Rabies is an acute, typically fatal, progressive encephalitis of humans and other mammals, caused by infection with virus species in the Lyssavirus genus of the Rhabdoviridae family. Virus present in saliva late in infection is generally transmitted to susceptible hosts by the bite of diseased animals. The dramatic nature of the signs and symptoms and the invariably fatal outcome of infection have long caught the imagination. The first definitive description of the disease is contained in Aristotle’s The History of Animals, written approximately 350 years BCE, although apparent reference to the disease and its consequences is made in the Laws of Eshnunna from present-day Iraq, dating back at least 2000 years BCE.

The genus *Lyssavirus* includes rabies virus (RABV) and twelve so-called rabies-related viruses. Based on phylogenetic relationships and antigenic properties, the genus has been subdivided into two phylogroups. Phylogroup 1 includes RABV, Australian bat lyssavirus (ABLV), Duvenhage virus (DUVV), European bat lyssaviruses 1 and 2 (EBLV 1 & 2), Aravan virus (ARAV), Khujand virus (KHUV) and Irkut virus (IRKV), whereas phylogroup 2 includes Lagos bat virus (LBV), Mokola virus (MOKV), and Shimoni bat virus (SHIBV) a recently-isolated virus from a bat in Kenya. West Caucasian bat virus (WCBV) from Russia is more divergent and is not a member of either phylogroup. Three related viruses, Bokeloh bat lyssavirus, Ikoma lyssavirus and Lleida bat lyssavirus, may be members of the genus but have not as yet been approved as species. Bats (order Chiroptera) are the principal reservoir hosts for the majority of lyssaviruses, whereas carnivores (order Carnivora) and bats (in the Americas only) maintain circulation of RABV. Current rabies vaccines appear to protect against infection with lyssaviruses in phylogroup 1, but afford no protection against phylogroup 2 or more divergent viruses.

**EPIDEMIOLOGY**

RABV is widely distributed around the world. Territories reported to be free of the virus are mainly islands and peninsulas. These include Great Britain, Ireland, Iceland, Sweden, Norway (apart from the Svalbard Islands to the north of the mainland), Denmark, Portugal, Spain, Gibraltar, Malta, Albania, Cyprus, Bahrain, Oman, Qatar, United Arab Emirates, Hong Kong, the Malaysian peninsula, Singapore, certain Indonesian and Philippine islands, Republic of Korea, Japan, Australia, New Zealand, Fiji, Hawaii and certain other western Pacific and Caribbean islands, Libya, Cape Verde, Sao Tome, Comores, Mauritius and Antarctica, but several of the countries mentioned in the Persian Gulf and South East Asia occasionally experience re-introductions of the disease. Several countries in western Europe have eradicated RABV as a result of successful oral vaccination campaigns in fox
Livestock Health, Management and Production › High Impact Diseases › Contagious diseases › Rabies

populations, but have nevertheless reported the presence of bat-associated lyssaviruses. In 1996, European bat lyssavirus 2 was also found in a bat in Britain, hitherto considered to be free of lyssaviruses. Apart from rare imported cases of the disease, Australia has always been free of RABV but ABLV has been recognized in fruit bats (flying foxes) as well as in insectivorous bats, and since November 1996, three people have died as a result of ABLV infection after being bitten or scratched by bats.

The distribution of rabies in South Africa by major host species. From Rabies Guide for the Medical, Veterinary and Allied Professions, 2nd edition (2010). Reproduced with permission from the Directorate Animal Health, Department of Agriculture, Forestry and Fisheries

