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Rabies Day Special: Bridging the Gap between Science and Safety

Popular Article

Rabies Day Special: Bridging the Gap between Science and Safety

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Introduction:

In the twenty-first century, rabies remains one of the most feared and serious hazards to public health. Untreated sickness manifests as a progressive encephalomyelitis that is always fatal and is caused by neurotropic viruses of the genus *lyssa virus*. Rabies is a neglected zoonotic disease that affects much of the world, with many human deaths happening in Africa and Asia in children under the age of 15. Rabies is thought to be under-reported in many areas, owing to a lack of surveillance and laboratory infrastructure, which is exacerbated by cultural or societal stigmas. In the absence of good data on disease incidence, policymakers and public health experts tend to prioritize rabies less. A more complete worldwide estimate has been provided by updating and adding country-specific data from published research and online surveys to estimates of the burden that were previously based on models of the incidence of dog bites. Based on preliminary statistics, it is estimated that rabies causes approximately 60,000 deaths worldwide each year, more than any other zoonotic disease combined. Due to the high proportion of children among these deaths, rabies is thought to result in more than 2 million DALYs (disability-adjusted life years) lost annually, at a cost to the economy of more than \$4 billion. Estimates of statistical life values have been utilized by other models to forecast the economic impact of rabies. These figures range from \$1.8 to \$2.2 million per human fatality; however, these figures do not account for livestock losses, post-exposure therapies, or the expense of immunization and diagnostic testing. It is estimated that the annual global expenses associated with canine rabies alone amount to tens of billions of dollars.

Etiology:

There are two components of the bullet-shaped Rhabdoviridae family of viruses that cause rabies. The ribonucleocapsid core is found in the second, more functional portion, whereas the first, which is the viral envelope, is thought to be more structural. The most typical way for the virus to spread is through the bite of an infected mammal, both domestic and wild, however saliva can also transfer the virus through cuts in the skin or mucous membranes. Additional ways to become infected include ingesting the virus, breathing it in aerosolized form, passing it through the placenta, and even receiving an organ transplant.

Epidemiology:

Rabies is thought to be the cause of between 30,000 and 70,000 deaths annually, with less developed nations being more affected. Few human cases are documented in the US, yet it might be because post-exposure prophylaxis is so often used and because there are preventative initiatives in place. Raising domesticated animals has only contributed to roughly 10% of rabies cases in affluent nations. On the other hand, the remaining cases are caused by wild creatures like foxes, bats, raccoons, and skunks. There have been anecdotal reports of rabies caused by transmission from rats, although small rodents and the rabbit family are generally thought to be safe since they are not likely to survive an inoculating wound from a rabid. Any mammal can transmit rabies. Knowing your region's animal carriers might assist you determine who can benefit from prophylaxis, as animal carriers differ by location.

Categories of contact with suspect rabid animal	Post-exposure prophylaxis measures
Category I - touching or feeding animals, animal licks on intact skin (no exposure)	Washing of exposed skin surfaces, no PEP
Category II - nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure)	Wound washing and immediate vaccination
Category III - single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure)	Wound washing, immediate vaccination and administration of rabies immunoglobulin/monoclonal antibodies

Pathophysiology:

The rhabdovirus targets the central nerves after viral transmission and spreads through the peripheral nervous system to cause encephalomyelitis. The initial signs of a viral illness in humans resemble those of any other nonspecific illness (fever, malaise, headache). After that, these mild symptoms could intensify into agitation, anxiety, and finally open delirium. Within the first several days following a rabid bite, tingling at the bite site is one extremely common symptom. It's interesting to note that the virus returns to the peripheral neurological system (PNS) after first spreading to the central nervous system (CNS), primarily attacking highly innervated tissues (i.e., salivary glands). Hypersalivation causes the "frothing," as seen in the films Cujo and Old Yeller, and individuals may experience severe pharyngeal muscular spasms at the sound, taste, or sight of water. We term this "hydrophobia." The infection eventually causes the entire neurological system to collapse completely, which results in an abrupt death. Animals typically pass away in ten days, but the incubation period after vaccination can extend anywhere from two weeks to six years, with an average of a few months. The site of exposure, the severity of the incision, and the viral load all influence the onset time. Ultimately, the virus damages the central nervous system, with the brainstem typically suffering the most. The inflammatory response triggers the toxic effects, which are accompanied by functional alterations that are not fully understood. Neurotransmission is ultimately thought to be impacted by the virus, and both virus-dependent and cell-dependent pathways may lead to apoptosis. Rabies is always lethal once clinical symptoms are observed.

Histopathology:

Autopsy examinations have shown that the brain is typically enlarged and congested, with an initial inflammatory process. Neuronal death is uncommon in most circumstances. Immunochemical labeling reveals virion deposits in the nerve cytoplasm. Negri bodies are frequently observed under light microscopy, although only in roughly two-

thirds of instances.

