Epidemiology, Prevention and Control Methods of Human Rabies: Review Article

Nibret Moges
Clinical Medicine Department, Faculty of Veterinary Medicine, University of Gondar, P.O. Box 196, Gondar Ethiopia

Abstract: Rabies is viral encephalitis, almost always fatal, caused by lyssavirus infection. It is associated with dysfunction of the neurons after entry of the rabies virus to the central nervous system, usually in the spinal cord. The only lesions are in the central nervous system and spreads from the site of infection occur only by ways of the peripheral nerves. The bite route is still regarded as the most important means of transmission. Although wild animals can be host for rabies, dogs and cat remain a most important source of human exposure. The disease is worldwide in distribution except in Antarctica. There is lack of accurate quantitative information on rabies both in humans and animals and little is known about the awareness of the people about the disease to apply effective control measures in many developing countries.

Key words: Epidemiology · Human Rabies · Prevention and Control · Worldwide

INTRODUCTION

The dictionary tells us that rabies is derived from the Latin rabere, “To rage or to rave,” as is the corresponding adjective rabid; rabere possibly may have earlier origins in the Sanskrit rabhas, for "Violence". The Greeks adopted their own word, lyssa, meaning "madness", for rabies; this in turn is still reflected in English in lyssophobia, described in oxford English Dictionary as “A morbid dread of hydrophobia, the symptoms of which sometimes simulate those of the actual disease [1].

Rabies is an encephalomyelitis caused by a neurotrophic virus that affects all species of warm-blooded animals [2, 3]. It was recognized in Egypt before 2300 B.C. and in ancient Greece, where it was well described by Aristotle. Perhaps the most lethal of all infectious disease, rabies also has a destruction of having stimulated one of the great discoveries in biomedical science.

Rabies is an invariably lethal; a cute viral disease of the central nervous system that affects all mammals and that is transmitted by infected secretions [4, 5]. It is caused by a number of different strains of highly neurotropic viruses. Most belong to a single serotype in the genus Lyssavirus (Greek Lyssa, rage or rabies), family Rhabdoviridae. The bullet shaped virion contains a single-stranded, negative-sense RNA genome. The virus multiplies in the salivary glands of an infected host [3, 6]. It is transmitted to humans or other animals by the bite of an infected animal whose saliva contains the virus; aerosols of the virus that can be spread in caves where bats roost; or by contamination of scratches, abrasions, open wounds and mucous membranes with saliva from an infected animal [7-9].

Rabies is a zoonotic disease [10]. It is widely distributed throughout the world with the exception of Australia, New Zealand, Japan, a number of European countries and some Caribbean Islands. Wild animals serve as a large and mainly uncontrollable reservoir of sylvatic rabies, which is an increasing threat to the human population and to domestic animals in many countries [6, 11]. Therefore, the objective of this paper was to review information regarding human rabies epidemiologyand its prevention and control methods.

Epidemiology
The Epidemiology of Human Rabies: An understanding of the epizootiology of rabies is necessary in evaluating the risk of exposure and the need for rabies post exposure prophylaxis (PEP) in humans. Rabies is found in mammals in all regions of the world except Antarctica [4].
The risk of developing rabies depends on the anatomic site and severity of the bite, the species inflicting the wound and probably the rabies virus variant [1]. Even the very severe exposure associated with wolf bites involving the head does not lead inevitably to rabies encephalitis. In this case, about 50-60 percent of the victims will develop rabies if they are not given post-exposure treatment with lesser bite, the risk is around 10-40 percent however, modern post-exposure treatment, instituted on the day of the bite can reduce the risk to virtually zero [12].

When a person is exposed to an animal suspected of having rabies, the risk of rabies transmission should be evaluated carefully. Risk assessment should include consideration of the species of animal involved, the prevalence of rabies in the area whether exposure sufficient to transmit rabies occurred and the current status of the animal and its availability for diagnostic testing [13].