Rabies was diagnosed for the first time on the African continent during an outbreak in dogs in the Eastern Cape Province of South Africa in 1893, although historical writings suggest that suspected rabies cases had previously occurred in that country some time prior to this, in dogs and in humans. The virus in dogs was apparently eradicated by August 1894 through muzzling, restriction of dog movements, and the destruction of stray animals, as rabies was not confirmed again in South Africa for 34 years after this. During this time however, there was mounting anecdotal evidence of an endemic form of the disease in small wild carnivores, including genets (*Genetta genetta*) and yellow mongooses (*Cynictis penicillata*). The disease was confirmed in 1928 in two children bitten by a yellow mongoose in the North-West Province, and since that time rabies has been diagnosed regularly in South Africa. Elsewhere in southern Africa, sporadic outbreaks of the disease occurred in the first half of the 20th century. Then, in 1947 a large outbreak of dog rabies originated in northern Namibia, sweeping south and east across the continent to reach Botswana, Zimbabwe and the
Livestock Health, Management and Production › High Impact Diseases › Contagious diseases › Rabies

Limpopo Province of South Africa by 1950. From here, the disease crossed into central Mozambique in 1952 and entered Swaziland in 1954. In 1961, dog rabies spread from the Maputo district in southern Mozambique into northern KwaZulu-Natal in South Africa. Apart from unconfirmed reports of the disease in the nineteenth century, KwaZulu-Natal had hitherto been free of rabies, and the epidemic which followed the introduction of the virus in 1961 was of an intensity unprecedented in South Africa. Vigorous efforts were made to control the disease through the vaccination of dogs and the prohibition of translocation of unvaccinated individuals, and these led to the outbreak in KwaZulu-Natal being finally brought to an end late in 1968. Rabies reappeared in the northern districts of KwaZulu-Natal, adjacent to the Maputo district of Mozambique, in 1976 at a time when there was an influx of refugees fleeing the unsettled conditions that followed the assumption of independence by Mozambique from Portugal. After its re-introduction into Kwazulu-Natal in 1976, dog rabies proved to be intractable. Currently, the entire South Africa is considered endemic for rabies, with a focus in dogs in KwaZulu-Natal extending into the Eastern Cape and Mpumalanga provinces, and outbreaks seen in Limpopo and Gauteng provinces.

Although all mammals are susceptible to infection with RABV, certain species are capable of sustained intraspecies maintenance of particular viral variants adapted to those species. Such reservoir species are found among members of the order Carnivora (in the families Canidae, Herpestidae, Procyonidae, and Mephitidae), and Chiroptera (bats - only in the Americas). Molecular epidemiology studies of RABV isolates reveal several distinct lineages, the most widely distributed of which is the cosmopolitan lineage, thought to have originated in Europe and spread to many parts of the world with the movement of dogs during colonial times. Within this lineage, strains may cluster by geographic region into particular clades, such as the Africa 1a (northern Africa) and Africa 1b (southern Africa) clades. Distinct clades are also represented by virus strains (so-called ‘biotypes’) circulating in particular host species. These are the result of genetic adaptation of RABV variants to those species. Hosts of a particular virus biotype tend to be more susceptible to lethal infection with that biotype, and tend to excrete virus of the adapted biotype more readily than other biotypes. This leads to improved maintenance of the virus biotype in populations of that host species (hence the designation as ‘reservoir hosts’); however, it must be noted that spillover of host-adapted strains to other species occurs frequently, with occasional adaptation to those species. Rabies infection with any strain of RABV is fatal in all species, with little evidence of a carrier state where virus is shed in the absence of clinical progression of the disease.

