Wildlife Health Australia

EXOTIC Eastern equine encephalitis

Fact sheet

Introductory statement

Eastern Equine Encephalitis virus (EEEV) is exotic to Australia. It is the most medically serious arthropod-borne encephalitic virus present in North America. The chances of EEEV becoming established in Australia are considered low, however Australian veterinarians should be aware that there was an outbreak of EEEV in captive emus (Dromaius novaehollandiae) in Louisiana, USA in 1991 with a high attack and fatality rate (Tully et al. 1992). Though unlikely, EEEV should also be considered as a differential during investigation of neurological disease in feral horses in Australia.

Aetiology

EEEV (colloquially referred to as "triple E") is an enveloped, single stranded RNA virus. It belongs to the family *Togaviridae*, within the genus *Alphavirus* (Calisher 1994). Its close relatives include Western Equine Encephalitis (WEEV), Venezuelan Equine Encephalitis (VEEV) and, in Australia, Ross River Virus (RRV). All of these viruses are arboviruses (arthropod-borne viruses) transmitted primarily by mosquitoes.

Natural hosts

EEEV has one of the broadest host ranges of any known virus, including several mosquito vectors, multiple reservoir species, several possible overwintering host species and many dead end hosts. The broad host range increases the likelihood that EEEV may spread to new areas, such as Australia. Several mosquito species are considered to be important vectors: *Culiseta melanura*, *Coquillettidia perturbans*, *Aedes vexans*, *A. canadensis* and *A. sollicitans*. The primary amplification hosts (those capable of infecting additional mosquitoes) are wading birds and songbirds (Scott and Weaver 1989; Calisher 1994). EEEV is capable of infecting multiple species of birds, mammals, amphibians and reptiles (Scott and Weaver 1989; Calisher 1994; White et al. 2011; Bingham et al. 2012). Ectothermic hosts (e.g. amphibians and reptiles) may play a key role as overwintering hosts, allowing year-to-year transmission of EEEV (Bingham et al. 2012; Graham et al. 2012).

World distribution

EEEV is endemic to the eastern United States of America (USA), from Florida to New England and as far west as Texas. EEEV also causes occasional outbreaks in the Caribbean and a far less dangerous strain is found in Central and South America (Calisher 1994).

Occurrences in Australia

EEEV is exotic to Australia and cases have never been reported within Australia.

Epidemiology

Transmission of EEEV is dependent upon amplification in competent vertebrate hosts and transmission between various hosts by mosquito vectors. Mosquitoes with generalist host preferences are frequently not the primary carrier of the virus but instead serve as “bridge vectors” that transmit the virus from more typical hosts to atypical hosts. Migrating birds are thought to be responsible for establishment of the virus throughout most of the Western Hemisphere.

Reservoir hosts maintain infections with high levels of EEEV in their blood and are not thought to develop illness. Birds are the typical reservoir host for EEEV, especially song birds, wading birds and other swamp birds (Scott and Weaver 1989; Calisher 1994); some rodents and reptiles may also be competent reservoirs (Arrigo et al. 2010; Bingham et al. 2012). The cycle is mostly dependent on a new population of susceptible hosts each spring and summer (i.e. bird hatchlings). After initial infection with EEEV, individual birds become immune to subsequent infection.

Mammals, particularly horses and humans, are considered “dead end” hosts for the virus. Infected mammals may either remain asymptomatic or develop disease. Occasionally, infections in horses and humans become serious and result in encephalitis and death. The incubation period in horses ranges from five to 14 days. Cases of EEE in horses usually begin 2–3 weeks after EEEV spreads to birds and human cases appear several weeks later again. White-tailed deer (*Odocoileus virginianus*), a dead end host, can suffer serious clinical disease (Kiupel et al. 2013).

Clinical signs

Information is primarily limited to domestic and laboratory animals; little is known about disease in wildlife. For clinical signs in humans see “Human health implications”.

Horses: fever and leukopenia during first 4–5 days of infection, progressing to ataxia, hyperexcitability, restlessness, depression, dramatic weight loss and a characteristic posture: drooping head and ears (Del Piero et al. 2001). Collapse may be followed by death (Walton 1992). Mortality rates are 80–90% (Scott and Weaver 1989).

Emus: depression and bloody vomiting and diarrhoea, 76% attack rate, 87% mortality rate (Tully et al. 1992).

Clinical signs in a range of other mammals (e.g. rodents, primates) and birds (turkeys, chickens, penguins, sparrows and cranes) include lethargy, fever, gastro-intestinal and neurological signs and death (Spalatin et al. 1961; Dein et al. 1986; Tully et al. 1992; Guy et al. 1993; Guy et al. 1994; Tuttle et al. 2005; Reed et al. 2007; Arrigo et al. 2010; Steele and Twenhafel 2010).