**Mortality and Morbidity Estimates:** In most areas of the world, accurate estimates of human rabies deaths are impossible to obtain because surveillance systems and regional laboratories are inadequate or nonexistent. Annual report of 2000 human deaths in Bangladesh, 1014 in China and 30,000 in India in the 1990s convey a rough estimate of the magnitude of mortality associated with rabies worldwide [1]. In Ethiopia, a total of 322 reported human deaths were recorded between 1990 and 2000 at zoonoses laboratory of EHNRI with an annual range of 17 to 54 cases and 95% of these were acquired from dogs. Among the reported fatal human rabies cases, 38.82% were children, 45.03% adults, 13.98% old people and 2.17% were unknown age [14].

Rabies is now present in all mainland Africa countries, including Madagascar. In 1998 only Libya and some African islands reported no cases of rabies. Human rabies is grossly underreported in Africa. In 1998, only 204 cases were notified to WHO, 91 percent were attributable to dog bites. The largest number, 43, occurred in Ethiopia [12, 14].

There are an estimated 55,000 human deaths annually from rabies worldwide, with about 31,000 in Asia and 24,000 in Africa. Of the sources of recent flourishing of rabies in East Asia is the pet boom. China introduced in the city of Beijing the “One-Dog Policy” in November 2006 to control the problem. India has been reported as having the highest rate of human rabies in the world, primarily because of stray dogs. As of 2007, Vietnam had the second-highest rate, followed by Thailand; in these countries to the virus is primarily transmitted through canines (Feral dogs and other wild canine species). Recent reports suggest that wild rabid dogs are roaming the streets. Because much cheaper pre-vaccination is not commonly administered in places like Thailand, the expense for lack of preparation with far more costly post-exposure prophylaxis can hit families hard [11,12].

In Ethiopia, during the last 3 years (1999-2002), post exposure antirabies treatment was given to 7,755 peoples in Addis Ababa and 137 fatal human rabies cases were recorded at the zoonoses laboratory of EHNRI [15]. In addition to deaths caused by rabies, millions of persons annually receive post exposure treatment (PET) for potential exposure to rabies virus. Many of these individuals receive vaccines of nervous tissue origin (NTO); which potentially result in thousands of serious adverse reactions. Along with the potential for adverse reactions with vaccines of NTO, there is concern over variability in antigen content. Experience in Pakistan and Nigeria with antirabies vaccines of little or no potency indicate that ineffective or even take (Lacking any antigenic value) biologicals may at times circulate in a number of countries [1].

Most human cases are reported in cities and are caused by the bites of rabid dogs. In those countries that have managed to control or eradicate canine rabies, even though they still have a wild cycle, the number of human cases has been reduced to very low level. Such is the situation in the US, where in 1938 there were 47 human cases, but recently the number has been down to between 0 and 3 a year [10].

**Rabies in Developing and Developed Nations:** From the public perspective, rabies remains a major threat only with in regions of Asia, Africa and South America where domestic dogs act as the major reservoir for the virus and the primary source for human exposures through animal bite. Within the broad category of developing countries, the geographic area of the tropics accounted for more than 99% of human deaths and approximately 90% of PETs for Rabies in 1985. The trend toward increasing global urbanization has meant that in 2000, approximately one half the world’s human population lives in cities compared with one-third in the 1970s. Disease such as rabies that are prone to transmission in crowded urban centers with inadequate public health infrastructures remain a constant or increasing threat in much of the world [16].
In general, rabies poses the greatest risk in cities (where dog and human populations reach their highest population densities). Rural or sylvatic rabies, involving rabies virus transmission from indigenous wild life, is a lesser threat in most regions of the world. Even in rural locations, dogs remain the most significant threat for rabies virus transmission to humans. In Mexico, where vampire bat and dog rabies co-occur, dog exposures account for approximately 81% of cases (Mainly urban) and vampire bats for approximately 11% of cases (Mostly rural). During an outbreak of rabies in Zimbabwe from 1980 to 1983, the majority of documented animal cases occurred in jackals, but dogs were the most serious threat to humans [1].

