Range of Rabies-A Review

G Yale¹, V Bhanu Rekha² and M GajendraGad¹

¹Epidemiology Unit, National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), (formerly, PD_ADMAS), Indian Council of Agricultural Research, Hebbal, Bengaluru- 560 024, India.

²Department of Veterinary Public Health and Epidemiology, Rajiv Gandhi Institute of Veterinary Education and Research, Puducherry-605009, India.

Abstract

Rabies is one of the oldest recognized zoonotic diseases in the world. Each year more than 10 million people endure protracted anxiety after exposure to an animal suspected with rabies. In 2011, rabies was still endemic in about 100 countries in the world where 2.5 thousand million people live. Rabies virus infects all mammals with affinity to carnivores, which spread the virus. Compartmentation of rabies results in the disease to be reported in one major host species in certain geographical areas while it is reported less frequently in the same species in other areas. This makes disease control difficult as control strategies have to differ based on reservoir host, spills over host, topography and ecology of region and socioeconomic status of the country. This review emphasizes the range of species rabies has been reported around the world accentuating the need for post exposure prophylaxis after exposure to species less likely known to have rabies.

Keywords: Rabies, host range, geographic distribution.

Introduction

Rabies is one of the oldest recognized diseases affecting all warm-blooded animals and remains to be the most important zoonotic disease in India (Menezes, 2008). Although rabies has been known for more than 4300 years and the name originated about 3000 B.C from the word ‘rabha’ rabies has been well documented and researched upon only from the 18th century (Takayama, 2005). For more than three millennia, rabies has been one of the best known and the most feared human disease. Each year, more than ten million people, many of whom are unvaccinated, endure protracted anxiety after exposure to an animal with suspected rabies (Deshmukh, 2004).

Smith et al. (1992) were the first to demonstrate that six genetic groups of rabies virus existed globally and four of them were distributed in Asia. The groups were distinguished by analysis of the 200-b region of the N genes from 87 rabies virus isolates from various parts of the world. Complete analysis of the nucleoprotein (N)-coding genes of 69 isolates from various parts of the world shows that least 11 phylogenetic lineages could be identified in accordance with their geographical localization and species of origin (Kissi et al., 1995).

Geographic range of rabies

Three principal global areas of rabies have been defined. These areas are (1) countries with enzootic canine rabies (all of Asia, Latin America, and Africa); (2) countries in which canine rabies has been brought under control and wildlife rabies predominates (Western Europe, Canada, and the United States); and (3) rabies-free countries (mostly islands, including England, Australia, and Japan) (De Serres et al., 2008).

In 2011, rabies was still endemic in about 100 countries in the world where 2.5 thousand million people live (Nandi and Kumar, 2011). Canine rabies is absent in the United Kingdom, Sweden, Norway, Australia, New Zealand, New Caledonia, Hawaii, French Polynesia and the Island of Reunion (Cliquet et al., 2003).

Asia: The record of rabies in Chinese history dates back to 556 B.C. in Master Zuo's tradition of the spring and autumn annals (Wu et al., 2009). Although no rabies case has been reported since 1957 in Japan, there are many areas where rabies is yet endemic or epidemic (Takayama, 2005; Tamashiro et al., 2007). Eight out of eleven member states of WHO Southeast Asia region (Bangladesh, Bhutan, Democratic People’s Republic of
Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste) are endemic for rabies (Gongal and Wright, 2011).

Community or stray dogs and to a lesser extent, unvaccinated pet dogs are responsible for sustaining endemic rabies in Thailand. Extensive research and stringent rabies control measures from the past two decades have reduced rabies in Thailand from 370 human rabies deaths in 1980 (±78) 100000) to 75 in 1996 (0±12) 100000) (Mitmoonpitak et al., 1998). Sri Lanka is among the top ten countries in the world that report the highest rate of human rabies deaths (2.8 per 1,000,000 in 2007) and potential rabid animal bites requiring post-exposure treatment (755 per 100,000 in 2003) (Kumarapeli and Friedlander, 2009) and control programs have been implemented from 1970’s (Nanayakkara et al., 2003)

