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Rabies: Eliminating a Deadly but Preventable Global Disease

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Introduction:

Rabies is one of the world's deadliest and most horrific diseases, and it remains a significant public health hazard in many regions of the world, particularly Africa and Asia. It is a highly zoonotic disease that remains endemic in many regions with poor vaccination coverage and limited public awareness. It is caused by the classical rabies virus of the *Lyssa virus* genus belonging to the *Rhabdoviridae* family.

The World Health Organization (WHO) classifies rabies as one of the 18 Neglected Tropical Diseases (NTDs) due to its persistent global burden. With an almost 100% case fatality rate, rabies ranks among the deadliest infectious diseases. More than 99% of human cases result from transmission through dog bites, and despite the availability of effective prevention strategies, rabies continues to cause an estimated 59,000 deaths annually, the majority occurring in Asia and Africa (Costa et al., 2018).

The fear of rabies leads to the unnecessary killing of numerous animals each year. While infected animals suffer from the severe symptoms of the disease, many healthy dogs are also inhumanely culled in misguided attempts to control its spread (Balaram et al., 2016).

India accounts for over one-third (35%) of global deaths and two-thirds (59.9%) of deaths occurring due to rabies in Asia. According to a study conducted in India in 2005, out of 140 rabid deaths, 91% were from rural areas, 62% were male, and 50% were children below 15 years of age. To avoid rabies, these animal bite patients must get prompt and thorough post-exposure prophylaxis (PEP). Therefore, in order to preserve the lives of these animal bite victims, the attending anti-rabies clinic (ARC) physician must administer the proper PEP, which includes a thorough wound wash, the entire course of anti-rabies vaccination (ARV), and wound injection of rabies immunoglobulin (RIG) in all category III bite cases.

It affects a wide range of mammals—including dogs, cats, livestock, and wildlife—and is transmitted through saliva via bites, scratches, or contact with mucous membranes (eyes, mouth, or open

wounds). Clinically, it presents in two forms: the furious form, marked by hyperactivity, aggression, excessive salivation, restlessness, and hallucinations; and the paralytic (dumb) form, characterized by progressive paralysis, lethargy, social withdrawal, and eventually coma. Despite the availability of effective vaccines and preventive treatments, its control remains difficult in many regions due to socioeconomic challenges, weak healthcare infrastructure, and lack of public awareness.

The World Health Organization (WHO), World Organization for Animal Health (OIE), Food and Agriculture Organization (FAO), and Global Alliance for Rabies Control (GARC) have set a collective objective to eliminate dog-mediated human rabies by 2030 (Rupprecht et al.,2019). This global target holds great significance for several reasons:

1. It is preventable.
2. It has substantial economic implications.
3. It necessitates a One Health approach.
4. It contributes to improved animal welfare.
5. It addresses health inequities.
6. It strengthens health systems.

History:

For centuries, rabies has instilled fear in human societies, as the bite of a rabid animal was long recognized as a certain sentence to a painful death. The word "rabies" comes from the Latin *rabere*, meaning "to be mad" or "rage," and in Sanskrit it is called *rabhas*, meaning "to do violence." A major milestone in rabies control came in 1885, when Louis Pasteur developed the first rabies vaccine and successfully treated Joseph Meister, a young boy bitten by a rabid dog. Pasteur inoculated him with a series of attenuated rabies virus preparations, and the boy survived, later serving as a caretaker at the Pasteur Institute. Alongside vaccines for cholera and anthrax, this achievement represented a turning point in rabies prevention, drastically reducing the disease's once inevitable fatality rate.

Host:

Most mammals are susceptible to rabies, but only a few act as reservoir hosts (Moges, N 2015). Several species, including dogs, jackals, wolves, foxes, raccoons, skunks, mongooses, and bats, are susceptible to the disease. Among these, dogs remain the primary source of human rabies transmission (Rupprecht et al. 2002). Reservoir hosts are generally categorized into two groups: terrestrial species and bats. Rabies may occur sporadically in individual animals or persist within populations in enzootic or epizootic forms (Balcha & Abdela, 2017). When the virus passes from a reservoir host to a non-reservoir species, the event is referred to as a "spillover."