Two biotypes of RABV occur in southern Africa, adapted to hosts belonging to the Canidae family (the canid biotype) and hosts belonging to the Herpestidae family (the mongoose biotype). In South Africa, the mongoose variant occurs principally in the yellow mongoose, although a number of early cases in genets (of the Viverridae family) gave rise to the misnomer ‘viverrid rabies’. Yellow mongooses, and mongoose rabies, are distributed over the central plateau of southern Africa. The major host species of the canid biotype in South Africa are dogs, black-backed jackals (Canis mesomelas) and bat-eared foxes (Otocyon megalotis). Rabies in jackals is predominantly seen in Limpopo Province and the adjacent North-West Province in the north, while rabies in bat-eared foxes has a geographic focus in the more arid western parts of the country (Northern and Western Cape Provinces).
Spillover infections into non-carnivorous mammals generally do not result in onward transmission of the virus from these dead-end hosts. A notable exception is rabies in greater kudus (*Tragelaphus strepsiceros*) in Namibia. Two extended epidemics have occurred, from 1975 through 1985 (during which an estimated 30,000 – 50,000 kudu died), and 2002 through 2012 (causing reductions of 30 – 70% in kudu populations). Epidemiological and phylogenetic evidence suggests that kudu populations are capable of maintaining the virus for extended periods (perhaps even indefinitely) following initial spillover of a canid variant, and that the virus is undergoing adaptation to its new host. Kudus are highly susceptible to infection by the oral route, and infected individuals excrete high concentrations of rabies virus in saliva. Rabies virus is not ordinarily resistant enough for indirect transmission to occur through contamination of the environment with infected saliva, and it is believed that transmission between kudus was favoured by their propensity to indulge in self and mutual grooming, and by the fact that oral transmission is facilitated by the mouth injuries which kudus sustain when browsing on the *Acacia* thorn trees which predominate in the affected area. Individuals sometimes browse in close proximity to each other, particularly when population densities are high, so that transmission of infection through contamination of vegetation is a possibility.

Rabies is ordinarily transmitted by bite, and the occurrence and concentration of virus in saliva varies with virus biotype and host species. Virus is usually present in the saliva of infected animals at the time of onset of discernible illness. Its presence may be intermittent and may terminate one or two days before death. Virus has been demonstrated in saliva or salivary glands up to 13 days before the onset of illness in dogs. Factors which determine the successful transmission of rabies include the dose, route of administration and biotype of the virus, and the susceptibility of the recipient. The severity, location and multiplicity of bites inflicted on the victim also influence the outcome of exposure to infection, and bites on the head and neck are generally associated with the shortest incubation periods and the highest mortality rates. In the host, the virus gains entry into nerve endings through nicotinic acetylcholine receptors in neuromuscular junctions, or through sensory nerve endings of the epithelial/subepithelial tissues and mucous membranes. Once virus has entered nerves, there is passive centripetal transport of subviral genome-containing particles by retrograde axoplasmic flow to the central nervous system (CNS), followed by spread within the CNS. Although infection is usually widespread in the brain in the agonal stages of the disease, there is a tendency for lesions to be most advanced and for highest concentrations of virus antigen to occur in particular locations; these localizations may account for characteristic signs of the disease. Thus, early selectivity for the limbic system which controls the emotions, with relative sparing of the neocortex, could explain the initial retention of alertness with manifestation of aggressiveness and loss of fear which often characterizes the disease. From the time that the infection reaches the central nervous system, passive centrifugal spread of virus by anterograde axoplasmal flow proceeds simultaneously with centripetal spread. Spread to the salivary glands coincides with widespread dissemination of infection in the brain.

Rabies can occasionally be transmitted through non-bite exposure. Contact of infected saliva with mucous membranes or broken skin of a susceptible host, through for example licking, can transmit the infection. Oral infection through the ingestion of infected milk has been recorded, although consumption of pasteurized milk should not pose a danger. While there are reports of people developing rabies after skinning and butchering the carcasses of infected animals, it has never been recorded that humans have acquired the infection by ingesting the tissues of infected livestock.
Aerosol transmission has been documented only in very unusual circumstances, including in two people who had separately visited a cave in the USA, home to a population of more than 20 million bats in which rabies virus infection was endemic. Infection has also been iatrogenically transmitted through organ transplantation from infected donors to recipients.

While unusual modes of transmission may be of interest in particular circumstances, it must be borne in mind that the vast majority of human exposures and deaths (> 90% worldwide) due to RABV infection result from contact with rabid dogs. Domestic dogs are the major reservoir in Africa and Asia, and effective control of the disease in dogs is a necessary component of rabies control plans in these regions.

