Bat lyssavirus infections

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Summary

Bats, which represent approximately 24% of all known mammalian species, frequently act as vectors of lyssaviruses. In particular, insectivorous bats play an important role in the epidemiology of rabies and some rabies-like viruses, while the haematophagous vampire bats are the major wildlife vector for rabies in Latin America. In contrast, the role of fruit bats (flying foxes) in the epidemiology of the recently discovered Australian bat lyssavirus is only just emerging. Information on the pathogenesis of lyssaviruses in bats is scarce. However, in general, mortality in bats infected via a natural route appears to be low, and seroconversion occurs in many of those that survive. While transmission of rabies from an infected bat may be via a bite, other routes are apparently also possible. Methods for the diagnosis of bat lyssavirus infections in bats and terrestrial mammals (including humans) are similar to the classical procedures for rabies. Measures for the prevention and control of these diseases are also similar to those for rabies, although additional innovative methods have been tested, specifically to control vampire bat rabies.

Keywords


Introduction

For almost two thousand years, rabies was thought to be transmitted almost exclusively by the bite of rabid dogs. However, in the early 20th Century, efficient methods emerged for the control of rabies in dogs, and subsequently, it became apparent that wildlife species, particularly carnivores, were also natural vectors. Such species have now become the major vectors of rabies in the developed countries of the world. In the 16th Century, following observations by the early Spanish explorers in the Caribbean, bats were among the first wildlife species to be associated with rabies (43). However, it was probably not until the 18th Century, when vampirism enjoyed some popularity in Europe, that the haematophagous bats of the Caribbean were dubbed vampire bats. A further 200 years then passed before the first scientific descriptions of rabies in vampire bats (Desmodus rotundus) appeared in Trinidad and South America (81). In 1953, a human death associated with a hoary bat (Lasiurus cinereus) in Florida was reported (10, 121), and this encouraged much greater surveillance of bats in North America. Similar activity followed in Europe, Africa and later in Australia, following the discovery of Australian bat lyssavirus (ABL). As a result, rabies and rabies-related viruses, collectively known as bat lyssaviruses, have now been isolated from many insectivorous, frugivorous and haematophagous bats throughout the world.

Bat species throughout the world number approximately 980, representing almost 24% of all known mammalian species (128). Bats belong to the order Chiroptera, and may be sub-divided into two suborders: the Megachiroptera (including fruit bats or flying foxes), and the Microchiroptera (insectivorous and vampire bats) (Table I). The aim of this paper is to review the current state of knowledge concerning infections of bats with bat lyssaviruses. In particular, lyssavirus infections of insectivorous bats throughout the world, rabies infection of vampire bats in Latin America, and ABL infection of fruit bats in Australia will be considered.

Insectivorous bats are present in most, if not all, regions of the world. Those species involved in the transmission of lyssaviruses are largely restricted to the following eight genera: Eptesicus, Myotis, Lasiurus, Lasionycteris, Pipistrellus,
<table>
<thead>
<tr>
<th>Sub-order</th>
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Taxonomy from Wilson and Reeder (128)
Genera infected with lyssaviruses from Amengual et al. (6), Baer and Smith (10), Constantine (21), Hooper et al. (48), Murshed and Standing (89), Smith et al. (103) and Swanepoel (109)
Tadarida, Miniopterus and Nycteris (100; S.A. Nadin-Davis, personal communication). Species of importance in North America include Eptesicus fuscus, Myotis lucifugus, Lasiusurus cinereus, L. borealis and Lasionycteris noctivagans, all of which are commonly found throughout the entire continent (although Lasiusurus spp. tend to avoid the colder northern regions). In contrast, Myotis silicilabrum and M. californicus are usually confined to the eastern and western regions, respectively, M. leibii and M. evotis are more common in the west up to Canada, and Tadarida brasiliensis. Lasiusurus semifolius, L. intermedium and Pipistrellus subflavus have a more southerly range extending into Central America. In the Old World, E. serotinus is the most important vector of lyssaviruses (6). The range of this species includes western Europe and northern Africa, and extends east through Asiatic Russia and the Himalayas to Thailand and the People’s Republic of China. Myotis dasycneme and M. daubentoni are also important but, although found in western Europe, the precise range of these species is poorly defined. Various species of Eptesicus, Miniopterus and Nycteris are widely distributed throughout Africa, but research into their role in the transmission of lyssaviruses is scarce (although Duvenhage virus was isolated from N. thebaica [55, 109]).

There is great variation in the biology of the species mentioned above. Some are gregarious (e.g. Eptesicus spp.) may have hundreds of animals in a colony, M. lucifugus from hundreds to thousands, and T. brasiliensis may number millions per colony), but others are solitary (e.g. L. noctivagans, all Lasiusurus spp. and most Myotis spp.). Some are seasonally migrating species (e.g. M. lucifugus may travel over 500 km, while M. dasycneme, M. daubentoni, L. noctivagans, L. cinereus, L. borealis and T. brasiliensis may all move 2,000 km), and others are sedentary (e.g. Eptesicus spp., most Myotis spp., L. seminolus and L. intermedium). Finally, there are species that live in houses, bridges and other buildings close to man (e.g. Eptesicus spp., M. lucifugus and T. brasiliensis), while others prefer natural sites such as trees, rocks, caves and crevices (e.g. Lasiusurus spp., L. noctivagans and most Myotis spp.). These variations are all likely to influence transmission and dispersal of lyssaviruses by different species of bats.

Within the family Phyllostomidae of the microchiropterans, three of the species feed on blood, namely: Desmodus rotundus (the common vampire bat), Diphylla ecaudata (the hairy-legged vampire bat) and Diaemus youngi (the white-winged vampire bat) (123). The geographical distribution of these three haematophagous species is generally limited to below 1,000 m altitude (although occasionally colonies have also been reported at over 2,000 m), in tropical and subtropical regions of Latin America (39, 110). Although all three species can transmit rabies, only D. rotundus will be considered in this paper, firstly, because it is the most common and has the widest geographical distribution, and secondly, of the three species, it is the primary wildlife vector for rabies, and therefore has the most important role in the epidemiology of the disease in this region. Diphylla ecaudata and D. youngi are less common, and mainly feed on the blood of birds.

In Australia and offshore islands, approximately seventy-five species of bats are found, including both megachiropterans and microchiropterans. These include at least twelve species of fruit bat (also known as flying foxes), all belonging to the family Pteropodidae (19). Only four of these are commonly seen on the mainland, as follows: the grey-headed flying fox (Pteropus poliocephalus), the black flying fox (P. alecto), the little red flying fox (P. scapulatus) and the spectacled flying fox (P. conspicillatus). In contrast, six families of insectivorous bats are present in Australia, with most species belonging to the family Vespertilionidae.