Epidemiology:

Rabies is estimated to cause around 59,000 human deaths annually across more than 150 countries,

with 95% of cases reported from Africa (35%) and Asia (60%). The burden of disease disproportionately affects poor rural populations, and nearly half of the cases are children under the age of 15 (World Health Organization, WHO).

According to the National Health Profile (NHP), India recorded a total of 2,863 rabies cases from 2005 to 2020, with over 75% concentrated in five states: West Bengal (43%), Andhra Pradesh (10%), Maharashtra (8%), Karnataka (7%), and Delhi (6%). In 2022, 307 persons died due to rabies in India. Delhi reported the maximum cases (48), followed by West Bengal (38), and 29 deaths each in Maharashtra, Karnataka, and Andhra Pradesh (Rubeshkumar et al., 2022).

Transmission:

- ✓ Rabies is predominantly transmitted through the bite of a rabid animal. The virus penetrates the skin barrier and enters tissues, where it establishes infection. Occasionally, it may also spread through contact of infected saliva with open wounds or mucous membranes.
- ✓ Wild carnivores and bats act as natural reservoirs, but domestic dogs (*Canis lupus familiaris*) are the primary vectors responsible for most of the human cases worldwide.

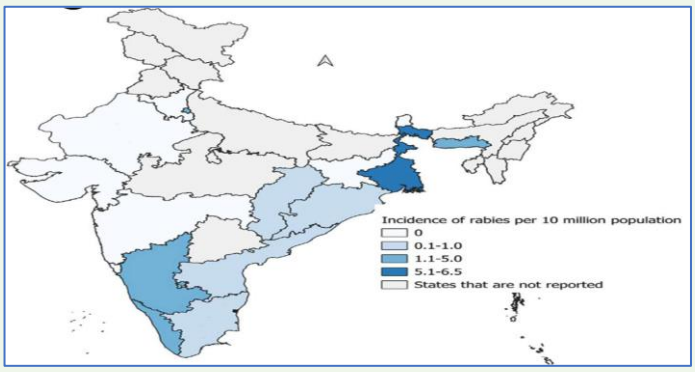

Fig- Incidence of rabies by India, 2020 (Rubeshkumar et.al, 2020)

- ✓ Humans and other species that do not play a role in spreading the virus and are considered dead-end hosts. Human-to-human transmission is extremely rare and has been reported only in cases of corneal or organ transplantation.
- ✓ While bites or scratches from infected animals are the most common sources of infection, transmission via contaminated objects or the environment is extremely unlikely.
- ✓ The disease can also spread through exposure to nervous system tissue or cerebrospinal fluid from infected animals.
- ✓ In rare cases, humans have contracted rabies by inhaling airborne virus particles, such as in laboratories working with live rabies virus or in caves densely populated with bats.

Incubation:

The incubation period varies with the amount of virus transmitted, virus strain, site of inoculation (bites closer to the head have a shorter incubation period), host immunity, and nature of the wound.

- In animals, the incubation period generally ranges from 1 to 3 months, though it may be as short as 10 days or, in rare cases, extend to several months or even a year. In dogs, symptoms typically appear within 21 to 80 days after exposure.
- In humans, the incubation period is usually between 1-3 months but can vary widely, from less than

a week to more than a year.

Clinical Manifestations:

In Animals: Rabies in animals generally manifests in two distinct forms: the furious form and the dumb (paralytic) form.

- Furious rabies often referred to as the "mad-dog syndrome," can affect all species. In this form, animals become highly irritable and may exhibit aggressive behavior, attacking humans and other animals using their teeth, claws, horns, or hooves, often without any provocation. These animals tend to lose their natural wariness and fear of both humans and other creatures.
- The dumb or paralytic form of rabies is characterized by ataxia and paralysis, particularly of the throat and jaw muscles, leading to excessive salivation and difficulty in swallowing.

In Humans: Rabies progresses through five distinct stages: incubation, prodromal phase, acute neurologic phase, coma, and death (or, in rare cases, recovery).

