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Rabies in the Modern World: Challenges and Prevention Strategies for Human Health

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ABSTRACT

Rabies is a viral zoonotic disease, spreading all over the world because of lack of proper control. The discovery of the first vaccine for rabies was done by Louis Pasteur with a desire to abolish or at least control rabies. Despite that, various characteristics of the virulence of rabies are not known. Contemptible or cautious vaccines for animals, in addition to human beings, are also available. Rabies among foxes and raccoons is going to be reduced by the use of vaccines.

Introduction

Rabies is the Latin word "Rabere" which means "to be mad." Rabies is a prehistoric viral zoonotic infection with a high case fatality rate [1]. More than 75% of infectious diseases that are newly emerging and 60% of infectious diseases that are known to affect humans are spread by animals [2]. Due to its high mortality rate, rabies is the zoonosis with the greatest public health concern. Rabies is commonly known as mad dog disease which is an acute, viral disease affecting the central nervous system. It usually spreads through bites from infected domestic dogs and wild carnivorous animals [3]. Rabies is also referred to as hydrophobia or lyssa, it has been recorded as early as 2300 B.C. in the Mosaic Esmuna Code of Babylon, causing fatalities in both dogs and humans [4]. While the Western Hemisphere has experienced rabies outbreaks since the 20th century, it remains endemic in nine Eastern countries. Wild animals that most probably acquire rabies in Western countries are raccoons, foxes, and bats [5].

Transmission and Spread

The rabies virus is usually transmitted through saliva, often through scratches or bites from infected animals. Rabies virus is discharged in saliva and it is passed on to the individual when it makes contact with undetermined cuts of the skin [6]. Dogs serve as the main source of rabies worldwide, and infected animals tend to exhibit aggressive behavior. In most of the countries, dogs are still causing rabies, and out of 10 people, 7 are being dead by rabid dogs in Western countries [7]. Notably, wild rabid animals may deviate from their usual behavior, becoming active during the daytime and posing a threat to humans. In Western countries, raccoons, foxes, and bats are the most common carriers of rabies [8]. The transmission cycle of rabies is shown in Figure 1.

Virus Characteristics

The virus of rabies belongs to the order *Mononegavirales*, the rabies virus has a negative-stranded RNA genome. This group of viruses is categorized under the *Rhabdoviridae* family. This group of viruses includes three genera of animal viruses [9]. Annually, rabies causes approximately 59,000 deaths worldwide, with a staggering 99% fatality rate [10]. Once symptoms manifest, there is no known treatment for the disease, leading to death within 1-2 weeks in animals and a similarly fatal outcome in humans [11].

Different Genotypes of *Lyssavirus*:

Isolation origin of different genotypes of rabies virus is shown in Table 1. The size of the genome of Genotype 1 (RABV) is approximately 12 kb, and it consists of five different types of structural proteins, namely the nucleo-protein (N), phospho-protein (P), matrix protein (M), glycoprotein (G), and RNA-dependent RNA-polymerase protein (L) [12].

Genotype	Genus Name	Origin of Isolation	Date of Isolation	References
1	Rabies virus (RABV)	Isolated from New World bats and dogs.	1768	[13]
2	Lagos bat virus	Isolated from frugivorous bats.	1956	[14]
3	Mokola virus	Isolated from Crocidura species.	1968	[15]
4	Duvenhage virus	Isolated from a human who died due to a bat bite.	1970	[16]
5	European bat lyssavirus 1	Isolated from Eptesicus serotinus bats.	1968	[17]
6	European bat *Lyssavirus* 2	Isolated from a human in Finland and mainly present in Myotis genus bats.	1985	[18]
7	Australian bat *Lyssavirus*	Isolated from one type of insectivorous bat and five species of flying fox bats.	1996	[19]

Table 1: Different Genotypes of *Lyssavirus*.

Pathophysiology and Symptoms

There is no cure for rabies once it reaches the brain through bypassing the protective blood-cerebrospinal fluid barrier, causing irreparable damage and ultimate death. The disease primarily affects warm-blooded mammals, including humans, while non-mammalian animals remain unaffected [20]. Rabies progresses through distinct phases: the prodromal phase, the excitation phase, and the paralytic phase with different sign and symptoms as shown in Table 2,3 [21]. Infected equines and herds (cattle, goat, sheep etc) may exhibit signs of distress, self-harm, and increased sensitivity to light as shown in Table 4. The Initial symptoms of rabies resemble those of the flu, including weakness, discomfort, and headaches, which then advance to neurological dysfunction, anxiety, confusion, and agitation. Unexplained paralysis and other neurological disorders may also arise [22, 23].

