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# Review on: Strategies for Preventing and Controlling Rabies Disease

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#### ABSTRACT

A virus called the Lyssavirus, which is a member of the Rhabdoviridae family, causes rabies, an infectious disease that damages the brain. It is regarded as a semi-zoonotic acute illness since infected animals usually pass away after exhibiting symptoms. Infected animals' saliva contains the virus, which is mostly spread by animal bites or contaminated saliva from all warm-blooded (homoeothermic) species. Though bats are also a major reservoir in the Americas, dogs are thought to be the most prevalent source of rabies transmission globally. Rabies can incubate for as little as four days or as long as six months, depending on the circumstances. The virus damages the nervous system after entering the body and making its way to the brain. After that, it moves to the salivary glands, where it can be bitten by humans or other animals. Clinical signs of rabies can mimic those of other neurological diseases such botulism, tetanus, and polio. As a result, laboratory validation is crucial, including diagnostic techniques such the mouse inoculation test, direct fluorescent antibody detection, and polymerase chain reaction (PCR). In this essay, the transmission, pathophysiology, treatment, prevention, and control of rabies are reviewed. Proactive preventative measures are essential to stop the spread of this lethal illness because of its high death rate.

Keywords: Lyssavirus, Zoonotic disease, Rhabdoviridae family, Polymerase chain reaction

#### INTRODUCTION

All warm-blooded animals, including humans, are susceptible to rabies, a virus that attacks the central nervous system [1], [2]. Once clinical signs start to show up, this zoonotic disease almost often results in lethal encephalitis in humans and other mammals [3]. Severe neurological symptoms precede paralysis and death as a result of the illness [4]. Rabies is still a fatal but preventable viral illness since there is no effective treatment once symptoms appear [5]. While wild animals serve as the primary hosts in developed regions, dogs are the predominant reservoirs of infection in the majority of underdeveloped countries [6]. Except for a small number of European nations, a number of Caribbean islands, Australia, New Zealand, and Japan, the disease is widespread The vast and mostly uncontrollable reservoir of sylvatic rabies found in wild animals is making the disease a larger hazard to both humans and domestic animals in many parts of the world [1]. Rabies is an acute viral infection of the central nervous system caused by a Lyssavirus belonging to the Rhabdoviridae family [4], [7]. Derived from the

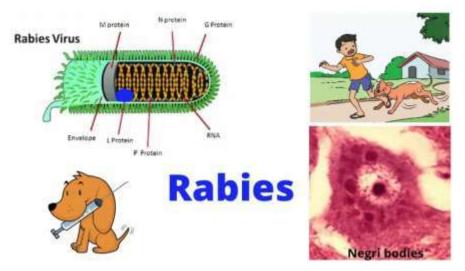
Greek word for "rod," "Rhabdo" describes the virus's characteristic rod- or bullet-shaped structure [1]. Rabies can infect any creature, including humans, cats, dogs, wild animals, and livestock. In animals, the illness typically progresses through three stages: prodromal, excitation (furious), and paralysis (dumb). Human transmission occurs most commonly by bites, scratches, or licks to broken skin or mucous membranes contaminated with infectious saliva [8]. Rabies is still a serious global public health concern, mainly in Africa, Asia, and Latin America, where it is estimated to cause 35,000 deaths annually [6]. The World Health Organisation (WHO) claims that rabies is a neglected tropical disease that mostly strikes impoverished and healthcare-poor countries [12]. According to current estimates, rabies kills approximately 55,000 people annually [7], and there is evidence that the illness is reemerging in a number of places [9]. The most important human transmission vectors are still domestic dogs [13]. However, with prompt medical attention, rabies can be avoided. The virus can be neutralised before it enters the nervous system by post-exposure prophylaxis (PEP), which consists of administering the rabies vaccine, using

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immunoglobulins, and providing prompt wound care [7], [14]. The risk of rabies transmission can be considerably decreased by raising public awareness and teaching communities about dog behaviour, how

to treat bite victims, and preventative measures [7], [9]. Thus, this review's main goal is to provide current knowledge about rabies prevention and control.



