International Journal of Basic and Applied Virology 12(2): 15-22, 2023
ISSN 2222-1298

DOI: 10.5829/idosi.ijbav.2023.15.22

Rabies Disease and Its Prevention and Control Strategies: A Review

Demirew Kidanemariam Gebrekiros

Ethiopia Agricultural Authority, Modjo Export Abattoir, Modjo, Ethiopia

Abstract: The rabies is an infectious disease, which defects the brain caused by the virus known as lyssavirus belonging to the family *Rhabdoviridae*. It is a semi-zoonotic acute disease because the rabid animal dies after illness. It is transmitted by all homoeothermic animals and the virus is secreted in the saliva of an infected animal. However, dogs are considered as high risk while in America, bat bites are also the cause of the spread of rabies. The incubation period of this disease is approximately up to six months long or in some cases; it is short up to just four days. Symptoms are produced after the completion of the incubation period. The virus gets entrance in the brain and causes damage there, after that it moves toward the salivary gland in order to transmit to other animals while biting or due to contamination of the saliva of an infected animal. The clinical signs and symptoms of this disease could be confused with some other diseases such as polio, tetanus and botulism. Hence, confirmatory diagnosis is done by using techniques including polymerase chain reaction, direct fluorescent antibody test and mouse inoculation technique. This paper reviews the transmission, pathogenesis, treatment, prevention and control of rabies since it is a highly fatal disease so preventive measures could be taken to fight against this infection.

Key words: Control · Rabies · Review · Prevention · Treatment

INTRODUCTION

Rabies is a deadly disease caused by a virus. It is the most severe zoonotic disease caused by harmful-RNAviruses from the Lyssavirus genus large-scale, Genetic variants of the genotype 1 Lyssavirus (The cause of classical rabies) are maintained in different parts of the world by different reservoir hosts within 'Host-adaptivelandscapes' [1]. The rabies virus is released in the saliva of an infected animal. The animal usually contracts rabies from the bite of an infected animal. The virus may also enter the body if the mucous membranes (the wet part of the eyes, nose, or mouth) or a scratch or break in the skin have contact with saliva containing the rabies virus. Once the rabies virus enters the body, it begins to multiply in the area near the entry site. If the infection is not stopped at this point, the virus will eventually invade the nerve cells in the area. Once the virus is in nerve tissue, it travels along the nerve to the center of multiplication (the brain). The virus may then spread to the salivary glands or other parts of the body. This incubation period lasts a varying amount of time; it can range from days to years, but the average length is 3-8 weeks [1].

In 1998, more than 33,000 people died worldwide because of rabies [1]. Most of those deaths occurred in tropical developing countries [2]. Canine rabies and hence human exposure can be controlled by intervening in the animal reservoir [3]. The domestic dog is the most important vector of human exposure [4]. Annual reports of the Ethiopian Health and Nutrition Research Institute indicated a total of 488 human deaths that occurred in 1964 and 1975 [5].

Empirical observation and models of the transmission of canine rabies indicate that rabies can be eradicated if 70% of the dog population is vaccinated repeatedly to achieve herd immunity [6, 7].

Stray dogs that are not accessible to mass vaccination can reduce the coverage achievement. Oral vaccines that could reach ownerless dogs are not yet on the market [8]. Non-selective elimination of stray dogs to reduce the reservoir population is no longer recommended as a strategy against rabies by WHO [9], since it increases population turnover and decreases herd immunity [10], while public opposition to dog removal can lead to the failure of rabies control programs [11]. In Ethiopia domestic dogs are the principal reservoir of rabies [12]. Studies on dog ownership pattern and awareness of

Corresponding Author: Demirew Kidanemariam Gebrekiros, Ethiopia Agricultural Authority, Modjo Export Abattoir, Modjo, Ethiopia.

rabies in Addis Ababa showed that 90.7% of the dog owners manage dogs for the safeguarding of their properties from theft out of which 52% of them are without regular vaccination [13]. World human mortality from endemic canine rabies was estimated to be 55 000 [14]. Though, rabies is one of the vaccine-preventable diseases, it is practically difficult and irreversible for medical treatment after the onset of clinical manifestation of the disease. In spite of the availability of safe and effective preventive tools in global market, the burden of the disease could not be reduced in developing countries [1].