**PATHOGENESIS**

The period of time between inoculation of virus and appearance of clinical signs is determined by factors including the inoculating dose and, for bite wounds, the site of inoculation. The incubation period following a bite exposure is usually between 20 and 90 days in humans and from two to eight weeks in dogs, but may rarely be as short as a few days or longer than a year. Incubation periods of 19 and 25 years, although not definitely proven, are suspected to have occurred in two human patients. Following inoculation via a bite wound, virus undergoes a variable period of replication at the
site of the bite, before gaining entry into the peripheral nervous system. This occurs through binding to
nicotinic acetylcholine receptors at the neuromuscular junction. Virus may also gain entry through
sensory nerve endings in epithelial/subepithelial tissues and mucous membranes. Once in the
peripheral nerves, virus travels by retrograde vast axonal transport to the central nervous system
(CNS). Rapid dissemination of virus in the CNS is associated with neuronal dysfunction. This
coincides with centrifugal spread along neuronal routes to peripheral sites, including the salivary
glands.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Clinical signs and pathology

Rabies should be suspected in cases of abnormal behaviour in animals, particularly when the affected
animal comes from an area where the disease is known to be active, or when there is a history that
suggests possible exposure to infection. Currently there are no reliable ante mortem tests for rabies
infection. Confirmation of a diagnosis therefore relies on demonstrating the presence of the virus or
antigen in the brain tissue post mortem. Animals with clinical signs suggestive of rabies, or displaying
any progressive neurological disease in a rabies-endemic area, should be euthanized for
examination. In certain circumstances where a dog has bitten humans or another animal/s, authorized
persons (state veterinary officials) may confine the animal and keep it under observation for 10–14
days (the maximum time period measured between the presence of virus in salivary glands and the
eventual onset of clinical signs). If the animal remains alive and healthy at the end of this period of
observation, it can be concluded that the probability that the animal was infectious at the time that it
inflicted the bite was very slight. Animals displaying signs of illness consistent with rabies during the
period of observation must however be euthanized and brain samples submitted for laboratory
examination. In cases where they are suspected of exposing humans to infection, wild animals, feral
dogs, or stray dogs whose owner cannot be traced, should be euthanized for examination.

Animals should be killed in such a manner as to avoid damaging the cranium. Protective clothing to
be worn while collecting specimens should include gloves, an impermeable apron and a face mask or
visor, and personnel should be immunized. The hippocampus is commonly used for the diagnosis of
rabies, but the distribution of virus antigen varies and it should be routine to take tissue samples from
a variety of sites in the brain. Brain specimens to be submitted for laboratory examination include 10–
20 mm³ blocks of cerebrum, cerebellum, hippocampus, medulla, thalamus and brain stem preserved
in duplicate in 50 per cent glycerol-saline solution for virological examination and in ten per cent
buffered formalin for histopathological examination. Where small animals are involved, half of the
brain (sectioned sagittally) may simply be placed in the glycerol-saline preservative and the other half
in the formalin. If preservative is not available, specimens may be stored in empty containers on ice
and submitted to the laboratory without delay. Adequate samples for making an accurate diagnosis
may also be collected in wide-bore, plastic drinking straws by a method which obviates the need to
skin the head and saw the cranium open: the occipital foramen is exposed with a knife and the
sample is collected by inserting the straw through the foramen and pushing it with a slight twisting
motion towards one of the eyes. The end of the straw containing the plug of brain tissue is cut off into
the container with preservative. Occasionally, virus antigen or infectivity may be demonstrated in
salivary glands and not brain, and it is recommended that samples of submaxillary salivary gland should also be submitted in glycerol-saline and formalin preservatives. Specimen containers are sealed tightly and packed in sufficient absorbent material to soak up the entire liquid contents of the container.