According to Jackson and Wunner[1] in countries where canine rabies is highest among human males and among individuals less than 20 years of age. The age and sex distribution of human rabies deaths generally mirrors the age distribution of dog bite victims, with a large proportion of victims under the age of 15 years. As Knipe and Howley[16] in these countries, very large numbers of doses of human vaccines are used and there is a continuing need for comprehensive, professionally organized and publicly supported rabies control agencies.

The actual risk of human exposure to rabies virus in developing countries is difficult to estimate. Surveys based on the experiences of foreign citizens from developed nations traveling or working overseas provide a range of values for rabies virus exposure or post exposure treatments of 0.2-6.2 per 1000 persons per month. These values vary with location and may not accurately reflect the risk to indigenous populations. In Thailand, it is estimates that over 200,000 persons received PET using tissue culture-derived vaccines in 1997 at a cost of approximately 10 million U.S. dollars [1].

In most developed countries, even those with modest disease burden, publicly supported rabies control agencies operate by different ways [16]. Human rabies in developed countries where tissue culture-derived vaccines and rabies immunoglobulin are available is a very rare disease. In the United States, the number of human rabies cases has declined dramatically since 1950s, concomitant with the decline of canine rabies. There has been a median of three human cases of rabies per year since 1990 and this number is higher than figures from Europe or Canada [1].

In the United States, Canada and Western Europe, where canine rabies has been controlled, dogs are responsible for very few cases. Rather, human rabies develops from bites of wild animals (Especially bats, raccoons, skunks and foxes) or occurs in travelers bitten by dogs elsewhere in the world. The increase in wildlife rabies in the United States and some other developed countries present a far greater risk to human than do dogs or cats [17].

In several countries of central and South America vampire-bat rabies is a threat to livestock and to the human population [11]. Among human rabies cases in the United States attributed to bat-associated variants, about 70% were caused by the silver-haired bat and eastern pipistrelle bat variants. However, only two cases were associated with a history of bat bite, as most bat exposures go undetected. Bat caves may contain aerosols of rabies virus and present a risk to spelunkers.

As Jackson and Wunner [1] a disturbing trend in recent cases of human rabies in the United States has been the inability to elicit a history of animal bite from the victim or close family members. Public health experts believe that a bat bite is still the most plausible explanation for these cases because documented instances of non bite routes of infection are exceedingly rare and generally have occurred under exceptional situations that are not comparable with those described for recent cases.

The most common explanation for the lack of history of a bat bite obtained from recent rabies patients or their close personal contacts are that patients failed to report an event perceived as insignificant or that the bat bite went unnoticed. The phenotype of rabies virus variants associated with bats may promote transmission via superficial wounds inflicted to peripheral body sites. All persons bitten by bat must receive post exposure rabies prophylaxis [17].

Routes of rabies virus transmission to humans: According to information provided by CDC, there are two possible routes of exposure to rabies; bite and non bite. Any penetration of the skin by teeth of a rabid animal constitutes a bite exposure. Nonbite exposure include scratches, abrasions, open wounds, or mucous membranes that come in contact with saliva or other potentially infectious material, example-brain or spinal cord tissue, from a rabid animal [18, 19].

Rabies virus cannot penetrate intact skin. Infection is usually the result of mammal bite, but is also possible if saliva contaminates damaged skin or even intact mucous membranes. On very rare occasions, virus has been inhaled as an aerosol. Those who handle infected
materials should be careful to avoid accidents with contaminated knives and needles, should always wear gloves and should avoid creating infective aerosols [12]. As Greene [5] described such air borne infections probably involve large quantities of aerosolized virus under condition of poor ventilation and susceptible exposed host.

Most commonly, transmission to humans takes place through exposure to saliva during a bite by an infected animal [4,19]. In a review of human rabies cases seen at Pasteur Institutes distributed around the world from 1927 to 1946, animal bites accounted for 99.8% of the 3,920 cases. However, sporadic cases of human rabies have been described following a variety of exposures. Saliva transmission by lick to mucus membranes, transdermal scratches contaminated with infectious material and even improperly inactivated rabies vaccines have resulted in infection [1, 4].

