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Rabies, A Deadly Disease in Dogs: Its Diagnosis and Prevention

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Abstract:

Rabies is an ancient but persistently significant zoonotic disease distinguished by its nearly 100% fatality rate once clinical signs appear. Caused by a neurotropic negative-sense RNA virus of the genus *Lyssavirus*, rabies affects all warm-blooded mammals and continues to impose a substantial global health burden, particularly in Asia and Africa. Despite the availability of highly effective vaccines, more than 59,000 human deaths occur annually, with children disproportionately affected. Transmission occurs primarily through the bite of infected dogs, which account for approximately 99% of human cases worldwide. The virus exhibits a complex pathogenesis, beginning with local replication in muscle tissue followed by rapid neuroinvasion, leading to progressive encephalitis. Clinical presentation varies from furious to paralytic forms, complicating early diagnosis. Although multiple laboratory techniques exist, confirmatory testing often requires specialized facilities, and no treatment is effective once symptoms develop. Prevention through timely wound care, rabies immunoglobulin, and appropriate pre-exposure or post-exposure vaccination remains the only life-saving intervention. The One Health framework—integrating human, animal, and environmental health—has shown marked success in several countries through mass dog vaccination and surveillance. Strengthening this multisectoral approach is crucial to achieving the global goal of "Zero by 2030," aiming to eliminate human deaths from dog-mediated rabies.

Introduction:

Rabies originates from the Latin term *rabere*, meaning "to be mad." It is one of the oldest known zoonotic viral infections and is characterized by an exceptionally high fatality rate. Globally, more than three-quarters of emerging infectious diseases and about 60% of established human infections are transmitted from animals. Because of its near-universal lethality once symptoms develop, rabies remains a major public health priority. This disease is caused by a RNA virus with a strong affinity for the central

nervous system. Once inside the host, the virus induces progressive deterioration of brain and spinal cord tissues, ultimately leading to fatal encephalitis in both humans and animals. The rabies virus (RABV) can infect virtually all mammalian species and is associated with a case fatality rate approaching 100%. It is found across most of the world, with the notable exception of rabies-free regions such as Australia and Antarctica. Every year, more than 15 million people undergo post-exposure prophylaxis, yet the virus still causes over 60,000 human deaths worldwide. Effective management of rabies relies heavily on widespread use of pre-exposure and post-exposure vaccines. The disease continues to be more prevalent in developing nations, where inadequate vaccination coverage and limited awareness contribute to higher transmission rates. The World Health Organization recognizes rabies as a multi-species infectious disease. Despite being preventable, the canine rabies virus variant remains responsible for most human deaths following the bite of an infected dog, a condition often termed dog-mediated rabies. International organizations, under the leadership of the World Health Organization, are collectively working toward the "Zero by 30" objective, aiming to eliminate human deaths from dog-mediated rabies by the year 2030.

Etiology:

The rabies virus is a bullet-shaped, enveloped, negative-sense RNA virus belonging to the *Lyssavirus* genus of the *Rhabdoviridae* family. Its genome encodes five major proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and the viral polymerase (L). The virus contains a helical ribonucleoprotein core surrounded by a lipid envelope. The N protein is vital for transcription and replication and is widely used in diagnostic assays, while the M protein governs virion assembly and budding. The G protein mediates attachment to host cell receptors and acts as the main neutralizing antigen. Classical rabies virus belongs to genotype 1 of the seven known lyssavirus genotypes, with the others, mainly bat-associated viruses, also capable of causing rabies-like neurological disease. The rabies virus is highly neurotropic and invariably causes fatal encephalitis. It is easily inactivated by common disinfectants, ultraviolet light, sunlight, drying, and exposure to air.

Epidemiology and Global Burden:

- **Current Global Situation:** Rabies remains a major public health problem, causing an estimated 59,000 human deaths every year, with the vast majority occurring in Asia and Africa. Children below 15 years of age represent about 40% of these deaths because of higher exposure through close contact with animals and delays in receiving proper treatment. In many endemic regions, weak surveillance systems and frequent misdiagnosis of rabies as other forms of acute encephalitis contribute to a significant underreporting of cases.
- **Transmission Dynamics:** Rabies is transmitted mainly through the bite of an infected animal, with domestic dogs responsible for roughly 99% of human infections worldwide. The virus, carried in the saliva, enters the body through broken skin or mucous membranes. Although rare, infection can also

occur through scratches, inhalation of virus-laden aerosols in laboratory or cave environments, and, in exceptional cases, via organ transplantation. The incubation period is highly variable, ranging from a few days to several years, though symptoms most often appear within one to three months. This variability depends on the amount of virus introduced, the location of the bite, and host factors. While the long incubation period allows time for effective post-exposure prophylaxis, it also makes tracing exposures and studying outbreaks more challenging.