India: A national multicentric study of human rabies in India also revealed that the annual incidence of human rabies was estimated to be 17,137 cases. The majority of the victims were male, adult, from rural areas and unvaccinated. The main animals responsible for bites were dogs (96.2%), most of which were stray dogs (Sudarshan et al., 2007). A survey in 2003 reported that the biting animal mainly responsible for human rabies death was dog (96.2%) of which majority strays (75.2%) followed by pet (11.1%), wild (3.5%); cat accounted for 1.7% in India (Bhuyan, 2012). Ichhpujani et al. (2008) reported that dog bites caused maximum morbidity (92%), followed by monkey (3.2%), cat (1.8%) and fox (0.4%) in India. Most bites were unprovoked (64.3%) by stray animals (64.7%). A study conducted on 250 animal bite victims in Pune showed that dog was the biting animal in 94.4% cases, followed by cat (2.4%), Jackal (1.2%), mongoose (1.2%), monkey (0.4%) and horse (0.4%)(Shetty et al., 2005). Andaman Nicobar and Lakshadweep islands are regions of India free of rabies (Sudarshan et. al., 2007). 

Europe: In Europe, red fox is the main reservoir of rabies (Gortzázar et al., 2007). Intense oral vaccination from 1978 proved better than traditional methods based fox population reduction (Artois et al., 2001). Despite this success, rabies appears to be re-emerging in some parts of Europe. This can be explained by a relaxation of vaccination campaigns in apparently rabies-free regions, an increase in fox densities and the expansion of new rabies hosts such as the raccoon (Holmala and Kauhala, 2006). Bat rabies was at its peak in Europe during 1980 to 1990 and later steadily decreased over time (Bourhy, 1992).

Africa: The principal reservoir host of rabies is dog in Kenya. Rabies was first confirmed in 1912 in Kenya, later was established as endemic and a threat (Borus, 1996). Awareness of lyssavirus other than rabies virus dates from the identification of Duvenhage virus in 1970 and was followed by detection of Lagos bat virus and Mokolain South Africa (Cohen et al., 2007). Lagos bat virus was isolated from frugivorous bats from Lagos islands of Nigeria in 1956 and Mokola virus from shrews in 1968 (Kemp et al., 1973).

Americas: During 1993 to 2002, 27 cases of human rabies from non-hematophagous bats were reported from the Americas (composed of 48 countries and territories) out of which 19 were from United States. Other species reported to have transmitted rabies to people were; monkeys (7 cases from Brazil), skunks (5 cases from Mexico and 1 from Peru), foxes (3 cases from Mexico), raccoons (2 cases from Brazil and 1 from El Salvador), pumas (1 case from Mexico), cats (38 cases) and cattle (3 cases) (Belotto et al., 2005). During the same period, 37,377 cases of rabies were reported in dogs, 22,902 raccoons, 12,964 skunks, 9232 bats, 5016 foxes and 31,187 cattle. In 2002, 17 countries reported canine rabies, highest from Brazil (457), Bolivia (108) and Mexico (105); 13 countries reported rabies in cats highest from USA (298) and Brazil (67) (Belotto et al., 2005).

Host range of rabies

Host range of a virus is the range of cell types and particularly host species a virus is able to infect. It can be defined as an inability of the virus to successfully adsorb and/or enter cells because of an incompatibility between virus capsid proteins (or virus envelope proteins) and the host receptor molecule or/and an incompatibility between the biochemistry of the virus and the biochemistry of the host. Tropism of virus can vary in terms of the breadth of the host range. Some viruses infect one or only a few species while others are capable of infecting a broad range of species. Rabies virus is one such virus with a broad host range infecting all mammals with affinity to carnivores, which spread the virus.

Compartmentation occurs with rabies, so that the disease is reported in one major host species in certain geographical areas while it is reported less frequently in the same species in other areas of endemic rabies. Therefore different species around the world play reservoir host to rabies virus in different regions.

