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Hendra Virus Re-visited

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Abstract: Hendra virus, a novel member of the family *Paramyxovirus* that has emerged from bats in Australia, causes fatal disease in livestock and humans. Eleven spillover events have been identified since the first description of the virus in 1994, resulting in a total of 37 equine cases and six human cases. All human cases have been attributed to exposure to infected horses; there is no evidence of bat-to-human or human-to-human transmission. Low infectivity and a high case fatality rate are features of Hendra virus infection in both horses and humans. The temporal pattern of spillover events suggests seasonal factors (plausibly be environmental, biological or ecological) as the proximate triggers for spillover. Minimisation of the future occurrence and impact of Hendra virus infections requires an understanding of the ecology of flying foxes, of virus infection dynamics in flying foxes, and of the factors that promote spillover. Management strategies seek to minimize the opportunity for effective contact between bats and horses, and limit potential horse-to-horse and horse-to-human transmission. Incomplete knowledge of the ecology of the virus, of the proximate factors associated with spillover, and the inherent difficulties of effectively managing wild populations, preclude a management approach targeted at bats.

Key words: Hendra virus; Bats; Zoonoses; Emergence; Epidemiology

Hendra virus is a novel zoonotic member of the family *Paramyxovirus*. With the closely related Nipah virus, it comprises the genus *Henipavirus*. Both viruses have emerged from wildlife, and both cause fatal disease in livestock and humans. Bats are the natural hosts of henipaviruses; evidence of infection is widespread in *Pteropus* bat species (flying foxes) across their range, and is becoming increasingly evident in other genera. Hendra virus, first described in 1994 in Australia, continues to cause sporadic equine and human cases in that country; Nipah virus, first described in Malaysia in 1999 following an outbreak of disease in pigs and attendant humans, now causes almost-annual clusters of encephalitic disease in humans in Bangladesh. The 'atypical' Hendra virus cases in eastern Australia in 2008 sharpened focus on virus strain diversity, pathogenicity and transmissibility, and on drivers for spillover from bats. There is increasing evidence that (like Nipah virus in Bangladesh) a cluster of Hendra strains exists, that aspects of the ecology and/or biology of flying foxes play a role in spillover, and that patterns of spillover

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are changing. This paper expands a previous discussions of Hendra virus emergence and management (6, 8). Emphasis is given to the importance of understanding agent and host ecology.

EMERGENCE AND EPIDEMIOLOGY

Hendra virus was first described in September 1994, in an outbreak of disease in horses in Australia. Twenty horses and two humans were infected, with the resultant deaths of 13 horses and one human (10). A further ten spillover events have been identified to date, resulting in a total of 37 equine cases and six human cases (Table 1).

Prior to the Redlands cluster in mid-2008, the predominant clinical manifestation in horses was an acute febrile respiratory syndrome (4, 5, 10), although minor neurological symptoms were sometimes observed. The Redlands cases exhibited symptoms of severe central nervous system involvement and an absence of respiratory involvement (7).

Low infectivity and a high case fatality rate are features of Hendra virus infection in both horses and humans. Infection appears not to transmit readily from bats to horses, nor from horse to horse, nor from horses to humans, however, once infected, horses have a 75% probability, and humans a 50% probability, of a fatal outcome. All six human cases of Hendra virus infection to date have been attributed to exposure to infected horses. There is no evidence of bat-to-human or human-to-human transmission (11, 13). Infection in flying foxes causes no evident disease, and appears widespread, both taxonomically and geographically; archived serum samples from the 1980s reveal an antibody prevalence similar to that evident in contemporary surveys, indicating that Hendra virus infection is endemic in Australian flying foxes.

DRIVERS OF EMERGENCE

In addition to Hendra virus, three other zoonotic agents are known to have emerged from flying foxes in the 1990's: the rabies-related Australian bat lyssavirus (ABLV) and Menangle virus in Australia, and the

Table 1. Confirmed Hendra virus cases, Australia

Location of event	Number of cases	Time of event
Mackay	2 horses & one human	August 1994
Brisbane (Hendra)	20 horses & two humans	September 1994
Cairns (Trinity Beach)	1 horse	January 1999
Cairns (Gordonvale)	1 horse & one human	October 2004
Townsville	1 horse	December 2004
Peachester	1 horse	June 2006
Murwillimbah	1 horse	October 2006
Peachester	1 horse	June 2007
Cairns (Clifton Beach)	1 horse	July 2007
Brisbane (Redlands)	5 horses & two humans	June 2008
Proserpine	3 horses	July 2008