Because of growing dog and human populations, the burden of human deaths from rabies and the economic costs will continue to escalate in the absence of concerted efforts and investment for control. As countries strive to reduce the number of human deaths and improve the availability of post-exposure prophylaxis, the costs will rise; however, if dog rabies control and ultimately elimination are achieved by mass dog vaccination, both the demand for post-exposure prophylaxis and the costs decline. National vaccination programs have widespread health benefits, particularly for the poorest communities in the world but it needs consistent and sustained commitment [15].

Despite being a preventable disease, rabies is continuing to cause immense human and animal death, claiming tens of thousands of human life and countless animal lives every year as well as significant economic loss mainly in developing countries including our country. This situation is related to the challenges in controlling rabies due to the wide host range and worldwide distribution, availability of many free-roaming dogs, limited access to control and lack of public and legislative awareness about the disease. With regard to the disease, limited investigations and researches are done which have no uniformity in their coverage and there is inadequate intersectoral collaboration on taking necessary measures to prevent and control rabies [16].

Therefore, the objectives of this paper were to review:

- To discuss the epidemiology, transmission, pathology, clinical manifestations, diagnosis, pathology, clinical manifestations, diagnosis, treatment and control of rabies infection.
- To discuss the recent strategies that are important to implement efficient control and eradication measures against rabies.

Rabies Disease

Aetiology: The causes of rabies are RNA viruses belonging to the genus *lyssavirus* within the family *Rhabdoviridae*, order *Mononegavirales* [17]. The genus includes the classical rabies virus (genotype 1) and six so-called rabies-related viruses, *Lagos* bat virus (genotype 2), *Mokola virus* (genotype 3), *Duvenhage* virus (genotype 4), European bat *lyssaviruses* 1 and 2 (genotypes 5 and 6) and the recently discovered Australian bat genotype 7. Each of these viruses is considered capable of causing rabies like disease in animals and humans [18].

Rabies virus (RABV) is the species which is responsible for most cases in human beings and animals [17]. The rabies virus transmembrane glycoprotein is involved in tropism and pathogenicity. It is the main protecting antigen, inducing a complete immune response with the production of virus neutralizing antibodies. Rabies virus is very sensitive to some environmental factors and is rapidly destroyed by direct sunlight, ultraviolet irradiation and heat at 60% for five minutes, lipid solvent (70% alcohol and ether), sodium deoxycholate, trypsin and common detergents [16].

Epidemiology

Distribution: Reservoirs of rabies vary throughout the world. Canine rabies is dominant in Africa, Asia, Latin America and the Middle East. In North America and Europe, canine rabies has been practically eliminated; rabies is maintained in wild life [19]. Some countries such as the United Kingdom, Ireland, Sweden, Norway, Iceland, Japan, Australia, New Zealand, Singapore, most of Malaysia, Papua New Guinea, the Pacific Islands and some Indonesian islands have been free of this virus for many years [20]. It has been reported that 98% of human rabies cases occurred in the developing countries of Asia, Africa and Latin America [21].

Host Range and Species Variations: All mammals are susceptible to rabies, but only a limited number of species also act as reservoir hosts [20]. Cattle with furious rabies can be dangerous, attacking and pursuing humans and other animals. Horses and mules frequently show evidences of distress and extreme agitation. Rabid foxes and coyotes often invade yards or even houses, attacking dogs and people [19].

Source of Infection and Transmission: The source of infection includes members of the families Canidae (dogs, jackals, coyotes, wolves, foxes and raccoon dogs), Mustelidae (e.g., skunks), Viverridae (e.g., mongooses) and Procyonidae (raccoons) and the order Chiroptera (bats). In Africa, evidence indicates that the primary rabies virus maintenance cycle is among domestic dogs although other carnivores maybe involved as non-maintenance population [22].