The initial symptoms of rabies are fever and often pain or an unusual or unexplained tingling, pricking, or burning sensation (paraesthesia) at the wound site. As the virus spreads through the central nervous system, progressive, fatal inflammation of the brain and spinal cord develops. Two forms of the disease can follow: furious or paralytic rabies.

- People with furious rabies exhibit signs of hyperactivity, excited behavior, hydrophobia (fear of water), aerophobia (fear of air), and death after a few days.
- Paralytic rabies, which accounts for about 30% of human cases, follows a slower and less dramatic course. Muscle weakness and paralysis begin at the site of infection and gradually spread. Eventually, the patient slips into a coma, followed by death. Once clinical symptoms appear, rabies is almost invariably fatal.

Diagnosis:

Rabies can be diagnosed both in vivo and post-mortem, though confirmation before death remains challenging (Bishop et al., 2013). While hydrophobia is a key symptom, no clinical sign is unique to rabies. Historically, the identification of Negri bodies (viral inclusion bodies) was used as a diagnostic method, but due to its low sensitivity and the availability of more accurate tests, it is no longer the primary diagnostic approach. Diagnostic tests often require animal brain tissue, limiting most definitive diagnoses to post-mortem examination. For accurate diagnosis, brain samples should be taken from at least two brain areas, typically the brainstem and cerebellum (Ugolini G, 2011). In animals, the direct fluorescent antibody test (dFAT) is the gold standard diagnostic method, detecting rabies antigen in brain tissue. Other diagnostic methods include reverse transcriptase polymerase chain reaction (RT-PCR), direct rapid immunohistochemistry (dRIT), and serological tests such as the fluorescent antibody virus neutralization (FAVN) test and the rapid fluorescent focus inhibition test (RFFIT). In humans, commonly used diagnostic

tests include dFAT, RT-PCR, and dRIT.

Management And Treatment Of Rabies:

Post-Exposure Prophylaxis (PEP):

1. **Wound Care:** Immediate and thorough cleaning of the bite or scratch with soap and running water for at least 15 minutes, followed by antiseptic treatment, can reduce the risk of infection.
2. **Rabies Vaccine:** A series of rabies vaccinations (usually 4 doses) is given within **14 days** of exposure. The doses are administered on days **0, 3, 7, and 14**, stimulating the body's immune system to defend against the virus.
3. **Rabies Immune Globulin (RIG):** Administered on day 0, RIG provides immediate passive immunity while the vaccine helps generate active immunity. It is injected directly into the wound site and, if necessary, at other sites away from the vaccine injection.
4. **Vaccinated animals:** If an animal that has been previously vaccinated for rabies is exposed to a potentially rabid animal, it should be immediately revaccinated and observed under quarantine for 10 days. If clinical signs of rabies appear during this period, **euthanasia or other control measures** may be required.
5. **Unvaccinated animals:** Unvaccinated animals exposed to rabies should be euthanized immediately to prevent further spread. In exceptional cases, if euthanasia is not feasible or acceptable, **strict quarantine combined with post-exposure vaccination** may be attempted, though this approach carries significant risks.

Pre-Exposure Prophylaxis (PrEP):

Recommended for individuals at high risk of exposure to rabies (e.g., veterinarians, animal handlers, wildlife workers and, travelers to high-risk areas). It involves **2–3 doses of rabies vaccine**, followed by booster doses depending on ongoing risk.

1. **Management of Symptomatic Rabies:** Once clinical symptoms of rabies appear, the disease is nearly always fatal.
2. **Supportive Care:** Intensive care is often provided to maintain breathing, hydration, and comfort, though it is rarely curative.
3. **Experimental Treatment (Milwaukee Protocol):** This involves placing the patient in a medically induced coma and administering antiviral drugs, but it has had very limited success.

PREVENTION and CONTROL:

1. **Vaccination**: Mass vaccination campaigns for domestic animals, particularly dogs, which are the main vectors of rabies transmission in humans, are essential.
2. **Animal control**: Management of stray animal populations includes **quarantine, vaccination, and, when necessary, humane euthanasia**. Quarantine regulations require that animals suspected of

rabies or exposed to the virus be isolated for monitoring.

