

ONE BITE, TWO WORLDS: UNDERSTANDING RABIES IN ANIMALS AND HUMANS

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Abstract

Rabies is a neurotropic viral zoonosis in which a seemingly routine animal bite can progress to a fatal neurological disease when appropriate preventive measures are delayed. Although the virus infects a wide range of mammals, the domestic dog remains the major link between animal infection and human rabies in many endemic regions. Rabies presents a distinctive public health challenge: once clinical signs develop, the disease is almost invariably fatal, yet infection following an exposure can be prevented effectively when timely and appropriate measures are taken. This article examines the disease across the complete transmission pathway, covering epidemiology, transmission, pathogenesis, clinical manifestations, laboratory diagnosis, post-exposure prophylaxis (PEP), treatment and supportive care, prevention, and One Health strategies. It also discusses the global objective of eliminating dog-mediated human rabies deaths by 2030. Current evidence indicates that human PEP and large-scale dog vaccination address complementary aspects of rabies control. While PEP protects individuals following exposure, sustained vaccination of dogs reduces viral transmission within the animal population and consequently lowers human exposure. Evidence from India further highlights the importance of strengthening rabies surveillance, ensuring timely and complete PEP, and maintaining effective canine vaccination programmes simultaneously. An integrated One Health approach, involving human and veterinary health services, diagnostic laboratories, communities, wildlife authorities, and local administration, provides a practical framework for advancing rabies control and supporting the long-term goal of elimination.

Keywords: rabies; rabies virus; dog-mediated rabies; zoonosis; veterinary public health; post-exposure prophylaxis; dog vaccination; One Health; Zero by 30.

Introduction

Rabies is an acute viral disease of the nervous system caused primarily by rabies virus (RABV), a member of the genus *Lyssavirus*. The disease affects humans as well as a broad range of domestic and wild mammals, including dogs, cats, cattle, buffaloes, horses, and wildlife species. Rather than being viewed simply as a “dog-bite disease,” rabies is more accurately understood as a zoonotic infection maintained within animal populations and transmitted to humans when saliva from an infected animal comes into contact with susceptible tissue. In many endemic regions, domestic dogs are the principal source of human infection, whereas

wildlife reservoirs, particularly bats, have a greater epidemiological role in certain other regions (WHO 2024; CDC 2025).

Rabies presents a distinctive public health paradox: it is one of the most lethal infectious diseases, yet it is also highly preventable. Once the characteristic neurological signs of rabies appear, the disease is almost invariably fatal. However, infection can generally be prevented when appropriate measures are initiated before clinical signs develop. Thorough wound cleansing, timely administration of rabies vaccine, and, when indicated, the use of rabies immunoglobulin

(RIG) or an appropriate recommended monoclonal-antibody product can substantially reduce the risk of the virus progressing to the central nervous system (WHO 2024). Consequently, the most critical opportunity for preventing rabies occurs immediately after exposure, rather than after the onset of illness.

Rabies also has particular importance in veterinary medicine and veterinary public health. Veterinarians may be among the first professionals to identify suspicious clinical features in animals, including abnormal aggression, unexplained paralysis, changes in vocalization, excessive salivation, or unusual behavioural patterns. Veterinary services contribute not only to the recognition and management of suspected cases but also to animal vaccination, bite-risk assessment, appropriate specimen collection, disease surveillance, public awareness, and outbreak response. Effective control of rabies therefore requires human and animal health sectors to work together, as both are integral components of the same prevention and elimination strategy.

Epidemiology

Rabies is reported on all continents except Antarctica, although the greatest burden remains concentrated in parts of Asia and Africa. The World Health Organization (WHO) estimates that rabies causes approximately 59,000 human deaths each year, while also noting that limitations in surveillance and reporting make the true global burden difficult to determine accurately. Children are disproportionately affected, and in many endemic regions, transmission from infected

dogs is responsible for up to 99% of human rabies cases (WHO 2024).