A rabies exposure is any bite, scratch, or other situation in which saliva, cerebral spinal fluid, tears, or nervous tissue from a suspect or known rabid animal or person enters an open wound or comes in contact with mucous membranes of another animal or person [23]. This mechanism enables the virus to transverse the dermal barrier and deposit the virus into tissues in which it can initiate infection [24].

The incubation period is both prolonged and variable. Typically, the virus remains at the inoculation site for a considerable time. The unusual length of the incubation period helps to explain the effective action of local infiltration of rabies immunoglobulin during human post-exposure prophylaxis, even days after exposure. Rabies has been transmitted by transplantation of tissues and organs from infected people [25].

Pathogenesis: The lyssavirus enters the body via abrasions or by direct in touch with mucosal membranes. It is not able to intersect undamaged skin. The rabies virus replicates inside the bitten muscle tissue and then it achieves entry towards the central nervous system [26]. The virions are passed in carrying vesicles [27] and move to the central nervous system (CNS) completely via rapid retrograde transport beside motor axons, by means of no uptake through sensory or sympathetic endings [28]. The entrance of virus inside tissues of the brain leads to death, usually through respiratory dysfunction and secondary metabolic and circulatory defects [29, 30].

Clinical Signs: It is investigated that as the disease becomes advanced, the animal shows strange behavior. Every verified suspicion of rabies must be established by the confirmatory report of laboratory test [31]. The primary clinical signs are frequently non-specific and can comprise anxiety, restiveness, anorexia or an improved appetite, nausea, diarrhea, a minor fever, dilation of the pupils, hyperactivity to any stimuli in addition to extreme salivation. The initial sign of post-vaccinal rabies is generally lameness in the vaccinated limb. The animals regularly comprise behaviorally and personality changes and might turn into either curiously aggressive or uncharacteristically dedicated [32].

Prodromal Stage: Following a definite incubation phase, the beginning of clinical symptoms starts. During this first stage which typically ends within 1-3 days, slight behavioral modification may occur, *i.e.* anger in domestic animals, daytime tricks in nocturnal animals, no fright of humans in the wild animals or else irregularities in the appetite [33].

Excitement (Furious) Phase: The furious type is described via agitation, wandering, weeping, polypnea, drooling and attacks upon other animals, community or unresponsive objects. Infected animals frequently ingest foreign items for instance firewood and gravel. The wild animals often drop their fright of humans and may harass humans or other surrounding animals that they would usually avoid (*e.g.,* porcupines). On the other hand, the nocturnal animals may be observable throughout the day. In cattle, strange attentiveness can be an indication of this phase [32].

Paralytic (Dumb) Phase: The "dumb" type of rabies is usually characterized by progressive paralysis. In this phase, the gullet and masseter muscles turn paralyzed; the animal might be incapable of swallowing and salivating abundantly. There may be a change in the voice of the infected animal due to laryngeal paralysis, including atypical bellowing in cattle and barking in dogs. In addition to that, there might be facial paralysis along with a dropping of the lower jaw. Ruminants may become isolated from the herd [34]. Furthermore, this stage is also characterized by the dropping of foamy salivary secretion and paralysis of hind limbs eventually leading complete paralysis followed by death [33]

Hydrophobia: The term stands for the fright of water is the historic synonym of rabies [35]. This condition refers to a collection of warning signs during the advanced phases of an infection in which the patients have obscurity in swallowing and taking water. Any mammal infected by the virus may reveal hydrophobia. In this condition, there is overproduction of saliva and the animal struggles to drink and could suffer from painful spasms of the muscular tissues within the throat as well as in the vocal cord. The virus remains in saliva and is spread due to the bite of a rabid animal [36].

Table 1: The diagnostic techniques for rabies disease

Techniques	Sample	Benefits/ disadvantages
Polymerase Chain Reaction (PCR)	Body fluids, saliva, Urine, cerebrospinal fluid	Applicable in all tissue conditions but, requires experienced technicians
Mouse Inoculation Technique (MIT)	Liver, brain, salivary glands, spleen and pancreas are the most appropriate sample	In this technique only fresh tissue is used for an accurate result
Direct Fluorescent Antibody Technique (DFA)	Similar to MIT	Applicable with most tissue sources. Not applicable in decomposed tissues.

