

European Bat Lyssavirus infection as a potentially zoonotic disease in the UK

Introduction

At the end of September 2002, immunofluorescence testing of a juvenile Daubenton's bat, *Myotis daubentonii*, revealed that the bat was suffering from rabies. The bat had developed behavioural abnormalities after having been rescued by a voluntary bat warden following a wing injury.

This was the first such case identified in the United Kingdom since 1996¹. [A diagnosis of lyssavirus infection was initially made using the fluorescent antibody test \(FAT\) on brain samples. This was subsequently confirmed by the rapid tissue culture inoculation test \(RTCIT\).](#)

The rabies virus isolated from the infected bat was subsequently typed as European Bat Lyssavirus (EBL) type 2a [genotype 6]².

Two months later, the death of a voluntary bat warden from rabies believed to be linked to a bat bite in Tayside, Scotland, was reported.

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Subsequently, on 20th November 2002, the Government's Deputy Chief Medical Officer issued an advisory letter to health care professionals in the UK entitled 'Suspected case of rabies in Tayside, Scotland' (CMO/CEM/2002/16). This letter is reproduced at the end of this document.

The key elements of this were:

- the information contained in the standard UK handbook 'Immunisation against infectious disease'³ that licensed bat handlers should have pre-exposure immunisation against rabies should be extended to all bat handlers include voluntary bat wardens (who may not be licensed); amending sections 27.3 and 27.4 of this book thus entitled all bat handlers to free rabies immunisation on the NHS;
- advice on post-exposure bite management.

The infection causative of death has been stated to be a European Bat Lyssavirus⁴, but no further typing information has yet been released; no infected bat has been directly identified; and the certainty with which a particular bat species may be implicated must be open to some doubt given that the bat warden concerned will have come into contact with very many species of bat.

This paper summarises and comments upon the extant literature available relevant to the management of European Bat Lyssavirus infection as a potentially zoonotic disease in the UK.

¹ 'Bat brings rabies to Britain'. *Commun Dis Rep CDR Wkly* 1996; 6 (24): 205. Available online at <<http://www.phls.org.uk/publications/cdr/CDR96/cdr2496.pdf>>

² 'European bat lyssavirus type 2 in a bat found in Lancashire'. Johnson N, Selden D, Parsons G, Fooks AR; *Veterinary Record*, 2002 Oct 12; 151(15):455-6.

³ 'Immunisation against infectious disease'. London: UK Departments of Health; HMSO, 1996.

⁴ 'Rabies death, Tayside'. 36/4702 SCIEH weekly report 26 Nov 2002, 36(2002/47): 301.

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Discussion

EBL infections in the UK: VLA surveillance of bats for rabies since 1986 has not directly identified any other cases of EBLV infection in bats other than the Lancashire case identified in this report and a case of EBLV type-2 [genotype 6] infection in a Daubenton's bat found in Newhaven and presumed to have originated in mainland Europe⁵.

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However, the isolation of EBLV 2 from a juvenile bat of a species common to Britain has raised the concern that EBLV 2 must now be considered to be endemic, all be it at a very low level; and although both quoted recent isolates have been made in Daubenton's bats, it is probably unsafe to assume that such endemicity is isolated to this one species.

Within Europe, lyssaviruses have been discovered in a wide range of bat species.

Bat species positive for Lyssavirus, Europe 1954-2000:

Species	Lyssavirus	Antibodies
<i>Eptesicus serotinus</i> (Serotine)	EBL1a & b	EBL1
<i>Pipistrellus pipistrellus</i> (Pipistrelle)	not characterised	not done
<i>Pipistrellus nathusii</i>	not characterised	not done
<i>Vespertilio murinus</i>	EBL1a	not done
<i>Myotis dasycneme</i>	EBL2a	not done
<i>Myotis daubentonii</i> (Daubenton's)	EBL2a & b	not done
<i>Myotis myotis</i>	EBL1b	EBL1
<i>Myotis natterei</i> (Natterer's)	EBL1b	not done
<i>Nyctalus noctula</i> (Noctule)	not characterised	not done
<i>Miniopterus schreibersii</i>	EBL1b	EBL1
<i>Tadarida teniotis</i>	not characterised	EBL1
<i>Rhinolophus ferrumequinum</i> (Greater horseshoe)	EBL1b	EBL1

[data from Muller R.W. quoted in 'European Bat Lyssavirus Infection in Spanish Bat Populations'. Serra-Cobo, J, Amengual, B., Abellan, C and Bourhy, H; Emerging Infectious Diseases 2000; 8\(4\): 413-420.](#)

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Whilst it has been reported that EBLV type- 1 [genotype 5] infections has crossed species into other mammals⁶, all be it in a very limited way, there is no supporting evidence that this may have happened so far in the UK in respect of either EBLV types- 1 or -2 [genotypes 5 & 6 respectively].