- **Regional Variations:** Rabies patterns differ widely across the world. In high-income countries, canine rabies has been largely eradicated through sustained vaccination efforts, and most human infections arise from contact with bats or exposures during travel to endemic regions. Conversely, dog-mediated rabies persists in many areas of Asia, Africa, and parts of Latin America, where dog vaccination rates remain low and access to human vaccines is limited. Wildlife reservoirs also vary by region: bats, skunks, raccoons, and foxes maintain distinct rabies variants in North America, while red foxes serve as the main reservoir in much of Europe. The spread of rabies into new wildlife populations, such as the expansion of raccoon rabies in the eastern United States, highlights the dynamic nature of rabies ecology and the ongoing need for flexible, region-specific control measures.

Pathogenesis:

Rabies lyssaviruses gain entry into the host through broken skin or by contacting mucous membranes, as they cannot penetrate intact skin. After entry, the virus initially replicates in local tissues, particularly within muscle cells and sometimes within macrophages. This early replication phase is essential because it allows the virus to access nearby peripheral nerves. The virus may remain and multiply in the muscle for up to about two weeks before it binds to nicotinic acetylcholine receptors at the neuromuscular junction. Once attached, the virus enters peripheral neurons and migrates toward the central nervous system at an approximate rate of 3 mm per hour. It reaches the spinal cord or brain primarily by fast retrograde axonal transport along motor neurons, rather than by uptake through sensory or autonomic nerve endings. After gaining access to the CNS, the virus spreads throughout neural tissues, ultimately causing fatal encephalitis. Death generally results from respiratory failure accompanied by metabolic and cardiovascular disturbances.

Clinical Signs:

Rabies is a zoonotic viral infection that causes a rapidly progressive and severe encephalitis. Once clinical signs develop, the disease is untreatable and almost always results in death. Although humans and animals often show comparable signs, the clinical picture can vary greatly among individuals. The illness is marked by profound neurological dysfunction that inevitably progresses to paralysis and death. In dogs, the classical course of the disease is described in three overlapping stages: the prodromal stage, the furious stage, and the paralytic stage. In both dogs and humans, the disease typically presents as either the

encephalitic (furious) form or the paralytic (dumb) form.

The incubation period in dogs is highly variable, ranging from about one week to several months. In dogs and cats, incubation commonly spans 10 days to 6 months, with many animals showing clinical signs within 1–2 months of exposure. In humans, the incubation period is even more unpredictable, extending from a few days to several years, most often between 2 weeks and 6 years—though the average duration is approximately 2–3 months. Numerous factors influence this variability, including the location and depth of the bite, the proximity of the bite site to the central nervous system, the quantity and strain of the virus introduced, and the age and immune condition of the affected individual. WHO reports highlight that bites received closer to the central nervous system are associated with significantly shorter incubation periods.

- **Prodromal phase:**

  After the incubation period, the earliest signs of rabies emerge as behavioural alterations. In dogs, the prodromal stage typically lasts 2–3 days and is marked by noticeable temperament changes—aggressive dogs may become quiet or withdrawn, while normally calm dogs may show irritability or aggression. Mild fever, dilated pupils, partial protrusion of the third eyelid, and increased salivation are also common. Some animals may bypass the furious phase and progress directly to paralysis. In humans, this stage often resembles a nonspecific viral illness. Patients may experience fatigue, loss of appetite, irritability, low-grade fever, headache, nausea, vomiting, cough, sore throat, and diarrhoea. A characteristic early feature is tingling, pain, or itching at the site of the healed bite, caused by viral activity along nerves. The human prodromal phase generally lasts 2–10 days before advancing to the next stage of disease.

- **Excitement (Furious) phase:**

  In the furious stage of rabies, dogs show easily recognisable signs such as extreme aggression, unpredictable behaviour, and a strong urge to bite or roam. Paralysis of the laryngeal and pharyngeal muscles causes a change in voice, difficulty swallowing, and excessive salivation. Some animals may experience convulsions and die before entering the paralytic phase. Cats are more prone to the furious form than dogs, and livestock may show hyperactivity, aggression, and drooling. In humans, this stage involves severe hyperexcitability, autonomic disturbances like hypersalivation and cardiac irregularities, and phobic spasms such as hydrophobia and aerophobia, often accompanied by hallucinations or delusions. Hydrophobia is not seen in dogs.

- **Paralytic (dumb) phase:**

  The paralytic stage appears when the furious phase is brief or absent. It is marked by increasing weakness, loss of coordination, and progressive paralysis leading to coma and death. In dogs, a classic sign is a “dropped jaw” due to masseter muscle paralysis, along with choking-like sounds, inability to

swallow, and heavy salivation. Paralysis starts in the bitten limb and spreads to the neck and head before cardiorespiratory failure occurs. In humans, the dumb form results from spinal cord involvement and may appear as flaccid paralysis, quadriplegia, transverse myelitis, or an ascending paralysis resembling Guillain–Barré syndrome. Coma eventually develops, and death follows within a few days.

Diagnostic Challenges:

Diagnosing rabies before death is often difficult because early clinical signs are vague and the available tests require specialised laboratory facilities. Common antemortem diagnostic approaches include direct fluorescent antibody testing on skin biopsies taken from the nape of the neck, RT-PCR analysis of saliva or cerebrospinal fluid, and detection of viral antigen from corneal impressions. These methods, however, may produce false-negative results in the early stages of illness, making repeat sampling and careful clinical evaluation necessary. For definitive confirmation, post-mortem examination of brain tissue using direct fluorescent antibody testing or immunohistochemistry remains the gold standard. There is ongoing work to develop rapid, easy-to-use diagnostic tools suitable for low-resource settings, as quick and accurate identification of the disease is vital for guiding infection control and advising exposed individuals.

