

RABIES: A HIDDEN THREAT EXPLORING DISEASE DYNAMICS AND FUTURE OPPORTUNITIES

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ABSTRACT

Rabies is a highly lethal viral zoonotic disease with significant mortality worldwide. Lyssaviruses, members of the family Rhabdoviridae, are primarily transmitted through the bite or saliva of infected animals. It is highly fatal in warm-blooded animals due to involvement of the CNS, five structural protein virus and causing acute progressive encephalitis. The incubation period varies greatly and depends on the depth of the wound. There is no effective treatment once the clinical signs appear. Effective rabies management requires immediate wound cleansing, followed by timely pre-exposure and post-exposure vaccination when needed. Recent advances have improved vaccine safety and immunogenicity through the development of embryo vaccines, modified live vaccines, tissue culture vaccines, cell culture vaccines, and inactivated vaccines, enhancing the safety and effectiveness of rabies prevention. This article provides a comprehensive overview of rabies, its pathogenesis and emphasizes the importance of early prevention, effective vaccination, and continued research for global rabies elimination.

Keywords: Lyssaviruses, viral encephalitis, vaccination, Hydrophobia, Human rabies immunoglobulin

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Introduction

The Word Rabies is derived from the Latin Word “rabere” meaning “to be furious”. It is highly Lethal, zoonotic illness with a 100% mortality rate. It is caused by the rabies virus, belonging to the genus “Lyssavirus”. It is non-segmented, single-stranded, negative-sense “RNA Virus [1]. Rabies is highly fatal in Mammals due to involvement of the nervous system. The most important feature of this virus is the presence of distinct genotype. The size of this virus is approximately 12Kb. This virus contains five structural proteins (Nucleoprotein protects RNA from RNase destruction, Phosphoprotein, Matrix protein, Glycoprotein, and RNA-Dependent RNA Polymerase [2]. Virions are composed of two structural units: an internal helical nucleocapsid composed of Nucleoprotein and viral genome RNA, and a lipid envelope derived from host cytoplasmic membrane during virus budding.

It is more prevalent in Asia, Africa, and South America. It is transmitted from one animal to another through the saliva of an infected animal (cats, dogs, bats), primarily via bites, scratches, or exposure through broken skin and mucosal surfaces. When the virus is inoculated, it first moves from the site of infection to the CNS, and secondly, it moves back peripherally, reaching the salivary gland and is transmitted to the other animal [3]. It is responsible for acute progressive encephalitis, and there is no cure when the clinical signs appear, but their early symptoms include Fever, Headache, pain at the bite site, Anxiety, hydrophobia, Aerophobia, Excessive salivation, Difficulty in swallowing, muscle spasm, paralysis, coma, and death. The diagnosis is based on clinical signs, laboratory tests such as fluorescent antibody test, mouse inoculation test, virus inoculation test, etc. Treatment is difficult once clinical signs appear, but options of pre-exposure or post-exposure are available. Pre-exposure vaccination with a schedule of 0, 7, 28 days reduces the administration of post exposure vaccination. Human rabies immunoglobulin in combination with rabies vaccine is essential because it neutralizes the virus and provides long lasting immunity [4]. To control the increase in rabies, public awareness through vaccination, and management of the dog population, but the rabies crisis has not yet been controlled because of the stray dog population. Continued research and international collaboration are expected to support the global goal of eliminating the dog mediated rabies. Ongoing research on the improvement of vaccine such as modified live vaccine, embryo vaccine, inactivated vaccines, mRNA-based, and DNA-based vaccine, to develop safer, more immunogenic, and cost-effective rabies vaccines.

Mechanism Of Action:

The rabies virus enters the body through the bite of an infected animal. After entering, it first replicates in muscle tissue near the bite wound. At the neuromuscular junction, the virus binds to the Nicotinic Acetylcholine receptor and then spreads to the Central Nervous System centripetally by retrograde Axon transport at a rate of about 50 to 100nm per day. The virus then spread away from the central nervous system centrifugally involving the peripheral nervous system, and then spread to the salivary Gland, skin, Heart and other Organs. But the Saliva is the main source of Transmission

of the disease. The incubation period varies greatly in rabid dogs. The length of the incubation period in dogs and cats is from 10 days to 6 months [5].

Clinical Signs:

Rabies is responsible for acute progressive encephalitis. There is no cure of disease when clinical signs appear. The clinical signs depend on the amount of virus entering the body and the infection away from the brain. Early symptoms include anxiety, restlessness, vomiting, mild fever, diarrhea, anorexia or increased appetite, pupil dilation, hyperactivity, and excessive salivation. The paralytic rabies is marked by paralysis. Hydrophobia, which means the fear of water, is the main sign. At the last stage, Heart failure and multiple organ system failure are seen [6]. The main clinical signs in humans are Fever, Headache, Hydrophobia, excessive salivation, Anxiety, Muscle spasm, Restlessness, paralysis, coma, and death due to respiratory failure.