Further studies will clearly be needed to determine the prevalence and characterisation of any strains that may have become endemic within the UK and to demonstrate which species of bat are affected. It is understood that such work will begin in the near future led by the VLA and sponsored by DEFRA.

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Management of human contacts of infected animals: The standard practice for the management of humans injured by native mammals in the UK has been predicated upon the assumption that no genotype of lyssavirus is endemic. As a result prophylactic treatment of persons has been dependent upon the demonstration of actual risk; that is, either contact with a known or suspected rabid animal abroad or in quarantine; or a native animal discovered to be infected after post-mortem examination.

Therefore, in the case of injury by an animal indigenous to the UK, no reporting of an incident known to the veterinary system is made to the health protection / public health system until

⁵ 'Ten-year survey of British bats for the existence of rabies'. Whitby JE, Johnstone P, Parsons G, King AA, Hutson AM; Veterinary Record, 1996 Nov 16; 139(20):491-3.

⁶ Rabies Bulletin Europe (RBE): 3 cases of transmission to Danish Sheep reported in RBE 3/98 & RBE 4/98 also 1 case of transmission to a stone marten in North Germany reported in RBE 3/01: accessed at <http://www.who-rabies-bulletin.org/> on 3/2/03.

after infection in the animal causing the injury has been confirmed. It appears that this system is still being operated.

Given that there must now be reasonable grounds for suspicion that EBLV type- 2 infection is now endemic in the UK, it would appear to be appropriate to revise this system. Consideration must be given to providing assessment and, if appropriate, prophylactic treatment at the time of injury. The need to bring forward the time of initiation of medical intervention is well illustrated in this case, where 16 days elapsed between a bite having occurred in an un-immunised human, and the diagnosis in the biting animal resulting in assessment and treatment of that human.

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Effectiveness of post-exposure treatment of human contacts of EBL: Standard recommendations for the post-exposure management of humans is based around the probability of exposure to rabies virus, that is, the likelihood that an infective dose has been inoculated, or otherwise breached skin or mucosal barriers, when set against the risks associated with the use of rabies immunoglobulins and vaccines. Particular caution has been exhibited in recent years by medical practitioners in the use of human pooled serum derived immunoglobulins, because of the potential risk of transmission of incompletely eliminated or screened viral and prion contaminants.

The treatment offered to the human contacts of the infected bat in this case was consistent with the advice offered in the DH guidance 'Immunisation against infectious diseases', which mirrors the risk and advised treatment categories advocated by the WHO⁷:

	exposure	treatment
Category I	Touching, feeding of animals or licks on intact skin no exposure	no treatment if history reliable
Category II	Minor scratches or abrasions without bleeding or licks on broken skin and nibbling of uncovered skin	use vaccine alone
Category III	Single or multiple transdermal bites, scratches or contamination of mucous membrane with saliva (i.e. licks)	use immunoglobulin plus vaccine

Note: Global sources of human immunoglobulin for post-exposure treatment will be discontinued by the companies that currently produce this product. Alternative sources including humanised mAbs and a cocktail of mouse mAbs are being considered by WHO.

However, this advice is primarily aimed at the post exposure management of humans exposed to genotype 1 (classical rabies virus).

Studies that elucidate the protective effect of vaccines based around the classical virus to other Lyssavirus group members are rare. Of the few studies that could be discovered concerning EBLVs, there appears to be evidence that classical virus based vaccines may not offer the same degree of protection to EBLV type-1 [genotype 5] as they do to their target genotype 1 viruses^{8,9,10}. Similarly, human immunoglobulins derived from volunteers immunised with classical rabies derived vaccines may not be as effective against EBLV-1 strains of disease as they are against classical disease.

