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RABIES VIRUS: CURRENT UNDERSTANDING OF TRANSMISSION, PATHOPHYSIOLOGY, AND PROPHYLAXIS

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Abstract

Rabies is a mortal viral condition of global community health importance, characterized by nearly 100% case fatality once clinical symptoms appear. Due to the virus a neurotropic, negative-strand RNA virus of the Lyssavirus within the family Rhabdoviridae, rabies affects a wide range of vertebrates and is spread by the bite of infected animals. Pet dogs remains responsible for human rabies deaths worldwide, particularly in developing regions, while wildlife reservoirs such as bats, foxes, raccoons, and other carnivores play a significant role in virus maintenance and spillover. This review comprehensively examines the etiology, structure, host reservoirs, modes of transmission, viral life cycle, and pathogenesis of rabies, with emphasis on neuroinvasion and immune evasion mechanisms. Clinical manifestations, including furious and paralytic forms, diagnostic challenges, and laboratory confirmation methods are discussed in detail. Furthermore, the review highlights current preventive strategies, vaccination programs, monoclonal antibody therapies, and wildlife control measures. Historical and modern vaccination approaches, alongside cultural and traditional practices, are critically evaluated. Despite being preventable, rabies continues to cause significant mortality due to gaps in awareness, access to vaccines, and timely medical intervention. Strengthening surveillance, mass vaccination of animal reservoirs, public education, and continued research into novel therapeutic strategies are essential to control rabies worldwide.

INTRODUCTION

The Sanskrit word rabhas, which means "to rage," or the Latin word rabere, which means "to rave," are the sources of the word rabies. The rabies virus, which is a member of the genus Lyssavirus (Greek Lyssa, meaning "frenzy") within the family Rhabdoviridae, is the cause of rabies, a viral zoonosis that continues to pose a serious threat to public health and is one of the leading infectious diseases that kill people globally with the highest case fatality rate Prevention is the main strategy because rabies encephalitis is nearly always lethal once it manifests. (Leung et al., 2007). The conventional furious type of rabies is the easiest to detect, but paralytic and unusual forms make diagnosis more difficult, especially when travelers contract the disease overseas. Travel-related rabies cases have brought attention to the significance of pre-travel vaccination and other preventative measures, and investigations have revealed potential risk factors and difficulties in clinical diagnosis and treatment (Carrara et al., 2013) Geographically dog bites are more common in Europe, Asia, and Africa, while bats are the primary cause of rabies in the Americas. Clinical signs include paralytic rabies, which is similar to Guillain-

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Barré syndrome, and furious rabies, which is marked by irregular consciousness and autonomic symptoms. Particularly for dog-associated rabies variations, the virus's capacity to avoid immune responses and apoptosis leads in limited central nervous system damage, limiting treatment success; nevertheless, in certain bat RABV instances, recovery may be possible if the immune response is swift (Hemachudha et al., 2013). It contain outbreaks, Ontario Ministry of Natural Resources implemented (TVR) strategies, like infection control (PIC) programs after raccoon rabies first appeared in North America near the New York/Ontario border. Nevertheless, the first raccoon rabies cases in Ontario it was declared between July and September 1999, followed by additional confirmed cases (Rosatte et al., 2001).

Causative agent

A CNS illness that is nearly always lethal is rabies. The rabies virus (RV) is the causal agent. (Dietzschold et al., 2008). A group of genetically similar viruses known as lyssaviruses have evolved to replicate in the control center of mammals. Genomic techniques revealed at least 7 potential genomes, only one fatal species (genotype 1) is thought to be the reason of this disease. (Rupprecht et al., 2002) (). The study examined the street rabies virus's ability to survive under different circumstances in the mucous glands. The heat inactivation of the virus was evaluated at 20°C and 37°C using bioassays on mice. At both temperatures, there was an initial rapid titre drop within 24 hours, followed by complete inactivation after 96 hours. The virus was most resilient at 5°C for 144 hours in substrate contamination experiments. Despite seeming dried, it was active for 24 hours on glass and plant leaves at 20–21°C and 48 hours on metal. The virus was rendered inactive in 1.5 hours by direct sunlight at 30°C, although it remained active for 20 hours in the absence of sunlight. (Matouch et al., 1987)

Host reservoir

The majority of wildlife diseases can infect several host species, but only a few number of species usually serve as long-term reservoirs that sustain and spread these pathogens. The majority of hosts lack the innate ability to aid in transmission, thus the pathogen's life cycle and host features determine whether a host is likely to serve as a reservoir. (Worsley-Tonks et al., 2020) For the majority of the 19th and 20th centuries. Bats are the ancestral reservoir of RABV, which has a historical connection to domestic dogs. Bats include a range of viral lineages, which were initially discovered in the early 20th century, despite RABV's limited geographic spread in the New World. The virus has now expanded to wild carnivores, primarily in the Caniformia suborder, after first spreading from bats to domestic dogs. These modifications show how RABV may adapt to a range of hosts, especially in North and South America. (Gilbert et al., 2018) The Rhabdoviridae family, which includes the bat and terrestrial rabies viruses, includes the rabies virus. (Albertini et al., 2007)

Domestic reservoir (carnivore)