India continues to be an important rabies-endemic country. A large community-based survey conducted during 2022–23 estimated approximately 9.1 million animal-bite incidents annually and modeled around 5,726 human rabies deaths per year. Dogs were responsible for the majority of reported bites. The study also identified incomplete access to, or incomplete completion of, recommended post-exposure vaccination as an important gap in rabies prevention (Thangaraj et al. 2025). These figures should be interpreted carefully because they represent modeled national estimates rather than a direct enumeration of individual rabies deaths.

The epidemiology of rabies varies considerably according to the reservoir species and ecological setting. In dog-mediated transmission systems, the virus is maintained primarily through dog-to-dog transmission, with humans becoming incidental or dead-end hosts. In wildlife-mediated systems, different reservoir species—including bats, foxes, raccoons, skunks, and other carnivores—may maintain distinct viral lineages. Livestock can also become infected, but they generally represent spillover hosts rather than the principal reservoirs responsible for sustained transmission to humans. Recognizing these differences is essential because effective vaccination, surveillance, and control programmes must be adapted to the reservoir species, transmission pattern, and ecological conditions of each region (Green, Carpenter, and Dunn 2011).

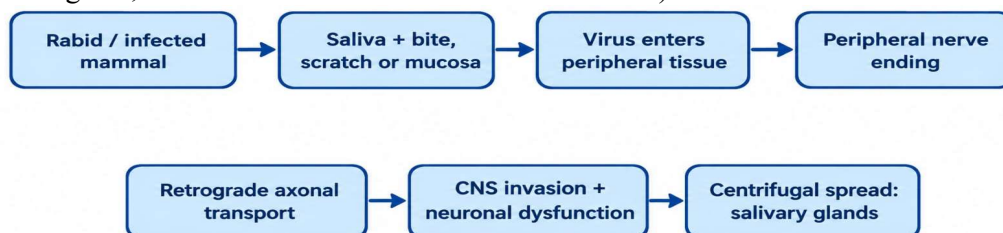


Fig. 1. Simplified transmission and neuroinvasion pathway. Source: based on Finke and Conzelmann (2005), Jackson (2005), and WHO (2024).

Epidemiological feature	What it means in practice
Reservoirs Domestic	Dogs are the major source of human rabies globally; wildlife reservoirs are important in several regions.

At-risk groups	Children, people in endemic rural areas, veterinarians, animal handlers, wildlife workers and laboratory personnel may face higher exposure risk.
Seasonality	Transmission patterns vary by host ecology, dog population dynamics, wildlife behaviour and local surveillance
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Control threshold	Sustained vaccination of roughly 70% of the dog population is widely used as a programmatic target to interrupt canine transmission.

Transmission

Rabies virus is transmitted mainly when saliva or nervous tissue from an infected mammal comes into contact with a bite wound, scratch, mucous membrane, or another area of broken skin. Although bites represent the most common route of transmission, exposure can also occur when a scratch becomes contaminated with infected saliva or when saliva contacts the eyes, mouth, or an open wound. Ordinary human-to-human contact has not been documented as a route of transmission; however, rare cases have occurred through transplantation of infected organs or tissues (WHO 2024).

Rabies virus does not survive well outside the host and is not efficiently transmitted through casual environmental contact. Therefore, simply touching or feeding an animal, or being licked on intact skin, does not constitute the same type of exposure as a bite or contact with damaged tissue. Proper risk assessment should take into account several factors, including the animal species, its vaccination and health status, the circumstances of the exposure, the location and depth of the wound, and whether infected saliva came into contact with broken skin or mucous membranes. Bat exposures require particular attention, as bites or scratches from bats can be small and may go unnoticed.

Following a suspected exposure, the most important immediate measure is to physically remove and inactivate the virus at the site of exposure. The wound should be thoroughly washed and flushed with soap and running water for at least 15 minutes, as soon as possible after the exposure, followed by prompt

professional assessment of the risk and need for further preventive measures. Irritating or potentially damaging substances should not be applied to the wound (WHO 2024).