Following the discovery that flying foxes were the likely reservoir of the morbilli-like Hendra virus in Australia (125, 130), surveillance of these animals was increased, particularly of those free-living individuals that were found sick or injured. In 1996, as a direct result of this activity, a newly recognised lyssavirus was discovered in a five-month-old female P. alecto from Ballina, New South Wales (40). The virus, which was originally called Ballina virus but which was later re-named Australian bat lyssavirus, has now been found in all four of the major species of fruit bats in Australia, and also in at least one species of insectivorous bat.

Importance for animal and public health

A priori, the chance of an insectivorous bat transmitting rabies virus to man, or any other terrestrial mammal, would be expected to be low. However, among the thirty-six indigenous cases of rabies diagnosed in humans in the United States of America (USA) since 1980, twenty-one (58%) were associated with bat virus variants. Although Eptesicus spp. (E. fuscus in North America, and E. serotinus in Europe) and Myotis spp. are by far the most common bats species that are found to be rabid, fifteen of the twenty-one human cases (71%) were linked with the silver-haired bat (L. noctivagans) (18, 46). Only one of the twenty-one cases had a clear history of being bitten by a bat. Given the numerous cases that were associated with only a vague history of exposure, it is almost mandatory for post-exposure treatment to be recommended, not only for someone directly scratched or bitten by a bat, but also in those situations where the presence of a bat has been noted in the company of a person, and where the possibility of a bat bite cannot reasonably be excluded.

Although lyssaviruses have been recognised in insectivorous bats in Europe since 1954 (6, 77), there have been only three bat-derived cases of lyssavirus infection in humans in Europe, all of which were reported in 1985 (66, 71). In the aftermath
of these cases, improved surveillance resulted in a marked increase in the number of lyssavirus diagnoses in bats. Approximately 100 bats per year were confirmed as being positive for lyssavirus from 1986 to 1990, and this then stabilised at twelve per year from 1991 to 1997 (6). It was not clear whether this peak in positive cases represented a transient epizootic in insectivorous bats in Europe, or if it was simply a consequence of a more intensive surveillance (or both).

Interestingly, until this time, transmission of bat lyssaviruses to terrestrial animals other than humans had seldom been reported, possibly because the typing of animal isolates is performed only rarely. However, in the summer of 1998, a sheep was found to have died following infection by a European bat lyssavirus (EBL) variant (EBL1) in Denmark (78). Furthermore, both antigenic typing and molecular epidemiological studies in Canada (S.A. Nadin-Davis, personal communication) suggested that a variant of bat origin (probably from Myotis spp.) was transmitted to a bovine in Ontario and to two red foxes on Prince Edward Island where it may then have become established in the fox population (27). Therefore, insectivorous bat lyssaviruses may be recognised more frequently in the future, not only in humans but also in animals.

The common vampire bat is the principal wildlife reservoir of rabies in tropical and subtropical Latin America. The introduction of cattle to this region by the Spanish explorers had important repercussions on the ecology of local vampire bat populations. The appearance of a massive new food source allowed vampire bats to proliferate, leading, in turn, to an increase in the prevalence of rabies, particularly in cattle and humans. Vampire bats cause heavy economic losses in those regions where cattle are farmed, accounting for approximately 100,000 cases of bovine paralytic rabies each year (1). However, even in rabies-free areas, cattle-owners encourage the destruction of the vampire bat because of the skin lesions and blood loss sustained by cattle (3, 122).

The vampire bat is also one of the most important vectors of rabies in humans. Since 1975, more than 490 cases of human rabies have been reported in Latin America involving haematophagous bats (80). A number of common factors associated with these cases have been identified, e.g. a reduction of cattle numbers in the region, lack of household protection against bats, and human colonisation of forested areas. At present, the domestic dog remains the primary rabies vector for humans in Latin America (urban rabies). Nevertheless, urban rabies should eventually be controlled in this region, as demonstrated by countries such as Mexico and Brazil where, following massive campaigns for dog vaccination, concomitant advances in the control of urban rabies have been achieved (76). With the decline in urban rabies, rabies transmitted by haematophagous bats is likely to become more important.

Australia has always been regarded as free of classical rabies, apart from occasional cases introduced by people who have contracted the disease while overseas (33, 68). Although ABL is clearly a lyssavirus belonging to the same serotype as classical rabies virus, it is nevertheless genetically distinct from rabies viruses of terrestrial mammals (41). However, whether this genetic difference reflects marked biological differences between the two viruses is not yet clear. To date, ABL has been responsible for the deaths of two women in Australia, one the subject of an unprovoked attack by a wild fruit bat, and the other a bat-carer who worked closely with fruit bats (5). However, retrospective studies have failed to identify any further human cases (96, 116), and furthermore, no cases of ABL have ever been recorded in domestic animals in Australia.

Following the recognition of ABL, pre-exposure vaccination with standard rabies vaccines was recommended to be undertaken by anyone professionally or recreationally exposed to bats (67). In addition, for anyone directly scratched or bitten by a bat, post-exposure treatment was recommended. Given the widespread distribution of fruit bats in Australia, the question of indirect contact between members of the public and fruit bats was more problematic, e.g. ascertaining the consequences of a large colony of fruit bats in a forest immediately adjacent to a school. While data from studies on classical rabies in bats might be helpful in addressing such issues, simple extrapolation to the situation in Australia could be dangerous.

Aetiology

Rabies and rabies-related viruses belong to the family *Rhabdoviridae* (from the Greek *rhabdos*, meaning rod), genus *Lyssavirus* (from the Greek *lyssa*, meaning madness). Louis Pasteur had postulated, as early as the 1880s, that such an agent caused rabies, and initially rabies virus was the only viral agent caused rabies, and initially rabies virus was the only recognised member of the genus. However, in 1956, the first rabies-related viruses were isolated in Africa and Europe (13, 14, 55), and currently four serotypes (14, 54, 97) and seven genotypes (14, 41) are recognised in the genus.