Source: Yousaf *et al*. [39]

Diagnosis: This disease can only be identified following the onset of the symptoms [33]. The diagnosis of rabies is carried out either *in vivo* or through autopsy [37]. The lyssavirus infection is not easy to diagnose via ante-mortem. While the hydrophobia is extremely suggestive, furthermore no medical signs of infection are pathognomonic for this disease. The historical reliance resting on the finding of accumulated Negri-bodies is no longer considered appropriate in support of the diagnostic evaluation, since of short sensitivity and alternative some laboratory- based tests have been developed for confirmation of infection [38]. The diagnosis of rabies virus is made by taking some part of tissue from the brain of the suspected animal. But mostly for confirmatory diagnosis samples from the brain stem and cerebellum are taken [39]. Brain smears are utilized for the human discovery of virus antigens by means of the fluorescent antibody test (FAT), designed mutually for human as well as for animal samples. In most animals, the direct FAT is suggested as a confirmatory diagnostic test. Other methods for the detection of this virus are mentioned in Table 1.

Prognosis: In non-vaccinated humans, rabies is constantly deadly following neurological warning signs developed. The vaccination following experience, post-exposure prophylaxis (PEP), is extremely victorious for the prevention of the disease if introduced within 6 days of illness. In the case of the major hindrance in the control of PEP, the treatment still has a possibility of victory [36].

Treatment: Just the once rabies warning signs have appeared, the treatment is generally supportive. The patients are sedated to manage their fear and pain. The basis of treatment is serious care support, counting paralysis, sedation, as well as ventilation. Ketamine is mostly suggested as a suitable mediator for these conditions [40]. Lyssavirus is simply inactivated by the sunshine and soap, in addition to aeration. The wound concern is essential for the hindrance of rabies infectivity. Among the investigational animals, rabies spread could nearly wholly have been prohibited via general wound treatment provided during the first 3 hours following disclosure of the virus [41]. The injured area should be rinsed carefully with antiseptic soap and water. After that povidone-iodine or alcohol should be applied in order to reduce the virus further [42].

Prevention and Control of Rabies: The vaccine against rabies was invented in 1885 by Louis Pasteur along with Emile Roux, prior to which nearly all human cases of rabies were lethal. The creative vaccine was produced by infected rabbits. In this procedure, the virus in the nervous tissue of rabbits was damaged by permitting it to dehydrate for about approximately five to ten days [43]. Furthermore, the human diploid cell rabies vaccine was discovered in 1967. While nowadays chicken embryo cell vaccines are available which are chea [44]. Another recombinant vaccine known as Raboral V-RG is in use within France, Belgium, Germany, in addition to the United States to avoid outbreaks in wild animals [45]. Human rabies can be stopped by supplying suitable rabies pre-exposure prophylaxis and timely local treatment of infected lesions combined in the company of proper rabies post-revelation prophylaxis [46]. The non-activated man vaccines are presented for veterinary workers, animal trainers, wildlife representatives, laboratory employees and others which are at higher risk of exposure [31].

Prevention and Control of Rabies in Animals

Vaccination of Domestic Animals: Rabies can be prevented in domesticated animals by vaccination and by the avoidance of contact with rabid wild animals. Vaccinating domestic dogs can substantially reduce the numbers of canine rabies and, most importantly, human rabies cases [25]. The most practical and cost-effective way to end canine rabies is mass dog vaccination, which saves the lives of both dogs and humans. In addition, farm livestock in endemic areas where clinical cases of rabies occur commonly should be vaccinated [31].

Removal of Stray Animals: Stray dogs are a health hazard in many countries, not only to people (with dog bites responsible for a large proportion of human infections, especially in children) but also to domestic and wild animals. They pose an animal welfare problem too. With no owners, it is hard to gain access to stray dogs to conduct parenteral vaccination [47].

