



Volant viruses: a concern to bats, humans and other animals

Introduction

Bats have a long and intimate association with viral diseases. There may be much to be learned from examining the disease ecology in this group of animals which would be to the benefit of humans, domestic animals and other wildlife species.

The status of bats and viral disease

Bats (Order Chiroptera) account for over 20% of all known species with over 1,100 species in 18 families. Until recently the families were grouped into two suborders, the Megachiroptera (Old World Fruit Bats) and Microchiroptera, but recent work shows the Microchiroptera to be paraphyletic with several families of insectivorous bats being more closely related to the Old World Fruit Bats than to other insectivorous bat families¹. Bats, the only truly volant (flying) mammals, play a pivotal role in maintenance of biodiversity in the ecosystems where they occur, being important insect predators, pollinators and seed dispersers^{1,2}.

Many bat species are threatened with extinction. The 1999 Action Plan for Australian Bats identified 36 species as threatened in Australia alone, primarily due to habitat loss and roost disturbance². The Action Plan also identified disease as a threatening process in flying foxes. Many bat species have a limited capacity to recover post-decline due to biological features such as relative longevity, late sexual maturity, seasonal breeding and low fecundity³. Populations that become reduced in size and genetic diversity are likely to remain vulnerable for long periods and, hence, be more susceptible to disease threats⁴.

Various authors have suggested infectious

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and paramyxoviruses identified in bats⁸. While many bat-borne viruses are important to public health the epidemiological significance of bats in the maintenance and transmission of infection has, with the notable exception of lyssaviruses, often been unclear.

Recently emerged viruses

Over the last 10 years, four previously unknown zoonotic viruses have emerged from bats in the Australasian region: Hendra virus, Australian bat lyssavirus, and Menangle virus in Australian bats; and Nipah virus, in a number of southeast Asian bat species (see Figure 1).

Hendra virus was first described in September 1994 in Australia, in an outbreak investigation of acute respiratory disease in a racing stable in the city of Brisbane⁹. Twenty horses and two humans were infected, 14 horses and one human fatally. In a further two identified foci of infection, in August 1994 (retrospectively diagnosed) and January 1999, a further three horses and one human were fatally infected^{10,11}. Most recently, in 2004, in two apparently separate, but spatially and temporally clustered spillovers, a further two horses were fatally infected and a human case non-fatally infected. All human cases have been attributed to exposure to infected horses. Hendra virus is a novel member of the family *Paramyxoviridae*, and has been allocated to the new genus *Henipavirus*. Epidemiological studies support flying foxes (*Pteropus* spp.) being the natural host of the virus¹². The mode of transmission to horses is unknown.

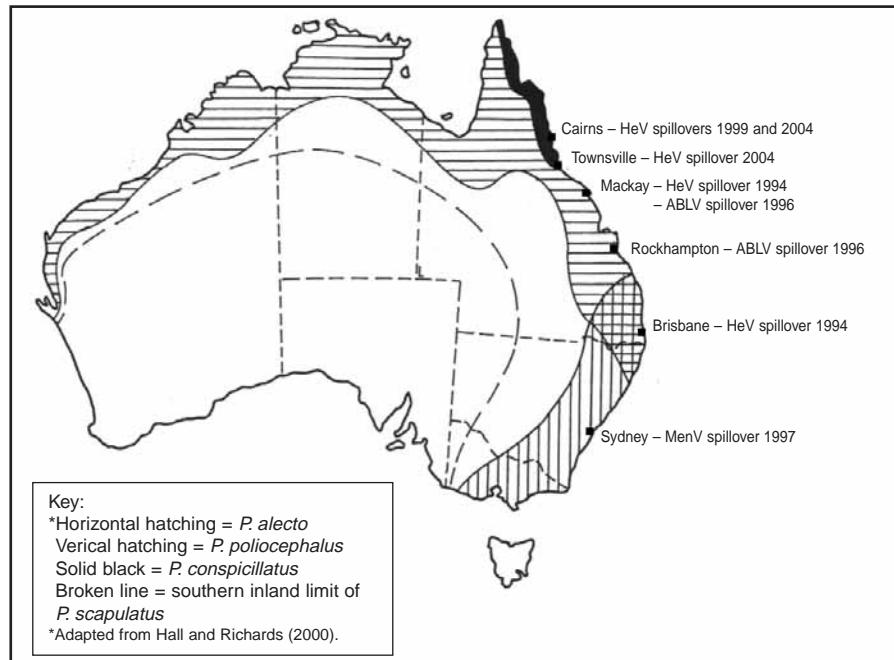
disease as a possible cause of mass mortality and mass abortion in bats in Australia and overseas^{4,6}. There are also reports of mortality events in flying foxes on several Pacific islands that are temporally associated with outbreaks of disease in humans or domestic animals^{6,7}. While such associations are suspicious, a clear causal link between infectious disease and bat population declines has yet to be established. Structured epidemiologic investigations of future outbreaks will help to address this.

The potential efficiency of many bat species as disseminator hosts of mammalian viruses has been previously noted, and is demonstrated by the spectrum of flaviviruses, alphaviruses, rhabdoviruses, arenaviruses, reoviruses,

In October 1996, a fatal rabies-like disease in a Queensland bat carer was attributed to Australian bat lyssavirus (ABLV)¹³. ABLV had been first described only six months earlier in a black flying fox (*Pteropus alecto*)¹⁴. Evidence of ABLV infection has



Fig 1. Map of Australia showing distribution of Australia's flying fox species and locations and dates of identified bat viral spillover events.



subsequently been found in insectivorous bats¹⁵ and exposure in the above human case was retrospectively attributed to a bite from a yellow-bellied sheathtail-bat (*Saccopteryx flaviventris*)¹⁶. A second fatal human case of ABLV occurred in December 1998, attributed to a bite from a black flying fox¹⁶. ABLV has strong serotypic, antigenic and sequence similarities to classical rabies virus, which is absent from Australia, but is phylogenetically distinct¹⁷. The extensive spatial and taxonomic occurrence of ABLV antigen and/or anti-ABLV antibody suggests that ABLV is endemic in Australian mega- and microchiropteran populations (Field HE; *unpublished data*).