**Laboratory confirmation**

Confirmation of a clinical diagnosis of rabies cannot be made by gross pathology or histology. The fluorescent antibody test (FAT) is the standard diagnostic test used to confirm a diagnosis. The FAT demonstrates the presence of rabies virus antigen in brain smears by means of immunofluorescence using antirabies fluorescein conjugate. The FAT takes only one to three hours to perform, and is of comparable sensitivity to mouse inoculation, with a concordance of 95 to 99 per cent between the two methods when the immunofluorescence test is performed by experienced investigators. The use of the FAT is limited by the costs of acquiring and maintaining a fluorescence microscope. A direct rapid immunohistochemical test (DRIT), employing a short formalin fixation of brain impression smears and requiring no specialized equipment, was shown to be 100% sensitive and specific when compared to the FAT. Supplementary tests include viral isolation in cell culture, mouse inoculation, polymerase chain reaction, and immunohistological tests. Histopathology on formalin-impregnated brain sections is not always informative for rabies infection but may help to exclude conditions in the differential diagnosis of rabies.

**Differential diagnosis**

Diseases which may be or have been, confused with rabies in southern Africa include distemper, infectious canine hepatitis, ehrlichiosis, cerebral babesiosis, toxoplasmosis, cerebral cysticercosis (caused by *Taenia solium*), tetanus, diminazine toxicity, pesticide (such as metaldehyde) and strychnine poisonings in dogs; cerebral theileriosis and babesiosis, thrombotic meningoencephalitis (caused by *Haemophilus somnus*) sporadic bovine encephalomyelitis (caused by *Chlamydophila pecorum*), botulism, lead, urea, chlorinated hydrocarbon and organophosphate poisonings, and cerebrocortical necrosis (caused by thiamine deficiency) in cattle; *coenurus cerebralis* (*Taenia multiceps*) coenuriasis in sheep; heartwater and a variety of plant poisonings (such as those caused by *Homeria* and *Morea* spp., *Matricaria nigellifolia*, *Cestrum* spp., *Cynanchum* spp., *Dipcadi glauca*) and the mycotoxicosis, diplodiosis, caused by the fungus *Diplodia maydis* in domestic ruminants; encephalomyelitis caused by equid herpesvirus 1 infection, tetanus, leukencephalomalacia (caused by fumonisin B1 produced by the fungus *Fusarium moniliforme*) and poisoning by *Senecio* spp. in horses; and pesticide poisonings in all animals.

**CONTROL/PREVENTION**

The mainstay of successful rabies control programmes is the immunization of a sufficient proportion of the main reservoir host population to achieve herd immunity and thus to prevent outbreaks of the disease. Domestic dogs are an important reservoir host of RABV across most of its range, and are the principal source of human infections. Rabies control programmes in these regions, that include Africa, Asia, and Latin America, must focus on vaccination to attain herd immunity in this species. The
proportion of a population that needs to be vaccinated to achieve herd immunity and thus control
disease, depends on the basic reproductive rate of the particular disease-causing agent. This is
known as $R_0$, and is defined as the average number of secondary infections produced by an infected
individual in an otherwise susceptible host population. $R_0$ determines whether a pathogen can persist
in such a population, and is valuable for assessing control options. When $R_0$ is less than 1, on
average each infectious individual infects less than one other individual, and the pathogen will die out
in the population. In contrast, when $R_0$ exceeds 1 there is an exponential rise in the number of cases
over time, and an epidemic results. $R_0$ has been estimated from rabies outbreaks in dog populations
around the world, and has consistently been found to be close to the extinction threshold of 1. These
low values of $R_0$ suggest that the critical vaccination coverage required to control disease should be
roughly between 20 and 40% (i.e. 20-40% of the dog population should be immune at any point in
time in order to prevent sustained outbreaks of rabies). Ideally, all puppies born into a population
should be vaccinated when they reach the age of 3 months (to prevent possible interference of
passively-transferred antibodies derived from vaccinated dams). This is possible in areas where dog-
owners are aware of the need for vaccination and have access to affordable veterinary services. Such
a situation has led to the elimination of dog-maintained rabies in many developed nations, including
the U.S.A. and countries in western Europe (although RABV is still maintained in wildlife hosts,
including bats, in the former). In developing countries by contrast, many dog-owners do not have
access to affordable veterinary services, and may not be aware of the need for vaccination. Rabies
control programmes are usually the responsibility of government, and are conducted as short-term
campaigns of mass vaccination, often in response to a rabies outbreak. Although low levels of
vaccination coverage are theoretically required to control dog rabies, the sustained control of the
disease in these situations is hampered by the decline in the proportion of the vaccinated population
that occurs following a mass vaccination campaign, as new susceptible dogs are born into the
population and vaccinated dogs die. In most dog rabies-endemic areas, dog birth rates are high and
therefore coverage levels decline rapidly. If coverage falls below the target threshold of 20-40%
before the next campaign, rabies transmission can be sustained and outbreaks persist. Therefore, the
vaccination coverage that should be achieved during any one campaign will depend on the
demographics (birth and death rates) of the particular dog population, as well as on the interval
between campaigns. Empirical evidence and theoretical studies show that annual campaigns
achieving 70% vaccination coverage in dog populations at each campaign are effective in controlling
and even eliminating rabies in the long term. Thus 70% vaccination coverage in annual campaigns
should remain a universal target for programmes that aim to eliminate dog-maintained rabies. Dogs
younger than three months are often presented by owners during these campaigns, and may be
vaccinated at this age.