Spillover infections of distinct rabies virus variants to non-maintenance (non-adapted, non-
reservoir) hosts occurs but does not typically result in sustained transmission (e.g. infection in domestic animals and humans are spillover). For ease of comprehension of host range of rabies, animals are categorized as pet, domestic and wild in this review.

Table 1: Rabies virus geographic and host range with genotype.

<table>
<thead>
<tr>
<th>Region</th>
<th>Reservoir Species</th>
<th>Genotype</th>
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<tbody>
<tr>
<td>Europe:</td>
<td>fox, bats</td>
<td>European bat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lyssavirus 1 &amp; 2</td>
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<tr>
<td>Asia</td>
<td>Dogs</td>
<td>Classical/Dog rabies virus</td>
</tr>
<tr>
<td>Africa</td>
<td>dog, mongoose, antelope</td>
<td>Lagos bat virus, Mokola virus</td>
</tr>
<tr>
<td>North America</td>
<td>foxes, skunks, raccoons, insectivorous bats</td>
<td>Classical rabies virus</td>
</tr>
<tr>
<td>South America</td>
<td>dog, vampire bats</td>
<td>Classical rabies virus</td>
</tr>
<tr>
<td>Australia</td>
<td>Insectivorous bats</td>
<td>Australian Bat Lyssavirus</td>
</tr>
<tr>
<td>Middle East</td>
<td>Wolf, dog</td>
<td>Classical/Dog rabies virus</td>
</tr>
</tbody>
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(Heaton et al., 1997, Adedeji et al., 2010)

Pet Animals

Dogs: Dogs are the reservoir of rabies in most of the countries around the world (Vaughn et al., 1965). Dogs are the reservoir species in eight of the eleven WHO Southeast Asian Region accounting for 96% of human rabies cases (Gongal and Wright, 2011). Each year, 21 000–24 000 people die in this region due to rabies which accounts for approximately 45% of worldwide human rabies deaths and approximately 4 million receive post exposure vaccine (Gongal and Wright, 2011). Dogs play reservoir host of urban rabies in Latin America too. Dogs are the primary source of infection for humans and other domestic animals. During 1990 to 1996, dogs were responsible for 80.6% of human rabies cases of Latin America in which the source of exposure were known (De Mattos et al., 1999).

Cats: Cats are diagnosed with rabies in raccoon rabies endemic regions of USA regularly (Krebs et al., 2000, 2003, 2004; Blanton et al., 2007, 2008, 2010). Cats are responsible for approximately 0.8% of human rabies annually in India (Wilde, 2005). In Latin America, cats get rabies through contact with dogs or through predation of bats and other small animals and transmit rabies to humans (Belotto et al., 2005).

Domestic Animals

Cattle: Rabies in cattle was reported way back in 1927 to 1947 in the state of New York, USA (Korns and Zeissig, 1948). The peculiarity of this case was that from 1925 an attempt to control rabies in urban dogs by controlling dog population started in the hope that dog and fox rabies endemic in the region would decrease or be eradicated. But as the dog population was controlled, rabies in fox and cattle started to increase. It is hypothesized that the reason for this was the seasonal increase of fox population that coincided during the time or the increase in fox population due to lack of competition from dogs. As fox rabies increased, grazing cattle were exposed more often and hence fox and cattle rabies were reported more while dog rabies and population decreased. Control strategies were altered to incorporate wider regions and more species simultaneously for better results (Korns and Zeissig, 1948). Rabies in cattle transmitted by bats has been reported in Central and South America by Carlos Arellano-Sota (1988). In 1971, 45% of rabies post exposure treatment in humans in France resulted from exposure to bovines (Soulebot et al., 1985).

Horses and Mules: Fifty-one cases of rabies were reported in horses, donkeys, and mules in 2001 and 52 cases reported during 2000 in the United States. Other reported cases of rabies in domestic animals included three goats and two swine (Krebs et al., 2002). Retrospective review of rabies in horses was done in Canada in 21 cases from 1970 to 1990 to determine the clinical signs of rabies in horses to improved clinical diagnosis of rabies in horses (Green et al., 1992).