Evaluation:

Without a documented history of rabid bites, rabies is frequently an excluding diagnosis. In the early stages, it may seem like influenza, Coxsackie, enterovirus, or herpes. Rabies can show in later stages with symptoms comparable to delirium tremens, tetanus, botulism, diphtheria, tick-borne illnesses, and Guillain Barre. Physicians frequently check CBC, electrolytes, cultures, CT, chest x-ray, and MRI, but are still unaware that rabies is to blame. Unless isolated in a rabies-specific viral culture, detected by polymerase chain reaction (PCR) in saliva, confirmed to have a positive antibody titer, or isolated in cerebrospinal fluid (CSF), the diagnosis may remain difficult until too late. Rabies can be confirmed using CSF, blood, saliva, tears, and tissue biopsies (neck, immunofluorescent stain). CSF investigation can reveal pleocytosis and allow the virus to be identified. According to the Centers for Disease Control and Prevention, no single test is sufficient to diagnose or rule out rabies. Finally, because the disease is rare, developed countries must maintain a high level of suspicion. If the biting animal can be euthanized and examined, post-exposure prophylaxis may be unnecessary. Public health may be able to help with animal experimentation.

Treatment / Management:

There is no effective treatment for rabies. Prevention is the mainstay of treatment, including domestic animal vaccination programs, education, and monitoring. Wound care is the first step in treating any individual with a feared rabies exposure. Appropriate wound care alone is almost 100% effective if initiated within 3 hours of inoculation. Scrubbing the wound and surrounding area with soap and water (solutions include a 20% soap solution, povidone, and alcohol solutions) and soaking for puncture wounds. After carefully cleansing the wound, apply a virucidal agent such benzalkonium chloride or povidone-iodine. When a bite from a recognized bat, skunk, raccoon, or fox occurs in the United States, it is promptly treated with rabies vaccine and rabies immune globulin. Consult the public health agency for any other bites. If a dog bite occurs outside of the US, it should be treated right away with rabies immune globulin and vaccination.

Afterward, the start of treatment is determined by the patient's history of vaccinations. A human diploid cell vaccine or a pure chick embryo cell vaccine administered intramuscularly twice day at a dose of 1 mL is a common course of treatment for patients who have already received vaccinations. Suppose the patient has not already been immunized. In that situation, treatment consists of administering 1 mL of one of the two vaccines described above intramuscularly on days 0, 3, 7, and 14 (and on days 28 if the individual is immunosuppressed). The vaccination dosage should be administered at a location apart from the second stage of treatment (human rabies immune globulin, or HRIG). These unimmunized individuals are also treated with human rabies immune globulin at a dose of 20 IU/kg, with the goal of infiltrating as much of the dose as possible surrounding the lesion. Any residual dose of human rabies immune globulin that has not been infiltrated into the wound is administered intramuscularly, as previously stated, at a distance from the vaccine site. The recommendations have just been modified in the United States. Because bats are the primary source of rabies in this area, everyone who awakens from sleep and discovers a bat in the room should be inoculated right away.

Differential Diagnosis:

- **Poisoning with belladonna alkaloids-** Tachycardia, dilated pupils, blurred vision, urinary retention, altered mental status, and dry and flushed skins are a few of the symptoms evident.
- **Stroke-** vertigo, dizziness, seizures, headaches, bell's palsy, drug withdrawal, dementia, electrolyte disorders,

acute infections, syncope, and alcoholism.

- **Jacob Creutzfeldt disease-** difficulty walking caused by problems with balance and co-ordination, slurred speech, numbness or pins and needles in different parts of the body, dizziness, vision problems, such as double vision, hallucinations (seeing or hearing things that aren't really there).
- **Brain tumor-** Brain imaging is always abnormal, and lesions may mimic demyelination, neoplasm, infarction, infection, and others. Such lesions can be faint, diffuse, and coalescent; and the presentation may include infarcts and hemorrhage paired with multifocal stenosis on vascular imaging.
- **Pseudotumor Cerebri**, this condition is not a brain tumor, but its symptoms mimic a brain tumor. Pseudotumor Cerebri most commonly afflicts obese adolescent girls and young women.
- **Encephalitis-** The diagnosis of rabies encephalitis is usually unmistakable and is based on the unique clinical symptoms. Hydrophobia, which is the most characteristic and widely known feature of rabies, was not present in our case. In a study by Chabra, 5% of patients with rabies did not have hydrophobia.
- **Tetanus-** Tetanus must be differentiated from other diseases that present with fever and rigidity such as strychnine poisoning, dental infections, drug reactions, hypocalcemia, meningitis, stroke, and stiff man syndrome.

Complications:

- Seizures** - Convulsive concussion, convulsive syncope, movement disorders, rigors, sleep-related events, or psychogenic non-epileptic spells.
- Fasciculations**-Fasciculation (muscle twitching) happens when a single peripheral nerve that controls a muscle is overactive, resulting in involuntary muscle movement.
- Psychosis**- hyperactivity, excitable behavior, hallucinations, lack of coordination, hydrophobia (fear of water) and aerophobia (fear of drafts or of fresh air).
- Aphasia** - It can impact your speech, as well as the way you write and understand both spoken and written language. Aphasia usually happens suddenly after a stroke or a head injury.
- Autonomic instability**
 - Balance problems.
 - Fainting or passing out (especially when standing up).
 - Nausea and vomiting.
 - "Brain fog," forgetfulness or trouble focusing.
 - Fast heart rate (tachycardia) or slow heart rate (bradycardia).
 - Pinpoint eye pupils or unusually wide eye pupils.
- Paralysis**- Paralytic rabies accounts for about 20% of the total number of human cases. This form of rabies runs a less dramatic and usually longer course than the furious form. Muscles gradually become paralyzed, starting from the wound site.
- Coma**- last Stage of rabies is the coma stage and usually begins within 10 days of stage 3. Patients may have ongoing hydrophobia, develop prolonged apnea periods, and have flaccid paralysis. Without supportive care due to cardiopulmonary failure, most patients experience death within 2 to 3 days after undergoes into coma.