Although RABV has a wide spectrum of hosts, non-wild dogs responsible for more than 98% of mammals cases also kill 59,000 people annually. (Mollentze and Brunker, 2018) Although they are insignificant in comparison to those spread by domestic dogs, wildlife can also spread the rabies virus. However, rabies is still widespread and poorly managed in domestic dog populations in most developing nations (Hampton et al., 2015).In well developed countries and other popular nations have all eradicated dog-mediated rabies. Dog-mediated rabies has remained a problem in these countries. (WHO, 2025) Although they are not viral reservoirs, domestic cats (Felis catus) are significant lyssavirus vectors. Cats are usually merely incidental hosts, infected with the lyssavirus that is most common in their area. There have been human cases of rabid cats in Europe, Asia, Africa, and the Americas. (Fehlner Gardiner et al., 2024)

Bats (chiroptera)

Although circulation in bats is geographically restricted to the fauna of the New World, bats are the ancestral reservoir of RABV, and a surprising diversity of species perpetuate various lineages of the virus. (Gilbert, 2018) All lyssaviruses are thought to have originated in bats. The primary cause this disease in humans and non-wild animals within Americas is the standard rabies (RABV) that found in bats throughout the continent. (Zendulková &

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Beranová, 2016) Throughout the Neotropics, agricultural growth and public health are at risk. In addition to causing decreased activity and paralysis before death, RABV-infected hosts frequently display increased hostility, which aids in transmission. (Cárdenas-Canales et al., 2022) The anatomical location in bat-acquired rabies is typically the face, the histological site of risk is typically restricted to the skin, and the virus may be well suited for epidermis entry than in dog-acquired rabies. Rabies contracted from bats is becoming more widespread. (Begeman et al., 2018)

Mode of transmission

Rabies is most commonly transmitted by the bite of infected animals, such as dogs and cats, because of their close proximity to humans (90%). Singh and associates (2017).The brain tissues of infected animals are the main way that the rabies virus spreads. (Ogbevoen & Ghahowa, 2010) Fig 01 demonstrate that the saliva of rabid animals and bites or scratches can transmit rabies to humans and other species. From the infection site, the virus travels through neurons to the central nervous system, where it multiplies, produces symptoms, and spreads throughout the body. Once symptoms manifest, the illness is nearly invariably fatal. (Mollentze & Brunker, 2018).Scraps and starches or open wounds exposed to saliva or other potentially infectious material from a rabid animal can result in non-bite rabies exposure. The danger of contracting rabies is not increased by other encounters, such as touching a rabid animal or coming into contact with its blood, urine, or excrement. (Fatima and others, 2023). In the United States, every rabid dog died within eight days of being ill. Saliva-contaminated scrapes are an uncommon way for the disease to spread; the disease rate is less than 50 times. A few cases have been connected to transplant surgery, despite the fact that the virus seldom spreads from person to person. **(Bano et al., 2017)**.

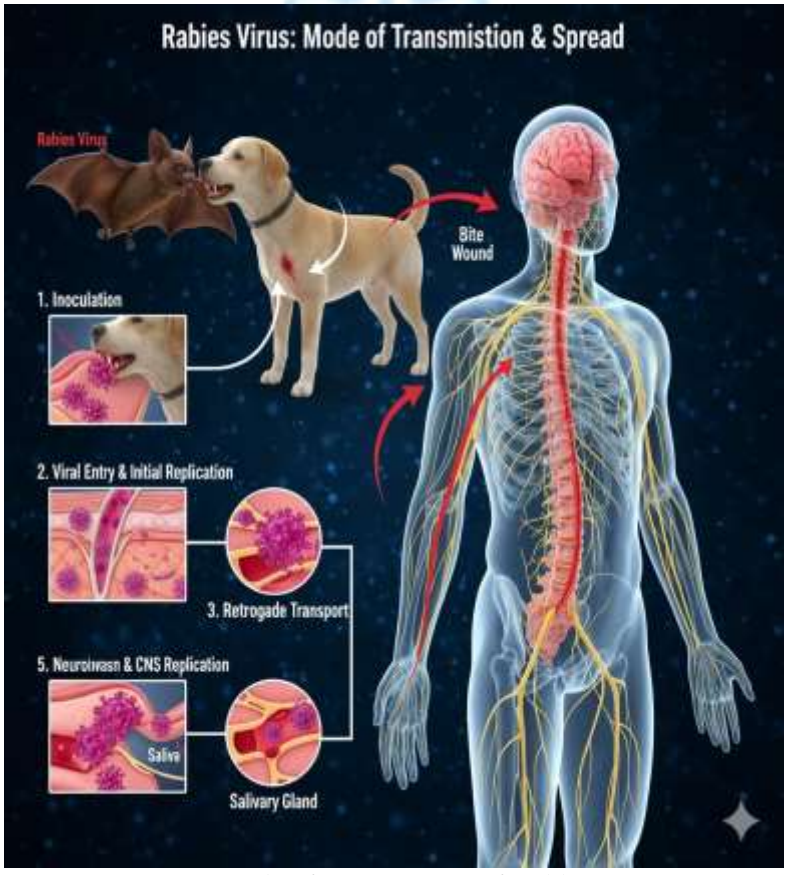


Fig. 01: Mode of transmission of Rabbies virus

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Structure of rabies

The Lyssavirus displays a well-organized structural composition that directly supports its infectivity and replication. Proteins form the largest portion of the viral structure, while lipids make up a significant fraction of the outer envelope. Smaller amounts of RNA and carbohydrates complete the virus's molecular framework. At its center, the virus contains a protein-RNA complex that serves as the genetic core and carries the viral genome (Wunner, 2003).A defining feature of the virus is its bullet-shaped morphology, which results from the precise arrangement of internal proteins around the RNA genome. The viral genome is a single-stranded RNA molecule that encodes only five essential structural proteins, reflecting its compact and efficient organization. These proteins include the nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and RNA-dependent RNA polymerase (L), each playing a distinct role in viral replication and assembly (Dietzschold et al., 2008).