Rabies in mules was reported in Manshehra, Pakistan. A total of 12 mules died showing clinical symptoms of rabies from a herd of 382 mules after being attacked by wild jackals. The disease was confirmed by Reverse Transcriptase–Polymerase Chain Reaction (RT-PCR) and mouse inoculation tests (Numan et al., 2011).

Goats and Donkeys: An epidemiological study of rabies in Sudan from 1992 to 2002 revealed that dogs, goats and donkeys were the main animals involved with rabies and the peak was found to be in January and February (Ah et al., 2006).

Sheep: A flock of 110 sheep housed in a cave as sheepfold in Shanxi province, China were attacked by a rabid dog which resulted in 36 deaths due to trampling...
and 15 deaths due to rabies in 2 weeks. The disease was confirmed by FAT and RT-PCR. This is the first confirmed sheep rabies outbreak reported in China (Zhu et al., 2011). In 1973, 30% of post exposure rabies treatment in humans in East Germany resulted from exposure to sheep (Smith et al., 1973).

Swine: Rabies outbreaks in swine were reported from 1968 to 1982 in Alberta and Saskatchewan provinces of Canada. A retrospective study with local veterinarians showed that skunk habitation and skunk rabies were more around these pig farms (Yates et al., 1983).

Wild Animals

Bears: Bears are considered as less susceptible to rabies, and only one single case of rabies in a polar bear (Ursus maritimus) has been reported in Canada in 1989. The most probable source of infection is bite from a rabid fox or scavenging a rabid carcass. Only polar bear hunters are at a risk of rabies from polar bears (Taylor et al. 1991). Eight cases of Black bear (Ursus americanus) were reported from Canada. Four of the bear had a history of violent behavior and two of the bears had attacked humans (Tabel et al., 2004). Black bears have been diagnosed with rabies in USA nearly every year (Kreb’s et al., 2000, 2004, 2005; Blanton et al., 2008).

Bats: During 2007, 49 states of United States of America and Puerto Rico reported 7,258 cases of rabies in animals and one case in a human. Relative contributions by the major animal groups were as follows: 2,659 raccoons (36.6%), 1,973 bats (27.2%), 1,478 skunks (20.4%), 489 foxes (6.7%), 274 cats (3.8%), 93 dogs (1.3%), and 57 cattle (0.8%) (Blanton et al., 2008).

In 2004, 46 persons died of rabies transmitted by vampire bats, mainly in Brazil (22cases) and Colombia (14 cases); 20 human cases of rabies were transmitted by dogs in all of Latin America (Schneider et al., 2005).

In 1999, ecephalitis was diagnosed in an Egyptian rousette bat (Rousettus aegyptiacus) that had been imported from Belgium and sold in a pet shop in southwestern France. The pet bat was infected with a Lagos batlyssavirus and resulted in the treatment of 120 exposed persons (Chomel et al., 2007). Vampire bats (Desmodus rotundus) are the only known reservoir host for sylvatic rabies in Latin America. During 1990 to 1996, vampire bats were responsible for 11.3% of human rabies cases of Latin America in which the source of exposure were known (De Mattos et al., 1999).

Deer: Since 1990, a total of 104 rabid deer have been reported in the United States. Possible deer to deer transmission of rabies through saliva and maternal activities has been observed. Since January 2007, a total of 11 rabid deer from 4 deer farms were identified within a 45 mile radius in a wildlife (fox, skunks and raccoons) rabies high prevalence region in Pennsylvania, USA. Bottle feeding and proximate management activities were considered high risk activities for rabies transmission to humans from captive deer (Petersen et al., 2012).

Elephants: Wimalaratne and Kodikara (1999) reported the first case of rabies in an elephant in Sri Lanka. The source of infection was not determined. The neutralizing antibody titer was found to be 0.68 IU/ml by Rapid Focus Fluorescence Inhibition Test where the level of neutralizing antibody in a normal elephant is 0.04 IU/ml. The antigen was confirmed by RT – PCR and the sequencing to be similar to the common Sri Lankan dog rabies variant.

