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Review Article

Rabies; General Overview, Zoonotic Importance, Prevention and Control

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Abstract

Rabies it is one of the most prevalent zoonoses that has been recorded over time. The terms used to describe rabies date back thousands of years, demonstrating how old the disease is. It is a contagious viral disease of the central nervous system (CNS) that causes convulsions, paralysis, excessive salivation, and an aversion to water in sufferers. In most cases, the condition results in the infected animal's death. Rabies is caused by a single stranded, negative-sense RNA virus of the order Mononegavirales, family Rhabdoviridae and genus Lyssavirus. Rabies is not uncommon among viral diseases in that it can affect a variety of victims, including all warm-blooded animals. The only place where rabies is not common is on islands. Except for Australia and Antarctica, many of the nations have rabies as an endemic disease. Over 55,000 people per year die from rabies worldwide, with 99% of those deaths occurring in Africa and Asia. Because of their preference for neural tissue (a condition known as neurotrophism), lyssaviruses can spread to the central nervous system and produce serious symptoms. The virus may remain dormant or continue to proliferate in nearby nerve tissues after a bite wound (and possibly skeletal muscle). The virus is typically spread through bites, with a smaller amount of transmission occurring through contact with rabid animal saliva on cuts, wounds, and mucous membranes. Since its inception in 1958, the direct fluorescent antibody (DFA) test has been extensively utilized on both humans and animals to identify the antigens of the rabies virus in the brain tissue. Renewed surveillance based on laboratory and variant typing is necessary for the prevention and control of rabies. In order to manage potentially exposed animals and help in the detection of new pathogens, precise and timely information and reporting are required. Viral introduction by the admission of infected animals is always a possibility. To understand the role that these animals play in disease transmission, it is still unknown how common rabies is in wild animals. For the purpose of finding newly imported RABV variations, ongoing monitoring of less common non-reservoir species is crucial.

Keywords: Rabies; Zoonotic; Prevention and Control

Introduction

Given rabies has existed for more than 4,300 years, it is one of the most prevalent zoonoses that has been recorded over time [1]. The terms used to describe rabies date back thousands of years, demonstrating how old the disease is. For instance, the Latin term "rabies" is a translation of the Sanskrit word "rabhas," which means "to commit violence." Early on, Roman writers understood that rabid dog saliva was infectious, referring to the infectious substance as a poison with the Latin name "virus" [2].

Acute, extremely contagious, and lethal to warm-blooded animals, rabies has a protracted and unpredictable incubation period [3]. It is a contagious viral disease of the central nervous system (CNS) that causes convulsions, paralysis, excessive salivation, and an aversion to water in sufferers. In most cases, the condition results in the infected animal's death [4]. The disease, an acute progressive encephalitis, causes behavioral abnormalities like agitation, excitement, and saliva dribbling. Initially, there might not be any symptoms, but rabies can cause discomfort, lethargy, head-

aches, and fever weeks or even years after a bite. Seizures, hallucinations, and paralysis follow these. Less than five examples of recovery are known to have taken place [4].

Over 55,000 people per year die from rabies worldwide, with 99% of those deaths occurring in Africa and Asia [5].

The name "lyssa virus," which refers to the genus to which rabies and viruses related to rabies belong, comes from the Greek word "lyssa" or "lytta," which means "madness." Democritus possibly provided the earliest known description of canine rabies about 500 B.C. Aristotle wrote about rabies in his Natural History of Animals, describing how the disease caused dogs to become irritable and how other animals got sick when they were bitten. In most regions of the world where the virus is enzootic, dogs and other carnivores continue to be the primary sources of human infection, therefore little has changed in the epidemiology of rabies [6].

History

The widespread and deadly sickness known as rabies affects both humans and animals. It has been around for a very long time [7]. Around 2300 BC, rabies was first identified in Egypt. Aristotle also accurately characterized rabies in ancient Greece. The Avesta (Persia) from the sixth century BC and the Susrutasamhita from the first century BC both included descriptions of canine rabies (India). In 1804 Zinke realized that the saliva from diseased dogs was contagious. Prior to Pasteur's discovery in 1885, there were no efficient preventive or curative treatments for animals. In 1881, Pasteur showed that the virus is neurotropic. Prior to the discovery and use of the rabies vaccine in 1885 by Pasteur, the structure and characteristics of the RABV were unknown. Joseph Meister, who had been severely attacked by a rabies-infected animal, received the rabies vaccine for the first time that same year. That day marked the advent of modern science in the age of infectious diseases, which focused on disease control and prevention. The RABV was recognized in 1903 by Remlinger and Riffat-Bay. In the 1940s, RABV first appeared in red foxes (Vulpes vulpes) in the Kaliningrad region. Within a few decades, it expanded to Central and Western Europe [8].

