

Guest Editorial

Rabies – A Veterinary Perspective**Dr. S. Abdul Rahman**

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Today with more than 70% of known pathogens being zoonotic in nature and with an alarming increase of emerging and re-emerging zoonotic diseases the concept of One World One Health has become more relevant than before.

Unless the medical and veterinary profession joins hands and works towards a joint strategy in controlling Rabies, its eradication will remain a distant dream and the disease will continue to be a neglected zoonosis.

Strategy

The strategy should be aimed at Elimination of Rabies, in India, Asia and all over the globe.

There are various means to achieve this eventually and the most important of them are:

Bring together veterinarians, scientists, wildlife experts, clinicians and public health officials

To share their experience in modern **rabies control**, and to agree on the strategies for the **prevention and control in reservoir animal species** and wild life

Historical Background

The early history of Rabies goes back to ancient civilizations of Indus Valley in India, Nile, Euphrates and Baghdad. The earliest description of rabies in wild animals was by Greek agriculturists although the Romans were the first to mention the disease in their essays. The role of animals especially dogs in the transmission was also known.

Aristotle stated that mad dogs could infect all creatures. The association of bite wounds with rabies was known before Hippocrates. Siptahin; a temple priest in Egypt described clinical signs of rabies and other infections around 1400BC. Pliny, the Roman historian, recognized rabies as a contagious disease of dogs that was transmitted to man.

Throughout the Middle Ages, there were many descriptions of rabid animals that destroyed farm animals and invaded cities. In 600 AD Prophet Mohammed informed his followers to wash a dog lick or wound seven times with water before performing prayers

Both furious and dumb rabies were probably known to both medical veterinarians and physicians. Tuberville, a French scientist was the first to differentiate between the types in 1576. He described the signs including the strained howling and stated the disease killed the animals in 3 or 4 days.

Introduction

Dogs constitute the main source of transmission of rabies though other animals are also involved. Today, there are over 400 million free-roaming dogs in the world with about one-half of the world's human population living in rabies endemic areas.

India has a dog population of 28 million out of which the stray dog population is around 80%. Ninety six percent of human rabies in developing countries is due to dog bites.

Children aged 5-15 years form about 40 percent of people exposed to dog bites in rabies-endemic areas. The majority of bites that occur in children go unrecognized and unreported

Rabies in Other Parts of the World

In 2008 USA reported 6,841 cases of rabies in animals and 2 cases in humans in 49 states and Puerto Rico to the CDC. Ninety three per cent of the animal cases in the USA

occurred in wildlife, raccoons (34.9%), bats (26.4%), skunks (23.2%) and foxes (6.6%), 7% were reported in domestic animals. Rabies cases were four times as many in cats than dogs

In Russia the epidemic situation for rabies had reached the highest levels of concern in Moscow. There were 257 animal rabies cases in 2009, more than 10-fold the means of previous years. Unprecedented measure to control the epidemic, like banning movements of pets to suburban cottages, canceling a show dog exhibition and mass immunization of wild and domestic animals have been planned. In Israel in 2009, 58 incidents of rabies have been reported against just 12 cases in 2008 and in Ghana, human dog bite cases have increased substantially during the last five years

Rabies in Animal

The reporting system of canine rabies is far from satisfactory. There is no coordination between various

agencies responsible for control programmes as a result, the authenticity of data available on the incidence of canine rabies in the country is doubtful.

There has been an increase in the incidence of rabies in cattle, sheep, goats, horses and cats as evinced by post-mortem reports from various veterinary colleges of the country.

Elimination of canine rabies constitutes the most effective means of controlling human rabies and avoiding expenses associated with prevention activities which could be better used for other public health priorities in the developing countries of the world such as India.

Clinical Signs of Rabies in various animals

The clinical signs of rabies in domestic warm-blood animals are highly variable, but similar in most species. Rabies should always be suspected if there is a sudden change in behavior, unexplained progressive paralysis and increased, decreased, or normal spinal reflexes.

Pyrexia may also be present. Clinical course is classically described as three, often overlapping phases:

- **the prodromal period**
- **the excitative or 'furious' stage**
- **The paralytic or 'dumb' phase.**

Not all animals' progress through all these stages and the presentation can be quite variable.

Excessive salivation, behavior change, abnormal posture, tenesmus, yawning, paraphimosis, photophobia, pica, sexual excitement, abnormal bellowing, aggression, increased libido, and decreased lactation are some of the common symptoms.

Symptoms in Cattle

Yawning, bellowing, in-coordination, decreased feeling in hind limbs, loss of tail movement, drooling saliva, "cud-dropping", inability to stand, hypersensitivity, aggression, paralysis.