Surrounding the core is a lipid bilayer envelope that originates from the host cell membrane. This envelope is embedded with trans membrane glycoprotein spikes that project outward from the viral surface. The glycoprotein molecules are arranged in closely packed trimetric formations, with approximately 400 spikes covering the viral envelope, enabling attachment to host cells and initiation of infection (Yousef et al., 2012).The internal nucleocapsid protects the viral RNA and ensures its stability during replication. Together, the envelope, glycoprotein spikes, and nucleocapsid give Rabies virus its distinctive visual identity and biological efficiency. Despite having a relatively simple and modular genome, the virus is highly effective in host invasion and disease progression (Rupprecht et al., 2023; You et al., 2025).

Function

The nucleoprotein (N) binds directly to viral RNA and forms the nucleocapsid, a structure essential for genome protection and replication. Each N protein encloses a short segment of RNA, creating a functional cytoplasmic complex required for viral replication (Singh et al., 2017).The phosphoprotein (P) supports viral RNA synthesis by assisting replication and transcription processes. The matrix protein (M) plays a key role in viral assembly and facilitates budding of new virus particles from the host cell.The glycoprotein (G) is the only rabies virus protein capable of inducing virus-neutralizing antibodies. Located on the viral surface, it forms spike-like projections that mediate host cell attachment and immune recognition (Rupprecht, 1996).The RNA-dependent RNA polymerase (L) is essential for viral RNA transcription and replication, driving the synthesis of new viral genomes (Cusabio Technology LLC, n.d.).

Virus life cycle

Once deposited in vivo, lyssaviruses must overcome at least three major obstacles: acquire entry into carrier cell and similar their constituent parts into virus particles and exit the cell (Rupprecht et al., 2002). Protein interactions between G and neurospecific receptors are essential for lyssavirus neurotropism and attachment/entry to target cells. The 1st cell surface recognition site for nAChR, has been found to cause (CVS) and at least four receptors for RAB have been identified (Zandi et al., 2021). The neuronal cell adhesion molecule (NCAM), the muscle version of the nicotinic acetylcholine receptor (nAChR), and the p75 neurotropic receptor (p75NTR) all bind to the rabies virus and/or facilitate its entry into cells. (Lafon, 2005) Saturable, pH-dependent, and competitive with unlabeled homologous viral particles, the rabies virus bound to the receptor peptide. Actin aids in clathrin-mediated endocytosis (CME), which is how RABV internalization happens after initial attachment. Intracellular trafficking takes place following viral invasion. Two models of retrograde trafficking have been put forth, according to which either only the viral capsids are carried or entire virions are divided into vesicles. (Guo et al., 2019) RABV enters the cell through the endocytic route following receptor engagement (Fig. 02). The endosomal compartment's acidic environment causes the viral glycoproteins to undergo a number of conformational changes that facilitate the fusing of the viral and endosomal membranes. A number of rhabdoviruses have had their pH dependence of fusion described. Around pH 6, fusion is at its best. (Albertini et al., 2012) The viral genome is then

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uncoated, releasing the viral RNP into the cytosol. Transcription occurs in the Negri body, a special "virus factory," using the RNP as a template. The G protein is translocated into the endoplasmic reticulum, while the other four viral proteins are made on free ribosomes, probably near the inclusion bodies. (Guo and others, 2019) The virus's polymerase generates five different mRNAs for each protein. The polymerase then transcribes the negative-sense genomic RNA into a positive-sense strand. The transition between genomic RNA transcription and replication is controlled by the quantity of N protein. (Yousaf and others, 2012). The full virion is created with genomic RNA and proteins in the inclusion bodies and Negri bodies during replication, and it is then discharged extracellularly through budding. (Guo and others, 2019).