#### **Rabies Disease**

#### **Etiology:**

The Lyssavirus genus, which belongs to the Rhabdoviridae family of bullet-shaped viruses with a single-stranded RNA genome, is the causal agent of rabies. Among the six so-called rabies-related viruses in the genus are the classical rabies virus (genotype 1), European bat lyssaviruses 1 and 2 (genotypes 5 and 6), Lagos bat virus (genotype 2), Mokola virus (genotype 3), Duvenhage virus (genotype 4), and the newly identified Australian bat genotype 7 [15]. The genus Lyssa virus includes the rabies virus as well as closely related viruses such as the Australian bat Lyssavirus, the European bat viruses 1 and 2, the Mokola virus, the Lagos bat virus, and the Duvenhage virus from Africa. All of these viruses are thought to be able to infect humans and animals with rabies-like illness. The following detergents can render the rabies virus inactive: sodium hypochlorite, 45-75% ethanol, iodine preparations, formaldehyde, phenol, ether, trypsin, β-propiolactone, and quaternary ammonium compounds. Additionally, a pH of less than 3 or a pH of more than 11 will inactivate it. Under UV light, this virus can harm itself. Drying and sunshine quickly deactivate it, and it cannot endure for extended periods of time in the environment in dried blood and secretions [16]

## **Epidermiology:**

**Distribution:** Globally, there are different rabies reservoirs. In Africa, Asia, Latin America, and the Middle East, canine rabies is the most prevalent kind. On the other hand, rabies in dogs has all but disappeared in North America and Europe, although the disease still exists in wildlife populations in America [17]. For many years, several areas have been free of rabies, including the UK, Ireland, Norway, Sweden, Iceland, Japan, Australia, New Zealand, Singapore, a large portion of Malaysia, Papua New Guinea, the Pacific Islands, and a number of Indonesian islands. Approximately 98% of human cases worldwide are recorded underdeveloped countries in Latin America, Africa, and Asia [18], [19].

Species and Host Range Variations: While many mammals are susceptible to rabies, only a few are true reservoir hosts [18]. Cattle, horses, and mules are examples of domestic animals that may experience cattle frequently severe symptoms; become aggressive, while horses and mules exhibit restlessness and agitation. Rabid foxes and coyotes are among the wild animals that can attack people or infiltrate residential areas, putting people and pets in danger [17].

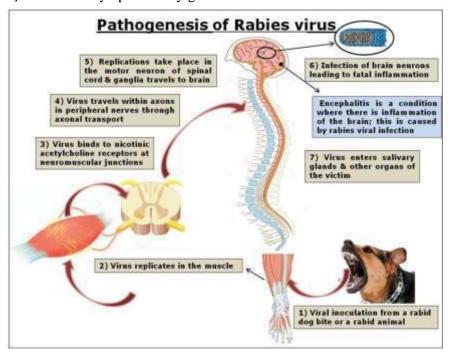
**Source of Infection and Transmission:** The Canidae (dogs, wolves, jackals, foxes, coyotes, and raccoondogs), Mustelidae (skunks), Viverridae (mongooses), Procyonidae (raccoons), and bats

(Chiroptera) are the primary animal reservoirs of rabies infection and transmission. Domestic dogs are thought to be the main reservoir in Africa, however other carnivores may occasionally add to cycles of transmission [20]. Exposure happens when an infected person or animal's saliva, cerebrospinal fluid, tears, or neural tissue enters the body through an open wound, mucous membrane, bite, or scratch. As a result, the virus is able to penetrate underlying tissues and get beyond the skin barrier [21], [22]. Rabies has an exceptionally lengthy incubation period that varies based on the virus load and exposure site. Before entering the neurological system, the virus frequently stays localised at the site of injection for weeks or even months. Rabies immunoglobulin post-exposure treatment can be effective days after exposure, which is explained by this delay. Rarely, organ or tissue transplants from sick people have also been used to spread rabies [23].

#### **Pathogenesis**

The aetiology Encephalomyelitis is caused by the Rhabdovirus, which attacks the encephalon after entering the peripheral nervous system and moving on to the central nervous system [24]. Human fever, pain, and headache are the first symptoms of nonspecific viral infections [25]. These first symptoms may give

rise to agitation, anxiety, and even delirium [26]. In the initial days following a rabies bite, one of the most common symptoms is a tingling sensation at the bite site [27]. The virus then moves from the peripheral nerves to the central nervous system after returning to the peripheral nervous system and concentrating on areas that are strongly innervated, including the salivary glands [28]. Hypersalivation in rabies patients can result in hydrophobia, a disorder characterised by sudden pharyngeal spasms at the sound, taste, or sight of water, in addition to tongue foaming [29]. The infection eventually becomes so severe that the nervous system totally fails, leading to immediate death [30]. Though the incubation period can normally last anywhere from two weeks to six years, animals usually die within 10 days following inoculation [31]. The incubation period is influenced by the virus load, wound severity, and bite site [32]. Ultimately, the virus causes more harm to the brainstem than to the rest of the central nervous system [33]. The harmful consequences and unnoticed functional changes are brought on by an inflammatory reaction [34]. The virus then alters neurotransmission, and apoptosis may be brought on by viral or cell-dependent processes [35]. Rabies is invariably lethal as soon as symptoms start to show [36].



