Wildlife Health Australia

EXOTIC Western equine encephalitis

Fact sheet

Introductory statement

Western equine encephalitis virus (WEEV) is a serious encephalitic virus endemic to western North America that affects multiple animal hosts and can cause mortality in a variety of mammals and birds, including captive Emus. Although it currently poses little danger to Australians, the spread of emerging infectious diseases such as West Nile Virus warrants guarded concern about this and other arboviruses colonizing Australia (see Prow et al. 2014). In addition, travellers to and from western North America may be exposed to this virus and therefore veterinarians, wildlife health professionals, and physicians should be aware of it. Given that most flights from North America originate from within the distribution of this virus, it could be predicted that this is among the most likely endemic North American virus to reach Australia.

Aetiology

WEEV is an enveloped, single stranded, positive sense RNA virus. It belongs to the virus family Togaviridae, within the genus *Alphavirus* (Calisher, 1994). Its close relatives include Eastern Equine Encephalitis Virus (EEEV), Venezuelan Equine Encephalitis Virus (VEEV), and in Australia, Ross River Virus (RRV). All of these viruses are arboviruses (arthropod-borne viruses) transmitted primarily by mosquitoes. The WEEV genome has similarities to North American EEEV, and antigenic segments similar to the Old World Sindbis virus. It is hypothesized that WEEV arose fairly recently as a result of recombination in a mosquito simultaneously infected with ancestral forms of these viruses (Hahn et al. 1988).

Natural hosts

WEEV has a broad host range encompassing several mosquito species that serve as vectors (primarily *Culex tarsalis*; Calisher 1994), numerous birds (primarily House Finches and House Sparrows) that serve as amplification hosts (hosts that can support blood levels of the virus that enable them to reinfect additional mosquitoes), and several species of dead-end hosts (hosts that do not develop high blood levels of virus and instead develop symptoms; e.g., humans, horses, squirrels, and a few other wild mammals). A secondary

transmission cycle involves the mosquito *Aedes melanimon* and the Black-tailed Jackrabbit (*Lepus californicus*) as an amplification host (Calisher 1994). Several amphibian and reptile species (e.g. garter snakes; Thomas and Eklund 1960; Thomas and Eklund 1962) are suspected overwintering hosts (hosts that are responsible for year-to-year transmission of the virus). In addition, and of particular interest to Australians, farm-raised emus experienced an outbreak in six flocks of emus over a 40-kilometre radius in Oklahoma (mid-western USA) in 1992, resulting in one emu death (Randolph et al. 1994).

World distribution

WEEV is endemic to the western Hemisphere and has been isolated from locations as far south as Argentina and as far north as British Columbia, Canada. Strains present in South America can cause disease in horses but are not implicated in severe human cases. The region of serious WEEV transmission and disease is from British Columbia east to Manitoba south through the western USA (specifically, the states of Washington, California, North and South Dakota, Montana, Minnesota, Wyoming, Utah, Colorado, Nebraska, New Mexico, and Texas; Calisher 1994).

Occurrences in Australia

To date, WEEV has not been reported in Australia.