Serotypes are defined by cross neutralisation studies and reactivity profiles with monoclonal antibodies, whereas genotypes are defined by phylogenetic analysis of viral genes (Fig. 1). Classical rabies virus, which has a world-wide distribution, belongs to serotype and genotype 1 (sero-genotype 1). Sero-genotypes 2 (Lagos bat virus), 3 (Mokola virus) and 4 (Duvenhage virus) have only been isolated in Africa, while genotypes 5 (EBL1) and 6 (EBL2) have only been found in Europe (13, 14, 55). Genotype 7 has been proposed for ABL (41), which is currently only known to exist in Australia. This virus appears to belong to serotype 1. All but serotype 2 are known to be associated with human deaths. In summary, it is important to note that, to date, all bat lyssaviruses isolated in the Americas belong to genotype 1,
ABL: Australian bat lyssavirus
EBL: European bat lyssavirus

Fig. 1
Radial phylogenetic tree of the lyssavirus genus estimated by comparison of the partial nucleotide sequence of the ectodomain of the glycoprotein

While all those isolated from Europe, Africa and Australia are rabies-related viruses belonging to genotypes 2, 4, 5, 6 and 7. While genotypes are differentiated on the basis of phylogenetic analysis, another characteristic that distinguishes lyssaviruses in genotypes 1, 4, 5 and 6 from those in genotypes 2 and 3 is pathogenicity in mice. The former are pathogenic in adult mice following inoculation via cerebral or peripheral routes, whereas the latter are only pathogenic when administered intracerebrally. In addition, only pathogenic lyssaviruses suppress the antigen-specific cell-mediated immune response in mice (88).

In general, lyssaviruses have a bullet-shaped morphology with one end round and the other flat (115) (Fig. 2). The diameter of the virus may range from 50 nm to 100 nm, and length...
from 100 nm to 430 nm, depending on the virus species, and on the presence of defective interfering particles. A lyssavirus virion is composed of a central ribonucleoprotein complex (RNP), tightly coiled and with helical symmetry. The RNP is composed of a ribonucleic acid (RNA) genome (approximately 12,000 nucleotides, single-stranded, negative polarity) that is intimately associated with multiple copies of the nucleoprotein (N protein), and of the polymerase (L protein) and its co-factor, the phosphoprotein (P protein). The bullet-shaped lipoprotein envelope, derived from the host cell during budding, surrounds the RNP, and embedded within this envelope are many knobbed spikes, each of which is a trimer of a glycoprotein (G protein). A fifth viral protein, the matrix protein (M protein), lies between the envelope and the RNP. This may be embedded in the inner layer of the envelope, or in the central axis of the RNP, or both.

While rabies virus can be grown in vitro on many cell types (115), the virus in vivo is extremely neurotropic. This specificity is mediated by the G protein which recognises neuro-specific receptors on the membrane of neurons. Candidates for the receptor include the acetyl-choline receptor (61), the neural cell adhesion molecule (N-Cam) (112) and the low affinity nerve growth factor receptor molecule (p75NTR) (120). In addition, phospholipids, gangliosides and carbohydrates are also involved in virus entry (119).

Once bound, the virus enters the cell via endosomes (115). As the pH decreases within the endosome, conformational changes in the G protein provoke fusion between the viral and endosomal membranes, and the RNP is delivered to the cytoplasm where viral expression and replication take place. Progeny virus eventually leave the host cell by budding.

**Epidemiology**

While many insectivorous and haematophagous bats are included among the vectors of sero-genotype 1 viruses, bats often appear to be the preferential vector species for the rabies-related viruses of sero-genotypes 2-7. Chiropterans are the exclusive vectors of five genotypes: genotype 2 preferentially circulates in the frugivorous megachiropterans of Africa (Eidolon and Epomophorus spp.) (109); genotype 7 in frugivorous and insectivorous species of Australia (48); genotype 4 in insectivorous bats of Africa (Miniopterus and Nycteris spp.) (55, 109); and genotypes 5 and 6 in insectivorous bats of Europe belonging to the Eptesicus and Myotis genera, respectively (6, 13, 14). Furthermore, although genotype 3 has been isolated from shrews, cats, a dog and a rodent (Lophuromys sikapusi) (109), the reservoir species has not been identified. Bats have yet to be excluded. These observations lend credulity to the hypothesis that many lyssaviruses were originally viruses of bats, and some were eventually transmitted to terrestrial species, principally carnivores.

Bats therefore appear to have a very prominent role in the epidemiology of lyssaviruses. While transmission of lyssaviruses from bats to terrestrial mammals has been reported only rarely (see above), transmission between different insectivorous bat species has been demonstrated by molecular epidemiological studies on rabies virus (6, 65, 100; S.A. Nadin-Davis, personal communication). In general, a particular species of bat seems to act as a vector for a specific variant of the rabies virus, suggesting a rather precise adaptation of virus to bat, and a long-term co-evolution between the two. However, exceptions occur, and a number of Myotis spp. are vectors for many different variants of rabies virus from other bat genera (S.A. Nadin-Davis, personal communication). The roosting habits and lifestyle of these bats may facilitate a rapid spillover of variants from other species. As Myotis variants have also been found in terrestrial species (e.g. cattle and foxes), the Myotis genus may be a favoured intermediate for lyssavirus interspecies transmission (and thus a preferred target for rabies surveillance). The L nattiwagans variant also apparently has great potential for interspecies spillover, given the great number of cases of human rabies caused by this variant in the USA (see above). This may be due to the unusual growth properties of this variant (73). Finally, circumstantial evidence suggests that EBL1 was transmitted from insectivorous bats to African fruit bats (Rousettus aegyptiacus) that had been held in a zoo in Europe (91).

These results highlight the contribution of molecular epidemiological studies, particularly over the last decade, to current understanding of the epidemiology of lyssaviruses, especially rabies. Through a combination of the polymerase chain reaction and rapid sequencing procedures, nucleotide and deduced amino acid sequence of viral proteins can now be obtained very rapidly. By judicious selection of the region of the genome to be sequenced (92, 99, 113, 114), isolates can be compared either across, or within, sero-genotypes. The subsequent construction of phylogenetic trees has indicated that, in general, lyssavirus isolates cluster into distinct lineages according to the following (56, 93, 98, 113):

a) geographical origin
b) whether the isolates are cosmopolitan or indigenous, and
c) vector species (suggesting that a number of variants are well adapted to their hosts).

As an example of the power of molecular epidemiology, the partial gene sequence of a rabies isolate can be used to identify the source of the rabies infection precisely, e.g. in a region such as Central or South America, where dog and vampire bat rabies are both present, it is possible to determine not only whether an isolate is of canine or chiropteran origin, but also its geographical origin (65).