Stray dogs, cats and ferrets should be removed from the community. Local health departments and animal control officials can enforce the removal of strays more effectively if owned animals are required to have identification and are confined or kept on leash. Strays should be impounded for at least three business days to determine if human exposure has occurred and to give owners sufficient time to reclaim animals [48].

Controlling Rabies in Wild Life: Rabies virus is maintained in populations of wild animals and occasionally spills over into domestic animals and humans. Immunization of wildlife by widespread distribution of vaccine-impregnated oral baits has shown variable success in arresting the propagation of rabies in raccoons and coyotes [49].

Quarantine and Movement Control: When there are reasonable groups of infected animals, they should be detained and isolated. Isolation of susceptible animals is possible by classical procedures of veterinary control which include quarantine measures, restriction of movement such as prohibition of free movement outside houses and farms, leashing, muzzling and surveillance of animals into and out of infected areas. The availability of secure accommodation for a period of up to six months is a factor in deciding whether to detain or destroy suspects. If rabies is confirmed in an animal in quarantine, any animals kept in close proximity to the rabid animal and animals released within the previous 15 days would need to be recalled. Such animals, if previously vaccinated for rabies, should be serologically tested for rabies antibodies. Dogs and cats entering from abroad will be quarantined and finally vaccinated before being released unless they are accompanied by valid vaccination certificates [50].

Isolation of Animals Exposed to Rabies and Euthanizing Them: Dogs, cats and ferrets that bite a human or another dog, cat, or ferret are subject to isolation and observation, or euthanasia and testing [49]. Unvaccinated dogs and cats exposed to rabid animals should be euthanized immediately. If the owner is unwilling to have this done, the animal should be placed in strict isolation for 6 months and vaccinated 1 month before being released [51].

Biosecurity: The most effective method of preventing the entry of rabies into a country free of the disease is the imposition of a quarantine period of 4-6 months on all imported dogs. This system has successfully prevented the entry of the disease in to island countries but has obvious limitations in countries that have land borders [52].

Pre-Exposure Vaccination in Animals: A number of recently developed, highly effective, thermo-stable, inactivated vaccines are available for veterinary use. The duration of immunity conferred varies from one to three years. Most veterinary vaccines are only registered for use in specific species, for example, dogs. All rabies vaccines registered for human and animal use must conform to established potency standards. Revaccination must be carried out every three years thereafter. Cattle and sheep may be vaccinated annually or every two to three years, depending on the vaccine manufacturer's instructions. Following an outbreak in domestic livestock, vaccination of animals without visible bite wounds is strongly recommended. All dogs and cats should be revaccinated 12 months after the initial vaccination regardless of the length of immunity period of the initial vaccine. Obtaining a booster vaccination immediately following exposure to a rabid animal is important to ensure adequate protection against the virus [53].

Post-Exposure Prophylaxis in Animals: A 5 doses of canine rabies vaccine administered on days 0, 3, 14, 21 and 35 along with murine anti-rabies antibody on day 0 may be effective in protecting a previously unvaccinated animal exposed to rabies. Regardless of the age of the animal at initial vaccination, a booster vaccination should be administered 1 year later. If signs suggestive of rabies develop (e.g., paralysis, seizures, etc.), the animal should be euthanized and the head shipped for testing [54].

Prevention and Controls of Rabies in Humans: To provide timely access to appropriate Post Exposure Treatment (Wound cleaning, vaccination and rabies immunoglobulin) to all human cases of dog bites suspected to be rabid; To increase knowledge and skills among animal and human health workers on rabies in general and post-exposure management [50].

Strategies for the prevention of human rabies are aimed at protecting those at highest risk of exposure, post exposure treatment and supportive management for the clinically ill. Specific activities will include

Early and Appropriate Post-exposure Treatment:

- Local treatment of wounds; reducing the rabies virus at the site of bite by washing the wound using of soap and water for 15 minutes.
- Rabies Immunoglobulin (RIG); the anti-rabies immunoglobulin provides passive immunity before vaccine takes effect.
- Human anti- rabies vaccines; use of the cell culture vaccines based on the management guidelines will be enhanced.