Epidemiology

Transmission of WEEV depends on interactions between mosquitoes and several vertebrate hosts. The primary mosquito vectors are *Culex tarsalis*, which feeds upon birds and mammals, and *Aedes melanimon*, which feeds primarily upon mammals. House finches and house sparrows, both of which are common around human dwellings in North America (house sparrows are also common near homes in eastern Australia), are the main amplification hosts; they support high levels of WEEV in their blood and are capable of reinfecting mosquitoes. Black-tailed Jackrabbits are also capable of supporting high levels of virus in blood (viraemia). In general, birds are not seriously affected by the virus; experimental infection with WEEV resulted in very low mortality in a wide range of North American birds (Reisen et al. 2003). After a single infection birds are immune to re-infection. Some mammals (including horses and humans) are incidentally exposed to WEEV via infected mosquitoes and can develop severe disease. Depending on the strain of WEEV, experimental infection can result in up to 100% mortality in mice (Steele and Twenhafel, 2010). However, mammalian hosts do not appear to support high levels of virus in their blood and therefore do not contribute substantially to the further transmission of the virus. Before 1954 very large outbreaks occurred occasionally and affected thousands or even tens of thousands of horses, with a case fatality rate of ~50%. In 1941 a severe outbreak occurred that affected thousands of people in the USA and Canada; the case fatality rate was ~8-15%. Risk factors in humans are rural residency, age (patients <10 years old are the most likely to develop severe complications), sex (males infected more often than females), outdoor activities or working environments, and proximity to mosquito breeding sites. However, since the 1950s incidence of human infection has declined to very low levels. Between 1954 and 1984 there were only ~34 human cases/yr reported in the USA, and only 5 cases from 1988-2008 (Davis et al. 2008). The decline in cases over the past century is probably associated with a general decline in outdoor activity among people in the USA, and also due to the dramatic loss of wetland habitats throughout the western USA, especially in California. However, there is some evidence that WEEV infections may be going underreported; several thousand cases of encephalitis in

California reported from 1990-1999 were never diagnosed and may have been due to arboviruses (Trevejo 2004).

Clinical signs

Clinical signs of WEE are highly variable; consequently, it is not possible to distinguish between infections with different encephalomyelitic viruses on a basis of clinical signs alone.

Humans: Encephalitis is most common in very young and old patients. Early stages of WEE include a suite of flu-like symptoms that are likely to be the only manifestations of the disease—chills, fever, headache, nausea, and vomiting that may last for about a week. A few days post-manifestation of symptoms the disease may progress to affect the central nervous system. Symptoms then include lethargy, drowsiness, nuchal rigidity, vertigo, and photophobia. Fatalities are rare, unlike with more serious encephalitides, WEEV rarely induces complications in patients that recover from encephalitis within two years. During this recovery period the patient may suffer from fatigue, headaches, and tremors. Adults typically make a full recovery, however, infants are more likely to develop severe motor or neural damage that may require prolonged physical therapy and care (Calisher 1994).

Macaques: Fever, inappetence, reduced activity, and tremors (Steele and Twenhafel 2010).

Horses: For the first five days post-infection symptoms are those of non-specific fever with leukopenia. General signs include lethargy, drooping ears, sluggish behaviour, abnormal gait, anorexia, and weight loss. In some cases, horses are very unbalanced and adopt a wide-legged stance, refusing to move. Severe neurological signs manifest at five days post-infection and may lead to the horse collapsing into convulsions with characteristic leg paddling; this late phase is often followed by coma and death. In symptomatic horses, mortality rates are 40-80% (Walton 1992).

Hamsters: Weight loss, rapid breathing, conjunctivitis, lack of co-ordination, seizures, and ultimately, death (Steele and Twenhafel 2010).

Emus: 10-50% morbidity. Anorexia, weight loss, prolonged sitting, sleeping and general drowsiness, leg weakness, S-shaped cervical curvature, lack of balance, abnormal breathing, and in some cases watery diarrhoea (Randolph et al. 1994).

Turkeys: Drowsiness, tremors, paralysis of the legs, high mortality (Woodring 1957).

Diagnosis

Diagnosis is accomplished by testing for WEEV-specific IgM antibodies in blood or cerebro-spinal fluid (CSF). WEEV can also be isolated from brain or CSF (Davis et al. 2008).

Clinical pathology

Humans: CSF pressure is typically elevated in cases with central nervous system involvement. CSF glucose levels remain normal, and protein content can also be normal or slightly elevated. Leukocyte counts are elevated, with polymorphonuclear cells most prevalent early in the infection and mononuclear cells most prevalent later (Calisher 1994). Hyponatremia may also occur (Davis et al. 2008).

Macaques: hyperglycaemia (Steele and Twenhafel, 2010).

Pathology

Humans: Encephalitic patients exhibit cranial oedema—accumulation of fluid between the brain and meninges that enclose it. Lesions are also usually present in several locations within the central nervous system, including the cortex, thalamus, pons, ganglia, and spinal cord (Calisher 1994).

Macaques: Leukocytosis and focal necrosis (Steele and Twenhafel 2010).