Etiology

Rabies is caused by a single stranded, negative-sense RNA virus of the order Mononegavirales, family Rhabdoviridae and genus Lyssavirus [9]. It is a neurotropic virus that is generally transmitted through bites from infected animals to susceptible host species including humans [10].

Epidemiology

Rabies is not uncommon among viral diseases in that it can affect a variety of victims, including all warm-blooded animals. The only place where rabies is not common is on islands. Except for Australia and Antarctica, many of the nations have rabies as an endemic disease. Bahrain, Cyprus, Hong Kong, Japan, Malaysia, Maldives, Qatar, Singapore, Lakshadweep, Andaman and Nicobar Islands of India, and Timor-Leste are among the Asian nations immune from rabies. Other nations that have achieved rabies-free status include Antigua and Barbuda, the Bahamas, Barbados, Belize, Falkland, Jamaica, Saint Kitts and Nevis, Trinidad and Tobago, Uruguay of the American subcontinent, Albania, E.Y.R. of Macedonia, Finland, Gibraltar, Greece, Iceland, Isle of Man, Malta, Portugal, Norway (aside from Svalbard), the United Kingdom, and Spain (aside from Melill + ceuta Africa's nations include Cape Verde, Congo, and Libya. Rabies has not been found in Mauritius, Reunion, or the Seychelles. Fiji, the Cook Islands, Vanuatu, Guam, French Polynesia, New Zealand, New Caledonia, the Solomon Islands, and Papua New Guinea are among the Oceana group of Islands that have achieved rabies-free status [11]. According to the World Health Organization (WHO), a nation can claim to be rabies-free if it has not experienced an indigenously acquired case of human or animal rabies in the previous two years as a result of surveillance and import restrictions. Nevertheless, despite the implementation of wildlife immunization programs, susceptibility to reintroduction from neighboring nations does persist [12]. Visitors to impoverished countries that care for pets often find it challenging to avoid stray dogs and cats, violating the precautions [13]. In order to prevent the entry of the virus, particularly with the import or introduction of diseased animals, any nation preserving the status of being rabies-free requires tight ongoing monitoring, quarantine of imported animals, and laws [14]. A current official list is required for a nation to be declared rabies-free. A country cannot become rabies-free just by having a rabies-related virus; this is also true for the United Kingdom and Australia [15]. Rabies was declared officially eradicated in the UK in 1920 [16]. However, one unvaccinated bat conservationist died in Dundee in 2002 after contracting RABV (European bat lyssavirus type 2) and not receiving POST EXPOSURE VACCINE [17]. When we look at the rabies situation in Asia, it is evident that the bulk of the developing countries on this peninsula are rabies fatality victims [18]. According to the WHO Global Vaccines Research Forum, more

than 3 billion people worldwide are at risk for dog rabies, and the Asian continent sees more than 30,000 annual fatalities, or one fatality every 15 minutes. But the unfortunate reality is that 15% of rabies-related deaths in those under the age of 15 involved children [12]. Although rabies still exists on the European continent, human rabies cases have virtually disappeared from most of the European countries, most likely as a result of the implementation of laws requiring vaccination of animals, particularly dogs. In various Asian and African nations, dog slaughterhouses are regarded as a critical risk factor in the epidemiology of rabies. RABV isolates found in Burkino Faso [19] and Vietnam [20] shared genetic similarities with isolates found in Mauritania and China, respectively. This suggests that RABV has spread internationally, which is alarming because it highlights the significance of dog trade and dog meat consumption in the rabies epidemiology.

