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An update on fatal zoonosis, rabies: Prevention, issues and approaches

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Abstract
Rabies is a fatal but preventable zoonosis occurs in most parts of the world resulting in loss of thousands of lives. Most deaths occur in developing countries due to lack of awareness regarding the cause, vector, pre-exposure and post exposure prophylaxis. This article represents some common questions about rabies and its occurrence, mortality, trending diagnosis, treatment and prevention as elimination of rabies throughout the world would save thousands of lives and would reduce the economic impact of the disease by reducing the requirement for pre and post exposure prophylaxis.

Keywords: Rabies, zoonosis, negribodies, dFAT, prophylaxis, Lyssa virus

Introduction
Rabies, a fatal viral zoonosis, occur in man and other warm blooded animals which persists in both developed and developing countries worldwide in spite of successful preventive public health measures and post exposure therapies. Zoonoses are the diseases which are naturally transmissible between vertebrate animals and man. Considering the years of life lost, rabies rank seventh among all infectious diseases in the world (Wyatt *et al.* 2007) [1]. It is the only communicable disease of man which can be regarded as 100% fatal. 4 out of 10 deaths are in children (WHO, 2017). 40% of people bitten by suspect rabid animals are children under 15 years of age (WHO, 2017). It is known by different names in different countries eg. Hydrophobia, Lyssa, Tollwat, Lytta, Rabere, Habhoo, Jalatanka, Lerage. Rabies in man occurs commonly in some areas of world, particularly in Iran, India, Phillipines, North Africa and Thailand. According to an estimation by WHO, almost 59,000 people die due to rabies every year (WHO, 2017). Australia, New Zealand, Fizi, Bahamas, Bahrain, Cyprus are the countries free from rabies. Japan is first in Asia to eradicate rabies. Globally estimates indicate that human mortality is higher in Asia, with the highest incidence and death reported in India. This is followed by Africa (Ali *et al.* 2015) [12].

Transmission, clinical sign and symptoms
Rabies is caused by Lyssa virus (-SS RNA, enveloped, inactivated at 56 degree celcius) which belong to family Rhabdoviridae. The virus is bullet shaped in structure and measures about 180-250 nm in length by 75 nm in diameter. The virus is present in the saliva of affected animals and most frequent method of transmission to humans is by bites, scratches or licks to broken skin or mucous membranes (Chernet *et al*. 2016) [14]. Most of the human cases are caused by the bite of an infected or rabid animal which is usually dog, cat, bat, wolf, jackal, fox, skunk, mongoose etc. (Singh *et al.* 2017) [6]. Domestic dogs are the main reservoir and source of rabies in Asia. Dogs are the causes of human rabies deaths in 99% of all cases (Yousaf *et al.* 2012) [3]. In South America and Mexico, the blood sucking vampire bat has been found to carry the infection for months without showing any symptoms and is a source of danger for man and animals there (Bano *et al*. 2017) [15]. Infection from man to man is very rare, probably during corneal transplantation. As the virus is neurotropic in nature it reaches the brain through nervous system from the site of bite. The distance of bite from the central nervous system is an important factor in reaching the virus in the brain. In man, virus can reach the brain from facial wound in 30 days, from the arm in 40 days and from the legs in 60 days (Kessels *et al.* 2017) [13].

The disease in man often initiate with some abnormal sensation at the site of exposure. Mild fever, headache, nausea and sore throat are common early complains. Hypersensitivity, anxiety, muscular spasms, pupillary dilatation, lachrymation, salivation and perspiration are evident. In the later stage because of the paralysis of muscles of deglutition, the patient develops the fear of water which gives the condition its common name-hydrophobia. The patient passes into delirium with generalized convulsion and finally death occur which invariably ensures is usually from respiratory paralysis**.**