Hoarse bellowing

Symptoms in Sheep

Clinical signs of sheep are very similar to cattle infected with rabies. In sheep and goats the incubation period maybe 2-4 weeks and may be extended to 17 weeks. The main difference is that a group of sheep will be infected, since an infected carnivore can easily bite more than one animal. There may also be aggressive wool pulling and no abnormal bleating. Other common signs are: sexual excitement, wool pulling, aggression, in-coordination and paralysis

Symptoms in Horses

Abnormal postures, lameness, weakness, depression, muscle in-coordination, inability to swallow and stand,

biting, aggression, hypersensitivity, and loss of anal tone.

Early clinical signs include pharyngeal paralysis, anorexia, depression, colic and ataxia.

Obscure lameness and posterior ataxia (in coordination) are relatively common early signs.

Over half of the clinical cases will be in the dumb form of rabies. However, the furious form will occur in 43% of infected horses. Hydrophobia (fear of water) is not a frequent sign in the horse. Insidious onset is the hallmark of equine rabies with reported initial clinical signs of lameness, colic, dysuria, priapism in addition to overt neurologic disease.

Symptoms in Pigs

Pigs infected with rabies are extremely rare due to most pigs being housed indoors.

Early clinical signs may include excitement, aggression, in coordination, excessive salivation, backwards walking, phantom chewing, lethargy, convulsions, paralysis and depression.

Death occurs within 2 days of clinical signs. Final stages of disease include depression, convulsions, and recumbency. The furious form of rabies is rare

Symptoms in Dogs and Cats

Cats consistently develop the furious form of rabies. However, the dumb form does occur.

The clinical signs include strange and abnormal behavior, abnormal meowing, photophobia, aggression, muscle tremors, and in coordination. Mandibular and laryngeal paralysis is rare in cat. Cats with clinical signs usually die in 3 to 4 days. The following phases are observed:

Prodromal Phase

Changes in temperament, photophobia, swallowing a variety of objects, and may become disoriented and wander aimlessly. Fixed stare, lose the ability to swallow, drool saliva, and develop a hoarse howl. Seizures or die suddenly during a seizure. The most characteristic sign is drooping of the jaw, the dog unable to eat may emit a choking sound and owners suspect that the dog has a bone in its throat. After 2-4 days the paralysis spreads and dogs become comatose and die.

Excitative Stage (2- 4 Days)

Animals become increasingly nervous, irritable and vicious, and are most likely to bite and attack. There is disorientation, difficulty in swallowing, and drooling and frothing of saliva.

Dogs may also show pica, i.e. eating unusual objects such as wood, stone, etc. The excitement phase may last up to a week. Sometimes animals progress directly from the prodromal phase to the paralytic stage.

Paralytic Phase

Muscular in coordination and convulsions gradually lead to generalized paralysis, coma and death. Although in classical rabies animals progress straight through the clinical signs to death, there are rare reports of recovery.

Rabies in Wildlife and Others

Examples of Rabies in Wild Life

Rabies in wildlife is a thorny issue. When is a disease part of natural selective?

For e.g. In the case of the Ethiopian wolf, with 500 left in Ethiopia, it is one of world's most endangered species. Dogs, wolves and people coexist in the high Afroalpine to such a close extent that wolves and dogs occasionally hybridize, making rabies transmission from dogs to wolves a very real threat. In 1991, 2003 and 2008 rabies wiped out 70% of affected wolf populations, a loss the species can ill afford.

Rabies in Antelopes in Namibia

The massive outbreak, affecting kudu antelopes (*Tragelaphus strepsiceros*), began early in 2008 in Namibia. 500 kudu bulls had succumbed to the disease. 20,000 antelopes also died during that epizootic. The social behavior of kudu is believed to be the contributing factor in transmission of rabies in this species through contact of infected saliva via mouth.

Sylvatic Rabies

Vampire bats are only found in Latin America and of the three recognized species, only the common vampire (*Desmodus rotundus*) feeds on mammals and thus could transmit rabies to humans. Fatal cases of human rabies transmitted by hematophagous (vampire) bats have reached new heights in Latin America. In 2004 (46 cases) and 2005 (55 cases) were reported. In 2005, 42 cases occurred in Brazil (41 in the Amazon region), 7 in Peru, 3 in remote communities of Colombia, and 2 in Ecuador, and 1 in Bolivia.