Consultations: Consultations that are typically requested for patients with this condition include the following:

- a) Neurologist: To evaluate and monitor the patient's neurological symptoms, such as confusion, agitation, paralysis, and seizures, which are characteristic of rabies.
- b) Infectious Disease Specialist: To confirm the diagnosis, determine the source of the infection, and guide antimicrobial treatment.
- c) Neurosurgeon: In rare cases, surgical intervention may be necessary to alleviate symptoms or manage complications.
- d) Public Health Specialist: To investigate the source of the infection, track potential contacts, and implement measures to prevent further transmission.

These consultations enable a comprehensive approach to managing rabies, ensuring timely diagnosis, treatment, and prevention of further spread. Prompt medical attention is critical, as rabies is almost always fatal if left untreated.

Vaccination:

Species	Age at Primary Vaccination	Revaccination
Dog & Cat	After 3 months of age *	3 years**
Cattle, Horse, Sheep & Goat	After 6 months of age *	2 years**
Ferret	After 3 months of age *	1 year**

Vaccination Programme: Post-Bite treatment (Post-exposure Prophylaxis)

In all species, repeated single dose of vaccine should be administrated (by the above recommended route) according to the following schedule-

Dose number	Timing
1 st	Day 0 (as soon as possible following bite/exposure)
2 nd	Day 3
3 rd	Day 7
4 th	Day 14
5 th	Day 28

Future Challenges:

Because rabies kills so many children, it should be considered a serious pediatrics disease. The combination of an existing rabies human vaccine with a conventional childhood immunization regimen should be prioritized in order to assure universal rabies vaccination of low-income children. This method would include rabies vaccine in the existing childhood Expanded Programme on Immunization (EPI) schedule. As part of a children EPI schedule, the addition of rabies vaccination to an existing multivalent pediatrics vaccine should ideally comprise a single-dose vaccine administered via a non-injectable route. Rabies, unlike other viruses targeted for eradication, will never be eliminated due to the prevalence of lyssaviruses in bats. The realistic goal for the twenty-first century is to increase efforts to eradicate rabies in dogs, resulting in a reduction in human mortality, a goal that has already been met in certain locations. The strategic approach for programs aimed at eliminating canine rabies should focus on a multidisciplinary core of disparate groups, including representatives from the public and private sectors (i.e.,

vaccine manufacturers, policymakers, scientists, veterinarians, and clinicians) with the overarching goal of eliminating human rabies. This joint interdisciplinary program, known as the One Health method, is a step toward rabies prevention through mass dog vaccination and humane dog population control. Financial assistance for these efforts will be required. Currently, philanthropic foundations, sponsors, and financial benefactors collaborate with global institutions to fund such projects. Along with these steps, the OIE has established an animal vaccine bank from which vaccine is distributed to various regions. The Food and Agriculture Organization of the United Nations has proposed a Progressive Control Pathway to Rabies Elimination, with the ultimate goal of maintaining rabies-free humans and animals. This support should extend beyond the community, district, national, and worldwide levels. In endemic areas, the development of novel diagnostic procedures for both ante-mortem and post-mortem diagnostic confirmation is critical to enable epidemiological assessment and, when possible, therapeutic alternatives evaluation. The OIE recommended a pathway for veterinary services to control rabies in dogs in order to increase veterinary services' compliance over time. Performance, vision, and strategy are the three important components. With this in mind, WHO, OIE, and the Food and Agricultural Organisation have suggested a strategy for eliminating human rabies transmitted by dogs in rabies-endemic countries, indicating that this be a feasible objective by 2030.

Summary:

Rabies is one of the worst infectious diseases, with a case fatality rate of nearly 100%. The disease has spread to all continents except Antarctica; the majority of cases are documented in Africa and Asia, with thousands of deaths recorded each year. However, the projected annual cases of nearly 60,000 of human rabies mortality are likely an underestimate. Almost all human rabies cases are caused by bites from infected dogs. Therefore, the most cost-effective method to eliminating the worldwide burden of human rabies is to reduce canine rabies rather than expanding the availability of human prophylaxis. Mass vaccination programs using parenteral vaccinations, as well as advancements in oral vaccines for animals; have enabled the eradication of rabies in terrestrial carnivores in various countries throughout the world. The ensuing decrease in cases of human rabies in such locations recommends the interdisciplinary One Health strategy to rabies control through mass vaccination of dogs and management of canine populations.

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