Menangle virus was first described in June 1997 in the investigation of an outbreak of reproductive disease in a New South Wales piggery¹⁸. Two piggery workers were subsequently found to have high neutralising antibody titres to Menangle virus. At the time of the outbreak, both workers suffered a severe febrile illness that was retrospectively attributed to infection with the virus, with exposure possibly resulting from contact with infected pig body fluids during assisted farrowings or autopsies¹⁹. Serological and epidemiological evidence suggests that

flying foxes are the natural host of Menangle virus (Field HE; *unpublished data*). Antigen has been identified in the faeces of flying foxes suggesting direct contact with faeces as a possible mode of transmission from flying foxes to pigs.

Nipah virus was first described in March 1999 in the investigation of an outbreak of disease in pigs and humans in Malaysia. In the course of the outbreak, 265 humans were infected, 105 fatally²⁰.

Figure 2. Authors AB left and HF right anaesthetise a spectacled flying fox (*Pteropus conspicillatus*) for Hendra virus surveillance. (Photo courtesy of Dr Jack Shield, Queensland Department of Primary Industries and Fisheries).



Infected pigs were identified as the primary source of human infection and over one million pigs were culled to control the outbreak. Wildlife surveillance identified the Malayan flying fox (*Pteropus vampyrus*) and island flying fox (*Pteropus hypomelanus*) as probable natural hosts of Nipah virus²¹. Subsequent studies have also found serological evidence of infection in Lyle's flying fox (*Pteropus lylei*) in Cambodia²². Nipah virus has strong serological and sequence similarities to Hendra virus, and is the second member of the genus *Henipavirus*²³. Recent reports from Bangladesh of the first person-to-person transmission of Nipah virus highlight the potential for apparent change in viral transmission dynamics and the urgent need for detailed study of bat viral ecology and increased understanding of spillover mechanisms²⁴.

Disease ecology and spillover mechanisms

A question that remains to be answered is why these zoonotic bat borne viruses have emerged at this point in time. Although it has yet to be established, it has been hypothesised that changes in flying fox ecology are driving disease emergence in these species¹². Flying foxes are particularly vulnerable to habitat



Figure 3. A little red flying fox (*Pteropus scapulatus*) is released post sampling for Hendra virus ecology studies (Photo Raina Plowright).



loss or modification due to the ephemeral nature of their food resources²⁵. Land use change has resulted in population decline, population concentration during resource scarcity, distributional changes and urbanisation of flying fox populations throughout the Old World Tropics^{5,7,25}. These processes could lead to emergence either by changes in viral dynamics or by increased contact with domestic animals and humans. We are currently conducting mathematical and simulation modelling along with temporal distribution studies to examine these hypotheses.

Another factor that may facilitate the role of bats as reservoirs of zoonotic diseases is their taxonomic status. Bats are placental mammals, ie, belong to the same subclass (Eutheria) as humans and most domestic animals and are hence more likely to host pathogens that can cross these species barriers than many other wildlife species.

Epidemiological models, supported by empirical studies, show host density and population size are strongly linked to the spread and diversity of directly transmitted pathogens²⁶. A large population size is required to meet threshold conditions for pathogen establishment²⁷ and to generate sufficient

susceptible individuals, through births or immigration, to allow pathogen persistence. Many colonial species of bats meet these criteria, with colony sizes frequently ranging from thousands to millions.

For pathogens with a short duration of infectiousness, followed by lifelong immunity (putative characteristics of Hendra and Nipah viruses²⁸), persistence in a population can be problematic. The disease spreads so quickly, and individuals recover so quickly that even a large population may not be able to generate enough susceptibles to avoid viral extinction²⁹. However, spatially heterogeneous populations with asynchronous dynamics may promote viral persistence due to a 'rescue effect' where infected populations seed susceptible populations 'rescuing' the virus from extinction. In this case, the complex spatial dynamics of bats, a consequence of a highly nomadic lifestyle tracking patchily distributed food resources, may promote persistence.

Concluding comments

To fully understand the factors that drive disease emergence we must attempt to understand these viruses and their hosts at a range of spatial scales. Currently we know a considerable amount about the

molecular biology of the viruses discussed^{17,30}, very little about the interaction between the viruses and their hosts^{28,31}, and even less about the biology of the viruses at the level of the host population¹². More studies at larger spatial scales are required to fill in the gaps in the understanding of disease emergence.

Hundreds of bat species have co-evolved with a wide range of viruses over millennia, and it is likely that the bats have evolved various mechanisms to cope with the presence of such pathogens. What is not known is how the dynamics of these pathogens may change in response to anthropogenic induced changes to bat ecology. As the pressure on bat populations increases, will bats become vulnerable to previously harmless pathogens? Will humans and domestic animals be increasingly exposed to bat viruses? Multidisciplinary research efforts are needed to understand these complex ecological interactions and prevent further emergence of bat borne infectious diseases.

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Figure 4. A little red flying fox (*Pteropus Scapulatus*).



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