The vampire bat is a non-migratory species which finds natural shelters either in the wild or associated with human habitation. Although temperature (22°C-25°C) and humidity...
Fig. 2
Structure of a lyssavirus
Design: P. Le Mercier, Lyssavirus Laboratory, Pasteur Institute, Paris
constructions in some subtropical zones of drainage and irrigation channels, and other man-made. The distribution of the common vampire bat in Central and South America is relatively stable, although new bridges, drainage and irrigation channels, and other man-made constructions in some subtropical zones of Mexico (e.g., northern Veracruz) have contributed to a slightly wider distribution of this species in some locations (35). The distribution of vampire bat species, in contrast, is more variable and less well-defined. This is demonstrated by changes in the distribution of the disease in Mexico. Despite relative stability in the distribution of the common vampire in Mexico, a dramatic increase in the distribution of vampire bats has been recorded in recent times. In the 1970s, an area comprising the States of Tamaulipas, Veracruz, and Tabasco bordering the Gulf of Mexico, and Quintana Roo on the Caribbean Sea, was free of rabies. This region represented approximately 38% of the area occupied by vampire bats in Mexico. However, rabies now affects most vampire bat populations in this area, only a small area of Tamaulipas being free (approximately 8% of the total area occupied by vampire bats) (12). This spectacular extension of the disease can be attributed to changes in the population density of vampire bats in and around this region (3).

Lyssaviruses have previously been associated with fruit bats in Africa (109) and Asia (103). The first recognised case of ABL in fruit bats in Australia was in 1996 (40), although the earliest recorded case was in January 1995. This was diagnosed retrospectively by identification of antigen in stored tissues (104). However, further attempts to pinpoint the advent of ABL in Australia have been thwarted by the paucity of stored sera or other appropriate tissues. Indirect evidence as to the length of time that ABL has been in Australia is conflicting. Hooper et al. showed that the nucleotide and amino acid sequences of the N protein from sixteen isolates of ABL collected from all regions of Australia were highly conserved (48). This uniformity might suggest that the virus has spread throughout the country only recently. Conversely, examples exist throughout the world of specific rabies virus variants where limited genetic variation of the variant indicates a state of equilibrium between the host and the virus, suggesting a long-term relationship (36, 100).

Certainly, a slight, but consistent, difference has been identified in the nucleotide sequences of isolates from pteropid bats compared to those few isolates from an insectivorous bat, the yellow-bellied sheath-tailed bat (Saccalaimus flaviventris) (48). This would be consistent with the view that ABL has existed in Australia at least long enough for two separate populations of the virus to evolve.

Sick and injured fruit bats in which ABL antigen has been demonstrated in the central nervous system (CNS) have been identified throughout much of the geographical range of the four major species. A serological survey of a mixture of healthy and sick fruit bats found that 16% were seropositive to ABL (48), thereby confirming the widespread distribution of the virus, and also suggesting that seropositive fruit bats are more common than those with overt disease. However, no data have been published on the seroprevalence of ABL in free-flying fruit bats in Australia. In addition, virtually no information exists on the geographical distribution of the disease, nor on the prevalence of the virus, in insectivorous bats of Australia.

Australian bat lyssavirus appears to primarily infect bats, at least in Australia. Despite an excellent regional veterinary laboratory system, and a long-standing interest among veterinary pathologists in wildlife disease, no disease that
could clearly be attributed to ABL has ever been reported in domestic or terrestrial wildlife species in Australia. The only recognised cases of infection in terrestrial mammals have been in two humans. Little, if any, work has been performed on the prevalence of ABL outside Australia.

The incubation period for lyssavirus infections of bats can range from weeks to months (15). Limited data suggest that the length of time may vary inversely with the dose of inoculum (9, 72) and, in addition, may be influenced by the ambient temperature. Experimental studies have found that hibernating bats appear to be resistant to infection, but that once infected, hibernation simply delayed the onset of clinical signs of disease. The disease continued to develop very slowly in hibernating bats (94, 108). Baer and Bales also suggested that longer incubation periods were generally associated with higher titres of virus in the salivary glands of bats (9).

**Pathogenesis**

Murphy et al. demonstrated that the pathogenesis of a vampire bat strain of rabies virus in hamsters was very similar to the pathogenesis of two other strains of rabies virus, and of Mokola and Lagos bat viruses (74, 75). This suggested a degree of uniformity in the action of lyssaviruses, at least following infection of terrestrial mammals. However, only fragmented data exist on the pathogenesis of lyssavirus infections in bats. Of the information that is available, most relates to rabies infections in insectivorous bats, little is available on vampire bat rabies, and almost nothing on fruit bats infected with ABL.

Many pathogenesis studies in the past have relied on intracerebral inoculation of bats using virus isolates from terrestrial mammals as the inoculum. However, the comparative studies by Baer and Bales (9) and Moreno and Baer (72) clearly showed that, for approximately the same dose of inoculum, intracerebral inoculation of bats resulted in higher mortality, more frequent infection of salivary glands, and earlier, more consistent excretion of virus in saliva than occurs with peripherally-inoculated bats. With hindsight, it appears that, in attempting to dissect the true pathogenesis of natural lyssavirus infections in bats, it may be prudent to consider only the results from those studies likely to simulate a natural infection in bats, i.e. peripheral inoculation with bat-derived isolates of lyssaviruses.

Baer and Bales conducted one of the most thorough pathogenesis studies in the late 1960s, using the insectivorous Mexican free tail bat (T. brasiliensis) (9). Having demonstrated that only approximately 20% of insectivorous bats (9/46) died following peripheral inoculation of up to 2,000 times the lethal dose 50 (LD50) of virus (including one that was found to be heavily infected at euthanasia, and therefore likely to have died), the researchers suggested that insectivorous bats were relatively insusceptible to disease following natural infection with bat isolates of rabies virus. Numerous other studies of insectivorous bats, summarised in Table II, support this contention (20, 24, 59, 105, 108). Similar mortality was demonstrated in vampire bats (16/42, 38%) inoculated with up to 5,000 LD50 of virus peripherally (72), and Aguilar Setién et al. (4) also demonstrated that vampire bats were less susceptible to a vampire bat isolate than foxes were to a fox isolate. However, Aguilar Setién et al. (4) also showed that mortality in this species could be much higher (34/38, 89%), when substantially more virus was inoculated (106 LD50). In addition, Delpietro and Russo (29) have reported that up to 50% mortality may occur when rabies is introduced into a wild population of vampire bats. Ressang et al. demonstrated the susceptibility of an Indonesian species of fruit bat (Pteropus vampyrus) to peripheral inoculation with rabies virus (90), while a recent study found that only 3/10 Australian fruit bats (P. poliocephalus) developed clinical signs of disease following peripheral inoculation with 105 tissue

**Table II**

Summary of results following experimental intramuscular inoculation of insectivorous bats with bat-derived lyssaviruses

