

# Rabies: 100% Preventable but Remains a Daily Threat to Millions around the World, a Comprehensive Review

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**Abstract-** Rabies is a serious viral disease of mammals that causes acute inflammation of the brain in animals. It is a zoonotic, fatal, and progressive neurological infection. The virus responsible for this belongs to the family Rhabdoviridae, genus Lyssavirus. It affects warm-blooded animals and the disease is prevalent throughout the world and endemic in many countries except Antarctica and Australia. The virus enters the body through a rabid animal bite. Currently, there is no specific treatment for rabies if clinical signs appear. We can control rabies through regular vaccination of ourselves and our pets.

**Index Terms-** Rabies, pathogenesis, transmission, prophylaxis, vaccination

## I. INTRODUCTION

Rabies is also called hydrophobia or rage. Rabies is a serious viral disease that causes acute inflammation of the brain in humans and other warm-blooded animals. Rabies is transmitted from rabid animals to humans. It can be transmitted when an infected animal scratches or bites human or other animals. It can also be transmitted through the saliva of an infected person or animal if it meets the mucous membranes of healthy animals or humans. In humans, most cases are seen due to the bite of rabid

dogs. About 99% of cases are reported having a history of rabid dog bites. By the time the symptoms will appear and now it is very late to save the life of an infected individual. However, a person who may have been infected with rabies can be treated effectively when seeks help at once. For treatment to be successful, it must be given before the appearance of symptoms. Without early treatment, it is usually fatal. Following the vaccination requirements for pets can be helpful in the prevention and control of this disease.

Rabies virus is a non-segmented, negative-stranded, RNA virus that belongs to the family Rhabdoviridae which includes at least three genera of animal viruses i.e., Ephemerovirus, Lyssavirus, and Vesiculovirus. Rabies virus belongs to the genus Lyssavirus. Many strains of this virus are species-specific and associated with different species.

Although rabies is an ancient disease, human rabies is a continuous problem in developing countries. In developing countries, it is often unrecognized until late during disease or postmortem because physicians are not familiar with the clinical manifestation of rabies disease. This disease can be prevented after exposure with the cleaning of wounds and administration of vaccines against rabies and rabies immune globulins. There is no established effective treatment once rabies develops, it is almost always fatal once symptoms occur.

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## II. HISTORY OF RABIES

Rabies is an ancient disease and its history is very long that is lost in antiquity. According to Athenodorus, it was first observed in human beings in the days of the Asclepiadae, the descendent of the god of medicine Aesculapius. The Greeks called rabies Lyssa which means madness. The disease in man is described as hydrophobia or rage because the infected individual is tormented at the same time with fear of water and thirst. The Latin word rabies is derived from an old Sanskrit word "rabhas" which means to do violence. Some 500 years B.C., Democritus is thought to have made the first recorded description of canine rabies. Aristotle, in the 4<sup>th</sup> century B.C., wrote it as dogs suffer from madness. This causes them to become seriously irritable and all animals they bite into becoming diseased. For the prevention of rabies, in ancient medical times, the attachment of the tongue (the frenum linguae) was cut and a fold was removed in which the causative agent was thought to be present. This idea was practiced until the 19<sup>th</sup> century when Louis Pasteur described the cause of rabies.

Fermi, in the review of a huge number of experiments, pointed out the difficulty of demonstrating rabies virus in the saliva. Bartarelli showed that the rabies virus reached the salivary glands of rabid dogs by peripheral nerves. He cut the nerve supply of one parotid gland in an animal, after which the animal was inoculated with the rabies virus. The gland with severed nerve supply contained almost no rabies virus, but those glands in which the nerve supply was left intact, produced rabies in other animals. Meanwhile, some scientists observed that the rabies virus could be found in the saliva of rabid dogs 2 or 3 days before the least clinical symptoms.

## III. HOW IS RABIES TRANSMITTED?

### A. *By infected animal bite.*

Rabies is transmitted when an infected animal bites a healthy animal or human which is the most common route, and contamination of scratch wounds by virus-infected saliva. However, there are certainly other routes that have been implicated in the past include through mouth mucous membranes, conjunctiva, genitalia, and anus. Aerosol transmission is also demonstrated in laboratory animals, in humans through rabies-infected bat caverns, and in many laboratory accidents because, in caves, there is the sprinkling of bat's urine and saliva. All animals including rodents, canids, and felines can transmit disease, but in 99% of cases human rabies is transmitted by a rabid dog bite and 0.1 to 1 % is through dog scratches. Vampire bats, insect bats, and flying foxes, all contain the rabies virus. In vampire bats, there are no clinical signs, but the virus is present in their saliva. Bats are considered a reservoir for the virus, but all other rabid animals can transmit disease and cause symptoms. Every bat bite should be vaccinated because it is a reservoir host, but every dog bite is not necessary to be vaccinated. There were five instances in humans in which disease is transmitted from one man to others through the transplantation of infected corneas. The non-bite exposures include

contamination of scratch, open wounds, abrasion, or mucous membrane by saliva or central nervous tissue from an infected animal.

