

## State of Globe: Rabies: The Lethality Since Antiquity!

Rabies, derived from the latin word “rabere” meaning rage or madness, in the late 16<sup>th</sup> century, is one of the most dreadful, fearful, highly infectious and lethal disease known to man since prehistoric days. With nearly 100% mortality and more than 100 years since the development of the rabies vaccine by Louis Pastuer and Emile Roux in 1885,<sup>[1]</sup> our effort to cure and eradicate rabies from our society is a distant dream. Although certain successes have been met, and few survivors namely Jeannafiesa an American teenager in 2004<sup>[2]</sup> and lately an Indian girl named Sarika a class 7<sup>th</sup> student, have been reported to be rabies free, our fight against rabies is far from over. According to the World Health Organization-sponsored National multicentric rabies survey in collaboration with the APCRI (Association for Prevention and Control of Rabies in India) and CVA (Commonwealth Veterinary Association), India continues to report 25,000-30,000 human rabies deaths, which accounts to 60% of global rabies death of 50,000.<sup>[3]</sup>

The bullet-shaped neurotropic lyssa virus type1 has a special affinity toward the nervous tissue. It is has a ssRNA nucleocapsid core and lipoprotein envelope. It is transmitted by the bites of dogs, bats, cats, jackals, wolves or *per se* any wildlife animal. Depending on the geographical location, the vector varies, with dog being the most common in Afro Asian countries, while bats and foxes are common in the US and Europe.<sup>[4,5]</sup> The incubation period commonly varies from 3 weeks to 8 weeks, and sometimes some years, depending on the site of the bite. Man is the dead end host; however, human to human transmission in case of cornea transplant may occur.<sup>[6,7]</sup> Once the virus is inoculated, it ascends with a speed of 12–14 mm/day to reach the spinal ganglion where rapid viral multiplication takes place. This is stage 1 of pathogenesis of rabies infection and it is at this stage that localized paresthesia begins at the site of the bite, which is a pathognomonic feature in rabies, and occurs in 50% cases of rabies. Sometimes, it is the only presenting complaint in a patient. Other non-specific symptoms like fever, malaise, anxiety, etc. are also present. Stage 2 begins

with continued rapid viral multiplication and now the virus travels with a greater speed of 200-400 mm/day to reach the central nervous system structures and salivary gland. It binds to the neuroreceptors of ACH, GABA and Glycine, and neurological manifestation begins.

Acute neurological manifestation can alternate between furious rabies where the patient is in an altered sensorium to apathetic rabies, which is a quieter form of rabies. According to the APCRI data, the most common symptoms are hydrophobia (95.7%), aerophobia (66.4%) and paralysis, and focal or generalized seizure takes place, followed by coma and finally death. Prompt diagnosis and Intensive Care Unit care are important.

The diagnosis is usually clinical. Laboratory investigations include an antigen detection test by immunofluorescence of the nuchal skin biopsy and virus isolation from the saliva and cerebrospinal fluid (CSF). NASBA (nucleic acid sequence-based amplification) can be used as a rapid diagnostic test in the saliva and CSF samples. Detection of neutralizing antibodies is not of much importance as it takes more than 1 week to appear in the serum or CSF. With the augmentation of neurological features, death is inevitable. Intensive care may increase survival,<sup>[8]</sup> but till date only four people have survived rabies.

Various protocols have been developed to deal with rabies. One such protocol developed by the university hospital of Wisconsin, also known as the Milwaukee protocol,<sup>[2]</sup> is highly successful. It includes ribavirin-, amantadine- and ketamine-induced coma. Treatment of rabies-stricken patients is mainly supportive. Vaccination in rabies is given post-exposure, except in high-risk groups like vet doctors and rabies researchers and lab workers where pre-exposure rabies vaccine is permitted. However, vaccination in rabies is not infallible and treatment failures are common due to poor and slow (more than 7 days) immunogenic response. Treatment includes standard wound care with no wound suturing. In a deep lacerated wound, delayed primary closure is practiced. The vaccine is derived from human cell culture and is given in five doses (0, 3, 7, 14 and 28), with a single dose of rabies immunoglobulin 20 IU/kg given 50% at the bite site and the remaining in the gluteal region. Doses remain the same for the adult or pediatric groups or for pregnant patients. Injection TT and antibiotics are also given to prevent secondary infection. Sometimes, compliance is the issue;

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therefore, five field visits can be reduced to three visits by administering two doses at Day 0 and one dose each on Days 7 and 21.

Vaccination was developed more than 100 years ago, but still we have rabies death, mainly due to financial limitations, poor public health infrastructure and awareness, especially in developing countries like India. The United States spends around \$563 million annually in rabies prevention,<sup>[9]</sup> whereas India spends less than half a million dollars. Till date, we do not have any study published to determine the prevalence of reservoirs of wildlife rabies. The WHO-sponsored trials found that India has approximately 25,000-30,000 human rabies deaths, which accounts for 60% of the global reported deaths of 50,000. Further, no anti rabies vaccine (ARV) is available for 79% of rural patients and 60% patients resort to indigenous treatment, with magico-religious being the most common (28.9%) followed by herbal medication (10.6%).

The National Rabies Control Pilot Project was recently approved by the Animal Welfare Board of India (AWBI), a statutory body under the Ministry of Environment and Forest that is financially choked. Mass sterilization of dogs and dog census are in the doll drums. The cost for sterilization per dog has increased to \$8, but the government contributes a meager amount of less than \$2. Mass vaccination of dogs is the most important measure that has to be taken to prevent rabies in humans. A two-prong strategy can be used. It can be curative and preventive. Curative includes mass euthanization of all the stray undomesticated dogs, something that was done lately in China. Preventive measures include declaring rabies a notifiable disease and incorporating it into in the Millennium Development Goal of 2020. It should also be a part of our national health policy. India should actively participate and contribute in the World Rabies Day, which is celebrated every year on 28<sup>th</sup> Sep, which also happens to be the death anniversary of Louis Pasteur. Also, the cost of vaccination will be greatly reduced if we the rabies vaccines in India. It should be incorporated in the PM's "make in India dream," which will ensure low cost and good quality vaccine. NGOs should be involved in creating awareness about the prevention and immunization against rabies. It should be made a part of the corporate social responsibility activity. Expert opinion should be sort from those countries where rabies is totally eradicated, like Taiwan, Sweden, etc., and their model should be carefully studied. An oral vaccine bait can be used for disease control of rabies in dogs, as used in cases of foxes in Canada.

The article authored by KK Sahu *et al.* has given an excellent preview of the status of rabies in the capital city of Uttar Pradesh, India. The epidemiological factors mentioned in the study, including the statistics, are of great help in extrapolating and assessing the gravity of the entire problem. Such an article from each state will undoubtedly project the true state of affairs in our country. This will go in a long way to eradicate the menace of this lethal disease.

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