<table>
<thead>
<tr>
<th>Bat species</th>
<th>Dose (MICLD50)</th>
<th>Mortality</th>
<th>Virus detected in</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>brain</td>
<td>salivary glands</td>
</tr>
<tr>
<td>Eptesicus fuscus</td>
<td>10^2.2</td>
<td>5/5 (100)</td>
<td>1/5 (20)</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Pipistrellus subflavus</td>
<td>10^2.2</td>
<td>0/2 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Myotis lucifugus</td>
<td>10^-1.1-2</td>
<td>0/5 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tedara brasiliensis</td>
<td>10^-2.0-3.0</td>
<td>2/28 (71^a)</td>
<td>1/2 (50)</td>
<td>1/2 (60)</td>
</tr>
<tr>
<td>Tadarida brasiliensis</td>
<td>10^-2.3-3</td>
<td>5/18 (28)</td>
<td>5/5 (100)</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Nycticebus bengalensis</td>
<td>10^-2-3</td>
<td>5/13 (38)</td>
<td>5/5 (100)</td>
<td>2/5 (40)</td>
</tr>
<tr>
<td>Lasiurus borealis</td>
<td>10^-2.0-3.0</td>
<td>4/20 (13)</td>
<td>4/4 (100)</td>
<td>4/4 (100)</td>
</tr>
<tr>
<td>Pipistrellus pipistrellus</td>
<td>10^-2-3</td>
<td>19/66 (29)</td>
<td>19/19 (100)</td>
<td>5/19 (25)</td>
</tr>
<tr>
<td>Total</td>
<td>40/170 (24)</td>
<td>35/40 (88)</td>
<td>12/40 (30)</td>
<td></td>
</tr>
</tbody>
</table>

MICLD50 = mouse intracerebral lethal dose 50% titre
a The criteria for a positive diagnosis in this study are unclear
b Only animals held at 25°C were considered. Although only 2 of 28 bats died, evidence of infection was found in 14 (50%) of the bats. The duration of the experiment was only 7 weeks
culture infective doses 50 (TCID\textsubscript{50}) of ABL (and only 1/7 when given 10\textsuperscript{3.7} TCID\textsubscript{50}) (K.A. McColl, T. Chamberlain, R. Lunt, K. Newbury, D. Middleton and H.A. Westbury, unpublished findings). Overall, these data not only suggest that vampire bats and fruit bats share the relative insusceptibility of insectivorous bats to lyssaviruses of bat origin, but also demonstrate a loose dose-response relationship between these viruses and bats (mortality is directly related to the dose of inoculum).

Many bats survive either natural infection or experimental peripheral inoculation with bat-derived lyssaviruses. Perez-Jorda et al. demonstrated that the prevalence of antibodies to EBL1 in wild European serotine bats (E. serotinus) varied throughout the year, with the maximum prevalence of 74% reached in the spring (83). Trimarchi and Debbie found that 9.6% of free-flying big brown bats (E. fuscus) and 2.4% of little brown bats (Myotis lucifugus) in New York State were seropositive to rabies virus (117). In experimental work on another insectivorous species (T. brasiliensis), Baer and Bales found that none of those that survived inoculation with rabies virus ever developed clinical signs of disease (9). However, approximately 10% were seropositive when the experiment was terminated. This proportion was much lower than that observed in the wild for the same species (17, 106), possibly because wild bats are repeatedly exposed to the virus, compared with the single exposure in this experiment. In addition, seroconversion in some of the experimentally infected bats may not have been detected as titres were only examined at the start and finish of the experiment, and may have waned to below detectable levels by the time the experiment was terminated.

This explanation may also account for the complete absence of seropositive animals among those vampire bats that survived experimental inoculation with rabies virus (72). The titre of these animals was not examined until a year after inoculation. In contrast, one study of a number of colonies of wild vampire bats demonstrated that up to 33% of clinically normal animals in a colony were seropositive (79). Evidence demonstrates that fruit bats that survive inoculation with ABL also seroconvert, but that serum antibodies may fall quickly, sometimes to below detectable levels less than two months post inoculation (K.A. McColl, T. Chamberlain, R. Lunt, K. Newbury, D. Middleton and H.A. Westbury, unpublished findings). As mentioned earlier, no data have been published on the prevalence of antibodies to ABL in free-flying fruit bats in Australia, but Agnomo \textit{et al.} demonstrated that, in a different species of wild fruit bat (\textit{Eidolon helvum}) in Nigeria, 5 of 50 (10%) were seropositive to rabies virus (2).

In addition to mature seropositive bats, Steece and Altenbach found that, in a wild population of \textit{T. brasiliensis}, seropositive female bats could protect their young by passive transfer of antibodies neutralising antibodies (106). The young later became infected as the maternal antibody waned. At about this time, rabies-specific immunoglobulin M (IgM) responses developed in juvenile bats, and these were soon followed by IgG responses.

While field and experimental observations indicate that many bats are insusceptible to disease following natural infection with bat isolates of lyssaviruses, some bats clearly do succumb to disease. However, no studies appear to have investigated why these particular bats die following infection, although Constantine has suggested that perhaps only immunocompromised bats are affected (23). In those animals that do develop disease, a long incubation period was usually observed, with concomitant high levels of virus in the salivary glands (9). Similar findings were demonstrated for vampire bats (72). Baer and Bales suggested that the high levels of virus excreted by those bats that are apparently destined to die might occasionally be sufficient to overcome the relative insusceptibility of other bats (9). These factors, in combination with the high population density of bats in most roosting sites, were thought to provide ideal conditions for the maintenance of enzootic rabies in bats.

While prenatal transmission of rabies virus in bats has been suggested, Constantine questioned these results, and has presented data to refute the claims (22). Aerosol transmission has also been suggested as a likely means of infection of bats, particularly those that live in dense colonies, and Baer and Bales have demonstrated experimental infection of an insectivorous bat via the intranasal route (9). Certainly, vampire bats are known to interact very closely with each other through mutual grooming, and through sharing food by regurgitation of ingested blood (126). However, natural transmission of rabies among bats is also likely to rely heavily on infected individuals biting others within the colony. In fact, biting is so frequent that Constantine felt that the incidence of rabies in large colonies of gregarious bats should be greater than that observed (23). A number of factors may explain why this is not the case.

Firstly, given the small size of bats, most bites inflicted will necessarily be superficial, possibly affecting the dermis only. A rabies isolate from silver-haired bats (L. noctivagans) has been found to have a much higher infectivity for fibroblast and epithelial cell lines than neuroblastoma lines, particularly when cultured at 34°C (73). This suggests that the virus may be better adapted to replicate in the slightly cooler superficial dermis in this (and possibly other) species of bat, indicating that the pathogenesis of the disease, particularly early events in the process, may be different from that observed in terrestrial mammals.