Fox: The present rabies epizootic in continental Europe has spread among red foxes (Vulpes vulpes) from 1940s. They act as vector and victim of rabies in Europe and are the main reservoir of the epizootic (MacDonal , 1981). In India, although dogs are primarily responsible for rabies in humans (96% of cases), foxes are responsible for 3% of the cases (1.7% jackals) (Wilde, 2005). In January 2011 a fox attacked dogs belonging to a meteorological station in the Svalbard archipelago, Norway. Rabies virus was detected in the fox’s brain post-mortem (Orpetveit et al., 2011). Rabies is regarded as endemic among the red fox and the arctic fox in northern and western areas of Alaska, with a cyclic occurrence of epidemics about every 3-4 years (Ritter 198; Mork and Presprud, 2004).

Marmosets: Eight cases of human rabies caused by a new rabies virus variant were reported in the state of Ceará, Brazil, from 1991 through 1998. Marmosets (Callithrixjacchus jacchus) were determined to be the source of exposure. Most cases occurred in persons who had tried to capture them and one case was transmitted by a pet marmoset (Favoretto et al., 2001)

Raccoons: The earliest report of enzootic rabies in raccoons (Procyon lotor) was reported from Florida, USA in 1947 which expanded gradually to north eastern states in 1960s and presently is endemic to whole of north east USA and Canada (Sobey et al., 2010). Rabies was introduced in the mid-Atlantic states in the 1970s by raccoons trapped in rabies-endemic zones of the southern United States (Woodford and
In Eastern Europe, raccoon dogs are becoming a new reservoir for rabies, in addition to the established red fox reservoir, as raccoon dogs have spread into new habitats from accidental release of animals raised for fur trade (Gylys et al., 1998).

**Reindeers and Seal:** In the high-arctic Svalbard islands of Norway, rabies was detected for the first time in 1980 when there was an outbreak in the arctic fox population. The outbreak spilled over to other species and was diagnosed in three reindeers and one seal (Odegard and Krogsrud, 1981).

**Rodents:** Rabies has also been reported in pet rabbits, ferrets and guinea pigs. Raccoon rabies virus was isolated from them and they had a history of exposure to raccoon or skunks. It is important to note that rabbits do not have vaccination for rabies and prevention from exposure is the only protective measure (Lackay et al., 2008). A farmer in Thailand, Phetchabun province incurred multiple bites from a rat in his bed inside a mosquito net. FAT, MIT and antibody tests revealed the rat to be infected with common Asian dog virus. Although rabies in rats is not common a bite from a rodent should not be ignored (Kamoltham et al., 2002).

Between 1985 and 1994, 368 cases of rabies in rodents and lagomorphs were reported by CDC, Atlanta. Highest cases were from woodchucks (*Marmota monax*) from regions with endemic raccoon rabies (Childs et al., 1997). During the same period Maryland Public Health department demonstrated that domestic animal and human rabies exposure due to rodents and lagomorphs represents a small but significant number of the total exposure to rabid animals by a screening that showed 12% of bites to humans by rabid animals were by rodents and lagomorphs (Moro et al., 1991) again accentuating the importance of the possibility of rabies through rodent bite to humans. A wood rat *Neotoma floridana* behaving abnormally was found by a group of children who attempted to catch it and one 6-year-old boy was bitten. Physician treating the child suggested investigation of the dead wood rat due to the high prevalence of wildlife rabies in North Carolina, USA which was diagnosed positive by mouse inoculation test (Dowda, 1981).

**Squirrels:** Venters and Jennings (1962) reported the first case of rabies in a flying squirrel in 1961 in Pinellas County, Florida, USA by Negri body staining, FAT and mouse inoculation test. Existence of concurrent rabies infection in yellow bats, without any evidence of the virus in the other mammals of the area, suggests that the flying squirrel was infected while investigating or capturing a moribund rabid bat. Further investigation of rabies in flying squirrel demonstrated that this case was an isolated one (Venters and Jennings, 1962). Rabies was reported in an Easter Fox squirrel by Cappucci et al. (1972) as an isolated case in California, USA which was shot down after displaying abnormal and aggressive behaviour. The squirrel was confirmed to have rabies by Negri body detection and FAT (Cappucci et al., 1972).