CONCLUSION AND RECOMMENDATIONS

The rabies is a viral disease which is fatal in nature, among unvaccinated human as well in animals. It can be controlled by proper awareness and immunization against the lyssavirus in both farm animals as well as pets. Rabies can be prevented by avoiding direct contact with the rabid animal, its mucous membranes and wounds and by giving proper training to wildlife workers, veterinarians, animal handlers and laboratory workers because prevention is better than cure. Adequate and appropriate strategies which are based on, One Health approach are necessary in order to implement efficient control and eradication measures against rabies endemic, especially in developing countries.

Based on the above conclusion, the following recommendations are given:

- Strict control of free-ranging dogs and mandatory rabies vaccination should be enforced.
- Establishing national animal rabies surveillance network is imperative.
- Post exposure prophylaxis should be decided to initiate or withhold according to postmortem diagnosis of the biting animal.
- Immediate washing of the wound with soap and water, application of human anti-rabies immunoglobulin and administration of tissue-culture rabies vaccine at 0, 3, 7, 14, 30 and 90 days after exposure.
- To reduce risk for emerging zoonoses, the public should be educated about the risks associated with related to wild and domestic animals and proper surveillance systems should be implemented.

REFERENCES

1. World survey of rabies No. 34 for the year, 1998. Geneva: WHO document; Available from: URL: http//whqlibdoc.who.int/hq/199/who_CDC_CSR_APH_99.6.pdf.
2. Warrel, D.A. and MJ. Warrel, 1995. Human rabies: A continuing challenge in the tropical world. Schweizenishe Wochenschnft, 125: 879-85.
3. Cleaveland, S., E.M. Feire, M. Kaare and P.G. Coleman, 2002. Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries. Bulletin of the WHO, 80: 304-10.
4. Wandeler, A.l., H.C. Matter, A. Kappeler and A. Budde, 1993. The ecology of dogs and canine rabies: a selective review Soentifique et Technique Office International des Epizooties, 12: 51-57.
5. Mebatsion, T., J.H. Cox and J.W. Frost, 1992. Isolation and characterization of 115 street rabies virus isolated from Ethiopia by using monoclonal antibodies: identification of 2 isolates Mokola and Lagos bat virus. J. Infectious Diseases, 166: 972-77.
6. WHO, 1987. Guidelines for dog rabies control. Geneva: World Health Organization; WHO documentVPH/ 83.43: Rev.1.
7. Coleman, P.G. and C. Dye, 1996. Immunization coverage required to prevent outbreaks of dog rabies. Vaccine, 14: 185-6.
8. WHO, 1998. Oral immunization of dogs against rabies. Report of the South WHO Consultation, Geneva, 24 25 July 1995. Geneva: World Health Organization, WHO document.
9. Bogel, K., 1987. Guidelines for Dog Rabies control. Geneva: WHO; June.
10. Matter, H.C., H. Kharmach, N. Haddad, S.C. Ben Youssef and R. Ben Khelifa, 1995. Test on three bait types for oral immunizationof dogs against rabies in Tunsia. American Journal of Tropical Medicine and Hygiene, 52: 489-95.
11. Beran, G.W., 1991. Urban rabies. In: Baer GM, editor. The natural history of rabies. Boca Racon (FL): CRC press, pp: 428-43.
12. Yimer, E., B. Neway, T. Girma, Y. Mekonnen, B. Yoseph, Z. Badeg, B.Mekoro and B. Abebe, 2002. Situation of rabies in Ethiopia: a retrospective study 1990-2000. Ethiop J. Health Dev., 16(1): 105-112.
13. EHNRI, 1997. Zoonoses and anti-rabies vaccine production annual report 1997. Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia.

