection. They are used orally in wildlife and by injection in cats, and are safe for all tested birds and mammals.
- **Inactivated (Killed) Vaccines:** These are commonly used for individual pets and large-scale dog vaccination programs. Killed vaccines are stable at room temperature and carry no risk of accidental infection, unlike live vaccines.

Oral Vaccination: Oral rabies vaccines are either modified live-virus or recombinant vaccines. Currently, the WHO recommends two oral vaccines for wildlife: the VRG recombinant vaccine and the highly weakened SAG2 vaccine.