



Rabies Virus: A Major Neglected Tropical Disease

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Abstract

Rabies is among the most neglected tropical diseases. The *Lyssavirus* genus causes rabies, a deadly zoonotic illness that affects mammals worldwide, including humans. Although pre-exposure and post-exposure prophylaxis (PEP) vaccines are now available, rabies still poses a serious threat to public health, especially in underdeveloped nations. This article looks at the dynamics of rabies transmission, clinical signs, difficulties in diagnosing the disease, and prevention measures. It highlights the vital importance of all-encompassing immunization programs, creative oral vaccination campaigns for wildlife, and joint ventures between the veterinary and medical fields. The World Health Organization's (WHO's) global aims for rabies elimination depend on improved surveillance and public education.

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Introduction

Zoonoses are illnesses or infections that people can naturally contract from vertebrate animals (1). Many zoonoses, such as echinococcosis, leishmaniasis, brucellosis, anthrax, rabies, leptospirosis, plague, taeniasis/cysticercosis, and schistosomiasis, are frequently overlooked. Most neglected diseases occur in developing nations due to poor environmental conditions and inadequate medical resources (2). Rabies is an extremely lethal and highly overlooked tropical disease. Controlling rabies is challenging because it is often disregarded as an endemic zoonotic illness (3). This most lethal viral zoonosis is spread by bats and can infect humans and other mammals, including pets, livestock, stray animals, and wildlife, causing fatal encephalomyelitis (4).

Rabies is a zoonotic viral disease caused by a virus from the *Lyssavirus* genus of the *Rhabdoviridae* family and the Mononegavirales order (5). This virus infects mammals and causes lethal encephalitis (6). The lethality of rabies in mammals is due to the involvement of the nervous system. It is caused by a neurotropic, negative-sense, non-segmented, and single-stranded RNA virus (5).

Rabies almost always results in death and is mostly spread from a rabid animal to a human through bites or scratches involving infectious saliva (7). Humans can contract the disease from both domestic and wild animals, usually through bites (7). Transmission typically occurs when an infected host's saliva is transferred to an uninfected animal. The most frequent way for the rabies virus to spread is through the bite or virus-containing saliva of an infected host (8).

Though rabies is a preventable viral zoonosis due to

the availability of vaccines, it remains a significant public health issue in developing countries (9). The rabies vaccine is used both to prevent rabies before exposure and for a while after exposure to the virus. Vaccinating dogs is highly effective in preventing the spread of rabies to humans and can be safely used across all age groups (10). However, these viruses can still infect dogs vaccinated with the currently available vaccines. Additionally, adopting oral rabies vaccination for stray and guard dogs in urban and rural areas, respectively, could be crucial (4). Therefore, this review aims to explore the rabies virus, a significantly neglected tropical disease.

Literature Review on Rabies Virus

Etiology

The causative agent of rabies is the *Lyssavirus* genus, belonging to the *Rhabdoviridae* family. It is a bullet-shaped virus containing a single-stranded RNA genome (11,12).

Species Affected

All species of mammals can potentially contract rabies, but only a limited number serve as reservoir hosts. These reservoir hosts are primarily members of the families Canidae (dogs, jackals, coyotes, wolves, foxes, raccoon dogs), Mustelidae (various skunks, ferret badgers), Viverridae (mongooses, genets), Procyonidae (raccoons), and the order Chiroptera (bats). Some unusual reservoirs have been proposed for specific variants, such as common/white-tufted marmosets (*Callithrix jacchus*) in parts of Brazil and greater kudu (*Tragelaphus strepsiceros*) in one region in Africa. While cats can be affected by rabies, cat-adapted variants have not been observed. Birds can be



infected with the rabies virus, as shown in experiments with orally or parenterally inoculated animals and in rare reports of naturally acquired infections (13).

Geographic Distribution

With some exceptions (particularly islands), the rabies virus is found worldwide. Some countries, such as the United Kingdom, Ireland, Sweden, Norway, Iceland, Japan, Australia, New Zealand, Singapore, most of Malaysia, Papua New Guinea, the Pacific Islands, and some Indonesian islands, have been free of this virus for many years (14). Rabies is a serious disease threat to humans, domestic animals, and wildlife. Worldwide, rabies kills about 50 000-100 000 people per year and countless domestic and wild animals (15,16).

Transmission

All warm-blooded animals can spread lyssavirus infections, and cold-blooded animals' cells can harbor virus replication (17). An animal's bite results in a cut or an open wound on the fur or mucous membranes, which allows the virus to enter and disseminate the illness (18). Because the virus is present in saliva, it primarily spreads through bites. In rare cases, saliva-contaminated scratches can also spread the disease, but at a rate that is roughly 50 times lower (19). Although there have been a few reported cases linked to organ transplant procedures, the virus rarely spreads from person to person (20).