Secondly, oral excretion of virus by infected bats may be limited. The data presented in Table II indicate that, for insectivorous bats, lyssaviruses were present in the salivary glands of only approximately 30% of infected animals that died. Clearly, these data give no indication of whether affected
animals had been excreting virus before, and during, the clinical phase of the disease. Salivary samples were collected throughout the course of infection in only two of the studies reported in Table II; too few to draw any definite conclusions. In one study on E. fuscus, all clinical samples were negative for virus (105), and in the other, on T. brasiliensis, virus was detected in the saliva in one of the five animals infected by the intramuscular route (9). In the same study, virus was also found in the saliva of two out of four other animals that died following subcutaneous or intranasal inoculation of virus.

Presumably, other oronasal tissues, apart from salivary glands, could also be responsible for excretion of lyssaviruses from bats. Constantine et al. (25) found virus and viral antigen in the nasal mucosa of five out of fifteen immature T. brasiliensis that were either dead or showing clinical signs of rabies. Viral antigen was also found in the ethmoturbinates in two out of five positive bats.

Data on excretion of rabies virus from vampire bats, and from fruit bats infected with ABL are scarce. One study on vampire bats has shown that a much higher proportion of these animals, compared with insectivorous bats, had virus in the salivary glands following peripheral administration of rabies virus. Moreno and Baer detected virus in the salivary glands of fourteen of sixteen animals (88%) following peripheral administration of rabies virus (72). Furthermore, virus was detected in the saliva of 75% of the bats in this study, in many cases before the onset of clinical signs of disease. In a small, preliminary study, Hooper et al. found ABL antigen in the salivary glands of only one out of eight wild Australian fruit bats that had antigen in the brain (48). Patterns of viral excretion in the saliva of experimentally infected fruit bats have yet to be determined.

For many years it has been suggested that bats not only excrete lyssavirus during the clinical course of the disease, but also that some may recover from infection, and continue to excrete virus in the saliva, often for months. These have been known as ‘carrier’ bats (81). More recently, the presence of carriers was demonstrated in two out of fourteen vampire bats inoculated intramuscularly with 10^3-10^6 mouse intracerebral lethal doses 50 (MICLD_50) of a vampire bat isolate of rabies virus (A. Aguilar Setién and F. Cliquet, unpublished findings). Neither bat had shown clinical signs of infection throughout a 600-day experimental trial.

However, Baer and Bales, working on an insectivorous species, T. brasiliensis (9), and Moreno and Baer, working on vampire bats (72), were unable to demonstrate any carrier bats among those that overcame experimental infection. Preliminary results from experimental inoculation of fruit bats (P. poliocephalus) with ABL suggest that, while a proportion of infected bats develop clinical signs of disease, many remain asymptomatic (K.A. McColl, T. Chamberlain, R. Lunt, K. Newbury, D. Middleton and H.A. Westbury, unpublished findings). Whether any of the latter excrete virus is currently unknown. Proving that carrier bats do not exist may be a difficult task, especially if the carrier state is uncommon in bat colonies.

Although little detailed information is available on events that occur in a bat after infection with a bat-derived lyssavirus, the work of Baer and Bales (9) and of Moreno and Baer (72) suggested that the disease would follow much the same course as observed with rabies virus infection of terrestrial mammals. Therefore, in insectivorous bats, it was not surprising that virus was cultured from the brain of all clinical cases, but never from any other organ in the absence of infection of the brain. This differed from the results of Sulkin et al. (107), who found that virus could be detected in the brown fat or salivary glands of insectivorous bats, even when no virus could be isolated from the brain. The limitation with the latter work was that a rabies virus of canine, rather than bat origin was used.

Baer and Bales (9) also detected virus in brown fat in three out of eight (38%) insectivorous bats, and in hibernating bats, brown fat has been suggested as a site of virus persistence (107). However, Kuzmin and Botvinkin found no significant difference between virus titres in brown fat of hibernating bats and others held at room temperature (59). There appeared to be no particular predilection for localisation of virus in brown fat in vampire bats, virus being found in this site in only two out of sixteen peripherally-infected bats (72).

While a number of studies have considered the lesions and events in the CNS of terrestrial mammals following inoculation with bat-derived lyssaviruses (34, 82, 118), no specific time-course study of events in the CNS of bats infected with similar viruses appears to have been performed.

Diagnosis and surveillance

While the proportion of lyssavirus-infected bats that show abnormal clinical signs may vary depending on the species of bat and the genotype of virus, the clinical diagnosis in affected bats may be based on signs that are similar for all species of bat, irrespective of the sero-genotype of virus involved. The main signs are an alteration in reflexes, loss of appetite, the onset of tremors and paralysis, and prostration. In vampire bats affected by rabies virus, the onset of clinical signs of disease is generally between 24 h and 96 h before death (A. Aguilar Setién, unpublished findings). Aggressive behaviour, as originally described in vampire bats (81), has rarely been observed in animals infected experimentally via a peripheral route of inoculation. Constantine has suggested that the fetus of rabies may only occur in bats following intracerebral inoculation of virus (23). However, aggressive behaviour has been recorded in some instances, both in naturally infected animals (45) and in experimental infections (105).
While not all bats infected with ABL develop clinical signs of disease, those wild bats that do show evidence of infection usually present neurological signs (40, 48, 104). Paralysis or paresis of hindlimbs and/or forelimbs are the most consistent findings. However, these changes may not always be clearly distinguished, due in part to the difficulty of conducting a careful clinical examination on a wild animal that could be infected with a lethal zoonotic virus. Aggression, clonic muscle spasms and altered vocalisation have also been reported, but these signs are not always restricted to ABL-infected bats.

At necropsy, no characteristic gross lesions are found in bats infected with lyssaviruses. Microscopic changes in insectivorous and vampire bats infected with rabies virus appear to be similar to those observed in terrestrial animals (i.e. a non-suppurative meningoencephalomyelitis). However, while the lesions associated with inoculation of bat lyssaviruses into terrestrial mammals have been described (34, 74, 75), there have been few, if any, definitive descriptions of the lesions in bats. Numerous references have been made to large eosinophilic intracytoplasmic inclusion bodies (Negri bodies) in bats, particularly in Perkinje cells and in neurones of the hippocampus, but these were noted as confirmation of diagnosis (before the advent of the fluorescent antibody test [FAT]), and were not usually accompanied by a full description of the lesions in the affected bat (17). In any case, the absence of Negri bodies does not necessarily imply freedom from infection with a lyssavirus. Hooper et al. have provided the most comprehensive description of histopathological findings in wild fruit bats infected with ABL (48, 49). While the basic lesions are a non-suppurative meningoencephalomyelitis and a ganglioneuritis, enormous variation was observed in the severity of the lesions, ranging from very severe to almost complete absence. No correlation appears to exist between the severity of the lesions and the severity of the clinical signs. When present, lesions in the CNS were characterised by necrosis and loss of neurones, diffuse and focal gliosis, perivascular cuffing and occasionally, the presence of Negri bodies in some neurones.