Pathogenesis

Because of their preference for neural tissue (a condition known as neurotrophism), lyssaviruses can spread to the central nervous system and produce serious symptoms. The virus may remain dormant or continue to proliferate in nearby nerve tissues after a bite wound (and possibly skeletal muscle). After a varied amount of time, the virus subsequently travels to neuromuscular junctions and neurotendinal spindles (days or weeks). The virus must travel through peripheral nerves in retrograde (centripetal or axoplasmic) flow for at least 21 days before reaching the CNS. The virus quickly advances to the brain after progressing in the CNS. Opposite to the initial injected site, the virus reaches the spinal cord or brain stem. Following this, the infection spreads to the other side's neurons before ascending bilaterally through the spinal cord or brain stem to the forebrain. The virus quickly advances to the brain after progressing in the CNS [21].

Transmission

The virus is typically spread through bites, with a smaller amount of transmission occurring through contact with rabid animal saliva on cuts, wounds, and mucous membranes. Exposures to the virus that aren't caused by bites include those from significant volumes of aerosolized rabies virus, organ transplants from rabies victims, contact with rabid animal saliva or nervous tissue, and scratches or mucous membrane contact [22].

Clinical signs

The majority of rabid animals exhibit signs of nervous system dysfunction. The most trustworthy warning signs are abrupt, severe behavioral changes and unexplained paralysis that gets worse over time. A rapid loss of appetite, symptoms of anxiety or unease, impatience, and hyperactivity are a few examples of behavioral changes. The animal might seek seclusion, or an antagonistic animal might change their ways. Wild animals may become unusually hostile and lose their fear of humans. It's possible to witness animals that are typically nocturnal out and about during the day.

The furious type of rabies, often known as the typical "mad-dog syndrome," can affect any species. However, it is most commonly seen in dogs. At the least provocation, the animal becomes agitated and may act brutally and aggressively by biting or clawing. The eyes are dilated, and the posture is anxious and vigilant. Noise can trigger an assault. These animals stop being wary and fearful of other animals. Young puppies are very lively and seek out human company, but they will bite even when petted and turn violent in a matter of hours. Seizures and a lack of muscle coordination are frequent as the condition worsens. Paralysis that worsens over time results in death.

The paralytic form of rabies, sometimes known as "dumb rabies," typically causes paralysis of the jaw and neck muscles, as well as excessive salivation and difficulty swallowing. Lower jaw drooping is a common condition. These creatures may not be aggressive and hardly ever bite. When touching the dog's mouth or administering medication to it with bare hands, people can become infected with this type. Within a few hours, death occurs once the body begins to gradually lose its ability to move [23].

Pathology

Although rabies is lethal and has severe neurologic symptoms, there aren't many or no obvious pathological changes in the central nervous system because of a mild inflammatory response. Peripheral nerves, the spinal cord, and the brain all exhibit degenerating ganglion cells after RABV infection, as well as perineural and perivascular infiltration of mononuclear cells and neuronophagia. Dis-

ease is produced by neuronal degeneration rather than neuronal death, which results in malfunctioning of neurons [24].

An early "axotomy reaction" to infection in gangliocytes is followed by a large number of autophagic compartments. Gangliocytes with advanced stages of degeneration have empty, partially membrane-bound vacuoles [25]. The most obvious inflammation is in the medulla and midbrain. The spinal cord is primarily impacted by rabies in its paralytic form. In the brainstem, hypothalamus, and limbic system, vascular abnormalities such thrombosis and hemorrhages are seen. The layer V cortical pyramidal neurons' axons and dendrites bead and swell as the disease progresses, the axons of the brainstem and the inferior cerebellar peduncle sustain more damage, and the axons of the cerebellar mossy fibers exhibit significant abnormalities. Vacuolations were seen ultra-structurally in axons and pre-synaptic nerve endings, as well as in cortical neurons with swollen mitochondria, the neuropil of the cerebral cortex, and in cortical neurons with axonal swellings. Routine HP investigations fail to reveal these fundamental neuronal abnormalities in RABV-infected neurons [26]. The RABV-infected neurons have intracytoplasmic Negri bodies, which are composed of nucleocapsid aggregates.

Diagnosis

Pre-clinical diagnosis

There are currently no tests that can detect rabies infection as soon as a person is thought to have been exposed to the virus. It becomes easy to diagnose rabies using a variety of diagnostic procedures once clinical signs start to emerge.