Table 2: Clinical Signs of Different Phases of the Rabies Virus in Animals

NO	Phase of Rabies	Clinical Signs and Symptoms	Reference
1	Prodromal phase	Heightened sensitivity to light and noise. Irritability. Aggressive behavior, particularly in cats. Increased alertness. Seeking refuge in dark places. Feelings of depression. Unprovoked attacks. Restlessness. Slight fever. Self-harm at the site of the bite. Impaired corneal reflex.	[24]
2	Excited phase	Aggressive biting and attacking. Signs of nervousness, such as irritability and weakness. Muscle tremors. Lack of coordination. Spasms. Difficulty swallowing. Dropping of the jaw, Coma, Paralysis leading to death.	[25]

Table 3: Clinical Signs of Different Phases of the Rabies Virus in Humans

No	Phase of Rabies	Clinical Signs and Symptoms	Reference
1	Furious form	Burning sensation at the sight of the bite. Itching. Gastrointestinal distress. Hyperactivity. Hallucinations. Excitable behaviour. Fear of water (Hydrophobia). Fear of drafts of air (Aerophobia).	[26]

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2	Paralytic form	Muscle paralysis starting from the bite area. Paralysis of the eyes, tongue, and lungs. Coma and eventual death.	[27]

Table 4: Signs and Symptoms of Rabies in Different Species

No.	Species	Signs of Rabies	Behavior and Activity	Reference
1	Cattle	Milk production abruptly drops, alerting cows, increasing eye and ear responses, and bellowing.	Abnormal behavior and heightened alertness.	[28]
2	Sheep and Goats	Ptyalism, restlessness, aggression.	Excessive drooling, restlessness, and aggression.	[29]
3	Equines	Colic-like signs, distress, and agitation, highly alert and responsive.	Signs of colic and extreme attentiveness.	[28]
4	Camelids	More common silent form, recumbency, ptyalism, hypersexuality, and biting behavior.	Frequently lying down, drooling, sexual behavior, and the tendency to bite.	[30]
5	Bats	Nocturnal behavior diminishes, lying motionless, unable to fly.	Reduced night activity, inactivity, and inability to fly.	[31]
6	Raccoons, Foxes, and Coyotes	Act like diurnal animals, ataxia and aggression, lack of fear towards humans, and attacking animals.	Daytime behavior, lack of coordination, aggression, no fear of humans, and attacks on other animals.	[32]
7	Rodents	Rarely infected, common in lab-reared.	Infrequent infection, mostly observed in laboratory settings.	[33]

Global Rabies Status by Country:

Rabies is a significant public health issue worldwide, particularly in regions with inadequate facilities of precautionary measures and healthcare. However certain countries have successfully controlled the disease through vaccination programs and public awareness initiatives. Particularly in Asia and Africa, still high rates of rabies transmission and rabies cases are noted. The status of rabies in different countries according to various studies are discussed in Table 5. To address this global challenge, ongoing efforts are concentrated on improving surveillance systems, vaccination, and sponsoring educational campaigns to elevate the awareness and control the transmission of rabies.

Table 5: Global Rabies Status by Country

NO	Country	Rabies Status	Year	References
1	Pakistan	2,000-5,000 human rabies cases.	2011	[34]
2	India	18,000-20,000 human rabies cases.	2011	[35]
3	Bangladesh	300,000 dog bites, 2,000-2,500 human deaths.	2011	[36]
4	European Union	9 cases in 2011, 3 cases in 2014.	2011, 2014	[36]
5	Africa	20,000 deaths annually.	2011	[37]
6	Thailand	Less than 25 deaths in 2011, 17 deaths in 2018, 40,000 dog Bites.	2011, 2018	[36]
7	Bhutan	814 human deaths from 1996 to 2009, less than 10% in 2011.	1996-2009, 2011	[36]

Prevention and Challenges

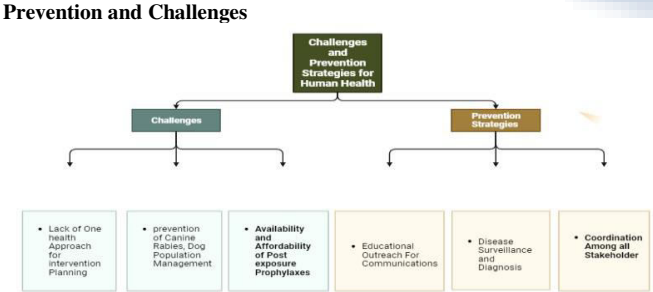

Figure 2: Challenges and Prevention Strategies for Human Health

Conclusion

Rabies is a dangerous viral disease that affects both animals and humans, primarily transmitted through bites. While preventive measures such as vaccines are available, the disease still poses a significant global threat, particularly in developing countries. Comprehensive one-health strategies, public awareness, and systematic vaccination programs remain crucial in controlling its spread and reducing its impact on communities.

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