Diagnosis:

The diagnosis is based on the history of exposure to a suspected rabid animal, clinical signs, and laboratory tests. There are several ways to diagnose rabies, such as first one is the Direct Fluorescent Antibody test (DFA), in which brain tissue is taken and fix it in a glass slide in acetone for 10 min, washed with PBS, and then stained with FITC-conjugated anti-rabies antibodies and observed under a fluorescent microscope. Apple-Green inclusion was observed in a positive sample. Mouse Inoculation test in which a brain sample from a suspected rabid animal is collected and suspended in Eagle's Minimum Essential Medium. After centrifugation, supernatant is collected and then inoculated into the mice. If the mice show clinical signs, it is humanely euthanized using a CO2 chamber, and their brain is examined by the direct fluorescent antibody test. The other main tests include Reverse Transcription Polymerase Chain Reaction (RT-PCR), Virus Isolation in cell culture, and Histopathological examination showing Negri Bodies [7].

Treatment:

There is no effective treatment for rabies once the clinical signs appear, but pre-exposure treatment options are available. Pre-exposure prophylaxis is a safe rabies vaccination given to individuals who are at high risk of exposure. This vaccination allows three intramuscular or intradermal injections with schedule on days 0, 7, and 28. The purpose of this vaccine is to prepare the immune system against the rabies virus. If a vaccinated person is later exposed through an animal bite, the immune system respond more rapidly and gives more protection. Pre exposure vaccine reduce the administration of post-exposure vaccination. Post-exposure vaccination is given immediately after a person has been bitten. Treatment should start as soon as possible. It involves the combination of Human Rabies Immunoglobulin (HRIG) and the rabies vaccine administration. The main benefit of this combination (HRIG) neutralizes the virus, and the rabies vaccine stimulates the immune system and provides long lasting immunity. HRIG vaccine is used as an inactivated vaccine (The vaccine is made from killed microorganisms that cannot cause disease but stimulate the immune response [8].

Prevention and Control:

There is currently no therapeutic intervention for a fatal disease that is preventable and incurable. Historically, Unani medicine describes its own approach to preventing and managing rabies. These traditional methods are based on the principles of detoxification. Once the toxin spreads to the body, keep the wound open and promote systemic detoxification. This approach uses purgative therapies to eliminate harmful humors. Classical unani formulations are DAWA-e-Zaraiyah and DAWA-e-Sartan use for the management of rabid dogs [9]. Human-to-human rabies transmission is rare but typically occurs through infected tissue or organ transplant. Standard precautions are not to share the biological material on mucosal surfaces or broken skin during procedures, such as intubation and suctioning, to reduce the risk of transmission [10]. However, with advances in medical sciences, rabies is now managed by evidence-based Treatments. It is crucial to reduce human rabies by effective control through vaccination and controlling the dog-mediated rabies population [11]. For animals that lack prior vaccination and encounter rabies exposure from an infected animal, it is necessary to euthanise (peaceful and painless death) the animal [12].

Public Health Significance:

The rabies crisis has not yet been controlled because there is a huge population of stray dogs and other rabid dogs, and they are freely attacking people. Concerns have been raised due to the mismanagement of stray dogs and the lack of vaccination [13]. Rabies virus needs a host, and it is unstable outside the body of a host and can be easily destroyed by sunlight, Heat and Drying. Effective prevention of rabies by giving awareness of strategies to the public, such as dog population management, vaccination, and use of personal protective equipment [14]. The economic impact on livestock results in the loss of milk and meat production, posing a public health risk. Effective strategies involve not only maintaining the vaccination schedule but also addressing environmental factors, such as control of the stray dog population through humane birth control, and safe disposal of animal carcasses to prevent exposure [15]

Future Prospectives:

Continued research and international collaboration are expected to support the global goal of eliminating dog-mediated human rabies in the future. Future rabies control depends on rapid diagnostic method, increasing public awareness, and improved vaccination. Use of genetically modified vaccines that alter the rabies viral genome by deleting the gene that encodes the phosphoprotein (protein that helps in replication) and matrix protein (protein that helps in the assembly and budding, which means the release of virus from the host cells). Modified live vaccine is also used to treat rabies by modifying the pathogenicity of the organism and to produce a powerful immune response without inducing clinical signs. Monoclonal antibodies are laboratory-made antibodies that provide passive immunity against the rabies virus. These antibodies bind and neutralize the virus at the wound site and prevent the virus from entering the nerve cells. They protect the body until the rabies vaccine stimulates the body to produce its own antibodies. These antibodies are used in category III rabies exposure. In addition, research is ongoing to develop the mRNA and DNA-based rabies vaccine,

which may provide safer, more effective, and long-lasting protection in the future.

Conclusion:

Rabies is a life-threatening zoonotic disease that remains a major public health concern worldwide, affecting both humans and animals. The virus causes a fatal infection when clinical signs appear. Early wound cleaning, timely vaccination, use of monoclonal antibodies, increase public awareness can successfully prevent the disease. The future of rabies control depends not only on medical advances but also on a one-health approach (where humans, animals, and environmental health are closely connected), strong public health policies, animal management, and collaborative efforts are essential to eliminate and control rabies. Continued investment in research, improved surveillance systems, and equitable access to vaccines and veterinary public health partnerships will play a crucial role in the sustainable elimination of rabies.

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