Infection with the virus may be indicated by symptoms such as hydrophobia or aerophobia, which are often specific to rabies. However, testing this early does not currently allow for the confirmation of a rabies diagnosis.

It would be possible to test the animal directly for the rabies virus if the suspected case of rabies was brought on by a bite from an animal that is still in the area, as might be the case if the animal was a neighbor's pet, for example. With earlier detection of the presence of the rabies virus, unneeded POST EXPOSURE VACCINE immunizations can be avoided, as well as the potential financial and emotional burden of treatment.

Clinical diagnosis

The incubation period following rabies virus exposure can range from one week to more than a year; nevertheless, the majority of persons start to exhibit symptoms within a few months. When symptoms are present, they could consist of:

- Tingling/Itchiness at the infection site
- Fever
- Hyperactivity and excited behavior
- Aggressiveness
- Hydrophobia
- Photophobia
- Aerophobia

The clinical diagnosis of rabies in humans must be confirmed by a number of tests because a diagnosis based solely on clinical presentation is challenging. Given how difficult it is to diagnose rabies, it is crucial that diagnostic tests deliver quick results that are dependable, sensitive, and specific.

Direct fluorescent antibody test

Since its inception in 1958, the direct fluorescent antibody (DFA) test has been extensively utilized on both humans and animals to identify the antigens of the rabies virus in the brain tissue.

A biopsy of the damaged tissues, such as the brain, is taken as part of the test and submitted to a lab to be checked for the presence of rabies. This is accomplished by applying fluorescently labelled antibodies to the tissue, then observing the fluorescent effect, which enables researchers to visualize and evaluate the outcomes.

Within a few hours, the DFA test is able to deliver quick findings. This test is furthermore accurate and focused on the rabies virus. The DFA test accurately identifies the presence of the illness in 95-99% of cases.

Other diagnostic techniques

The sensitivity and specificity of direct fast immunochemistry (IHC) assays are also considered sufficient. This is a good substitute for DFA testing, especially to increase rabies monitoring in endemic areas.

It is also possible to identify rabies in living people using intravitam methods. It is extremely challenging to get a precise diagnosis of rabies in animals since the sensitivity of tests might vary greatly depending on the infection stage, immune system, and appropriate testing methods. It is possible to detect the presence of rabies using samples of brain tissue, skin tissue, urine, or saliva [27-31].

Differential diagnosis

- Botulism
- Encephalitis
- Guillain-Barre Syndrome
- Herpes Simplex
- Herpes Simplex Encephalitis
- Poliomyelitis
- Tetanus [32].

Management

- Wound treatment: The wound should be thoroughly cleansed as soon as possible after the occurrence by running the water for several minutes and washing with soap or detergent and water. Applying the appropriate disinfectant and treating the wound should be done immediately. Alcohol between 40 and 70 percent, povidone-iodine tincture, or aqueous solution are acceptable disinfectants. Any time saliva comes in contact with mucous membranes like the mouth, nose, or eyes, it is important to immediately wash them thoroughly with clean water. Primary suture might exacerbate the wound's damage and raise the possibility of rabies virus infection of the nerves. It needs to be avoided or delayed until postexposure therapy has started. Sutures (including the infiltration of local anesthetic) should be postponed in patients who require HRIG until HRIG has been infused into the wound [33].
- Vaccination: It might be challenging to decide whether to begin immunizations and may be necessary to seek professional guidance. An evaluation of the risk should consider: The possible rabies exposure's location (country) influences whether the animal is likely to be rabid. If exposure took place in a place where rabies is not present, post-exposure vaccination may not be necessary, magnitude of exposure, clinical characteristics of the animal, its level of immunization, and if it is available for observation or testing (usually only applies to dogs, cats, and ferrets) types of animals (if known). The choice to begin vaccination should be made as soon as possible so that post-exposure vaccination can begin right away and continue while the animal is being watched or while waiting for the results of laboratory testing. Since the bat rabies virus has been found to replicate in epithelial cells, superficial scratches and bites, especially those from bats, should be handled carefully [34]. Even if there is no prior history of animal bites, the discovery of a bat in a room occupied by a child who is unable to credibly describe being bitten may be cause for alarm, especially if the child was asleep. To eliminate any potential interaction, an assessment is necessary. However, the possibility of contracting rabies in humans after being exposed to bats without being bitten or coming into close contact (for instance, a bat flying into a room, being seen by one or more adults, and being safely removed from the area or leaving without coming into contact with anyone) is incredibly slim [35]. Post-exposure vaccination may be started and stopped if the affected dog, cat, or ferret is able to be watched for 10 days and is still healthy at the end of that time. While the majority of nations utilize a five-dose regimen, several have recently switched to the WHO-recommended four-dose regimen, which involves injecting the vaccine intramuscularly at 0.1 mL on days 0, 3, and 7 and 14. Rabies immunoglobulin is advised for both category II and category III exposures under this shortened regimen. A fifth dosage at day 28 is still advised in cases when the immune system is weakened [36]. While significant adverse effects, such as Guillain-Barré syndrome and allergic responses, are uncommon, minor injection site reactions are frequent and more likely to happen after an intradermal immunization [37]. For individuals who are immunocompromised, specialized counsel is required. To determine if an appropriate immune response has been generated following vaccination and whether more boosters are necessary, they may require further observation. Those who have had the first vaccination only need two booster shots, administered intramuscularly on days 0 and 3, or intradermally in four doses in one visit; Rabies immunoglobulin is not necessary [38].
- Rabies immunoglobulin: There are several rabies immunoglobulin preparations on the market, but due to worldwide shortages and expensive prices [39,40], access to them is restricted. At the location of exposure, rabies immunoglobu-