Another method that has been widely used in attempts to control dog rabies is culling (the widespread
killing of hosts regardless of infection status). This is based on the assumption that, if host densities
are sufficiently reduced, rabies will be unable to invade or persist in the population. Although the
assumption that rabies transmission rates increase with host density is intuitively appealing, there is
no evidence that this is the case in domestic dog populations. Although some culling efforts have
succeeded through strict authoritarian policies that led to the removal of almost 100% of the dog
population, in almost all cases culling has been ineffective in controlling dog rabies, despite the
removal of significant proportions of the total dog population. For example, nearly 300,000 dogs were culled over a four-year period in Flores, Indonesia in response to a rabies outbreak on that island in 1997. Rabies was still endemic in 2004, even though the total dog population had been reduced by around half. There is no evidence today that culling operations have any significant effects on controlling rabies, and can instead provoke considerable upset in communities, as the vast majority of free-roaming dogs ('strays') in many societies globally are in fact owned. Historically, outbreaks have been brought under control through movement restrictions of dogs, and killing suspect rabid and exposed (bitten) animals. With the advent of effective animal vaccines, mass vaccination has become the mainstay of successful dog rabies control.

Oral vaccination programmes making use of modified live or recombinant vaccines in species-appropriate baits have been used with great effect to control rabies in wildlife in Europe and North America. Successes include the virtual elimination of fox rabies from western Europe, elimination of several variants of RABV in parts of Canada and the USA, and the maintenance of a \textit{cordon sanitaire} against the westward expansion of raccoon rabies in the eastern USA and Canada. Uptake of baits by target and non-target species is assessed by the incorporation of biological markers such as tetracycline, which is deposited in bone and can be demonstrated in cross-sections of teeth, or sulphadimethoxine, a serum marker. Although in the majority of dog populations well-organised mass vaccination campaigns are capable of attaining vaccination coverage of 70% using injectable inactivated vaccines, oral vaccination could be implemented in dog populations where geographic or cultural factors make achieving this target more difficult.

There is no cure for clinical rabies in humans. Prevention of the disease in humans following exposure to a rabid animal relies on prompt flushing of any bite wounds with water, and soap if available, for at least five minutes, followed by timely receipt of post-exposure prophylaxis (PEP). The flow diagram below provides a useful approach for medical and veterinary professionals to the person with a suspected rabies exposure.
1. Assess the risk of transmission (page 36) and category of exposure (see B below).
2. Record full details and history of the incident.
3. If risk of rabies is considered, proceed as indicated in the flow chart.