Treatment:

Because rabies is caused by a virus, there is no curative treatment once clinical signs appear. The disease is almost universally fatal, and after central nervous system symptoms develop, mortality approaches 100%, even in individuals who previously received pre-exposure vaccination. Management at this stage is limited to supportive care. Preventing rabies through timely vaccination remains the only effective strategy. Both human and equine-derived rabies immunoglobulins are available to provide passive immunity when exposure occurs.

If a person or animal is bitten by a suspected rabid animal, immediate wound care is essential. The bite site should be thoroughly washed with soap (preferably carbolic soap) and water for at least 10 minutes to reduce viral load and lower the risk of secondary bacterial infection. The wound should then be examined for foreign material such as broken teeth. It should be left open to heal by second intention, as suturing increases the chance of bacterial growth and infection. Rabies immunoglobulin should be administered promptly as part of post-exposure management.

Vaccination:

Rabies has no medical cure and is almost always fatal once symptoms appear, so only supportive care can be given at that stage. The main way to control rabies today is through proper management and vaccination of stray animals, especially dogs. Poor vaccination coverage in stray populations makes rabies a continuing threat. When a person is bitten or exposed to saliva from a rabid animal, immediate treatment

with rabies immune globulin and the rabies vaccine can prevent the virus from causing disease. Survival depends greatly on early treatment and the body's ability to mount an immune response.

Pre-exposure vaccination is recommended for pets, stray animals, veterinarians, animal handlers, laboratory workers, and travellers visiting high-risk regions. It helps the body build immunity before any exposure. If a bite occurs, post-exposure vaccination becomes essential. After thorough washing of the wound, rabies immunoglobulin and a series of vaccine doses are given within 28 days to block the virus and stop its spread in the nerves. Human rabies immune globulin is injected into and around the bite site as early as possible. Rabies vaccines work by stimulating antibody production. For animals, recombinant, inactivated, and live attenuated vaccines are used; inactivated vaccines are also used for humans.

- ***Pre-exposure vaccination:*** Dose 1: 1 ml (IM), at 0 days. Dose 2: 1ml (IM), 7 days after dose 1. Dose 3: 1ml (IM) between 21 or 28 days after dose 1
- ***Post-exposure vaccination:*** No previous vaccine history, then 1ml (IM) vaccine at 0, 3, 7, 14, 30, and 90th days after the bite. Vaccine history within one year, then 1ml (IM) vaccine at 0 and 3rd day after the bite. Vaccine history between 1-5 years, then 1ml (IM) vaccine at 0, 3, and 7th days after the bite.

Zoonotic Impact and One Health:

Rabies is a deadly zoonotic disease, and controlling it effectively requires the One Health approach, which links the health of humans, animals, and the environment. Every year, nearly 59,000 people die from rabies worldwide. Although dogs are the main source—responsible for about 99% of human cases—other animals such as bats and wild mammals also act as important reservoirs. Rabies spreads to humans mainly through the bite of an infected animal and is almost always fatal once symptoms appear. To eliminate this disease, the World Health Organization promotes the global goal "Zero by 2030," aiming for zero human deaths from dog-mediated rabies by the year 2030. Achieving this target involves environmental management, widespread vaccination of both humans and animals, and strict control of stray dog populations. Several countries have shown the effectiveness of this strategy. For example, Bangladesh reduced rabies deaths from 1,500 to 200 between 2012 and 2015. Bhutan and Sri Lanka also reported major progress through mass vaccination campaigns and coordinated One Health programs. However, the disease remains common in countries like India, Nepal, and Pakistan due to insufficient vaccination, large numbers of stray dogs, and a lack of awareness. Strengthening the One Health framework, especially through stray dog management and routine immunisation, is the most reliable pathway for rabies prevention and long-term eradication.

Conclusion:

Rabies remains one of the most lethal yet entirely preventable zoonotic diseases, posing a persistent threat to both human and animal health worldwide. Its continued prevalence in many low- and middle-income countries reflects gaps in vaccination coverage, surveillance, public awareness, and stray dog

management. Although no curative treatment exists once clinical signs develop, timely wound care, appropriate post-exposure prophylaxis, and strategic pre-exposure vaccination provide highly effective protection. Strengthening diagnostic capacity, especially in resource-limited settings, also remains essential for early case recognition and outbreak control. Sustainable elimination of dog-mediated rabies requires coordinated One Health action that integrates human health systems, veterinary services, and environmental management. Countries that have successfully reduced rabies burden demonstrate that large-scale vaccination of dogs, combined with community education and improved access to prophylaxis, can produce rapid, measurable progress. Achieving the global "Zero by 2030" target will depend on sustained political commitment, intersectoral collaboration, and continued investment in prevention strategies. With these efforts, global eradication of human deaths from rabies is an attainable and realistic goal.

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