Diagnosis

Blood or cerebrospinal fluid (CSF) using an ELISA. Virus levels in blood are typically too low for effective use of PCR (Davis et al. 2008). Older diagnostic tools include haemagglutination inhibition assays, neutralization assays (Davis et al. 2008) and isolation of live virus from brain tissue (Calisher 1994), however, these techniques must be conducted under Biosafety Level 3 conditions (Davis et al. 2008).

Clinical pathology

Whooping cranes (*G. americana*): elevated aspartate transaminase, gamma-glutamyl transferase, lactic acid dehydrogenase and uric acid (Dein et al. 1986).

Pathology

Emus showed pronounced haemorrhaging within the intestinal tract, lesions in the spleen and liver, necrosis of hepatocytes, the spleen, intestinal mucosa, and the lamina propria of the intestine, no lesions in the CNS (Tully et al. 1992; Veazey et al. 1994).

Most other affected animals show inflammation and lesions throughout the CNS (Del Piero et al. 2001), vasculitis, splenitis and hepatitis (Steele and Twenhafel 2010) (Guy et al. 1993; Guy et al. 1994; Reed et al. 2007).

Differential diagnoses

In feral horses, other arboviruses e.g. Ross River Virus, Japanese Encephalitis Virus. In emus, other causes of mass mortality, including Salmonellosis and Erysipelas in farmed emus, should be considered.

Laboratory procedures and diagnostic specimens

Blood and CSF for ELISA (Davis et al. 2008). Brain can be used to isolate and culture live virus (Calisher 1994).

Treatment

Antiviral drugs have limited efficacy against EEEV; most treatment is geared toward limiting the severity of encephalitic symptoms (Davis et al., 2008). Physical therapy is often required during recovery (Calisher 1994).

Prevention and control

Mosquito control is the most effective method of minimising EEEV activity. An effective vaccine has been developed for emus (Tengelsen et al. 2001) and an approved and moderately effective EEEV vaccine is available for horses in endemic areas (Davis et al. 2008; Pandya et al. 2012). No approved vaccine is currently available for humans. A very expensive live attenuated vaccine, used by the US Military, may be obtained by researchers who frequently work with the virus. Vaccine research has surged in recent years and results look promising (Pandya et al. 2012; Carossino et al. 2014). Avoiding swamps, wearing long clothing and limiting night time outdoor activity are all recommended to reduce mosquito exposure, especially during outbreaks (Calisher 1994).

Surveillance and management

Wildlife disease surveillance in Australia is coordinated by the Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia's States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au. There are no cases of EEE in the national database.

Research

Current research in endemic areas has focused either on development of a vaccine (e.g. Padya et al. 2014), viral pathogenesis (e.g. Steele and Twenhafel 2010), or the ecology and epidemiology of mosquito-host interactions involving EEEV (e.g. Bingham et al. 2012; Graham et al. 2012).

Human health implications

An average of eight human cases of neurological disease result from EEEV infection annually in the USA. Most systemic infections end in complete recovery after 1–2 weeks and many remain subclinical. If the infection

becomes encephalitic, the disease becomes very dangerous. The most serious symptoms and consequences are manifested in young children and elderly patients. Mortality is high in cases that proceed to encephalitis (Calisher 1994). In many surviving patients brain lesions have lasting, debilitating consequences (intellectual impairment, personality disorders, seizures, etc.), with only 3% of patients making a full recovery (Ayres and Feemster 1949).

The high mortality rate, poor recovery rate, lack of an effective vaccine and potential application as a biological weapon ranks EEEV as the most medically serious arthropod-borne encephalitis in North America.

Conclusions

EEEV is exotic to Australia. The virus has a very broad host range, with a range of mosquito vectors. Infection can cause serious neurological disease in humans and a wide range of other vertebrate hosts. The primary amplification hosts are wading birds and songbirds. Geographic spread of the virus is considered possible.

References and other information

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Acknowledgements

We are extremely grateful to those who had input into this fact sheet and would specifically like to thank Sean P. Graham and Crystal Kelehear.

Drafted: 28 February 2016.

To provide feedback on this fact sheet

Wildlife Health Australia would be very grateful for any feedback on this fact sheet. Please provide detailed comments or suggestions to admin@wildlifehealthaustralia.com.au. We would also like to hear from you if you have a particular area of expertise and would like to produce a fact sheet (or sheets) for the network (or update current sheets). A small amount of funding is available to facilitate this.

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