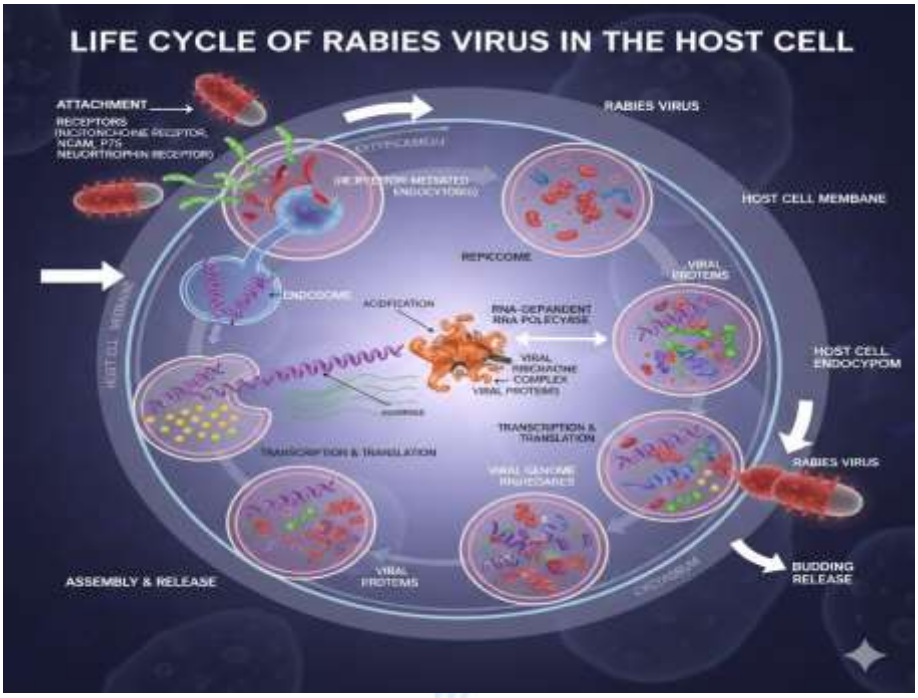


Fig. 02: Life cycle of Rabbies virus

The pathogenesis

Humans typically contract the virus by the bite of a mad animal carrying contaminated saliva. Less frequently, fresh saliva from a non-wild animal might contaminate an open cut, scratch, abrasion, or mucous membrane, spreading the virus. In rare cases, organ or corneal transplants, as well as aerosol inhalation, can spread the virus. (Rupprecht and others, 2002) A rabid animal's bite can inoculate subcutaneous tissues and muscles with infectious saliva, which then initiates the rabies virus's replication in the affected muscle tissue through attachment to nAChR at the neuromuscular intersection. (Kumar et al., 2023) The eclipse phase, also known as the incubation stage, typically lasts few months, though it may differ from weeks to years. .

The incubation period, which is unaffected by the location of the bite or the clinical manifestation, is an intriguing feature of rabies. 3 For the most of the incubation period, RABV remains in the muscle as a low-replication-rate, or "smouldering," infection38 that is restricted to the muscle location that was injected. (2013) Hemachudha et al. RABV enters peripheral neurons by uptake mediated by dynamin and clathrin at the plasma membrane. Endocytosed viruses are then transported intact and inside endosomes from the distal neurites to the site of fusion at the cell body. Somal fusion is required for infection to be successful. (Whelan and Piccinotti, 2016)The virus subsequently uses retrograde axoplasmatic transport channels to penetrate the

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central nervous system. A. Both motor and sensory fibers may be impacted, depending on the animal. Once within the central nervous system, the virus multiplies rapidly, causing harmful effects on nerve cell function. (WHO Collaborating Center for Research & Surveillance on Rabies, n.d.) The neural pathway, which involves retrograde transport along spinal tracts to the medulla oblongata and enhances fusion efficiency with neuronal membranes through pH-dependent conformational changes in the G protein, and the transcellular pathway, in which viral particles infect cerebrovascular endothelial cells by binding the G protein to neural cell adhesion molecules or low-density lipoprotein receptors, are the two ways the virus enters the central nervous system (CNS). (Muhetaer, 2025) The virus spreads centrifugally from the central nervous system to the rest of the body, especially the salivary glands, via the peripheral neurons. At this stage, active viral replication occurs with budding, particularly in the salivary glands, resulting in increased salivary viral concentrations. (Leung et al., 2007)

Clinical diagnosis

The death rate from diseased rabid dog bites is 65% to 80% depending on the location, severity of the wound, and salivary viral concentration particularly if blood ensues. (Bolzan and Consales, 2007) This disease can take up to six months to incubate, while it can take as little as four days in certain situations (Bano et al., 2017) Behavioral changes may take place during the prodromal period. Dogs who are normally sociable may become shy and seek out quiet places, or they may become snappy and agitated. Conversely, aggressive and extremely stressed dogs may become friendlier than usual. (Fekadu, 1993) Early on, common flu-like symptoms like fever, nausea, headache, appetite loss, exhaustion. Additionally, indicators of abnormal sexual behavior, such as hypersexuality, priapism, frequent ejaculation, and other abnormal sexual activities, may be the representation. (Tian et al., 2019) Objective indicators of nervous system malfunction start to appear during the acute neurological phase. Both individuals with encephalitic rabies and some with paralytic forms may experience mental impairment, but the encephalitic group is more likely to experience it. (Hemachudha et al., 2002) Agitation, wandering, sobbing, polypnea, drooling, and attacks on other animals, the community, or unresponsive items are characteristics of the encephalitic (furious form). Animals that are infected often consume foreign objects, such as gravel and firewood. (Bano at el., 2017) The dog has extreme agitation, restlessness, and occasionally the desire to wander. Its desire to bite anything it comes across makes it the most deadly at this point. Most often, paralysis of the laryngeal muscles results in an altered phonation, which is a distinctive high-pitched bark. (Fekadu, 1933). Phobic spasms are a common occurrence for all encephalitic rabies patients, however they do not happen when drowsiness and coma take control. Aerophobia and hydrophobia can appear independently. (Hemachudha at el., 2002) Periods of clarity, agitation, disorientation, and autonomic dysfunction interspersed with spasms in response to touch, auditory, visual, or olfactory inputs are classic signs of brain involvement. (Bolzano and Consoles. 2007) when the recitative phase is very brief or nonexistent, the paralytic phase (dumb rabies) takes place. The "dropped jaw" that results from masseter muscular paralysis is the most distinctive symptom. (Fekadu , 1993) Additionally, the gullet muscle becomes paralyzed, making it difficult for the animal to swallow and causing copious amounts of salivation. (Bano et al., 2017) Because there is no aggressiveness, this type of the illness is very challenging to diagnose. The main cardinal indicators are barely noticeable and show up late. About 50% of patients experience phobic spasms. (Hemachudha et al, 2002)

Laboratory diagnosis

Timely administration of post-exposure prophylaxis depends heavily on accurate laboratory confirmation of rabies in both humans and animals. Rabies diagnosis can be performed either during life or after death, depending on the availability and condition of samples (Consoles & Bolzano, 2007). One of the most reliable diagnostic methods is the direct fluorescent antibody test (dFA), which is widely regarded as the gold standard. In humans, this test is commonly applied ante mortem using skin biopsy specimens, while in animals it is performed on fresh brain tissue (Hanlon & Nadin-Davis, 2013).The dFA