Human to Human spread is always theoretical danger to those close to the patient for saliva, tears, respiratory secretions and urine contains virus and patients with rabies may cough, spit and even bite. However, transmission of rabies from one person to another has been proved only in a group of patients who received infected corneal transplant grafts, transmission by breast milk and transplacentally has been proved in animals but not in humans. A number of women with rabies encephalitis have been delivered of healthy babies [5, 12].

In the United States, ingestion of unpasteurized milk from rabid cows has been treated as a possible exposing to virus. Scratches from a rabid animal potentially could be contaminated with virus shed in saliva and in the United States are often treated as an exposure, but documented cases of this injury leading to rabies are rare [1].

The benefits and costs of rabies preexposure prophylaxis for travelers to rabies endemic countries have been assessed and although not necessarily economical, the practice is likely to continue for important non-economic reasons. The current recommendations for U.S. residents are to consider preexposure immunization when traveling to high risk locations with in countries where rabies is endemic and where access to medical care could preclude the ready availability of PET [1].

Prevention and Control Methods: Historically, several key events have contributed to the control of human rabies: the development of a human rabies vaccine (1885), the discovery of the diagnosis Negribody (1903), the use of rabies vaccines for dogs (1904s), the addition of rabies immune globulin to human postexposure vaccination treatments (1954), the growth of rabies virus in cultured cells (1958) and the development of diagnostic fluorescent antibody test (1959) [17].

There Are Two Approaches to Prevention of Rabies in Humans: Pre-exposure and post-exposure. Pre-exposure vaccination is desirable for all persons who are at high risk of contact with rabid animals such as veterinarians, animal care personnel, certain laboratory workers and spelunkers. Persons traveling to developing countries where rabies control programs for domestic animals are not optimal should be offered pre-exposure prophylaxis [9, 17, 20, 21]. However, pre-exposure prophylaxis does not eliminate the need for prompt post-exposure prophylaxis if an exposure to rabies occurs [17]. So immediate treatment after exposure is essential for all individuals known or suspected of having been exposed to a rabid animal [20].

Pre-exposure Vaccine Regime: 1 dose of cell culture or purified duck embryo vaccine on days 0, 7, 28 a few days variation is acceptable. The dose in 1 standard intramuscular dose (1ml or 0.5 ml according to vaccine type). The vaccine may be given intradermally (0.1ml on day 0, 7, 28) except in anti malarial chemoprophylaxis (e.g. chloroquine) is being used concurrently, when intramuscular injections are preferable, since the antibody response may be impaired if the intradermal method is used WHO [22] and this will provide 2 years of protection [21]. Booster (Or serologic confirmation of adequate level) is given depending on the individual’s continuing risk category [16].
CONCLUSIONS

In more than 99% of human rabies cases, the virus was transmitted by the bite of a dog and over 90% of persons who receive postexposure treatment live in areas where canine rabies is present. WHO advocates canine rabies control as the only long term, cost effective means of eliminating or preventing most human cases [23]. Increased travel of humans, along with intentional and unintentional translocation of animal (including known potential rabies-reservoir species), has made the recognition of clinical rabies and its prevention of increasing importance [4].

RECOMMENDATIONS

Unvaccinated dogs and cats exposed to a rabid animal 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. Animals with expired vaccinations need to be evaluated on a case-by-case basis. Dogs and cats that are currently vaccinated should be revaccinated immediately, kept under the owner’s control and observed for 45 days. In unvaccinated humans, rabies is almost always fatal after neurological symptoms have developed, but prompt post-exposure vaccination may prevent the virus from progressing [24].

The first protective measure is local treatment of the wound. The wound should be washed immediately with soap and water, detergent, or another substance that inactivates the virus. The World Health Organization Expert Committee on Rabies also recommends the installation of antirabies serum around the wound [16, 21].

The pre-exposure schedule for rabies vaccination is 3 doses, given at the following times;

Dose 1: As appropriate
Dose 2: 7 days after Dose 1
Dose 3: 21 days or 28 days after Dose 1

For laboratory workers and others who may be repeatedly exposed to rabies virus, periodic testing for immunity is recommended and booster doses should be given as needed [21].

REFERENCES