### B. *Risk factors of rabies include*

Bite of a dog infected with rabies, Injection of a live modified vaccine in immunocompromised patients, laboratory persons or researchers working in the laboratory with rabies virus, having pets at home, dealing with zoo animals, and having pre-bite or post-bite of infected animals.

## IV. WHO CAN GET RABIES?

All mammals can get rabies, including humans or it can infect all warm-blooded animals. The most common reservoirs of rabies include wolves, foxes, and raccoons which are highly susceptible, humans, dogs, cats, sheep, goat, cattle, buffalo, and horses which are moderately susceptible, and birds are rarely infected.

## V. INCUBATION PERIOD

The incubation period is defined as the period between the invasion of a pathogen till the onset of clinical signs and symptoms. The incubation period of rabies is variable and may range from 2 to 8 weeks and may extend up to 24 weeks.

## VI. PATHOGENESIS OF DISEASE

Much of what is known about rabies pathogenesis is learned from the experiments or studies performed on laboratory animals e.g., rodents. After the entry of virus or inoculation when a rabid animal bites into the subcutaneous tissues and muscles, the virus starts its replication in the connective or striated tissue at the site of entrance and then enters the peripheral nerves through the neuromuscular junction by binding with the nicotinic acetylcholine receptors. In the spinal cord, its multiplication occurs. After this, it starts spreading to the central nervous system in the endoneurium of Schwann cells of motor and sensory axons and reach the grey matter of the brain. After the bite, the virus reaches the ganglion in the spinal cord and then to the brain through centripetal force. Then it causes encephalitis and continues spreading throughout the whole body and infects salivary glands. After infecting the salivary glands, the virus appears in the saliva. Viruses multiply in deep tissues due to less oxygen.

## VII. SEMIOLOGY OR CLINICAL SIGNS

Generally, there are three stages of rabies, but the fourth phase is also considered, known as the atypical phase. Following are the phases or stages of rabies

- A. Prodromal stage or dumb form
- B. Furious stage
- C. Paralytic stage
- D. Atypical stage
- A. *Prodromal or dumb form*

This stage lasts for 2 to 4 days. Animals pass this phase unnoticed. The signs of this stage include erratic behavior which

means whenever the animal is a pet, it has strange behavior with the owner.

### B. Furious stage

This stage lasts for 2 to 4 days, as in the previous stage. In this stage, many changes are observed in the animals. The animals become furious, there is an increase in body temperature or fever, abnormal gait, chewing, biting non-food items, aimless wondering, dilation of the pupil, and spasm of the eye, eyeball, or cornea.

### C. Paralytic form

This stage lasts for 2-4 days, as in the previous stages. This is the typical form of rabies because everyone can identify this stage. In this stage, there is paralysis of lower motor and cranial nerves, and death will occur within 3 to 7 days after the appearance of this stage. Cranial paralysis results in the following symptoms

- Animals suffer from ascending paralysis, and paralysis of biting organs.
- Laryngeal paralysis that results in voice change.
- Pharyngeal paralysis that results in dysphagia (abnormal eating), drooling of saliva, irregular contraction of pharyngeal tissue, when saliva will finish, the mouth will become dry.
- Masticatory paralysis results in irregular chewing and hanging jaws.
- Generalized paralysis results in disorientation, struggling gait, convulsion, seizure, and champing (aggressiveness).
- Death will occur due to respiratory paralysis.

### D. Atypical stage or form

Vampire bats are considered reservoir hosts.

## VIII. LABORATORY DIAGNOSIS

Rabies is diagnosed based on clinical signs in antemortem cases. Most tests in the case of rabies are not sensitive. If we perform the histopathology of the brain of a rabid animal, we can see inclusion bodies in the slide. Other tests for rabies include the DFA test which stands for Direct fluorescent antibody test, mouse inoculation, tissue culture, and molecular analysis e.g., detection of virus RNA. If the DFA test of the animal is positive, then we inject some pieces of brain intra-cerebrally into the mouse for further confirmation. If we perform tests on the frozen sample, then all the above tests may give false-negative results, so avoid freezing of the sample. Keep the sample at 4° C and liquid ice is not required because it may freeze the sample.