14. Fekadu, M., 1997. Human rabies surveillance and control in Ethiopia. In: Proceedings of the Southern and Eastern Africa Rabies Group Meeting Nairobi, Kenya 4-6 March.
15. WHO, 2013. World Health Organization Expert Consultation on Rabies. Second report: Technical Report Series 982. Geneva, Switzerland, pp: 8-67.
16. Finnegan, C., S. Brookes and A. Fooks, 2002. Rabies in North America and Europe. J. R. Soc. Med., 95: 9-13.
17. Johnson, N., A. Vos, C. Freuling, N. Tordo, A. Fooks and T. Muller, 2010. Human rabies due to lyssa virus infection of bat origin. Veterinary Microbiology, 142: 151-59.
18. Warrell, M., 2001. Rabies encephalitis and its prophylaxis. Practical Neurology, 1: 14-29.
19. Kahin, 2005. The Merck Veterinary Manual. 9 ed. Merck & Co; INC. White house Station, N.J., USA, pp: 1067-1071.
20. OIE, 2008. Manual of diagnostic tests and vaccines for terrestrial animals, Rabies.
21. Dacheux, L., O. Delmas and H. Bourhy, 2012. Human rabies encephalitis prevention and treatment. Progress since Pasteur's Discovery Biologicals, 40: 61.
22. Eyob A., W. Beruktayet, N. Ayalew and D. Yetayew, 2016. Assessment of the Knowledge, Attitude and Practices of Rabies in Arada Sub City Addis Ababa, Ethiopia. Intl. J. Basic & Appl. Virol., 4(2): 41-52, 20155(2): 14-19.
23. Permpalung, N., S. Wongrakpanich, S. Korpaisarn, P. Tanratana and J. Angsanakul, 2013. Trend of human rabies prophylaxis in developing countries toward optimal rabies immunization. Vaccine, 31: 4079-4083.
24. Belotto, A., C. Leanes, M. Schneider, H. Tamayo and E. Correa, 2005. Overview of rabies in the Americas. Virus Res., 111: 5-12.
25. Kumar, P., S. Ganguly, R. Wakchaure, P. Par, K. Qadri, T. Mahajan, N. Dalai and S. Shekhar, 2015. Rabies, its Zoonotic Threat and Strategies for Adoption towards Public Health Welfare: A Review. Int. J. Phar. & Biomedi. Rese., 2(6): 26-29.
26. Ugolini, G., 2007. Use of rabies virus as a transneuronal tracer of neuronal connections: implications for the understanding of rabies pathogenesis. Develop. Biologic., 131: 493-506.
27. Klingen, Y., K.K. Conzelmann and S. Finke, 2008. Double-labelled rabies virus: live tracking of enveloped virus transport. J. Virol., 82(1): 237-245.
28. Hemachudha, T., G. Ugolini, S. Wacharapluesadee, W. Sungkarat, S. Shuangshoti and J. Laothamatas, 2013. Human rabies: neuropathogenesis, diagnosis and management. Lancet Neurol., 12(5): 498-513.
29. Bishop, G.C., D.N. Durrheim, P.E. Kloeck, J.D. Godlonton, J. Bingham and R. Speare, 2003. Rabies guide for the medical, veterinary and allied professions. Rabies Advisory Group, South African Department of Agriculture and Health, Pretoria.
30. Shite, A., T. Guadu and B. Admassu, 2015. Challenges of Rabies. International Journal of Basic and Applied Virology, 4(2): 41-52.
31. Chernet, B. and A. Nejash, 2016. Review of rabies preventions and control. Int. J. Life Sci., 4(2): 293-301.
32. Banyard, A.C., D.L. Horton, C. Freuling, T. Müller and A.R. Fooks, 2013. Control and prevention of canine rabies: the need for building laboratory-based surveillance capacity. Antivir. Res., 98(3): 357-364.
33. WHO, 2013. World Health Organization Expert consultation on rabies, 2nd Report (No. 982).
34. Yang, D.K., E.K. Shin, Y.I. Oh, K.W. Lee, C.S. Lee, S.Y. Kim, J.A. Lee and J.Y. Song, 2012. Comparison of four diagnostic methods for detecting rabies viruses circulating in Korea. J. Vet. Sci., 13(1): 43-48.
35. Smallman-Raynor, A. Cliff, P. Haggett and Matthew, 2004. World atlas of epidemic diseases. Arnold, London, pp: 51.
36. Mustafa, M., E.M. Ellzam, A.M. Sharifa, M.S. Rahman, M.M. Sien and M.K. Nang, 2015. Rabies a zoonotic disease, transmission, prevention and treatment. J. Dent. Med. Sci., 14(10): 82-87.
37. Consales, C.A. and V.L. Bolzan, 2007. Rabies review: immunopathology, clinical aspects and treatment. J. Venomous Anim. Toxins Trop. Dis., 13(1): 5-38.
38. Abera, E., A. Assefa, S. Belete and N. Mekonen, 2015. Review on Rabies, with Emphasis on Disease Control and Eradication Measures. International Journal of Basic and Applied Virology, 4(2): 60-70.
39. Yousaf, M.Z., M. Qasim, S. Zia, U.A. Ashfaq and S. Khan, 2012. Rabies molecular virology, diagnosis, prevention and treatment. Virol. J., 9(1): 1.
40. Jackson, A.C., M.J. Warrell and C.E. Rupprecht, 2003. Management of rabies in humans. Clin. Infect. Dis., 36: 60-63.