Pathogenesis

Rabies has a distinctive neuroinvasive mechanism that allows the virus to reach and spread through the nervous system. After entering peripheral tissues, the virus can infect nerve endings and travel toward the central nervous system through retrograde axonal transport. Once within the nervous system, viral spread occurs along interconnected neuronal pathways. At later stages, the virus can move centrifugally from the nervous system to peripheral tissues, including the salivary glands, facilitating the presence of infectious virus in saliva and thereby promoting transmission to another host (Finke and Conzelmann 2005; Jackson 2005).

Severe rabies should not be understood simply as a consequence of extensive neuronal destruction. Experimental and pathological studies indicate that neuronal dysfunction, changes in cellular processes, and complex virus–host interactions make important contributions to the neurological manifestations of the disease. Rabies virus can also influence both innate and adaptive immune responses, which may allow it to reach neural tissues before an effective protective immune response has been established (Jackson 2005).

The incubation period of rabies is highly variable. It commonly extends over several weeks to months, although both shorter and considerably longer periods have been reported.

Factors such as the site of exposure, amount of virus introduced, severity of the wound, distance of the exposure site from the brain, and individual host characteristics can influence the time required for clinical disease to develop.

Once the virus has established infection within the central nervous system and neurological signs have appeared, the preventive window for conventional post-exposure prophylaxis (PEP) has essentially closed. At this stage, clinical management is primarily focused on intensive supportive and palliative care, rather than routine post-exposure prevention (CDC 2026; WHO 2024).

Clinical Manifestations

Human rabies

Human rabies usually begins with a nonspecific prodromal phase, during which affected individuals may experience fever, weakness, headache, malaise, anxiety, or unusual sensations such as pain, tingling, or burning around the site of exposure. As the infection progresses and the nervous system becomes involved, more severe neurological manifestations may develop, including agitation, confusion, hallucinations, difficulty swallowing (dysphagia), excessive salivation, and painful spasms of the pharyngeal muscles. These spasms may be triggered by attempts to drink and, in some cases, even by moving air. This characteristic response accounts for the terms hydrophobia and aerophobia.

Two major clinical forms of human rabies are commonly recognized. Furious rabies is characterized by episodes of marked hyperactivity, agitation, hallucinations, autonomic dysfunction, and painful pharyngeal spasms. In contrast, paralytic rabies is dominated by progressive muscle weakness and paralysis and may closely resemble other neurological disorders. The paralytic form is particularly challenging from a diagnostic perspective because the absence of prominent agitation or other classic features may delay clinical recognition (WHO 2024; CDC 2026).

Animal rabies

Clinical manifestations in animals vary according to the species, stage of infection, and individual animal response. Important warning

signs may include sudden behavioural changes, unexplained aggression or unusual tameness, altered vocalization, aimless wandering, excessive salivation, difficulty swallowing, dysfunction of the jaw or throat, incoordination, progressive weakness, and paralysis. In dogs, rabies may appear as a furious form, a dumb or paralytic form, or a combination of both. Cattle and horses may show predominantly neurological abnormalities and behavioural changes, and the disease may be confused with other causes of encephalitis, neurological dysfunction, or paralysis (Green, Carpenter, and Dunn 2011).

Diagnosis

Although clinical suspicion is an important starting point, laboratory confirmation is essential whenever feasible. Clinical diagnosis can be challenging because the early manifestations of rabies may resemble those of several other infectious and neurological diseases. Furthermore, there is no single simple bedside test that can reliably exclude rabies in an exposed person before clinical symptoms appear. Once rabies is suspected, sample collection, testing, and interpretation should be guided by appropriate public-health and laboratory specialists (WHO 2024; CDC 2025).

For the diagnosis of rabies in animals, brain tissue is the principal specimen used for post-mortem confirmation. Direct fluorescent antibody testing (DFA/dFAT) remains an important reference method. Other approaches, including direct rapid immunohistochemical tests and molecular techniques such as reverse-transcription polymerase chain reaction (RT-PCR) and real-time RT-PCR (RT-qPCR), can complement conventional diagnostic methods. These techniques are particularly useful when sample quality or laboratory capacity presents a challenge. Studies conducted in India have demonstrated useful agreement between DFA, rapid immunohistochemical methods, and RT-PCR, with RT-PCR also showing value when testing decomposed specimens (Prabhu et al. 2018).