lin delivers passive antibodies. Before patients see an active immune response, it is administered just once, as quickly as feasible, and within seven days of the initial vaccination dosage [41]. The suggested dosage is 20 IU/kg. The entire dose should be given locally near the wound, if at all feasible.

Prevention and control

Renewed surveillance based on laboratory and variant typing is necessary for the prevention and control of rabies. In order to manage potentially exposed animals and help in the detection of new pathogens, precise and timely information and reporting are required. Viral introduction by the admission of infected animals is always a possibility [42]. This aids in explaining disease epidemiology and assessing the need for successful vaccination programs for both domestic and wild animals. All the animals brought in for rabies diagnosis should be recorded and reported, and electronic laboratory reporting and notification of rabies in animals should be implemented in order to evaluate the trends in surveillance. For giving the best information on animals, point location, history of vaccination, RABV variation (if rabid), and exposure to rabid animals are crucial. Standard public health reporting methods must also be incorporated in this regard [43-45]. To determine the precise prevalence of rabies in humans and animals, extensive epidemiological data are required. For the effective management and elimination of this devastating illness, more active partnerships are needed both inside and beyond the nation. The risk to people, domestic animals, and wildlife is dramatically increased by the creation of new RABV variations or the introduction of non-indigenous viruses. The following actions make up a swift and thorough reaction for effective disease management and eradication

- Characterization of the RABV at regional reference laboratory, national and international level.
- Identification and control of the source of entry of virus.
- Enhancement of laboratory-based surveillance in domestic and wild animals.
- Increased rate of vaccination in animals against rabies.
- Restriction of animal movement.
- Control of vector population is required.
- Coordination of a multi-agency response [46].
- Provision for public and professional outreach and education.

Because rabies is a zoonotic disease, proper measures should be followed while treating suspected or confirmed cases. All veterinary staff members must be appropriately safeguarded. The salivary glands, saliva, and central nervous system of affected animals are potential sources of infection [47]. Strict personal hygiene practices and the use of barrier protection while handling bodily fluids, sick animals, and post-mortem specimens greatly reduce the risk of disease transmission. In order to decide whether POST EXPOSURE VACCINE is necessary by observing the possibility of rabies under veterinarian's notice, the proper authorities and all in-contact persons should be taken care of [48]. In order to raise public awareness, mass media campaigns and seminars should emphasize the link between dog meat trade, consumption, and rabies in relation to public health [49]. Dogs being transported should have a sufficient rabies vaccination history that is well-documented.