3. **Wildlife management:** In areas where rabies is widespread among wildlife, **oral rabies vaccines (ORV)** are distributed in bait form to immunize wild animal populations.
4. **Public health measures:** Public education on avoiding contact with wild animals and the danger of rabies is a vital component of prevention efforts. Rabies surveillance and reporting help monitor outbreaks and guide control strategies.

Type of Prophylaxis	Route of Administration	Dose of Vaccine	Day of Dose
Pre-exposure prophylaxis	Intradermal	0.1 ml/dose	Day 0, 3, 7, 14 & 28
	Intramuscular	1 entire vaccine vial	Day 0, 3, 7, 14 & 28
Post- exposure prophylaxis	Intradermal	0.1 ml/dose	Day 0, 7 & booster on either day 21 or 28
	Intramuscular	1 entire vaccine vial	Day 0, 7 & booster on either day 21 or 28
Re-exposure	Intradermal	0.1 ml/dose	Day 0 & 3
	Intramuscular	1 entire vaccine vial	Day 0 & 3

Table 1. Rabies Vaccination Schedule (Source: National Guidelines for Rabies Prophylaxis, 2019)

Importance Of World Rabies Day:

World Rabies Day was initiated in 2007 by the Global Alliance for Rabies Control (GARC) in collaboration with the US Centers for Disease Control and Prevention (CDC), with support from international health organizations including The World Health Organization (WHO), The World Organization for Animal Health (OIE), The Pan-American Health Organization (PAHO), and The Food and Agriculture Organization (FAO). It is celebrated annually on 28th September, the death anniversary of Louis Pasteur, who developed the first rabies vaccine. This day serves as a global platform to bring together stakeholders from different sectors in a united and coordinated effort to eliminate rabies worldwide.

WHO-India Strategic Framework for Rabies Elimination (2019–2030):

Zero by 30 is the global strategy adopted by the World Health Organization (WHO), the World Organization for Animal Health (OIE), the Food and Agriculture Organization (FAO), and the Global Alliance for Rabies Control (GARC). The plan, launched in 2018, aims to achieve zero human deaths from dog-mediated rabies by 2030.

Government Control Programs for Rabies in India:

India has implemented several government schemes to combat rabies, each with its own specific focus and objectives:

1. **National Rabies Control Program (NRCP):** Focuses on **mass vaccination of dogs**, public awareness campaigns, training of healthcare workers, disease surveillance, and strengthening laboratory support.
2. **National Health Mission (NHM):** Providing free rabies vaccines and immunoglobulin, supporting

the NRCP, and integrating rabies prevention into primary healthcare services.

3. **Animal Welfare Board of India (AWBI):** Promoting animal birth control (ABC) programs, responsible pet ownership, and financial assistance to NGOs.
4. **National Rural Health Mission (NRHM):** Integrating rabies prevention into primary healthcare services and training rural health workers.
5. **National Vector-Borne Disease Control Program (NVBDCP):** Collaborates with NRCP to implement and strengthen rabies prevention measures.

State and Municipal-Level Initiatives:

1. Kerala: Comprehensive rabies control with mass dog vaccinations and awareness campaigns.
2. Goa: Successful control model with high vaccination rates and no recent human rabies deaths.
3. Tamil Nadu, Maharashtra, Karnataka: Active programs for dog vaccination and birth control.

Strategic Approaches For Future Control:

To break the boundaries of rabies control, a multi-faceted approach is required:

1. **Global Collaboration:** Strengthening international cooperation and funding for rabies control programs can enhance global efforts to reduce the burden of the disease.
2. **One Health Approach:** Integrating human, animal, and environmental health strategies can improve rabies control efforts, particularly through coordinated vaccination campaigns and surveillance systems.
3. **Innovation and Research:** Continued investment in research and development of new vaccines, diagnostics, and therapeutic interventions is crucial for overcoming existing limitations and achieving long-term control of rabies.

Challenges In Rabies Prevention And Control:

1. Limited Access to Healthcare.
2. Low Public Awareness and Education.
3. Lack of a proper surveillance system.
4. Scanty Resources.
5. Social and Cultural.
6. Vaccines and PEP are not accessible.
7. Stray Dog Populations.
8. Wildlife Reservoirs.

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