

Rabies: The Mad Dog Disease

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ABSTRACT

The Rabies virus belongs to the genus *Lyssavirus* which is a member of *Rhabdoviridae*. It is a zoonotic disease that commonly affects bats, foxes, and dogs. When a rabid animal bites a susceptible organism, the virus moves toward the brain through peripheral nerves and then from the brain toward different organs. It has three major phases: the **prodromal phase**, the **excitation phase**, and the **paralytic phase**. Diagnosis of rabies is very difficult because most animals may die without showing any clinical signs or develop a dumb phase or paralytic phase. In order to prevent this from happening, we must dispose of the carcasses of dead rabid animals properly and follow the vaccination schedule in live susceptible hosts.

Introduction:

The Rabies virus contains a negative-strand RNA genome. This genome exists in 2 families including *Paramyxoviridae* and *Rhabdoviridae* [1]. *Rhabdoviridae* is further divided into two genera *Vesiculovirus* and *Lyssavirus*. *Vesiculovirus* comprises a Vesicular Stomatitis Virus containing unsegmented negative RNA strand [2]. *Lyssavirus* comprises rabies virus and also rabies-related viruses that have been isolated from Africa and Europe [3,4]. The length of *Lyssavirus* is 12kb [5,6]. *Lyssavirus* virion is composed of 2 structural units: a lipoprotein envelope and an internal helically coiled ribonucleocapsid that is tightly packed in the genome so that it is insensitive to ribonuclease activity [7]. Both transcription and replication start at the 3' end and progress toward the 5' end [8].

Host Spectrum:

Rabies is a zoonotic disease. It has been reported in many species including dogs, cats, cows, horses, mules, wolves, bats, foxes, and humans. Dogs are more susceptible to the rabies virus and when a rabid dog bites other animals or humans, this virus is transferred to their bodies. The transmission of rabies to humans depends upon the contact of rabid animal to a wound or injury by rabid animal. The wild animals are more susceptible to get the disease and transfer to pets and humans.[9].

Epidemiology:

In rabies-endemic areas, dogs are responsible for 98% of human fatalities from rabies. It is known to prevalent form ancient times and In 1989, 2,499 humans died due to rabies in European areas [10]. According to World Health Organization (WHO), more than 30,000 people die every year in Asia due to rabies. A high death rate was experienced in India in 2004 caused by the rabies virus [20]. In China, more than 3,000 rabies cases were reported in 2006-2007 [21]. In Sri Lanka, almost 100 human deaths were reported due to the bites of unvaccinated stray dogs [22]. Pakistan is also facing an increase in rabies cases. In Karachi, 25-30 rabies cases are treated every day. In Africa, 24,000 deaths are reported every year including poor communities and children [23]. These statistics are sufficient to prove that rabies is an evergreen issue globally.

Pathogenesis:

The incubation period of rabies varies from a week to several months. It depends upon the site of exposure/ bite wound, dose, and viral strain. In some experiments, it was noticed that the length of the incubation period is inversely proportional to the quantity of the virus [11]. The virus is introduced into the body through a bite wound or laceration. After inoculation, it replicates in muscles, or the connective tissue present at the site of entry (Figure 1). Then, it migrates to the central nervous system via peripheral nerves, and then from CNS it spreads to all other body parts [18, 19].

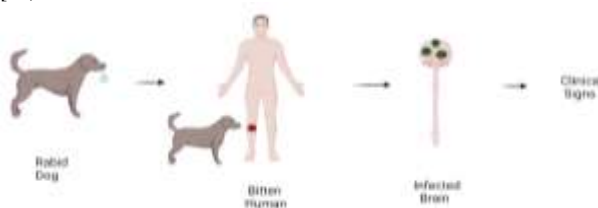


Figure 1. Pathogenesis of Rabies virus (RABV)

Published on: 25 FEBRUARY 2023

<https://biologicaltimes.com/>

15

To cite this article: Zainab. Rabies: The Mad Dog Disease. Biological Times. 2023 February; 2(2): 15-16.