Standard laboratory techniques used for the diagnosis of rabies in terrestrial mammals may also be used to confirm lyssavirus infections of bats (70, 114). Viruses may be detected, by the FAT (28), either directly in infected tissues, or after culturing infected tissues on susceptible cells (8, 53, 124). An enzyme-linked immunosorbent assay (ELISA) that detects RNP antigens in infected tissues may also be used (e.g. rapid rabies enzyme immuno-diagnosis [RREID]) (84). Bat lyssaviruses produce no cytopathic effect in tissue culture. Intracerebral inoculation of suckling or weaned mice may also be used to isolate viruses (58). Monoclonal antibodies have been developed for the identification of rabies virus and non-rabies lyssaviruses, and these have been used for demonstration of viral antigen in tissue culture, fixed or frozen tissue sections, and in fixed impression smears of the brain (101). Lyssaviruses can also be detected by electron microscopy (50). The rapid fluorescent focus inhibition test (RFFIT) is generally used to detect anti-lyssavirus antibodies (102), although an ELISA has also been developed (85).

Since many bat lyssaviruses, notably those from Europe and Africa, are quite different from classical rabies virus, it is important that a broadly-reactive diagnostic tool be available. One candidate may be the RREID ELISA which is capable of detecting RNP antigen of all available lyssaviruses (87). Recent work has indicated that in ABL-infected bats showing obvious histological lesions, the FAT may only be very weakly positive (K.A. McColl, T. Chamberlain, R. Lunt, K. Newbury, D. Middleton and H.A. Westbury, unpublished findings). In fact, an inverse relationship appears to exist between the severity of histological lesions in the CNS, and the amount of viral antigen as detected by the FAT.

**Prophylaxis and treatment**

Measures for the prevention of rabies in humans have been well documented (129). The recommended standard protocols for pre-exposure immunisation and post-exposure treatment would be appropriate for people dealing with rabies in insectivorous or vampire bats in the Americas (see section above entitled ‘Importance for animal and public health’). However, in Europe, dealing with rabies-like lyssaviruses in insectivorous bats may present special problems. It has been clearly demonstrated that classical rabies vaccines (based on genotype 1 viruses) do not offer the same protection against genotype 5 viruses (EBL1) as that afforded against genotype 1 viruses. Furthermore, the Pitman Moore (PM) strain of vaccine clearly results in weaker protection than the Pasteur virus (PV) strain (51, 60). In addition, only a small proportion of humans vaccinated with classical vaccines develop a helper T lymphocyte response (as measured by specific interleukin-2 production) against EBL1 (47, 86). Therefore, when post-exposure treatment of humans exposed to genotype 5 viruses calls for administration of hyperimmune serum (to complement vaccination), equine rabies immune globulin (ERIG) is indicated rather than the human counterpart (HRIG). This is because the former is prepared with the PV strain, while most of the available human sera are obtained from individuals vaccinated with the PM strain.

Measures for the control of ABL in Australia must await a better understanding of the epidemiology and pathogenesis of the disease. Currently, the only recommendations for prophylaxis apply to people who, for either professional or recreational reasons, might be exposed to the virus. As vaccination studies with laboratory rodents have shown that human and animal rabies vaccines can protect mice against intracerebral challenge with ABL (48), people in high-risk situations are advised to undergo pre-exposure vaccination (67). This includes both administration of rabies vaccines, and also subsequent monitoring of antibody titres to ensure that a protective titre develops, and is then maintained.
Post-exposure treatment depends on the level of risk involved. All wounds should be washed, and all exposed people should undergo a vaccination course. However, only those in high-risk situations should receive rabies immunoglobulin (infiltration of the full dose around the wound, when anatomically feasible; otherwise, half the dose applied around the wound, and half administered intramuscularly). When vaccination is required, the simultaneous use of immunosuppressants should be avoided. A woman in Australia who was possibly exposed to ABL had been treated with prednisone for many years. She failed to develop a protective antibody titre despite having undergone post-exposure treatment with a vaccine booster one year later (26).

Traditional means of control of bovine paralytic rabies associated with vampire bats have included the preventative vaccination of cattle, and reduction of bat numbers. The latter has been achieved by destroying bat shelters (e.g. with fire or explosives), but these measures have often resulted in the simultaneous loss of beneficial insectivorous and frugivorous bats.

During the 1970s, methods based on the use of anticoagulants were introduced to control vampire bats. Initially, a number of individual bats were captured, and an anticoagulant was applied to their bodies. Following the release of the treated animals, other members of the colony became contaminated with the anticoagulant during sessions of mutual grooming (62). In this way, each treated individual was capable of poisoning ten to forty other animals in the colony. Later, the application of anticoagulants to vampire bat-induced skin lesions in domestic animals was found effective as vampire bats often return to the site of pre-existing bites (38). Eventually, the anticoagulants were administered systemically to cattle. Final blood concentrations are innocuous to the host but lethal to vampire bats (95, 111). Because of the slow reproductive cycle of the vampire bat, anticoagulants have proved a useful long-term strategy for the control of these animals. However, the cumulative effect of anticoagulants may also have a negative impact on predators and scavengers, both directly and through contamination of the environment. For this reason, an alternative method of control has been investigated.

The possibility of forming immune barriers to the transmission of vampire bat rabies has been examined, as this strategy has been used with a number of other wildlife reservoirs of rabies virus (16, 30). Haematophagous bats have been vaccinated orally with a recombinant vaccinia rabies glycoprotein, and this has been found to confer protection if administered between eighteen and thirty days before challenge (4). Such work may also be of importance with bat species in other regions of the world since, in recent years, many human cases of rabies have been shown to be caused by viruses of bat origin (15).

A reduction in the number of bats in a particular region, by whatever means, is only ever a temporary means of controlling bat numbers, unless populations in adjoining areas are also controlled (7). This is because the availability of food in the treated area quickly attracts bats from adjacent regions, resulting in rapid re-population. Furthermore, bachelor males which have been expelled from a colony may travel up to 100 km in order to join, or found, a new colony. Such trips can spread rabies into previously uninfected regions, particularly if the offending male can excrete the virus for long periods.