Adapted from references (1)

previously mentioned Nipah virus in Malaysia. While improved surveillance and diagnostic capabilities can enhance the detection of emerging diseases, neither explains emergence *per se*. Global travel and trade, encroachment of human activities into wilderness regions, urbanization, climatic changes and agricultural intensification are factors widely recognised as common drivers of emergence (9). For diseases with wildlife reservoirs, factors that alter wildlife population structure and migration patterns are argued to precipitate disease emergence (3) by promoting the movement of pathogens beyond their ecological niche. The increasing urban presence of flying foxes in many Australian cities and towns (attributed to the more reliable and abundant food resources in these areas) (12), the associated changes in flying fox movement patterns and population dynamics, and the increased probability of human and domestic animal contact, are consistent with this hypothesis. Indeed, it is evident that flying fox populations across their global range have been impacted by such processes, and it is plausible that this ecological disruption has driven the emergence of multiple pathogens from flying foxes in recent decades. However, what is less clear are the proximate triggers for spillover; those factors or circumstances that determine why spillover events occur in some years and not others, or at some times of year and not others. The temporal pattern of Hendra virus spillover events suggests the possibility of seasonal factors being these proximate triggers. Such factors could plausibly be environmental, biological or ecological. This contention is supported by Plowright *et al* (2008), who reported reproductive and nutritional stress in flying foxes to be associated with an increased risk of infection.

HOST MANAGEMENT STRATEGIES

Effective disease management requires an understanding of the epidemiology of the disease (knowledge of its cause, maintenance and transmission, host range, and the nature of the host-agent relationship), an ability to detect disease (surveillance and diagnostic capabilities) and political/public/industry support. Broadly, current strategies for the management of Hendra virus and other bat-associated pathogens are directed at minimising direct or indirect contact with the natural host, monitoring intermediate hosts, improving biosecurity on farms, and better disease recognition and diagnosis (8). The strategies for Hendra virus are reviewed here.

The sporadic nature of Hendra virus spillover from flying foxes to horses, the low infectivity for horses, the absence of direct flying fox-human transmission, and the inherent difficulties of managing wildlife populations have resulted in a primary focus on management strategies for horses rather than flying foxes. These include promotion of both awareness and risk minimisation strategies in the Australian horse-owning and veterinary communities (and thus, early reporting), prioritised diagnostic testing of suspect cases (early detection), and movement restrictions on suspect and in-contact horses pending test results (early response) (2). Human contact with suspect cases should be minimised and appropriate personal protective equipment and protocols used (1). Confirmed equine cases are euthanased and deep-buried or incinerated; in-contact humans must immediately notify public health authorities; facilities such as stables and yards potentially contaminated by infectious body fluids are chemically decontaminated; in-contact horses are isolated on property, clinically monitored and serially tested for anti-Hendra virus antibodies. Detailed protocols are available (1). A cross-protecting experimental Nipah virus vaccine has been developed, but commercial development of a vaccine has not occurred to date. Australian veterinarians have a high awareness of Hendra virus, and exclusion testing is now routinely undertaken for horses exhibiting suspect clinical signs (1). Veterinarians involved in suspect disease investigations should follow detailed protocols (1), as horses have been the source of infection for all human cases.

Field *et al*. previously observed breed (thoroughbred), age (>8 yo) and housing (paddocked) to be consistent horselevel risk factors for index cases (5). These risk factors have been evident in subsequent spillovers. Thus, on the basis of the limited available epidemiological information, avoiding keeping horses in paddocks with trees that are attractive to bats, avoiding placing feed bins or watering points under trees attractive to bats, and stabling horses or moving them away from areas of bat activity should decrease the risk of exposure.

CONCLUSION

Minimisation of the future occurrence and impact of Hendra virus infections requires an understanding of the ecology of flying foxes, of virus infection dynamics in flying foxes, and of the factors that promote spillover - the factors that create the 'epidemiologic bridge' from flying foxes to horses. Host management strategies seek to minimize the opportunity for effective contact between the flying foxes and horses, and limit potential horse-to-horse and horse-to-human transmission. Incomplete knowledge of the ecology of the virus, of the proximate factors associated with spillover, and the inherent difficulties of effectively managing wild populations, preclude a management approach targeted at the natural host. Strategies for horses emphasize early detection and response; strategies for humans emphasize risk assessment and management, minimal contact and use of defined personal protective equipment and protocols.

It is notable that neither the indiscriminate nor targeted killing of bats is contemplated as an effective host management strategy. Apart from philosophical and ethical considerations, such a strategy with nomadic species such as flying foxes is biologically flawed, and may cause a net influx of bats to a resultant niche vacuum. The forced movement of roosting flying foxes (flying foxes communally roost in trees, frequently in groups of thousands) by sustained noise, smoke, flags has been attempted with mixed (and typically temporary) success. Permanent removal of flying fox roosts can only be guaranteed by the removal of the roost trees. The evidence indicates that Hendra and Nipah virus are 'old' viruses (10). They likely have co-evolved with flying foxes, remaining harmlessly in this niche until relatively recent (and primarily anthropogenic) ecological changes precipitated their emergence.

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