In 2004, number of human cases of rabies transmitted by wildlife (in most cases the vampire bat) exceeded those transmitted by dogs. In 2005, 13 cases of canine-transmitted human rabies in Latin America were reported, compared with 60 cases of bat-transmitted human rabies (55 from hematophagous bats).

Control of Rabies in Animals

The veterinary component of the Rabies control programme has always had a step motherly attitude whenever such programmes have been initiated by Government agencies and it is only recently that organisations such as APCRI and RIA which have given impetus to canine Rabies control programmes.

Areas for discussion for this topic will mainly focus on, dog rabies control using parenteral vaccination, oral vaccination of stray dogs, and complementary measure to control the dog population such as responsible dog ownership, the control of food resources, sterilization of dogs (ABC programs), establishment of animal shelters and culling.

Rabies control by oral vaccination will be of high significance and will encompass oral vaccination programmes currently implemented, field trials, and evaluation of bait delivery systems.

Recommendations of the World Health Organization, Alliance for Rabies Control, U.S. Centers for Disease Control & Prevention, Animal Welfare Board of India, National Association of State Public Health Veterinarians, National Animal Control Association and World Society for the Protection of Animals need to be followed for eradicating canine rabies by pursuing a focused vaccination strategy, using good quality three-year vaccines.

The ASEAN Secretariat has taken a bold decision to eliminate rabies by 2020; while SAARC is also trying to move towards human rabies elimination. Though many international non-government and humanitarian organizations are involved in animal birth control and rabies vaccination activities in urban areas in some countries, a strong international partnership will be needed to execute a comprehensive rabies elimination programme in the South-East Asia region. WHO has been providing technical support to member countries to launch such a programme.

Recent positive developments in South Asia and South-East Asia towards rabies elimination need to be enforced and supported through international partnerships and funding.

Political commitment, development and execution of comprehensive rabies elimination programmes and community participation are prerequisites for successful rabies elimination.

Necessary tools and methods for control and prevention of dog and human rabies are available, and human rabies elimination has been demonstrated in Europe, America and some countries of Asia. Coordination among major stake-holders, international partnerships, political commitment and regional cooperation are major challenges.

A programme focused on mass vaccination of dogs and animal birth control is largely justified by the future savings in human rabies prevention. This is where dog owners, civic societies, animal welfare and non-government organizations need to play a proactive role.

A concerted effort between the human and animal health sectors can achieve the goals of rabies elimination.

OIE developed international standards to guide Veterinary Services and supporting institutions in fulfilling their responsibility to control stray dog populations, thereby respecting animal welfare standards and taking account of the newest scientific knowledge available should be a priority in rabies control.

But successful rabies control and eradication requires raising public awareness of rabies, collaboration with other professions involved, namely the public health sector and non-healthcare services of municipalities.

Control of rabies is an international public good not only for the current generation, but most importantly for all future generations!

Since 2007, the OIE, along with its partners, has been strongly supporting and promoting the World Rabies Day held every year on the 28th of September. The in-depth studies of OIE have revealed that the National Veterinary Services of many developing or in-transition countries need to increase their financial and technical capacity to effectively control rabies.

This needs to be carried out through a sustainable high quality vaccination campaigns in dogs to increase accurate laboratory diagnosis to rule out rabies infection in dogs, which can avoid unnecessary and costly post-exposure treatment of humans since post-exposure treatment in humans is about 20-100 times higher than the vaccination of a dog against rabies.

Oral and parenteral vaccinations are strongly recommended particularly for wildlife and canine rabies control. Massive depopulation of animals is not recommended.

Complementary approaches including animal birth control (ABC) for dogs should also be considered. Rabies vaccines must adhere to OIE and WHO international quality, efficacy and safety guidelines. Cost-efficiency must be considered. Evaluation of vaccination campaigns in reservoir species should be pursued to include rabies surveillance and post-vaccination monitoring. Vaccination of dogs is the most important control measure adopted in the country. However, the quality of vaccines, and their antigenicity, the maintenance of cold chain are some of the factors which are responsible for the vaccination failures, which has led to an increase in the incidence of rabies in spite of vaccination.

Vaccinations

Different types of vaccines are available. They are: Nerve tissue vaccines [NTV] (still used in Pakistan and Bangladesh), Suckling mouse brain, purified rabies vaccine [PRV], Tissue culture vaccines [TCV]. **DOSE:** 1 ml Age at primary vaccination should be 12th - 13th week followed by a booster after a month (21 days)- Occasionally

recommended earlier than 3 months. If vaccinated before 3 months, to be repeated at 13th week. The route of administration is Intramuscular or subcutaneous. Booster to be given annually and, subsequently annual or triennial. Regarding adverse reactions or events there is currently no epidemiological data about adverse events or vaccination failure. Accidental human exposure to vaccine,

Post-exposure Antirabies Vaccination

Wound management and vaccination should be done. The schedule for vaccinated dog is as follows:

Immune status is considered protective if dog has undergone minimum of 2 vaccinations.