Complications

- Seizures
- Fasciculations
- Psychosis
- Aphasia
- Autonomic instability
- Paralysis
- Coma
- Death

Conclusion

To understand the role that these animals play in disease transmission, it is still unknown how common rabies is in wild animals. For the purpose of finding newly imported RABV variations, ongoing monitoring of less common non-reservoir species is crucial. Since the RABV as such can spread by saliva contact with both mucous membranes and torn skin, strict barrier precautions must be used. Although it might differ depending on jurisdiction, it is crucial from the veterinarians' perspective that they notify the right authorities along with the proper reporting of the condition. To further reduce the risk of disease spread and raise public awareness of precautions for those living in rural areas and those working in abattoirs, medical and veterinary professionals must be knowledgeable about the path of rabies transmission. It is crucial that everyone who comes into touch with the patient reports to the doctors and prioritizes POST EXPOSURE VACCINE [50].

Bibliography

1. Takayama N. "Clinical feature of human rabies. (In Japanese)". *Nippon Rinsho* 63.12 (2005): 2175-2179.

2. Steele JH and PJ Fernandez. "History of rabies and global aspects. 1- 24, in the natural history of rabies (G. M. Baer, ed.)". CRC Press, Boca Raton, Florida (1991): 620.

3. AWOYOMI O., *et al*. "Socioeconomic factors associated with non-vaccination of dogs against rabies in Ibadan, Nigeria". *Nigerian Veterinary Journal* 28.3 (2007): 59-63.

4. BEARD M. "Woman dies of rabies after Nigerian dog bite". Independent Newspaper, The London (2001).

5. WORLD HEALTH ORGANIZATION. "Expert Consultation on Rabies". *Technical Report Series* 931 (2005): 44.

6. George M Baer. "Commentary on rabies; Defining the rabies problem". *Public Health Reports* 113.3 (1998): 245

7. Blancou J. "History of surveillance and control of transmissible animal diseases". *Paris: Office International des Epizootics* (2003): 193-219.

8. Hanlon C and Childs J. "Epidemiology. In: Jackson A, editor. Rabies scientific basis of the disease and its management". Oxford: Elsevier (2013): 61-122.

9. WHO. "World Health Organization: Rabies, countries or areas at risk". WHO Rabnet/CDC (Data source) and WHO Public Health Information and Geographic Information Systems (Map production). ©World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland (2013).

10. Knobel DL., *et al*. "Reevaluating the burden of rabies in Africa and Asia". *Bulletin of the World Health Organisation* 83 (2005): 360-368.

11. Yousaf MZ., *et al*. "Rabies molecular virology, diagnosis, prevention and treatment". *Virology Journal* 9 (2012): 50.

12. Dutta JK and Dutta TK. "Rabies in endemic countries". *The British Medical Journal* 308 (1994): 488-489.

13. Meslin FX. "Rabies as a traveler's risk, especially in high endemicity areas". *Journal of Travel Medicine* 12.1 (2005): S30-S40.

14. Mudur G. "Foreign visitors to India are unaware of rabies risk". *The British Medical Journal* 331 (2005): 255.

15. Castrodale L., *et al*. "Rabies in a puppy imported from India to the USA, March 2007". *Zoonoses Public Health* 55.8-10 (2008): 427-430.

16. McKay N and Wallis I. "Rabies: a review of UK management". *Emergency Medicine Journal* 22 (2005): 316-321.

17. Pounder D. "Bat rabies". *The BMJ* 326.7392 (2003): 726.

18. Fooks AR., *et al*. "Intracerebral delivery of small interfering RNAs (siRNAs) using adenoviral vector protects mice against lethal peripheral rabies challenge". *Virus Research* 163.1 (2007): 11-18.

19. Hampson K., *et al*. "Estimating the global burden of endemic canine rabies". *PLOS Neglected Tropical Diseases* 9.4 (2015): e0003709.

20. De Benedictis P., *et al*. "Phylogenetic analysis of rabies viruses from Burkina Faso, 2007". *Zoonoses Public Health* 57.7-8 (2010): e42-e46.

21. Nguyen AK., *et al*. "Molecular epidemiology of rabies virus in Vietnam (2006-2009)". *Japanese Journal of Infectious Diseases* 64.5 (2011): 391-396.

22. Greene CE., *et al*. "Infectious Diseases of the Dog and Cat". W. B. Saunders Company, Philadelphia (1990): 365-383.

23. Centers for Disease Control and Prevention. "Rabies Prevention-United States, Recommendations of the Immunizations Practices Advisory Committee (ACIP)". *Morbidity and Mortality Weekly Report* 40.3 (1991): 1-19.