**Clinical Manifestations** 

Animals with rabies start acting strangely and erratically as the disease worsens. Laboratory diagnostic testing is required to confirm any suspected



condition. Anxiety, restlessness, nausea, diarrhoea, moderate fever, dilated pupils, hypersensitivity to stimuli, excessive salivation, and lack of appetite or occasionally increased hunger are examples of early clinical symptoms, which are frequently ambiguous [37]. Lameness in the afflicted leg is frequently the initial symptom of post-vaccinal rabies. Usually, affected animals exhibit noticeable temperamental changes, becoming either excessively loving or abnormally aggressive [38].

### 1.Prodromal Stage

The onset of the first clinical signs follows a variable incubation time. Subtle behavioural changes like irritation in domestic animals, odd activity patterns in nocturnal species, lack of anxiety towards humans in wild animals, and peculiar feeding habits are characteristics of this early stage, which lasts for around one to three days [39].

#### 2. Excitement (Furious) Stage

Attacks on people, animals, or inanimate things, loud vocalisations, rapid breathing, copious drooling, and obvious agitation are characteristics of the angry variety. Rabid animals frequently gnaw on odd items like sticks or stones. When wild animals lose their innate fear of people, they may attack animals they would ordinarily avoid, such porcupines. During the day, animals that are nocturnal may become active. Prolonged object focus or staring can also be a sign of this stage in cattle [38].

#### 3. Stage of Paralysis (Dumb)

The main symptom of the paralytic or "dumb" form of rabies is gradual muscular paralysis. Drooling may increase as a result of the jaw and throat muscles becoming inflexible, which makes swallowing challenging. Laryngeal paralysis can change vocalisation, causing dogs to bark abnormally or

cattle to bellow unusually. Facial paralysis, drooping of the lower jaw, and isolation from the herd in ruminants are common. This stage is also marked by foamy salivation, hind limb weakness, and ultimately complete paralysis followed by death [40].

#### 4. Hydrophobia

Hydrophobia, literally meaning "fear of water," is a classical sign in advanced rabies [41]. It refers to the difficulty and pain in swallowing fluids due to throat spasms, causing affected animals to struggle when attempting to drink. Excessive salivation is common, and painful spasms of the throat and vocal cord muscles occur. The virus persists in the saliva, facilitating transmission through the bite of an infected animal [42].

#### Diagnosis of rabies

Usually, rabies cannot be identified until clinical signs appear. Both living patients and post-mortem autopsies can be used for diagnosis [43]. It is still difficult to detect lyssavirus infections antemortem. There are no symptoms that are actually pathognomonic for rabies, despite the fact that hydrophobia is thought to be quite suggestive. Negri bodies have historically been utilised for diagnosis, but this method is no longer regarded as trustworthy because of its poor sensitivity. For confirmation, more precise laboratory-based methods have been created. Tissue samples are typically taken from the brain, especially the brainstem and cerebellum, in order to make a conclusive diagnosis in animals [44]. Brain smears are subsequently examined using the fluorescent antibody test (FAT), which is applicable to both human and animal materials. The direct FAT is the accepted confirmatory diagnostic method for animals [45]. Additional techniques for this virus's detection are listed in Table 1.

Table1: The diagnostic techniques for rabies disease.

Techniques	Sample	Benefits/disadvantages
Polymerase Chain	Body fluids, saliva, Urine,	Applicable in all tissue conditions
Reaction (PCR)	cerebrospinal fluid	but, requires experienced technicians.
Mouse Inoculation	Liver, brain, salivary glands,	In this technique only fresh tissue is
Technique (MIT)	spleen and pancreas are the	used for an accurate result.
	most appropriate sample.	
Direct Fluorescent	Similar to MIT	Applicable with most tissue sources.
Antibody technique (DFA)		Not applicable in decomposed tissue.



Source: Yousaf et al. [45]

#### **Prognosis**

Once neurological symptoms start to manifest, rabies is nearly usually fatal in uninfected people. However, if given during the first six days following exposure, post-exposure prophylaxis (PEP) by vaccine is quite successful in preventing the illness. Treatment may still have a probability of effectiveness even in cases when delays make PEP more difficult to execute [42].

#### **Treatment**

The only available treatment options for rabies are supportive care once the disease's clinical symptoms appear. Sedation is frequently used to reduce pain, agitation, and fear in patients. Intensive care techniques like sedation, assisted ventilation, and paralysis therapy are frequently used in management. In these situations, ketamine has been suggested as an appropriate agent [46]. Sunlight, washing, and air exposure can easily deactivate the rabies virus (Lyssavirus). As a result, effective wound care is essential to avoiding infection. Thorough wound care within the first three hours of virus exposure can virtually stop the spread of rabies, according to experimental research. To further lower the viral load, the suggested strategy calls for thoroughly cleaning the wound with soap and water before using an antiseptic such povidone-iodine or alcohol. [47], [48].