SOCIO-ECONOMICS

It is estimated that 55,000 people die each year from rabies, and 7 million people are exposed to the virus. Most of these people live in resource-poor countries, where life-saving PEP is not always available or affordable. Rabies control strategies that incorporate mass vaccination of dogs have the potential to be more cost-effective in preventing human rabies deaths than strategies relying on administration of PEP alone, with dog vaccination strategies becoming more cost-effective within 5-6 years of the onset of mass dog vaccination campaigns. These economic benefits are due to the relatively high costs of PEP compared with delivery of dog vaccination, and the escalating costs of PEP over time as rabies incidence continues to rise. However, cost-effectiveness models assume a linear relationship between dog rabies incidence and demand for human PEP, which may not hold true in real-world settings. For example, dog vaccination has been associated with an increased demand for PEP in some parts of Asia, possibly due to increased awareness of the disease both in bite victims and in medical staff. Although provision of PEP to people exposed to rabies is one of the most cost-effective health interventions as measured by cost per death averted (US$200/death averted compared to childhood immunization through the Expanded Program on Immunization at US$205/death averted), it can still be out of financial reach of many bite victims. Vaccine shortages are common in developing countries, and patients may need to travel long distances, often to several clinics, to obtain vaccines. Studies have shown that switching from intramuscular administration of PEP to equally efficacious intradermal regimens will result in significant savings in the volume of
vaccine required to treat the same number of patients, which could mitigate vaccine shortages, and would dramatically reduce the costs of implementing PEP.

The burden of rabies falls disproportionately on one of the most vulnerable sectors of society, namely children, and particularly those in marginalized rural populations. Children from 5-15 years old have an increased risk of exposure, and a higher probability of being bitten on the head, face, or neck, resulting in a relatively high proportion of childhood rabies deaths. Bite victims who live furthest from health facilities and those who are in lower socioeconomic brackets undergo longer delays before receiving PEP, which increases the risk of developing rabies. Even in countries where governments provide vaccine free of charge, considerable costs can be incurred by patients for travel and accommodation (often including the cost of an accompanying family member, in the case of child bite victims), according to the number of clinic visits required (four or five, for intramuscular regimens).

Few data are available on livestock losses due to rabies. It is likely that the extent of losses is underreported. In South Africa, 1,449 cases in cattle were confirmed by laboratory testing from 1992 through to 2006, compared to 4,741 cases in dogs during this same period. A particular problem of livestock rabies occurs in Latin America, where haematophagous bats (vampire bats) that feed on cattle carry RABV. Prior to the advent of safe, effective tissue culture vaccines for animals, it was estimated that rabies killed over 500,000 cattle in a year in Latin America and parts of the Caribbean, at a cost of over US$47 million at the time. The cost of preventing these losses through vaccination of cattle in such areas where spillover occurs from maintenance hosts is borne by farmers.

IMPRESSANT OUTBREAKS

The outbreak of dog rabies that swept across southern Africa in 1947-1950 established the virus in dog populations across the region. The outbreak that followed in KwaZulu-Natal in 1961-1968 was of an unprecedented intensity in South Africa, although it is noteworthy that the disease in dogs was eliminated through intensive vaccination efforts. The virus was reintroduced in 1976, and this region has remained the primary geographic focus of human rabies cases in the country since. Analysis of annual incidence data spanning the 30-year period from 1971-2000 revealed that rabies epidemics in southern and eastern Africa cycle with a period of 3-6 years and show significant synchrony across the region. It is thought that movement of infected dogs and co-ordination of control efforts are important in generating these synchronous cycles across the region.

Significant outbreaks in wild carnivores include the steady westward spread of rabies in red foxes from the time of the Second World War from an original focus in eastern Poland, reaching France by 1968. Many countries in Europe each reported several thousand cases of the disease in foxes per annum in the 1970s and 1980s. The elimination of rabies in red foxes in western Europe through the use of oral vaccines is one of the great success stories in rabies control. Other important outbreaks in wild carnivores have occurred in North America. These include the epidemic of raccoon rabies in the eastern USA, believed to have been initiated by human movement of raccoons from a population in the south-eastern USA in which rabies was endemic, for the purpose of restocking dwindling local populations. The number of cases of raccoon rabies increased from 21 in 1980, soon after the introduction, to over 3,000 in 1997, making it one of the most intensive outbreaks of animal rabies
ever recorded. Several notable outbreaks of rabies in skunks occurred in northern Arizona from 2001-2009. Although skunk-associated virus variants are seen in several parts of North America, the outbreaks in Arizona occurred outside these areas, and were found to be caused by a RABV variant associated with brown bats. Phylogenetic analysis revealed that each of the six outbreaks was caused by an independent introduction of bat-associated RABV into the skunk population, with further spread in these terrestrial hosts. Although it is generally accepted that RABV originally evolved in bats and later shifted to carnivores, examples of such cross-species transmission events are rare, and the Arizona outbreak provided scientists with the opportunity to study the mechanisms of lyssavirus host shifts.