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test relies on antibodies labeled with fluorescein isothiocyanate (FITC). These antibodies specifically bind to rabies virus antigens, such as the ribonucleocapsid or nucleoprotein (N). When the virus antigen is present in a fixed tissue sample, the labeled antibodies attach firmly and remain visible after washing. The bound complexes can then be detected under a fluorescence microscope, allowing rapid and specific identification of the virus (Duong et al., 2016).Effective rabies surveillance is essential for early outbreak detection and assessment of control strategies. To support postmortem diagnosis, especially in field conditions, the direct Rapid Immunohistochemical Test (dRIT) was developed. This method uses biotin-labeled monoclonal antibodies along with a streptavidin–peroxidase system to detect rabies virus antigens. The test demonstrates sensitivity comparable to the fluorescent antibody technique and can provide results within one hour (Fooks et al., 2009). Due to its low cost and minimal equipment requirements, dRIT is particularly valuable in resource-limited settings (Hemachudha et al., 2002)

RABIES: TREATMENTS AND PREVENTION

Since there is no cure for rabies, efforts must be directed towards prevention. Disease-prevention strategies target rabies-transmitting animals and may involve treating an individual after exposure. The adoption of community-wide rabies vaccination for domestic animals has significantly reduced the incidence of rabies in Europe. While the majority of urban domestic animals receive many vaccinations. By administering rabies immune globulin the vaccine, as soon as feasible after exposure, symptoms can be avoided before they manifest. The patient's immunological response and prompt care are essential for survival. Rabies is almost always lethal if left untreated. Scientists have devised post-exposure and pre-exposure prophylactic techniques as new treatments (Yousaf et al., 2012).

Protocols for Treating Rabies

One hour after infection, treatment began with local infiltrations and inoculations of quaternary ammonium compounds, interferon, antirabies gamma-globulin, and local anesthetics (Kaplan et al., 1962, pages 765–775). The Milwaukee and Recife Protocols place a strong emphasis on cerebral vasospasm monitoring, sedation, electrolyte control, and antiviral medication; host immunity and the length of the incubation period determine survival (Ledesma et al., 2020; Jackson, 2004). Rabishield and Twinrab are examples of monoclonal antibodies that have demonstrated preventive and post-exposure effectiveness (Schumacher et al., 1989). Palliative care, nourishment, hydration, and rest are all components of supportive care (Bintang et al., Year).

The Pathophysiology of the Rabies Virus

Since the infectious rabies virus was initially isolated from cloned complementary deoxyribonucleic acid, rabies virus-based vaccines have developed. Studies have demonstrated that cell culture passages can decrease the virulent wild-type rabies virus. While the pathogenic rabies virus avoids them, it triggers host innate immune responses. Additionally, by stimulating cluster of differentiation 4 positive T cell-dependent and independent B cells, a live replication-deficient rabies virus vaccination can elicit strong immunological responses. Using a variety of techniques for enhancing immunogenicity and safety through genetic engineering, this continuing research attempts to produce therapies based on live-attenuated rabies virus to treat clinical rabies (Zhu and Guo, 2016, page 279).

Historical Views on Vaccination against Rabies

Louis Pasteur created the first rabies vaccinations for post-exposure prophylaxis in 1885, using cell-cultured rabies virus and rabid rabbit spinal cord. The most recent vaccine, the purified Vero cell vaccine, is approved in more than 100 nations. Equine and human rabies immunoglobulin choices are problematic because to side effects and expense, especially in developing nations (AuthorLastName et al., 2015). Pasteur's realization that post-exposure prophylaxis was necessary to prevent symptomatic disease marked the beginning of human rabies vaccinations. Pasteur administered a series of inoculations from the desiccated spinal cord of an infected rabbit to nine-year-old Joseph Meister in July 1885 after he was attacked by a rabid dog. The treatment worked despite the risks, and Pasteur's later work with Jean-Baptiste Jupille, a fifteen-year-old shepherd, won praise from all around the world.

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Pasteur's vaccine experienced substantial changes over the course of the following fifty years as colleagues experimented with the timing of inoculation and techniques for preparing rabbit spinal cords. A. New Pasteur Institutes were established as a result of the global dissemination of this technology. Despite some correlation with partial inactivation resulting in paralysis or hypersensitive reactions, phenol-based virus inactivation techniques were established in the early 20th century to lower vaccine-induced illness risks. Pasteur's original method was progressively displaced by this new approach, which persisted until the 1950s (Dacheux, Delmas, and Bourhy, 2011).