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⁷ WHO Expert Committee on Rabies, 8th report – 1992, published as WHO Technical Report Series 824. Available at <<http://www.who.int/emc/diseases/zoo/rabies.html>>

⁸ 'Efficacy of rabies vaccines against Duvenhage virus isolated from European house bats (Eptesicus serotinus), classic rabies and rabies-related viruses'. Fekadu M, Shaddock JH, Sanderlin DW, Smith JS. Vaccine 1988 Dec;6(6):533-9.

⁹ 'Bat lyssavirus infections'. McKoll KA, Tordo N, Aguilar Setien A. Revue Scientifique et Technique 2000;19(1):177-196.

¹⁰ 'T and B cell human responses to European bat lyssavirus after post-exposure rabies vaccination'. Herzog M, Fritzell C, Lafage M, Montano Hirose JA, Scott-Algara D, Lafon M. Clin Exp Immunol 1991 Aug;85(2):224-30.

One of these studies has suggested that vaccines based upon the Pitman Moore (PM) strain offers weaker protection than vaccines based upon the Pasteur strain (PV)⁹ against EBLV type-1 [genotype 5], without reference to protective effects against EBLV type-2 [genotype 6].

The only peer reviewed article that could be discovered that specifically refers to the protective effects of rabies vaccine against EBLV type- 2 [genotype 6], suggests that Pasteur strain vaccines do elicit virus neutralising antibodies against genotypes 1, 4, 5 and 6¹¹.

There is experimental data that suggests, at least in rodent models, that the cross-protection between RABV vaccines (PM, PV & LEP strains) and other Lyssaviruses (EBLVs, DUUV, MOK, LB) is not necessarily complete¹².

None of these studies on there own are comprehensive but together, they would suggest that protection is less than 100%. The degree of protection offered appears dependant on both the vaccine strain used and the challenge virus genotype. No one has looked at all the genotypes versus one vaccine]

Studies for both cross-protection and cross-neutralisation for the EBLVs are underway at the VLA in collaboration with two other WHO collaborating centres in Germany and France, respectively.

In summary:

- the management of EBLV type-2 infections in humans has not been well studied, probably because where EBLVs have been endemic for longest, infection with EBL 1 strains have been the predominant zoonotic threat;
- the evidence for the effectiveness of both rabies vaccines targeted at classical disease and immunoglobulins derived from volunteers immunised using such vaccines, is not unequivocally established in respect of either EBLV type-1 or EBLV-2;
- however, the little evidence that is available suggests that:

post-exposure treatment using current genotype 1 targeted vaccines / immunoglobulins from donors primed with genotype 1 targeted vaccines is more likely to be effective against EBLV type-2 infections than EBLV type-1;

that vaccines derived from Pasteur strains and immunoglobulins raised in volunteers primed with Pasteur strain vaccines should be preferred to those derived from Pitman Moore strains where exposure to either EBLV types- 1 or -2 disease is suspected. This is likely to be more critical where EBLV type-1 exposure is suspected.

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¹¹ 'Evidence of two lyssavirus phylogroups with distinct pathogenicity and immunogenicity'. Badrane H, Bahloul C, Perrin P, Tordo N. Journal of Virology 2001; 75(7):3268-3276.

¹² Schneider, 1982; Dietzschold et al., 1987; Lafon et al., 1988; Fekadu et al., 1988; Herzog et al., 1991; & VLA, unpublished.

Conclusions

1. The prevalence of European bay lyssavirus infections in the bat population in the UK needs to be established to:
 - 1.1. determine whether or not such infections are endemic;
 - 1.2. and if such infections are endemic, what is the prevalence of infection and which species and lyssavirus variants are involved.
2. Until such time as evidence may be offered to the contrary, the management of bat bites of any species should be predicated upon an assumption that EBLV ~~type-2~~ has become endemic amongst bats in the UK.
3. There is no evidence to suggest that such an assumption need to be made in respect of any other indigenous mammalian species in the UK at the present time¹³.
4. National policy on the management of bat bites has already been changed to respond in part to this possibility. In addition to those developments signalled in the CMOs advisory letter (CMO/CEM/2002/16), however, it is suggested that the following matters also need to be taken into account:
 - 4.1. that whilst post-exposure treatment using the current genotype 1 targeted vaccines / immunoglobulins from donors primed with genotype 1 targeted vaccines available in the UK is likely to be effective against EBLV ~~types-1~~ and ~~-2~~ infections, the effectiveness of such treatment is likely to be lesser if EBLV ~~type-1~~ exposure has occurred;
 - 4.2. and, therefore, that consideration be given to using vaccines derived from Pasteur strains and immunoglobulins raised in volunteers primed with Pasteur strain vaccines for the management of post exposure treatment where exposure to EBLV ~~type -1~~ or ~~-2~~ disease is suspected, especially if the risk of EBLV ~~type-1~~ infection needs to be considered.
 - 4.3. The current custom and practice of notification to the public health / health protection services of a bat bite only after demonstration of lyssavirus infection in the biting animal must be changed. It should be a mandatory requirement that all bites (outside of groups having specific occupational policies and advisory services) be immediately notified in order that prophylactic treatment may be commenced at the same time that steps are being taken to test the biting animal for lyssavirus infection.