Outbreaks of rabies in previously-free territories are always significant events, due to the potential for establishment of the virus in reservoir populations and the daunting task of preventing human deaths and of eventually eradicating the virus. A recent example occurred on the Indonesian island of Bali, where rabies was introduced in 2008. The first human death was confirmed in November that year, and cases continued to climb, reaching a peak in 2010 of 11 deaths in one month. To date, more than 140 people have died. Early attempts to control the disease focussed on culling dogs, and were largely unsuccessful. Once sufficient resources were mobilized, island-wide mass vaccination campaigns of the estimated 350,000 dogs on the island began. Although challenging, as dogs are not routinely handled by owners and need to be trapped in nets for vaccination, three rounds of mass vaccination have seen over 600,000 doses of vaccine delivered. Human rabies deaths have declined from 83 in 2010, to 26 in 2011, and just 7 in 2012.

FAQS

1. **What is the earliest age at which dogs may be vaccinated against rabies?**

   All dogs (and cats) regardless of age may be safely vaccinated. Dogs and cats younger than three months may be vaccinated. Ideally they should be vaccinated again at three months, followed by a third vaccination within 12 months.

2. **What role do bats play in the transmission of rabies in southern Africa?**

   Infections of bats with RABV have only been confirmed in the Americas. In southern Africa, two bat-associated lyssaviruses (Duvenhage and Lagos bat virus) have been isolated. Lagos bat virus has not been associated with human disease, but has been isolated from two cats in South Africa and Zimbabwe, as well as a water mongoose. Duvenhage virus was isolated from three human rabies patients following exposure to bats, two in South Africa and one in Kenya. A fourth lyssavirus, Mokola virus, has been found in cats and a dog in South Africa and a human in Nigeria, but is not currently associated with bats.

3. **If a dog is positive for rabies, what should be done about the other dogs in the household that were in contact with it?**

   If the other dogs have valid and up-to-date vaccination certificates, they can be given a
booster dose and revaccinated again 3 days later. They should be observed for any signs of rabies for 6 months. If the dogs were not vaccinated, they must be euthanized under the supervision of a veterinarian or authorised person.

4. **Do rodents pose a risk of rabies to humans?**

   Mice and rodents commonly found in and around dwellings or kept as pets, have not been implicated as vectors of rabies.

5. **Does eating meat from a rabid animal pose a risk to humans?**

   Ingestion of cooked meat from rabid animals has not been implicated in the transmission of rabies virus to humans. However, these cases should still be treated as category 2 exposures, requiring the administration of vaccine. There are reports of people acquiring rabies while skinning and butchering carcasses of rabid animals, so these cases (along with slaughtering) should also be treated as category 2 exposures. If injuries are sustained during slaughtering, these are considered category 3 exposures.

6. **Can birds contract rabies?**

   Although birds are susceptible to experimental infection, virus is restricted to the central nervous system and cannot be transmitted to other animals. Early reports of disease in European birds of prey have not been confirmed, and there are no recent records of disease in birds.

7. **Can rabies be transmitted between people?**

   Human-to-human cases have been reported although they are not well documented. Two cases in Ethiopia were reported whose only known exposure was contact (bite/saliva) with family members who had died of rabies. Several cases have been associated with organ transplantation from infected donors. Although natural human-to-human transmission is likely rare, anyone in direct contact with rabies patients should employ barrier nursing techniques to minimize the risk of transmission of the virus via saliva or other secretions.

**REFERENCES**