Modern vaccines and Prophylaxis

In order to prevent rabies in pets and wildlife, vaccinations are essential. Dogs and cats need several doses of rabies virus vaccines to develop immunity. There are two commercially available oral rabies vaccines for wildlife, including live-attenuated and live-recombinant varieties. Raccoons and foxes are successfully immunized with the vaccinia virus that expresses the rabies virus glycoprotein, but people may experience negative effects. The SAG-2 vaccine, which is derived from the SAD strain and is used for foxes in Europe, is safe and immunogenic in dogs; nevertheless, inoculated dogs have low levels of virus-neutralizing antibody titers. Since smallpox was eradicated in 1980, the development of live virus vaccines has been crucial.For diseases including rabies, poliovirus, and yellow fever, several live virus vaccines have been developed, mostly for animals. Using liquid virus-containing sachets in bait, which trigger immunological responses when consumed, is an efficient way to vaccinate wildlife. SAD Bern and its variants are the main strains utilized. Reversion mutations have been related to some occurrences of vaccine-induced rabies, despite the fact that rabies in people has been successfully reduced by up to 96% in Europe. Furthermore, different species respond differently to these vaccines; for example, certain strains are ineffective against striped skunks (Smith et al., 2019). For high-risk individuals, pre-exposure prophylaxis for rabies is advised. It consists of three injections that prime the immune system for possible exposure, encourage recall during actual exposure. Treatment for post-exposure prophylaxis, which includes wound care and active and passive immunization for the patient, is customized based on infection risk, wound severity, and the biting animal's vaccination status (Kaye et al., YEAR; Bintang et al., Year). The Zagreb regimen is used while administering the pure chick embryo cell vaccination in Indonesia. In order to neutralize the virus, rabies immunoglobulin is frequently added to vaccinations administered within weeks after the bite. Because it has fewer adverse effects than equine rabies immunoglobulin, human rabies immunoglobulin is recommended. For both human and equine rabies immunoglobulin, the Ministry of Health recommends particular dosages and methods of administration (Bintang et al., Year).

Conventional Medicine and Cultural Customs

Folklore about rabid bites in Ethiopia emphasizes the use of plant-based medications and herbal emetics to purge the poison over a forty-day period (Pankhurst, 1970). Charmed pots, topical applications of urine and mustard oil, cauterization, and the use of armlets were among the treatments used in India. Additionally, several suggested plant-based and veterinary treatments were applied to animals. These techniques are still anecdotal and have not been scientifically tested; failures frequently result in fatalities (Beasley, Wallace, Coetzer, Nel, and Pieracci, Year).

Strategies for Global Prevention and Control

With 500,000 people seeking post-exposure treatment each year and an estimated 40,000 to 50,000 deaths. The World Health Organization advises administering human or equine rabies immunoglobulin as soon as possible in addition to rabies vaccinations; the vaccine is not enough for post-exposure efficacy. The main strategies for preventing rabies include mass vaccinations, community collaboration, public education, and enforced laws. Coordinated management measures are effective, as evidenced by successful examples like Malaysia's canine rabies eradication (Wilde et al., 2005; Rupprecht, Hanlon, and Hemachudha, 2002). Timely post-exposure therapy, pre-exposure, animal immunization, public education, and continuous research into medicines, monoclonal antibodies, and vaccine methods are all necessary for effective prevention. To guarantee timely modern

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intervention and lower mortality, knowledge of traditional medicinal practices is crucial.

REFERENCES:

Aghahowa, I. J., & Ogbevoen, E. S. (2010). Rabies in Nigeria: A review. African Journal of Microbiology Research, 4(18), 1872–1879.

Albertini, A. A. V., Baquero, E., Ferlin, A., & Gaudin, Y. (2012). *Molecular and cellular aspects of rhabdovirus entry. Viruses, 4*(1), 117–139.

Albertini, A. A. V., Schoehn, G., Weissenhorn, W., & Ruigrok, R. W. H. (2007). Structural aspects of rabies virus replication. Virus Research, 127(2), 1–17.

Ashwini, M. A., Pattanaik, A., & Mani, R. S. (2024). *Recent updates on laboratory diagnosis of rabies. Indian Journal of Medical Research, 159*(1), 48–61

Bano, I., Sajjad, H., Shah, A. M., Leghari, A., Mirbahar, K. H., Shams, S., & Soomro, M. (2017). A review of rabies disease, its transmission and treatment. Journal of Animal Health and Production, 4(4), 140–144.

Beasley, E. A., Wallace, R. M., Coetzer, A., Nel, L. H., & Pieracci, E. G. (2022). Roles of traditional medicine and traditional healers for rabies prevention and potential impacts on post-exposure prophylaxis: A literature review. PLoS Neglected Tropical Diseases, 16(1), e0010087.

Begeman, L., GeurtsvanKessel, C., Finke, S., Freuling, C. M., Koopmans, M., Müller, T., Ruigrok, T. J. H., & Kuiken, T. (2018). Comparative pathogenesis of rabies in bats and carnivores, and implications for spillover to humans. The Lancet Infectious Diseases, 18(4), e147–e159.

Beranová, K., & Zendulková, D. (2016). Rabies in bats [Article in Czech]. Klinická mikrobiologie a infekční lékařství, 22(2), 68–74.

Bintang, A. K., Basri, M. I., Lotisna, M., & Carrey, M. (2025). *Rabies: Diagnostic, treatment, and prevention*. Department of Neurology, Faculty of Medicine, Hasanuddin University

Brunker, K., & Mollentze, N. (2018). Rabies virus. Trends in Microbiology, 26(10), 886–887.

Cárdenas-Canales, E. M., Stockmaier, S., Cronin, E., Rocke, T. E., Osorio, J. E., & Carter, G. G. (2022). Social effects of rabies infection in male vampire bats (Desmodus rotundus). Biology Letters, 18(9), 20220298.

Carrara, P., Parola, P., Brouqui, P., & Gautret, P. (2013). Imported human rabies cases worldwide, 1990–2012. *PLoS Neglected Tropical Diseases, 7*(5), e2209.

Consales, C. A. & Bolzan, V. L. (2007). Rabies review: immunopathology, clinical aspects and treatment. *Journal of Venomous Animals and Toxins including Tropical Diseases*, 13(1), 5–38.

Dacheux, L., Delmas, O., & Bourhy, H. (2011). *Human rabies encephalitis prevention and treatment: Progress since Pasteur's discovery*. Infectious Disorders – Drug Targets, 11(3), 251–299.