#### **Prevention and Control of Rabies**

In 1885, Louis Pasteur and Emile Roux created the rabies vaccine, which came before In addition to the United States, France, Belgium, and Germany also utilize Raboral V-RG to prevent outbreaks in wild animals [49], [50]. Appropriate rabies preexposure prophylaxis, prompt local treatment of infected lesions, and appropriate rabies post-revelation prophylaxis can all help prevent human rabies. The non-activated man vaccinations are offered to those who are more likely to be exposed, such as veterinary professionals, animal trainers, wildlife representatives, laboratory personnel, and others [51], [52].

# **Controlling and Preventing Rabies in Animals**

a) Mass dog vaccination:

Up to 99% of human rabies cases are transmitted by dogs. To stop transmission, at least 70% of dogs must receive vaccinations [53].

b) Dog Population Management:

Increasing vaccination rates and reducing the number of stray dogs are achieved through sterilisation, registration, and humane culling where required [54].

# Separation of Rabies-Expected Animals and Euthanasia

**Them:** A dog, cat, or ferret may be removed, observed, or put down and tested if it bites a person or another dog, cat, or ferret. When unvaccinated dogs and cats come into contact with rabid animals, they should be put down right away. The animal should be vaccinated one month before to release and kept in tight isolation for six months if the owner refuses to have this done [55].

**Biosecurity:** Placing all imported canines under quarantine for four to six months is the best way to stop rabies from entering a nation that is rabies-free. This strategy has been successful in completely preventing the disease from entering island nations, but it clearly has limitations in nations with boundaries of land. [56].

Animal Pre-Exposure Vaccination: Some recently developed inactivated vaccines for veterinary use are very efficient and thermostable. This exemption may be granted for a period of one to three years. Dogs are among the specific species for which the bulk of veterinary vaccinations are approved exclusively. There are potency standards for all rabies vaccines that are authorised for use in both humans and animals. Revaccination is required every three years after then. The vaccine manufacturer's instructions will determine whether cattle and sheep should be immunised annually or every two to three years. It is highly advised to vaccinate domestic livestock that do not exhibit obvious bite wounds after an outbreak. Regardless of the duration of the initial vaccination's protection period, all dogs and cats should have a second vaccination 12 months after the first one. For sufficient protection against the virus, a booster shot



should be obtained as soon as possible after coming into contact with a rabid animal [57].

Animal Post-Exposure Prophylaxis: Five doses of the canine rabies vaccination on days 0, 3, 14, 21, and 35, along with a murine antirabies antibody on day 0, may help protect an unprotected animal from rabies. No matter the animal's age, a booster shot ought to be administered a year following the first dose. Animals should be put down and their heads submitted for inspection if they exhibit signs of rabies, such as seizures, paralysis, etc. [58]. Human Rabies Prevention and Controls: Prompt action is crucial to preventing human rabies following probable exposure.

## **Controlling and Preventing Rabies in Humans:**

The key to preventing rabies in humans after suspected exposure is prompt availability to postexposure prophylaxis (PEP), which includes complete wound cleaning, immunisation, and rabies immunoglobulin (RIG) delivery. For rabies control and management to be effective, human and animal health professionals must increase their knowledge and abilities. The protection of those most at risk of exposure, post-exposure prophylaxis, and supportive care for patients who are clinically affected are the three main goals of rabies prevention methodologies. The following are important preventive measures:

- Immediate wound care: Washing bite wounds thoroughly and promptly with soap and running water for at least 15 minutes greatly lowers the virus load at the injection site.
- The administration of rabies immunoglobulin (RIG) provides passive immunity, which helps to bridge the gap until vaccine-induced active immunity is established.
- Anti-rabies vaccinations for humans: Using contemporary cell culture-derived vaccines in compliance with advised protocols guarantees dependable and efficient protection.

#### **CONCLUSION**

A deadly viral zoonotic illness, rabies poses a major threat to public health. Despite being found all over the world, it is significant in emerging nations like Ethiopia. This is a result of the high number of stray dogs that are common. This virus poses a hazard to African wild dogs (Lycaon pictus) and Ethiopian wolves (Canis simensis) in Africa. Only when the virus is injected into a bite wound or mucous membrane can it spread. Although avoidable, the condition is incurable. The two main strategies for preventing rabies in animals are vaccination and avoiding contact with diseased animals. Human and animal exposure to rabies can be prevented in the majority of cases by educating the public about the disease's transmission routes and avoiding wildlife interaction. Given the above-mentioned conclusions, the following recommendations could be made. It is crucial to educate the public about the prevention, control, and mechanism of transmission of rabies. Application of international law to aid in the prevention and management of infectious illnesses. Establishing guidelines for stray dog management, rigorously controlling dogs that are let to roam freely, and mandating rabies vaccinations are all crucial.

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