Diagnosis

Detection of the rabies virus or its specific components through World Health Organization (WHO) and OIE-recommended standard laboratory tests is essential for an accurate diagnosis of rabies (21). This diagnosis is crucial in animals to facilitate timely post-exposure prophylaxis (PEP) in humans, which involves vaccination and concurrent immunotherapy initiated after potential exposure to rabies risk. Rabies diagnosis can be conducted either while the animal is alive (in vivo) or after death (post-mortem) (22). However, ante-mortem diagnosis of rabies infection can be challenging, and confirmation typically requires laboratory tests performed post-mortem on central nervous system (CNS) tissue extracted from the skull (23). While hydrophobia is highly suggestive, no clinical signs are pathognomonic for rabies. The historical reliance on detecting Negri bodies is no longer considered sufficient for diagnosis due to its low sensitivity. Instead, alternative laboratory-based tests have been developed to definitively confirm rabies infection (24).

Clinical Sign of Rabies

In animals, the clinical signs of rabies are often not definitive (25). Symptoms can include noticeable changes in behavior, loss of appetite, fever, alterations in vocalization (such as changes in the sound of a dog's bark),

heightened excitability, aggression, paralysis (especially in the lower jaw), and increased salivation (26). Infected animals typically show signs of CNS disturbance, with slight variations among species. The clinical course of rabies can be divided into three phases: prodromal, excitative (furious), and paralytic or end-stage (26,27).

Treatment

Pre-exposure management of rabies, as recommended by the WHO, involves preventive immunization for all personnel handling infected or potentially infected materials. This immunization protocol includes three injections administered at 0, 7, and 28 days. Serological testing to measure antibody levels should be conducted 1–3 weeks after the final immunization. Individuals working in laboratories should undergo re-evaluation every six months, while other diagnosticians should be re-examined every two years. Booster vaccinations are recommended if antibody levels fall below 0.5 international units (IU) per mL, even without serological monitoring. For those without access to serological testing, a booster vaccination should be administered annually, followed by subsequent immunizations every 1–3 years (28-30).

To control rabies after exposure, any animals that come into contact with a confirmed or suspected rabid animal must be placed under rigorous quarantine for six months. Before being released from quarantine, or even one month beforehand, a rabies vaccination should be given. For PEP in domestic animals who have not received vaccinations, there are currently no licensed biologicals available. According to (31,32), rabies vaccinations by themselves do not consistently shield animals against the disease. When determining whether an animal is past due for a booster shot, veterinarians should examine each case individually, considering variables such as the level of exposure, the amount of time since the last shot, the number of shots given in the past, the animal's present health, and the local rabies epidemiology (33,34).

Prevention and Control of Rabies

Rabies is a globally prevalent and legally notifiable disease, except in bats. Unlike many infections, rabies can be prevented through timely immunization, even after exposure (35). Modern rabies vaccines are available for dogs, cats, and domestic livestock species. Dogs, cats, and ferrets that have never been vaccinated and are exposed to a rabid animal should be euthanized immediately. Rabies vaccine should be administered upon entry into quarantine or up to 28 days before release, following pre-exposure vaccination recommendations (36). Regardless of vaccination status, a healthy dog, cat, or ferret that is exposed should be confined and observed daily for ten days from the time of exposure (37).

Controlling rabies is primarily the responsibility of veterinary authorities, but demonstrating the public health

significance and benefits of disease control can encourage the health sector to take action. Integrating efforts between the medical and veterinary sectors is crucial for effective disease control (38-40). Key aspects of rabies prevention and control in humans include responsible pet ownership, regular veterinary care, vaccination, and public education initiatives. Individuals at high risk, including rabies researchers, laboratory workers, veterinarians, their staff, and animal handlers, should receive pre-exposure immunizations. For those exposed to rabies, prompt PEP, which includes local wound treatment along with human rabies immunoglobulin and vaccine administration, can prevent the development of the disease in humans (41, 42).

Conclusion and Recommendations

Rabies is among the most neglected tropical diseases. Rabies remains a significant global health threat, particularly in regions with inadequate resources for disease control and prevention. This zoonotic disease, caused by the Lyssavirus genus, affects mammals worldwide, posing a lethal risk to humans and animals alike. Despite the availability of effective vaccines for dogs, cats, and livestock, rabies persists as a neglected tropical disease in many developing countries.

Based on the above conclusion, the following recommendations are forwarded:

- The three primary goals of prevention should be to encourage responsible pet ownership, guarantee routine veterinary care, and support extensive immunization campaigns.
- Developing knowledge regarding the symptoms, prevention, and transmission of rabies depends largely on public education.
- The World Health Organization's 2030 target of eradicating rabies as a threat to public health depends on sustained research, surveillance, and international cooperation.

Authors' Contribution

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Competing Interests

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