## IX. TREATMENT

Currently, there is no specific treatment available if the onset of disease or clinical signs appears.

### A. How can we protect ourselves and our animals?

The best and effective protection against rabies infection is solely the vaccination of pets and avoidance of risk factors that

have been discussed before. Dog and cat require vaccination. Make sure you are vaccinating your animals and keep your animals indoor to avoid their contact with other wild or rabid animals. If the rabid animal is captured, always fire the animal from a distance and never try to euthanize the animal.

### B. Prophylactic measures

There are two types of prophylactic measures in animals and humans

1. Pre-exposure prophylaxis (PrEP)
2. Post-exposure prophylaxis (PEP)

Pre-exposure prophylaxis

(1) In dogs and cats

- Inject the first shot of vaccine against rabies at the age of 3 months because before 3 months, there is no production of antibodies due to the absence of receptors.
- Inject the second booster shot of the vaccine 2 to 3 weeks after the first shot.
- Inject the third shot at the age of 6<sup>th</sup> months.
- After this, give the fourth shot every year.

Post-exposure prophylaxis

(2) In dogs, cats, sheep, goats, and small calves

- Inject the first two (double) shots on 0 days or we can say on the day of biting.
- Inject the second single shot on the 7<sup>th</sup> day after the first shot.
- And finally, administer the third single shot on the 21<sup>st</sup> day after the first shot.

(3) In donkeys, horses, and cows

- Inject the first three (triple) shots on 0 days.
- Inject the second two (double) shots on the 7<sup>th</sup> day after the first shot.
- And finally, Inject the third two (double) shots on the 21<sup>st</sup> day after the first shot.

(4) In Buffalo and camels

- Inject the first four shots on 0 days.
- Inject the second three (triple) shots on the 7<sup>th</sup> day after the first shot.
- And finally, give third three (triple) shots on the 21<sup>st</sup> day after the first shot.

(5) In hippo, rhino, and elephants

- Inject the first five shots on 0 days.
- Inject the second four shots on the 7<sup>th</sup> day after the first shot.
- And finally, give third four shots on the 21<sup>st</sup> day after the first shot.

(One single shot of rabies vaccine is equal to 1 CC or 1 ml.)

*Precaution-* Do not give all the shots at the same point in animals. Change site in every shot. All shots should be given subcutaneously in different sites at the same time in both pre-exposure and post-exposure.

### C. Protocol in Humans

#### Pre-exposure prophylaxis

- Inject the first single shot of vaccine against rabies
- Inject the second single shot of vaccine against rabies on the 3<sup>rd</sup> day after the first shot.
- Administer the third single shot of vaccine on the 7<sup>th</sup> or 14<sup>th</sup> day after the first shot.

#### Post-exposure prophylaxis

- Administer the first single shot on 0 days.
- Administer the second single shot on the 3<sup>rd</sup> day after the first shot.
- Administer the third single shot on the 7<sup>th</sup> day after the first shot.
- Inject the fourth single shot on the 14<sup>th</sup> day after the first shot.
- Finally, administer the fifth shot on the 21<sup>st</sup> day after the first shot.

The recommended site for human vaccination against rabies is the deltoid muscle preferably the lateral side of the deltoid muscle.

### D. Management of wound

#### (1) If the wound is superficial and not bleeding

- Bleeding should be encouraged to increase oxygen or to make an oxygenated environment.

#### (2) If there is a large wound

- Stop bleeding as soon as possible to avoid blood loss.

#### (3) Small wound but bleeding

- Washing with soap or alcohol (ethanol) is approved.
- Dip biting area in benzalkonium chloride for 2 hours.
- Scrubbing biting site under running water is required.

#### (4) Perforating wound or wound at the abdominal cavity

- Explore the wound and observe inside the cavity to manage the internal wound.

#### (5) Wound at the thoracic region

- First, ensure negative pressure and then manage the wound.

The wound must be opened after 2 or 3 days to ensure the oxygenated environment, and then apply a bandage. Generally, we leave the wound open. After all these protocols, we must provide antibiotics, antipyretic, NSAID, wound healing agents, symptomatic treatment and antiseptic, etc.

## X. CONCLUSION

Rabies is a zoonotic disease that can spread from rabid animals to normal animals, even humans. It is 100% preventable but remains a threat to millions of people around the globe. We can prevent this disease through vaccination and proper management. We must vaccinate ourselves and our pets. Currently, there is no specific treatment against rabies if clinical signs appear so that we must manage and prevent its spread by following the recommended protocols.

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