Phases and Clinical Signs:

There are three phases of rabies:

a. Prodromal phase

In the prodromal phase, behavioral changes occur. The animal becomes shy, and the body temperature rises. Pupils may dilate and salivation may also occur [11].

b. Excitation phase

In the excitation phase, the animal becomes very furious and restless. Paralysis of the pharyngeal muscles takes place which makes swallowing difficult and hypersalivation is also observed [11].

c. Paralytic phase

In the paralytic phase or dumb phase of rabies, paralysis of masseter muscles take place which results in a dropped jaw. Sometimes, choking sounds are also present [11].

A rabid animal may die without showing any clinical signs or develop dumb rabies [11]. Therefore, it is challenging to diagnose rabid animals timely.

Confirmatory and Differential Diagnosis:

Rabies-suspected cases must be carefully examined to rule out other neurological diseases like canine distemper, cerebral babesiosis, ehrlichiosis, pesticide or diminazene poisoning, old dog encephalitis, granulomatous encephalomyelitis [16]. For confirmatory diagnosis, brain samples can be taken from two locations, the **brain stem**, and **cerebellum** [16]. WHO recommended techniques for the diagnosis of rabies are Direct Fluorescent Antibody test, Mouse Inoculation technique, Tissue Culture Infection Technique, and Polymerase Chain Reaction (PCR) [17]. In humans, tests are also performed on samples of serum, saliva, and skin biopsies of hair follicles at the nape of the neck [16].

Control:

For control of rabies, the United States follows some measures that include proper disposal of carcasses of rabid animals and quarantine of the infected animals for almost 6 months. An important measure in the control of rabies is to vaccinate all stray dogs as well as pet dogs.

a. Pre-Exposure Prophylaxis:

The people who are at greater risk to be infected with this virus like veterinarians, lab attendants, and animal handlers must be pre-immunized with serological monitoring every 6 months. When the antibody titer falls below a standard value which is 0.5 IU/ml, a booster dose must be given and a serum sample must be tested every year [10].

b. Post-Exposure Prophylaxis:

When the rabid dog bites, wash the wound vigorously with soap for 7-10 minutes. Apply anti-bacterial ointment and anti-tetanus injection. Debride the wound if necessary and infiltrate with hyper-immune globulins (HRIG) [12]. HRIG attacks the virus and inhibits its progression in the host's body [19].

c. Vaccination:

Vaccinate the susceptible individuals with a single dose on days 0, 3, 7, 14, and 28. Also, inject Human RIG on day 0 [13,14]. For previously immunized individuals, 2 doses are recommended on days 0 and 3. HRIG is contraindicated in previously immunized persons [13]. WHO on rabies 8th report, 1992 [10], states that vaccination schedule depends upon the type and potency of available vaccines. The WHO-approved vaccination regimens are given in Table 1 [12,15]:

Table 1. WHO-approved vaccination regimens for Rabies [12,15]

No.	Name of the Vaccination Regimen	Doses	Route	Days for Shot
1.	5-dose 'Essen' Intramuscular regimen	5	Intramuscular	0, 3, 7, 14, 28
2.	2-1-1 'Zagreb' Intramuscular regimen	4	Intramuscular	0, 0, 7, 21
3.	2-site 'Thai Red Cross' Intradermal regimen	8	Intradermal	0, 0, 3, 3, 7, 7, 28, 90
4.	8-site 'Oxford' Intradermal regimen	8	Intradermal	0, 0, 7, 7, 7, 7, 28, 90

Conclusion:

Rabies is a zoonotic disease and spread mostly through dogs and other domestic and wild animals, but it can be successfully eradicated by following some important preventive measures and vaccination schedules. If a dog bites you, wash the wound with carbolic soap for at least 10 minutes vigorously and consult a doctor immediately. The studies are needed to develop anti-rabies drug as well as proper vaccination strategies should be adopted to eradicate rabies from the world.

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