One dose following bite from a suspected or rabid dog.

Schedule for Unvaccinated Dog is as follows:

Rabid dog bite: Euthanasia preferred. Under isolation and observation if owner unwilling.

Suspected: Under observation for 10-15 days. Vaccination on 0, 3rd, 7th, 14th, 28th and 90th [optional] days.

Rabies Control in Wildlife

There are many sophisticated and modern methods of rabies control in various rabies wildlife reservoirs especially foxes and raccoon dogs

Stray Dog Control

Control of stray dog population is a priority to control Rabies. However due to strict laws pertaining to euthanasia of dogs, animal birth control programmes have been initiated in most metropolitan cities of the country with limited success. The sheer magnitude and logistics of catching, neutering and releasing of such a huge number of strays has been a constraint in the successful outcome of the programme. The stray dog control programme includes

1. Animal Birth Control Programme

In 2001, the Government of India passed the Dog Control ABC Rules which made it illegal to kill a dog unless it was terminally ill or badly injured and a nationwide ABC programme was started. The control of stray dogs which was being done by Municipal corporations, in most cases with horrific consequences was handed over to Animal Welfare Organizations through out the country. Enforcement is still weak and sporadic mass killing does still take place on occasion in a knee-jerk reaction to complaints from the public, but usually only where no effective ABC programme has been set up.

There have been many success stories of this programme and the following two examples are cited here.

The Blue Cross of India Chennai and People for Animals have carried out well over a 1,000 spays every month for the last several years. Every year that went by there has been a drop in the number of rabies cases, from a

high of 120 reported human cases in Chennai in 1996 to five cases in 2004 and zero in 2009.

Encouraged by the Chennai story, the Ministry of Environment & Forests is now working out a roadmap for a rabies free India which hopefully will be in place in a few months. If the program is properly implemented, India will no longer be the largest contributor to the world's human rabies cases as it is at present.

The Marwar Trust, located in Jodhpur, is dedicated to the control of stray dog populations and canine rabies in Jodhpur. Since 2004, the Trust has undertaken a high-intensity Animal Birth Control and rabies vaccination program. 48,000 dogs have been sterilized and vaccinated. Alongside this program, the Trust organizes dog-bite prevention and rabies awareness lessons in the local schools

“Adopt a Village” Programme for Rabies Control in India

A joint programme with Global Alliance for Rabies Control, Rabies in Asia Foundation and the Commonwealth Veterinary Association has been set up in India. In this programme ten villages surrounding Bangalore and Pune, will benefit from a programme aimed at reducing the incidence of human and animal rabies through improved educational awareness and mass vaccination of dogs. A large number of medical and veterinary partners will work together in the target villages to educate people in their own language with sensitivity to their customs.

The Gates Foundation/WHO Project

At the end of 2008 the Bill and Melinda Gates Foundation (GF) agreed to fund a 5 year project (2009-2013) for human and dog rabies elimination in parts of the Philippines, South Africa and Tanzania. The goal of this project is to prevent human rabies through the control and eventual elimination of canine rabies, creating a paradigm shift in human rabies prevention in Africa and Asia.

The project which is managed by the WHO will demonstrate in today's context in Asia and Africa the feasibility and sustainability of human rabies prevention through dog rabies elimination, and catalyze similar initiatives in Africa and Asia within the next decade.

Since project initiation in early 2009 much has been achieved in Kwa Zulu Natal (KZN), Republic of South Africa, to reach project objectives. For example, dog ecology studies across the province to determine required baseline data as well as advocacy and “primary canine health care” activities were initiated in 2009. These activities are essential preparation for mass vaccination campaigns aiming to reach more than 600,000 dogs during 2010. The “primary canine health care” concept

developed in KZN aims at providing dog owners with more than free rabies immunization services. General health care and reproduction control are also provided to help secure participation in dog mass vaccination campaigns and responsible dog ownership.

In the Philippines the first phase of the project covers the Western Visayas and 2 provinces of Central Visayas with a human population of 8.7 million. The Western Visayas (region 6) have consistently reported the highest number of animal bite patients of the entire Visayas.