Hamsters: Necrotic brain lesions, lymphocyte infiltration, haemorrhage (Steele and Twenhafel 2010).

Mice: The brain exhibits neuronal necrosis, swelling, mild lymphocyte infiltration. Lesions in the lungs, liver and heart. Inflammation and necrosis in the bone marrow, skeletal muscle, cartilage and peripheral nerves (Steele and Twenhafel 2010).

Emus: Congestion of the meninges, brain, liver, spleen, kidney and mesenteric blood vessels. Lesions in the meninges and brain: multifocal, moderate lymphocytic, histiocytic and heterophilic meningitis in the meninges of the cerebrum and cerebellum. Dilation and congestion of blood vessels in the meninges and neuropil. Mild axonal degeneration (Randolph et al. 1994).

Differential diagnoses

Symptoms of WEEV infection could easily be confused for those caused by other viruses that are far more likely to infect Australians at home or on vacation (e.g., Ross River virus, Japanese encephalitis virus). Of course, these and many other possibilities would need to be eliminated before a case of WEE in Australia could be confirmed.

Laboratory diagnostic specimens

Blood or CSF can be used to test for WEEV-specific antibodies (Davis et al. 2008). WEEV can be isolated from brain or CSF. Haemagglutination or neutralization procedures can also be conducted, but these require live virus (Calisher 1994).

Laboratory procedures

Enzyme-linked Immunosorbent Assay (ELISA) procedures rely on combination of small blood or CSF samples in a 96-well plate coated with antibodies reactant to WEEV-antibodies (antibody-antibody binding). The antibody complex is conjugated with a fluorescent enzyme. The plate is run through a machine that can determine the amount of fluorescence emitted by the enzyme-antibody complex, and thus determine the amount of virus-specific antibody present in the sample. ELISA kits are commercially available and typically include all reagents and instructions necessary for completion of the assay.

Treatment

Treatment of WEEV focuses on controlling the severity of encephalitic symptoms (fever reduction, maintaining electrolyte balance and hydration, maintaining respiration, controlling seizures, and decreasing cranial pressure; Calisher 1994).

Prevention and control

A vaccine is available for horses however, a vaccine developed for humans is experimental and only available to researchers and the US Military (Calisher, 1994). Control measures focus on prevention of mosquito-human interactions. Mosquito control programs have been extremely effective in the western US and may have contributed to the steady decline in WEE cases over the past 50 years (Trevejo 2004). These control methods include water diversion and application of pesticides (Trevejo 2004). An unintended consequence of massive (e.g. 90%) conversion of wetlands to croplands in California was the elimination of mosquito breeding habitats.

Surveillance and management

Wildlife disease surveillance in Australia is coordinated by 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.

Surveillance methods include routine testing of mosquitoes and sentinel chickens for infection with WEEV. Although methods differ between different municipal surveillance programs, these programs continue in the western USA despite the low incidence of human infection and provide a potential early warning system in the event of an outbreak (Trevejo 2004).

Statistics

There are no reports of WEEV in Australia's National Wildlife Health Information System.

Research

Early research on WEEV focused on epidemiology and control and became a model for arboviral epidemiological research. Success in mitigating the effects of this virus in the western USA may be due in part to these classic, determined research efforts. More recent research has involved quantifying encephalitic cases in the western US (Trevejo 2004) and vaccine development (Carossino et al. 2014).

Human health implications

Although the case fatality rate for WEE is quite low, encephalitic viruses are always a cause for guarded concern. WEEV was a considerable public health concern in the western USA during the first half of the 20th century when it was responsible for large outbreaks in humans and horses.

Conclusions

WEEV currently poses little threat to humans and has never been confirmed in Australia. However, in the past it was a considerable public health issue in the western USA to both humans and horses. Given that mosquitoes and sentinel chickens routinely test positive for the virus, WEEV is still a concern in the western USA and flights destined for Australia from California are thus a possible route for spread of this virus. In the event that WEEV established in Australia, emus and equids would likely be adversely affected.

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To provide feedback on this fact sheet

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