Daher, E. D. F., da Silva Júnior, G. B., Ferreira, M. T., Barros, F. A. S., Gurgel, T. M., & Patrocínio, R. M. S. V. (2005). *Renal involvement in human rabies: Clinical manifestations and autopsy findings of nine cases from Northeast of Brazil.* **Revista do Instituto de Medicina Tropical de São Paulo, 47**(6), 315–320.

Dietzschold, B., Li, J., Faber, M., & Schnell, M. (2008). Concepts in the pathogenesis of rabies. Future Virology, 3(5), 481–490.

Duong, V., Tarantola, A., Ong, S., Mey, C., Choeung, R., Ly, S., Bourhy, H., Dussart, P., & Buchy, P. (2016). Laboratory diagnostics in dog-mediated rabies: An overview of performance and a proposed strategy for various settings. *International Journal of Infectious Diseases, 46*, 107–114.

Dürr, S., Naïssengar, S., Mindekem, R., Diguimbye, C., Niezgoda, M., Kuzmin, I., Rupprecht, C. E., & Zinsstag, J. (2008). *Rabies diagnosis for developing countries*. PLoS Neglected Tropical Diseases, 2(3), e206.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Fatima, M., Iqbal, T., Shaheen, L., Salma, U., Siddique, R., Ali, R., Rehman, A. U., & Usman, S. (2023). Transmission dynamics of rabies virus. In L. Aguilar-Marcelino, M. A. Zafar, R. Z. Abbas, & A. Khan (Eds.), Zoonosis (Vol. 3, pp. 386–397). Unique Scientific Publishers.

Fehlner Gardiner, C., Gongal, G., Tenzin, T., Sabeta, C., De Benedictis, P., Rocha, S. M., Vargas, A., Cediel Becerra, N., Gomez, L. C., Maki, J., & Rupprecht, C. E. (2024). Rabies in cats—An emerging public health issue. Viruses, 16(10), 1635.

Fekadu, M. (1993). *Canine rabies*. *Onderstepoort Journal of Veterinary Research*, 60(4), 421–427.

Fisher, C. R., Streicker, D. G., & Schnell, M. J. (2018). The spread and evolution of rabies virus: Conquering new frontiers. Nature Reviews Microbiology, 16(4), 241–255.

Fooks, A. R., Johnson, N., Freuling, C. M., Wakeley, P. R., Banyard, A. C., McElhinney, L. M., Marston, D. A., Dastjerdi, A., Wright, E., Weiss, R. A., & Müller, T. (2009). *Emerging technologies for the detection of rabies virus: Challenges and hopes in the 21st century*. PLoS Neglected Tropical Diseases, 3(9), e5309.

Franka, R., & Wallace, R. M. (2018). *Rabies diagnosis and surveillance in animals in the era of rabies elimination*. Rev. Sci. Tech. Off. Int. Epizoot., 37(2), 359–370.

Gilbert, A. T. (2018). Rabies virus vectors and reservoir species. Revue Scientifique et Technique (International Office of Epizooties), 37(2), 371–384.

Guo, C., and Zhu, S. (2016). Control and treatment of rabies: from prevention to potentially curative measures. Article 279, Viruses, 8(11).

Guo, Y., Duan, M., Wang, X., Gao, J., Guan, Z., & Zhang, M. (2019). *Early events in rabies virus infection–Attachment, entry, and intracellular trafficking*. *Virus Research*, *263*, 217–225.

Hampson, K., Coudeville, L., Lembo, T., Sambo, M., Kieffer, A., Attlan, M., Barrat, J., Blanton, J. D., Briggs, D. J., Cleaveland, S., Costa, P., Freuling, C. M., Hiby, E., Knopf, L., Leanes, F., Meslin, F.-X., Metlin, A., Miranda, M. E., Müller, T., Nel, L. H., Recuenco, S., Rupprecht, C. E., Schumacher, C., Taylor, L., Vigilato, M. A. N., Zinsstag, J., & Dushoff, J. (2015). Estimating the global burden of endemic canine rabies. PLOS Neglected Tropical Diseases, 9(4), e0003709.

Hanlon, C. A., & Nadin-Davis, S. A. (2013). *Laboratory diagnosis of rabies*. In A. C. Jackson (Ed.), **Rabies (3rd ed., pp. 409–459)**. Academic Press.

Hemachudha, T., Ugolini, G., Wacharapluesadee, S., Sungkarat, W., Shuangshoti, S., & Laothamatas, J. (2013). *Human rabies: Neuropathogenesis, diagnosis, and management. The Lancet Neurology, 12*(5), 498–513.

Hemachudha, T., Ugolini, G., Wacharapluesadee, S., Sungkarat, W., Shuangshoti, S., & others. (2013). *Human rabies: Neuropathogenesis, diagnosis, and management*. **The Lancet Neurology, 12**(5), 498–513.

Hemachudha, T., Ugolini, G., Wacharapluesadee, S., Sungkarat, W., Shuangshoti, S., & Jiraporn, V. (2013). *Human rabies: Neuropathogenesis, diagnosis, and management*. Neurology Asia, 18(12),

Jackson, A. (2005). Recovery from rabies. New England Journal of Medicine.

Kaplan, M. M., Cohen, D., Koprowski, H., Dean, D., & Ferrigan, L. (1962). Studies on the local treatment of wounds for the prevention of rabies. Bulletin of the World Health

Kaye, A. D., Perilloux, D. M., Field, E., Orvin, C. A., Zaheri, S. C., Upshaw, W. C., Behara, R., Parker-Actlis, T. Q., Kaye, A. M., Ahmadzadeh, S., Shekoohi, S., & Varrassi, G.