In humans, antemortem diagnosis may require examination of multiple specimen types.

Saliva, nuchal skin biopsies, and cerebrospinal fluid (CSF) can be evaluated using molecular or antigen-based diagnostic methods. Serum and CSF may also be examined for rabies virus-neutralizing antibodies when clinically appropriate. Importantly, a negative result from a single specimen does not necessarily exclude rabies. Because viral shedding and detectability can vary over time, serial sampling and testing of multiple specimen types may be necessary under expert laboratory and public-health guidance.

Diagnostic approach	Main role	Key limitation/consideration
Direct fluorescent antibody test	Reference test for infected animal brain tissue	Requires suitable tissue, trained laboratory staff and fluorescence microscopy.
RT-PCR / RT-qPCR	Detects viral RNA; useful for confirmation and molecular epidemiology	Sensitivity depends on specimen type, timing, RNA quality and assay design.
Direct rapid immunohistochemistry	Practical antigen detection in some laboratories	Requires validated reagents and quality assurance.
Serology	Assesses neutralizing antibody response in selected human contexts	Interpretation depends on vaccination history and timing.
Clinical + exposure assessment	Determines urgency of PEP and differential diagnosis	Clinical assessment cannot replace laboratory confirmation when confirmation is required.

Post-Exposure Prophylaxis (PEP)

Post-exposure prophylaxis (PEP) is the most time-sensitive intervention following a potential rabies exposure. Its purpose is to prevent the virus from establishing infection and reaching the nervous system. The main components of PEP are: (1) immediate and thorough wound cleansing, (2) administration of rabies vaccine when vaccination is indicated, and (3) administration of rabies immunoglobulin (RIG) or a recommended monoclonal-antibody product for severe exposures when indicated under the applicable protocol (WHO 2024).

The WHO exposure categories provide a practical framework for understanding when PEP is required. Category I refers to contact that does not constitute an actual exposure, such as touching an animal or being licked on intact skin. Category II includes minor scratches or abrasions without bleeding and generally requires proper wound care along with rabies vaccination. Category III involves more significant exposures, including transdermal bites or scratches, contamination of mucous

membranes or broken skin with saliva, and certain direct exposures to bats. These exposures require wound cleansing and vaccination, together with passive immunization when indicated (WHO 2024).

Treatment and Management

Once clinical rabies has developed, there is no reliably effective curative treatment. Management is therefore directed primarily toward intensive supportive care, symptom control, prevention of complications, appropriate infection-control measures, and compassionate communication with the patient and their family. Given the extremely high fatality associated with clinical rabies, preventing infection before neurological disease develops remains far more effective than attempting to treat established disease (WHO 2024).

Patients with suspected or confirmed rabies may require intensive-care support to maintain the airway and breathing, including mechanical ventilation when necessary. Care may also involve management of fluid and

electrolyte disturbances, seizures, severe agitation, autonomic instability, and other complications associated with neurological disease. Several experimental treatment approaches, including protocolized deep sedation and combinations of antiviral or immunomodulatory agents, have been attempted in individual cases. However, the

available evidence remains limited and inconsistent. Reviews of the Milwaukee and Recife treatment approaches have emphasized that these protocols should not be regarded as established or reliably effective cures for rabies (Ledesma, Lemos, and Horta 2020; Zeiler and Jackson 2016).