Collection of baseline data on dog population and rabies cases were completed in the area at the end of 2009. Social preparation, health promotion and **advocacy activities as well as dog vaccinator training and preventive immunization** were conducted during the 1st quarter of 2010. Dog registration and rabies vaccination are now being initiated. Some 650,000 doses of dog rabies vaccine are being dispatched to cover the requirements of the western Visayas.

Sri Lanka Project

Blue Paw Trust (BPT) is a non-profit organization in Sri Lanka having a humane dog population and rabies management project called “Dog Managed Zones” (DMZs) as a reasonable solution to the roaming dog population

The existing dogs in an area remain within a controlled environment and are not dumped at other locations. A DMZ is an area which is enclosed adequately and therefore restricts entry and exit of roaming dogs. It contains a limited number of dogs that are sterilized and vaccinated against rabies and are generally healthy. The presence of these animals, due to their natural territorial behavior, helps prevent unknown roaming dogs from entering the premises. Components of the program include:

- existing dogs remaining within the zone;
- sterilization of all dogs within the premises and buffer zone (males and females);
- initial and follow up annual vaccination;
- feeding stations for all dogs within the zone away from public areas;
- proper garbage disposal and control;
- staff education concerning rabies control, bite prevention, feeding methods and garbage disposal; and
- encouragement of staff to promote this important service to free their community of rabies

Non Surgical Dog Population Control

Non-surgical sterilants can enhance Rabies control. In late 2008, the Found Animals Foundation and its strategic partner the Alliance for Contraception in Cat &

Dogs (ACC&D) announced a pledge of \$75 million for the creation of a non-surgical sterilant for cats and dogs. The Found Animals Foundation has put forth the \$25 million Michelson Prize in Reproductive Biology along with the companion Michelson Grants program which offers up to \$50 million to advance research on promising non-surgical approaches. EsterilSo ITM is also being used in field clinics throughout much of Latin America, including Mexico where 10,000 dogs were sterilized using the product. This new sterilization product can provide a low cost, effective, culturally acceptable alternative to surgical castration, and is an important tool in high volume sterilization programs for male dogs. Working with key stakeholders, animal welfare organizations, and governments, will help build sustainable, safer and healthier communities in developing nations

New Directions in Rabies Ecology

Studying rabies through an ecological lens provides researchers and public health practitioners with a better understanding of the remarkable emergent (and re-emergent) properties of the rabies virus.

The human health hazard and economic expense of control make rabies an insidious disease worthy of elimination; nonetheless, the very properties that make it a tenacious and dangerous disease, also make rabies ecology fascinating. Rabies is a remarkably resilient disease for such a fragile RNA virus, exemplified by its persistence in North American wildlife. Despite elimination of rabies in domestic dogs in the US and hundreds of millions of dollars spent on control efforts each year, the virus continues to circulate among multiple wildlife species including skunk, gray fox, raccoon, mongoose, and bats. The success of the rabies virus hinges on TWO factors:

- Rabies can persist in wildlife reservoirs for decades, despite high morbidity and mortality rates, and
- Rabies can successfully switch reservoir hosts to occupy empty host niches.

By studying the ecological and virological factors that promote the emergence and re-emergence of rabies, we can advance our understanding of how to control rabies outbreaks

Our understanding of rabies disease ecology has increased substantially with the advent of molecular ecological techniques. Host ecology has benefited from

supplementing traditional radio-telemetry studies of habitat use with population genetic approaches.

With these techniques, we can more accurately estimate population wise dispersal, as well as identify barriers to dispersal across the landscape to predict the potential emergence of rabies.

Similarly, using molecular epidemiological approaches with the virus, we can reconstruct the history of an outbreak, infer the source of the outbreak, and trace how rabies spreads across the landscape.

The molecular ecology of both host and pathogen can be placed in a geographical context so that we can predict how land use and land cover affect rabies emergence.

Although these factors have been investigated separately, a holistic approach to the study of rabies is missing; thus, it is unknown how virus, host and environment interact to maintain rabies on the landscape.

Ecological genomics provides a new frontier in which we can study the ecology of rabies. As whole genomes become cheaper and easier to sequence, our understanding of the molecular underpinnings of transmission and immunology advance

Bridging our knowledge of how rabies genes function in a laboratory setting with our understanding of how the virus propagates in nature is the challenge for the next generation of rabies ecologists. How different genotypes and phenotypes of host and pathogen interact with the environment will inform our ability to predict disease outbreaks, and ultimately assist us in controlling rabies.

The celebration of World Rabies Day every year since 2007 has contributed in advocacy, awareness and education for rabies prevention and control in countries of the region where it is endemic.

Let us hope that we will be able to launch a campaign for human rabies elimination by 2020

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