Krebs, J. W., Mondul, A. M., Rupprecht, C. E., & Childs, J. E. (2001). Rabies surveillance in the United States during 2000. Journal of the American Veterinary Medical Association, 219(12), 1687–1699.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Kumar, A., Bhatt, S., Kumar, A., & Rana, T. (2023). *Canine rabies: An epidemiological significance, pathogenesis, diagnosis, prevention, and public health issues*. **Comparative Immunology, Microbiology and Infectious Diseases, 97**, 101992.

Lafon, M. (2005). *Rabies virus receptors. Journal of Neurovirology, 11*(1), 82–87.

Ledesma, L. A., Lemos, E. R. S., & Horta, M. A. (2020). *Comparing clinical protocols for the treatment of human rabies: The Milwaukee protocol and the Brazilian protocol (Recife)*. Revista da Sociedade Brasileira de Medicina Tropical / Journal of the Brazilian Society of Tropical Medicine, 53, e20200352.

Lentz, T. L. (1990). *Rabies virus binding to an acetylcholine receptor α-subunit peptide. Journal of Molecular Recognition, 3*(2), 82–87.

Leung, A. K. C., Davies, H. D., & Hon, K.-L. E. (2007). Rabies: Epidemiology, pathogenesis, and prophylaxis. *Advances in Therapy, 24*(6), 1345–1357.

Matouch, O., Jaros, J., & Pohl, P. (1987). Survival of rabies virus under external conditions [Article in Czech]. Veterinární Medicína (Praha), 32(11), 669–674

Muhetaer, M. (2025). *Analysis of pathogenesis and mechanism of rabies. Theoretical and Natural Science, 93*, 39–44.

Pankhurst, R. (1970). *The history and traditional treatment of rabies in Ethiopia*. Medical History, 14(4), 378–389.

Piccinotti, S., & Whelan, S. P. J. (2016). Rabies internalizes into primary peripheral neurons via clathrin-coated pits and requires fusion at the cell body. PLoS Pathogens, 12 (7), e1005753.

Rosatte, R., Donovan, D., Allan, M., Howes, L. A., Silver, A., & et al. (2001). Emergency response to raccoon rabies: Introduction into Ontario. *Journal of Wildlife Diseases, 37*(2), 265–279.

Rosekrans, J. A., and D. G. Hankins (2004). A succinct overview of rabies prevention and treatment for medical professionals. Mayo Clinic Proceedings, 79(5), 671-676

Rupprecht, C. E. (1996). *Rhabdoviruses: Rabies virus*. In S. Baron (Ed.), *Medical microbiology* (4th ed.). University of Texas Medical Branch at Galveston.

Rupprecht, C. E., Hanlon, C. A., & Hemachudha, T. (2002). *Rabies re-examined*. The Lancet Infectious Diseases, 2(6), 327–343.

Schumacher, C. L., Dietzschold, B., Ertl, H. C. J., Niu, H.-S., Rupprecht, C. E., & Koprowski, H. (1989). Use of mouse anti-rabies monoclonal antibodies in postexposure treatment of rabies. *The Journal of Infectious Diseases*, 160(2), 326–330.

Singh, R., Singh, K. P., Cherian, S., Saminathan, M., Kapoor, S., Manjunatha Reddy, G. B., Panda, S., & Dhama, K. (2017). Rabies – epidemiology, pathogenesis, public health concerns and advances in diagnosis and control: A comprehensive review. Veterinary Quarterly, 37(1), 212–251.

Smith, S. P., Wu, G., Fooks, A. R., Ma, J., & Banyard, A. C. (2019). *Trying to treat the untreatable: Experimental approaches to clear rabies virus infection from the CNS. Journal of General Virology, 100*(8), 1171–1186.

Tian, Z., Chen, Y., & Yan, W. (2019). *Clinical features of rabies patients with abnormal sexual behaviors as the presenting manifestations: A case report and literature review*. **BMC Infectious Diseases, 19**, 679.

Wilde, H., Khawplod, P., Khamoltham, T., Hemachudha, T., Tepsumethanon, V., Lumlerdacha, B., Mitmoonpitak, C., & Sitprija, V. (2005). Rabies control in South and Southeast Asia. *Vaccine*, 23(17–18), 2284–2289.

World Health Organization Collaborating Centre for Rabies Surveillance & Research. (n.d.). *Transmission and pathogenesis*. Rabies – Bulletin – Europe. Retrieved December 27, 2025

World Health Organization. (2025). Epidemiology and burden of disease. World Health Organization.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Worsley Tonks, K. E. L., Escobar, L. E., Biek, R., Castaneda Guzman, M., Craft, M. E., Streicker, D. G., White, L. A., & Fountain Jones, N. M. (2020). Using host traits to predict reservoir host species of rabies virus. PLOS Neglected Tropical Diseases, 14(12), e0008940.

You, Y., Yang, F., Lin, S., Chen, Z., Shu, S., Yu, Y., He, B., Cao, Y., & Lu, G. (2025). Rabies virus glycoprotein: Structure, function, and antivirals. hLife.

Yousaf, M. Z., Qasim, M., Zia, S., Rehman Khan, M., & Khan, A. (2012). Rabies: Molecular virology, diagnosis, prevention and treatment. Virology Journal, 9, 1-50.

Zandi, F., Goshadrou, F., Meyfour, A., & Vaziri, B. (2021). *Rabies infection: An overview of lyssavirus-host protein interactions. Iranian Biomedical Journal, 25*(4), 226–242.