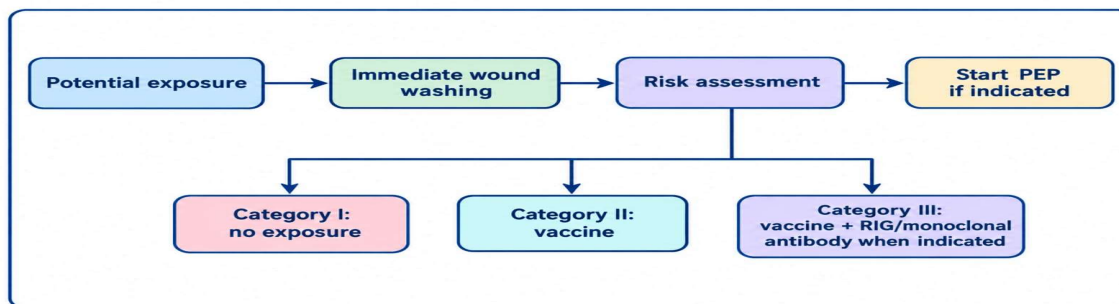


Fig. 2. Simplified PEP decision pathway. Source: author-created synthesis based on WHO (2024) and CDC (2026). Exact schedules vary by prior vaccination status and national guidance.

In animals, management is determined by several factors, including the species, vaccination status, nature of the exposure, and applicable local regulations. Animals suspected of having rabies should be separated from people and other animals and handled only by appropriately trained veterinary or public-health personnel. Decisions regarding diagnostic testing, observation, quarantine, vaccination, euthanasia, or other control measures should be made by the competent authority in accordance with relevant regulations. These measures serve two important purposes: protecting people from further exposure and generating reliable epidemiological information for disease-control efforts.

Prevention

Effective rabies prevention depends on a layered and coordinated approach rather than a single intervention. The first layer is preventing infection in animal populations, particularly through sustained vaccination of dogs. The second involves reducing human exposure through responsible animal handling, awareness, and bite-prevention education. The third is ensuring rapid access to appropriate post-exposure prophylaxis (PEP) following an exposure. The fourth is strengthening surveillance and laboratory capacity, allowing

unusual events and potential outbreaks to be detected, investigated, and controlled promptly.

For dog-mediated rabies, mass dog vaccination is the principal population-level intervention. Both mathematical modelling and field studies support maintaining high and sustained vaccination coverage, commonly around 70% of the dog population, to interrupt transmission within dog populations. Importantly, vaccination programmes must include free-roaming and community dogs, rather than focusing exclusively on owned animals. Where conventional approaches based on catching and injecting dogs cannot achieve adequate coverage, alternative strategies, including oral vaccination and combined vaccination approaches, are being investigated (Lavan et al. 2017; Morters et al. 2013; Wallace et al. 2023).

Indiscriminate dog culling is not a substitute for vaccination. Removal of animals can create vacant ecological space that may subsequently be occupied by other, potentially unvaccinated dogs, while population turnover can maintain susceptibility within the population. Consequently, effective and humane rabies control should integrate responsible dog ownership, appropriate population management, sterilization where suitable, sustained vaccination, and community participation rather

than treating these measures as independent interventions.

Prevention Checklist

- Vaccinate dogs regularly according to veterinary recommendations and the applicable vaccination schedule.
- Prevent uncontrolled roaming and breeding of dogs wherever practical and appropriate.
- Educate children about safe and responsible behaviour around animals.
- Report animals showing suspicious or unusual behaviour to the appropriate veterinary or public-health authority.
- Wash bite and scratch wounds immediately with soap and running water for at least 15 minutes.
- Complete the prescribed PEP regimen without interruption.
- Ensure a reliable supply of rabies vaccines and immunoglobulin or other recommended passive-immunization products at appropriate healthcare facilities.
- Strengthen integrated surveillance by improving coordination and information sharing between veterinary and human health services.

One Health Approach

Rabies is a classic One Health disease because its transmission and control involve interconnected aspects of veterinary medicine, human health, ecology, and community life. A single exposure may involve several sectors: a health professional may treat the person who was bitten, a veterinarian may assess the suspected animal, a laboratory may examine the animal specimen, local authorities may be responsible for managing free-roaming dogs, and community members may determine whether and how quickly an exposure is reported. When these activities operate independently, important opportunities for prevention, diagnosis, and control can be missed.