Diagnosis

Rabies is a neglected zoonotic disease that causes one death every 15 minute worldwide (WHO, 2017). The main burden lies on developing countries in Asia and Africa, where surveillance and disease detection is hampered by absence of adequate laboratory facilities and/or the difficulties of submitting samples from remote areas to laboratories (Nishizono *et al*. 2008) [4]. Current diagnostic tools are not suitable for detecting rabies infection before the onset of clinical sign and unless the rabies specific signs of hydrophobia or aerophobia are present (WHO, 2017). Rabies is difficult to diagnose because, in the early stages, it is easily confused with other diseases or with aggressiveness. Traditional rapid seller's staining and histopathological methods are still in use for diagnosis. Direct immuno fluorescent test (dFAT) is gold standard test and most commonly recommended for diagnosis in fresh brain tissues by both OIE and WHO (Duong *et al.* 2016) [5]. The RTPCR assays proved to be a sensitive and specific tool for routine diagnostic purposes particularly in decomposed samples (Lechenne *et al.* 2016) [9]. Cerebral inclusion bodies called Negri bodies (intracytoplasmic) are 100% diagnostic but are found in only about 80% of the cases. If possible, the animal from which the bite was recieved should also examined for rabies.

Treatment

Immediately after being bitten, the site should be treated with alcohol, iodine solution or carbolic acid after proper washing with soap with water followed by vaccination. The first dose of vaccine is given as soon as possible after exposure, with additional doses on days 3, 7, 14, 28 after the first. For pre exposure vaccinated patient, only the post exposure vaccinations on days 0 and 3 (intramuscularly into the deltoid region. In infants, the lateral thigh is recommended.

Economic impact of treatment

Treating a rabies exposure, where the average cost of rabies post exposure prophylaxis (PEP) is US$ 40 in Africa, US$ 49 in Asia can be a catastrophic financial burden of affected families whose average income is around US$ 1-2 per person.15 million people each year receive post exposure prophylaxis to prevent rabies but the disease remains neglected and highly under reported (Preiss *et al.* 2018) [11].

Control and Prevention

The use of inactivated tissue culture-derived vaccines is highly effective at preventing the development of rabies and very few failures are recorded (Hicks *et al.* 2012) [2]. Current approaches for rabies control are directed towards provision of effective post exposure prophylaxis to animal bite victims (Garg *et.al.* 2017) [10]. World Rabies Day, 28th September is celebrated annually to raise awareness about rabies prevention and to highlight progress in defeating this horrifying disease. The low level of commitment to rabies control is partly attributable to challenges in laboratory diagnosis and lack of adequate surveillance to indicate the disease burden (Mani *et al.* 2016) [7]. One Health is an initiative that seeks greater integration of human and veterinary medicine in areas as diverse as infectious disease control and comparative and translational medical research (Day *et al.* 2017) [8]. The WHO, the world organization for animal health, FAO of united nation and the global alliance for rabies control have revealed plan to end human death from dog-transmitted rabies by 2030 (ZERO BY 2030).

- There should be Vetico-medicos cooperation as it is a dreadly zoonotic disease.
- There should be whole hearted administrative support for disease investigation and control.
- There should be political will, adequate resources and diligent programme management related to rabies control and prevention as rabies is 100% vaccine preventable.
- Strict quarantine measures to be are to be adopted especially of imported canine population.
- Set up of modern laboratory in the city, district and town level to study the disease process and to extend rapid diagnosis.
- People's awareness has to be increased through mass media, group discussion, seminar in both urban and rural levels.
- Vaccination programme should be made obligatory for dog owner by municipality, corporation and other statutory bodies.
- Elimination programs revolve around mass dog vaccination campaigns, where atleast 70% of the dog population should be covered in order to break the cycle of transmission in dogs and to humans (WHO, 2017).
- Adequate transport facilities to be made to dispatch the materials for quick diagnosis.
- All dogs over age of three month shall be registered for licensing within one month of reaching this age (WHO 1984).
- Every year more than 15 million people worldwide receive a post bite vaccination. This is estimated to prevent hundreds of thousands of rabies deaths annually.

Conclusion

Almost all cases of human rabies result from bites from infected dogs. Even though rabies is fatal it is preventable with currently available tools but access to latest tools and techniques is limited in countries with highest disease burden. Increasing knowledge regarding wound washing, seeking post-exposure prophylaxis and the need to vaccinate dogs are likely to result in more effective prevention of rabies. The cooperation between medical and veterinary sectors also needed to eradicate rabies globally.

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