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¹³ [Experimental studies are underway in ferrets and foxes to confirm this assumption. Work in dogs and cats is planned but still subject to formal approval.](#)

MESSAGE FROM DR PAT TROOP, DEPUTY CHIEF MEDICAL OFFICER

Date: 20 NOVEMBER 2002 Reference: CMO/CEM/2002/16

Dear Colleague

SUSPECTED CASE OF RABIES IN TAYSIDE, SCOTLAND

You will probably be aware from media reports, that a patient with suspected rabies is being treated at Ninewells Hospital, Dundee, Scotland. He was admitted with mild neurological symptoms which have since developed into a progressive illness consistent with a rabies-like illness. Initial laboratory tests were inconclusive for the rabies virus; results from further tests are awaited.

The patient may have been infected with European Bat Lyssavirus (EBL). He is known to have had prolonged close contact with bats over many years, and to have been bitten by a bat at least once during the incubation period for the disease.

Since 1996, EBL has been isolated from two Daubenton's bats in the UK. In September 2002 EBL was isolated from a bat that had bitten an individual in Lancashire, and EBL was also isolated from a bat in Sussex in 1996. Both victims were given post-exposure prophylaxis (vaccination) and no human disease was reported.

EBL is less virulent than the common strain of rabies virus, but it has been associated, very rarely, with human infection in other Northern European countries. All available evidence indicates that the threat from these bats to the general public, or to pets and domestic animals, is extremely low. Bats are naturally timid creatures which are hibernating at this time of year. However, those engaged in bat conservation activities who handle bats routinely are at greater risk. They should be advised to exercise particular care, for example by wearing bite-proof gloves, and they should be vaccinated. If they have not already been vaccinated against rabies, they are advised to come forward for pre-exposure immunisation.

Pre-exposure immunisation

Pre-exposure immunisation with human diploid cell rabies is available free from the NHS for certain groups of people listed in the Department of Health's (DH) 1996 Guidance Immunisation Against Infectious Disease, sections 27.3 and 27.4. This list includes licensed bat handlers. Additionally, it is now recommended that the free vaccination should also be offered to people who regularly handle bats, and not just licensed bat handlers. The DH Guidance is currently being updated to reflect this new advice. People continuing to handle bats should also have booster rabies vaccination every 3-5 years.

Arrangements for obtaining vaccine for pre-exposure immunisation
Stocks of vaccine can be obtained from the Public Health Laboratory Service (PHLS) Virus Reference Division on 0208 200 4400.

Post-exposure prophylaxis

As a result of media coverage of this incident, it is possible that some bat handlers will report having been bitten or scratched by a bat. Guidance on treatment for such people can be obtained from the PHLS Virus Reference Laboratory. Current advice is that if such an event had occurred within the previous 2 years, and if the individual in question is fully immunised against rabies, they should be offered 2 doses of vaccine. If, however, the individual is previously unimmunised or incompletely immunised, they should be offered 5 doses of vaccine. For those who are previously unimmunised, and who have been bitten by a bat that is known, or strongly suspected, to be rabid, then immunoglobulin should be offered in addition to a full course of vaccine.

Further information

The Public Health Laboratory Service (PHLS) has prepared advice on EBL, based on "Frequently Asked Questions", which can be accessed via the advice on rabies generally on the PHLS website at www.phls.org.uk/topics_az/rabies.menu.htm. Further general health advice is available from NHS Direct on 0854 4647. Should one of your patients require information about having bats in their house they can contact the UK Bat Helpline on 0845 130 0228.

Enquires regarding the circulation of this message should be directed to Kim Norman or Allison Lee on 020 7972 5349 or Allison Lee on 020 7972 5691