An effective One Health rabies programme should integrate at least five major

functions. These include human healthcare services for rapid assessment and access to PEP; veterinary services for dog vaccination, animal assessment, and diagnostic testing; laboratory services for disease confirmation and molecular surveillance; community-based systems for bite prevention, exposure reporting, and responsible animal ownership; and local administrative and environmental services for dog-population management and coordination of control activities. The objective is not simply to bring different sectors together, but to establish mechanisms through which they can share information, coordinate interventions, and respond to risks using a common understanding of the local epidemiological situation.

India provides an important example of the potential benefits of such coordinated action. In Goa, an integrated programme combining mass dog vaccination, public education, and strengthened surveillance was associated with the elimination of human rabies during the study period and a 92% reduction in monthly canine rabies cases. More than 95,000 dogs were vaccinated, with coverage of approximately 70%, while educational activities reached a large number of children (Gibson et al. 2022). This experience illustrates the potential impact of sustained, coordinated rabies-control measures. However, the findings should not be assumed to apply uniformly to every region, as differences in resources, dog populations, ecology, healthcare access, and programme implementation can substantially influence outcomes.

Rabies Elimination

The global target commonly known as “Zero by 30” aims to end human deaths caused by dog-mediated rabies by 2030. The strategy is based on a clear epidemiological principle: when rabies transmission is effectively controlled within the dog population, the risk of human exposure and infection decreases substantially. Human post-exposure prophylaxis (PEP) remains an essential component of this strategy because it protects individuals following exposure and prevents deaths from infections that may still occur during the elimination process. However, PEP alone cannot

eliminate rabies because it does not remove the source of infection within the animal reservoir.

Rabies elimination cannot be achieved through a single vaccination campaign. It requires sustained and repeated dog vaccination with high population coverage, dependable disease surveillance, rapid investigation of suspected animal cases, accessible PEP, adequately trained personnel, laboratory diagnostic capacity, community participation, and long-term financial and institutional support. Mathematical modelling studies indicate that elimination is feasible, but they also demonstrate that factors such as vaccination coverage, dog birth rates, dog population density, and continuity of control programmes have a major influence on the outcome (Townsend et al. 2013).

In India, one of the major challenges is translating established policies and strategies into effective large-scale implementation. Recent national evidence indicates that animal-bite exposures continue to occur, completion of recommended vaccination following exposure remains incomplete in some settings, and a substantial burden of human rabies persists. India's National Action Plan for Rabies Elimination (NAPRE) is aligned with the global 2030 target, but achieving meaningful progress requires sustained coordination among human health services, veterinary authorities, laboratories, local administration, and communities. In other words, the success of rabies elimination depends not only on having an appropriate policy framework, but also on consistent and coordinated implementation at the ground level (Thangaraj et al. 2025; Phukan 2026).

Conclusion

Rabies demonstrates an important principle of veterinary public health: even a

disease with an exceptionally high case-fatality rate can be controlled when prevention acts before the virus establishes infection in the nervous system. Following exposure, the virus can progress from peripheral tissues toward the central nervous system, whereas effective prevention intervenes at an earlier stage through prompt wound cleansing, appropriate post-exposure prophylaxis (PEP), and sustained vaccination of dogs.

For veterinary students and professionals, the practical lesson is equally important. Every suspected rabies exposure should be approached as a One Health event. This requires consideration of what happened to the exposed person, the circumstances and condition of the animal, whether the animal can be safely assessed or tested, whether the exposed individual has initiated the appropriate PEP, and whether the incident has been reported to the relevant authorities. At the population level, effective control depends on combining disease surveillance, sustained dog vaccination, community education, and reliable access to essential human biological products. At the individual level, prompt wound care and professional risk assessment should never be delayed.

Rabies elimination therefore does not depend on the discovery of a single "miracle drug." The essential preventive and control tools are already available. The continuing challenge is to deliver these interventions consistently, equitably, and through coordinated human and animal health systems. Veterinary medicine has a central role in this effort because controlling rabies within its animal reservoirs, particularly dog populations, provides one of the most sustainable ways to reduce human exposure and protect human lives.

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