24. Jackson AC. Pathogenesis. In: Jackson AC, Wunner WH, editors. "Rabies". 2nd edition. London: Elsevier Academic Press (2007b): 341-381.

25. Rossiter JP., *et al*. "Selective vulnerability of dorsal root ganglia neurons in experimental rabies after peripheral inoculation of CVS-11 in adult mice". *Acta Neuropathologica* 118.2 (2009): 249-259.

26. Jackson AC. "Rabies pathogenesis update". *Rev PanAmaz Saude* 1.1 (2010): 167-172.

27. http://www.ncbi.nlm.nih.gov/pubmed/16878462

28. http://www.who.int/mediacentre/factsheets/fs099/en/

29. http://www.who.int/rabies/home_diagnosis/en/

30. http://www.nhs.uk/Conditions/Rabies/Pages/Introduction.aspx

31. http://www.who.int/rabies/human/antigendetection/en/

32. https://emedicine.medscape.com/article/220967-differential

33. Wilde H., *et al*. "Failure of postexposure treatment of rabies in children". *Clinical Infectious Diseases* 22 (1996): 228-232.

34. Morimoto K., *et al*. "Characterization of a unique variant of bat rabies virus responsible for newly emerging human cases in North America". *Proceedings of the National Academy of Sciences of the United States of America* 93 (1996): 5653-5658.

35. De Serres G., *et al*. "Bats in the bedroom, bats in the belfry: reanalysis of the rationale for rabies postexposure prophylaxis". *Clinical Infectious Diseases* 48 (2009): 1493-1499.

36. Rupprecht CE., *et al*. "Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the advisory committee on immunization practices". *Morbidity and Mortality Weekly Report* 59. RR-2 (2010): 1-9.

37. Bernard KW., *et al*. "Neuroparalytic illness and human diploid cell rabies vaccine". *JAMA* 248 (1982): 3136-3138.

38. World Health Organization. "WHO expert consultation on rabies: second report". WHO Press (2013).

39. Knobel DL., *et al*. "Re-evaluating the burden of rabies in Africa and Asia". *Bulletin of the World Health Organization* 83 (2005): 360-368.

40. Sudarshan MK., *et al*. "An epidemiological study of animal bites in India: results of a WHO sponsored national multi-centric rabies survey". *Journal of Communicable Diseases* 38 (2006): 32-39.

41. Castrodale L., *et al*. "Rabies in a puppy imported from India to the USA, March 2007". *Zoonoses Public Health* 55 (8-10): 427-430.

42. Blanton JD., *et al*. "Rabies surveillance in the United States during 2008". *Journal of the American Veterinary Medical Association* 235.6 (2008): 676-689.

43. Deb R., *et al*. "Infectious diseases of cattle". New Delhi: Satish Serial Publishing House (2012): 224.

44. Fisman DN. "Taking the bite out of rabies, putting teeth into one health". *Annals of Internal Medicine* 160.2 (2012): 132-133.

45. Seneschall C and Luna-Farro M. "Controlling rabies through a multidisciplinary, public health system in Trujillo, La Libertad, Peru". *Pathogens and Global Health* 107.7 (2013): 361-366.

46. Weese JS. "A review of equine zoonotic diseases: risks in veterinary medicine". *Proceedings Annual Convention AAEP* 48 (2002): 362-369.

47. Beran GW. "Zoonoses in practice". *Veterinary Clinics of North America: Small Animal Practice* 23 (1993): 1085-1097.

48. Dzikwi AA., *et al*. "Knowledge, attitude and practice about rabies among children receiving formal and informal education in Samaru, Zaria, Nigeria". *Global Journal of Health Science* 4.5 (2012): 132-139.

49. CDC. "Investigation of rabies infections in organ donor and transplant recipients - Alabama, Arkansas, Oklahoma, and Texas, 2004". *Morbidity and Mortality Weekly Report* 53 (2004): 1-3.

50. Rajendra Singh., *et al*. "Rabies - epidemiology, pathogenesis, public health concerns and advances in diagnosis and control: a comprehensive review". *Veterinary Quarterly* 37.1 (2017): 212-251.