**Skunks:** Rabies has been reported to be endemic in skunks (*Mephitis mephitis*) from 1964 in Northern (Montana and neighboring states) and Southern central (Arizona and neighboring states) USA and Canada (Engeman et al., 2003). Skunks are host to three strains of skunk rabies virus and fox, bat and raccoon rabies virus making rabies control more difficult (Jojola et al., 2004). Skunks are the second highest wild animals to be diagnosed with rabies after raccoons in USA (Blanton et al., 2010). In 1995, 1.4% of post exposure prophylaxes in humans were due to exposure to skunks in Pennsylvania, USA (Moore et al., 2000).

**Mongoose:** The epidemiology of rabies in mongoose and the outbreaks caused in livestock by mongoose has been studied by Everard et al., (1974) in Grenada. The study revealed 18.9% of the caught wild mongooses to have rabies neutralizing antibodies indicating high transmission rate of rabies among mongooses (Everard et al., 1974). Wilde (2007) reported a human death due to a bite from a rabid mongoose in South Africa.

**Wolves and Jackals:** Ethiopian wolves brain smears from two carcasses in the wild were found to be positive for rabies by FAT. Rabies virus was isolated from the brains by mouse inoculation. The virus was identified as a minor variant of the serotype 1 rabies virus found in domestic dogs and wild canids of Africa (Sillerö-Zubiri, 1996).

Rabies is endemic in South Africa, in addition to domestic dogs, canid rabies is currently sustained by black-backed jackals (*Canis mesomelas*) in the and bat-eared foxes (*Otocyon megalotis*) in the Cape region which is transmitted to humans frequently (Zulu et al., 2009). Rathod et al. (1997) reported extensively about the rabid wolf attacks on villagers in Jalgaon district of Maharashtra, India. Rabid fox attacks have been reported in large numbers in the past decade especially in the Deccan plateau of central India (Suja et al., 2004).

**Other mammals:** In the late 1970s and early 1980s, a rabies epidemic occurred in free-ranging greater kudus (*Tragelaphus strepsiceros*) in Namibia (Huschle,
Other wild animals in which rabies was reported includes Mongoose (Herpestes javanicus), Bobcats (Lynx rufus), Groundhogs (Marmota monax), Coyotes (Canis latrans), White-tailed deer (Odocoileus virginianus), River otters (Lontra canadensis), Opossums (Didelphis virginiana), Fishers (Martes pennanti), Ringtail (Bassariscus astutus), Buffalo bison (Bison bison), Chinchilla (Chinchilla lanigera), Mink (Mustela vison), Ground squirrel (Spermophilus sp.), Beavers (Castor canadensis), Wolf (Canis lupus), Cougar (Puma concolor), Musk rat (Ondatra zibethicus), Caribou (Rangifer tarandus), Badgers (Taxidea taxus), Chipmunk (Tamias striatus), wapiti or elk (Cervus elephas), Weasel (Mustela sp.), Wolf-dog hybrid (Canis lupus x C familiaris), Javelina (Pecari tajacu), Llama (Llama glama) (Tabel et al.,1974; Krebs et al., 2000, 2003, 2004; Blanton et al., 2007, 2008, 2010).

Birds
Rabies has been experimentally induced in birds by Jorgenson et al. (1976) who fed carcass of an experimentally infected rabid skunk to a great horned owl. The bird developed antibodies detected by passive hemagglutination. 27 days after ingestion andrabies antigen was detected in pharyngeal swab and corneal smear and on day 52 and 87 respectively. Clinical signs of rabies were not detected in the bird. Gough and Jorgenson also (1976) found rabies antibodies through passive hemagglutination in 23 birds out of 362 wild birds. Although birds are not regarded important carriers of rabies these studies demonstrate the potential of predator or carrion feeders to initiate a rabies viral infection.

References


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