41. Dean, D.J., G.M. Baer and W.R. Thompson, 1963. Studies on the local treatment of rabies-infected wounds. Bull. World Health Org., 28(4): 477.
42. Gautret, P., J. Blanton, L. Dacheux, F. Ribadeau-Dumas, P. Brouqui, P. Parola, D.H. Esposito and H. Bourhy, 2014. Rabies in nonhuman primates and potential for transmission to humans: a literature review and examination of selected French national data. PLoS Negl. Trop. Dis., 8(5): e2863.
43. Geison, G.L., 1978. Pasteur's work on rabies: Reexamining the ethical issues. Hasting Center Rep., 8(2): 26-33.
44. Ly, S., P. Buchy and N.Y. Heng, 2009. Rabies situation in Cambodia. PLoS Negl. Trop. Dis., 3(9): e511.
45. Reece, J.F. and S.K. Chawla, 2006. Control of rabies in Jaipur. India by the sterilisation.
46. Tojinbara, K., K. Sugiura, A. Yamada, I. Kakitani and N.C. Kwan, 2016. Estimating the probability distribution of the incubation period for rabies using data from the 1948-1954 rabies epidemic in Tokyo. Prev. Vet. Med., 123: 102-105.
47. Pastoret, P., S. Van, N. Gucht and B. Brochier, 2014. Eradicating rabies at source. Rev. Sci. tech. off. Int. Epiz., 33(2): 509-516.
48. Petros, A. and M. Yalemtsehay, 2014. Rabies and its Folk Drugs Remedies in Ethiopia: A Review, International Journal of Basic and Applied Virology, 3(2): 22-27.
49. Nibret, M., 2015, Epidemiology, Prevention and Control Methods of Human Rabies: Review Article, Intl. J. Basic & Appl. Virol., 4(1): 22-27.
50. Centers for Disease Control and Prevention (CDC), 2011. Rabies. OIE Terrestrial Manual Report, pp: 1-20.
51. Centers for Disease Control and Prevention (CDC), 2001. Compendium of Animal Rabies Prevention and Control, National Association of state public veterinarians. Morbid. Mortal Weekly Rep, pp: 1-7.
52. Radostits, O.M., C.C. Gay, K.W. Hincheliff and P.D. Constable, 2007. Diseases associated with viruses and chlamydia: Veterinary Medicine, a Textbook of the disease of Cattle, Sheep, Pigs, Goats and Horses. 10 ed. London: Saunders Elsevier Published Ltd, pp: 1384-1387.
53. Murray, K., K. Holmes and C. Hanlon, 2009. Rabies in vaccinated dogs and cats in the United States. Javma., 235: 691-95.
54. Asefa, D., P. Mahendra, M. Hailu, H. Abraham and D. Ritwik, 2015. Rabies: A major fatal viral disease of humans and animals in Ethiopia. Journal of Natural History, 11(2): 19-25.