 Perspectives

The best known of the lyssaviruses, rabies virus, reportedly kills at least 60,000 humans annually (46), the vast majority of these deaths being associated with the canine rabies cycle in underdeveloped countries (urban rabies). However, rabies in wildlife (sylvatic rabies) is also recognised throughout the entire range of the disease, and is particularly important in the developed countries of the world where urban rabies has been controlled. In these countries, awareness of the role of bats in the epidemiology of rabies is increasing.

Although the importance of vampire bats as vectors of rabies is already recognised, the role of insectivorous and frugivorous bats might easily be overlooked. However, as already mentioned, twenty-one of thirty-six cases of rabies in humans in the USA between 1980 and 1997 were shown to have originated from insectivorous bats and, importantly, in all but one or two cases, the manner of transmission could not be identified. Furthermore, two human deaths associated with ABL-infected fruit bats have been reported in Australia, a continent considered to be free of endemic rabies. With the increasing use of molecular epidemiological methods to characterise virus isolates, it is not unreasonable to expect that a greater proportion of the human deaths that have been attributed to rabies in the past, will be recognised as bat variants of rabies virus and of other lyssaviruses in the future. The two major consequences of this are discussed below.

Firstly, given that classical serotype 1 rabies vaccines provide little, if any, protection against genotypes 2, 3 and 5 (11), the development of a broad-spectrum anti-lyssavirus vaccine should be a high priority. Through the use of deoxyribonucleic acid (DNA) immunisation techniques, such vaccines have recently been developed for mice (11, 31, 51) and dogs (89). A chimeric G protein, encoded by a single recombinant gene comprising equal proportions of the rabies virus (genotype 1) and Mokola virus (genotype 3) G genes, was shown to protect against most lyssavirus genotypes, although ABL was not available for testing (11). Other combinations of G genes may be more appropriate for a particular geographic region, e.g. an EBL1-rabies chimera may be useful to protect against all lyssaviruses in Europe (51). Currently, lyssaviruses associated with insectivorous
bats in Europe cause little apparent disease. However, it may not be outrageous to suggest that foxes in Europe could become vectors for EBL1 variants, in view of:

a) the recent demonstration of EBL1 in sheep in Denmark
b) the isolation of insectivorous bat rabies variants from cattle and foxes in Canada, and
c) the current extensive oral vaccination campaigns in Europe that are effectively creating a fox population that is strongly immune to genotype 1 viruses.

In this scenario, the new vector would present a risk of transmission to both animals and humans, particularly as current commercial rabies vaccines would not be protective. A chimeric EBL1-PV gene in a recombinant vaccinia virus for oral vaccination of foxes may overcome this problem.

Secondly, a better understanding of the epidemiology and pathogenesis of bat lyssavirus infections will enhance prevention and control of these diseases. There is a clear deficiency in knowledge of these aspects of lyssavirus infections of bats in general, but particularly for the non-rabies genotypes. It is difficult to provide informed advice on the control and prevention of these diseases when basic data are not available.

However, in situations where information appears to be sufficient to develop control programmes, it is important not to become complacent. For example, in Latin America there is a tendency to believe that the vampire bat rabies problem has been solved through vaccination of cattle and the use of anticoagulants. In reality, unprecedented increases have been recorded in the number of people infected by vampire bats, and the number of young cattle that die of rabies despite being born into vaccinated herds (36, 80). Studies on the dynamics of vampire bat populations, the spread and persistence of rabies virus in these populations, and the immune response of young cattle to rabies virus are important issues that need to be addressed.

Clearly, much remains to be learnt about bat lyssavirus infections around the world. While few will be surprised by the increasing recognition of the importance of bat-transmitted rabies, in the early years of the new millennium many of the other bat lyssaviruses are also likely to emerge from relative obscurity.

Acknowledgement
The authors would like to thank Dr Y. Rotivel for her critical reading of the section of the paper dealing with treatment and prophylaxis in humans.

Infections dues au lyssavirus des chauves-souris
K.A. McColl, N. Tordo & A. Aguilar Setién

Résumé
Les chauves-souris, qui représentent environ 24 % de l’ensemble des espèces mammifères connues, sont souvent des vecteurs de lyssavirus. Les chauves-souris insectivores jouent un rôle important dans l’épidémiologie du virus de la rage et de certains virus apparentés ; la chauve-souris hémophaghe (vampire) est le principal vecteur de la rage sylvatique en Amérique latine. Quant aux chauves-souris frugivores (roussettes), leur rôle dans l’épidémiologie des nouveaux lyssavirus récemment découverts en Australie, dits lyssavirus des chauves-souris australiennes, vient à peine d’être établi. La pathogénie des lyssavirus chez les chauves-souris est peu connue. Toutefois, les chauves-souris infectées par voie naturelle ne succombent que rarement à cette infection et des anticorps apparaissent chez la plupart des sujets qui survivent. Les chauves-souris infectées transmettant la rage essentiellement par morsure, mais...
Infecciones por lyssavirus del murciélago

K.A. McColl, N. Tordo & A. Aguilar Setién

Resumen
Los murciélagos, que representan aproximadamente un 24% de todas las especies de mamíferos conocidas, ejercen con frecuencia de vectores de los lyssavirus. Los murciélagos insectívoros desempeñan una función de especial importancia en la epidemiología del virus de la rabia y algunos otros virus afines. Los murciélagos hematófagos (vampiros), por su parte, constituyen el principal vector salvaje de la rabia en América Latina. En marcado contraste con esos casos, apenas se empieza a conocer ahora el papel de los murciélagos frutívoros (zorros voladores) en la epidemiología del lyssavirus australiano del murciélago, un microorganismo recién descubierto. Se tiene poca información sobre la patogénesis de los lyssavirus en los murciélagos. No obstante, la mortalidad de murciélagos infectados por vía natural parece ser en general baja, y muchos de los animales supervivientes desarrollan anticuerpos. Un murciélago infectado puede transmitir la rabia por mordedura, aunque parece que también hay otras vías de transmisión posibles. Los métodos para diagnosticar la presencia de infecciones por estos lyssavirus, tanto en murciélagos como en otros mamíferos terrestres (y en el hombre), son semejantes a los procedimientos clásicos utilizados para diagnosticar la rabia. Las medidas de prevención y control de esa infección son también similares a las que se usan para la rabia, aunque además se han ensayado otros métodos complementarios y novedosos para luchar específicamente contra la rabia transmitida por murciélagos vampiros.

Palabras clave
References


