ROSS RIVER VIRUS

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Keywords: horse; Ross River virus; Alphavirus; mosquito-borne; horse; zoonosis

Summary
Ross River virus is an arthropod-borne virus (arbovirus) and the cause of the most common mosquito-borne human disease in Australia, being frequently associated with a debilitating polyarthritis. Serological evidence would indicate that subclinical infections with the virus are widespread in horses in many areas of the country. Clinical disease can occur in horses, with affected animals displaying any or all of the following signs: pyrexia, inappetence, lameness, stiffness, swollen joints, reluctance to move, ataxia, mild colic and poor performance. Persistence of certain clinical signs such as limb soreness and impaired performance for months or even years has also been reported in a small percentage of cases. The horse is considered a possible amplifying host for the virus, with the ability to develop a high-titred viraemia and infect various mosquito species.

Introduction
Ross River virus is closely related to Getah virus in terms of its taxonomic classification, ecology and the nature of the clinical disease it can cause in horses. In contrast to Getah virus, however, Ross River virus is also an important human pathogen (Russell 2002). It is an arthropod-borne virus or arbovirus that can be transmitted by a wide range of mosquito species and which is endemic in Australia, in Papua-New Guinea and certain islands in the South Pacific (Spradbrow 1972; Russell 1994, 1996, 2002; Azuolas 1998). Disease caused by Ross River virus is the most common arboviral infection of man in Australia. It is a nonfatal disease that is characterised principally by a debilitating polyarthritis syndrome (Fraser 1986; Russell 1994). Joint pain, limb soreness and locomotor difficulties can persist for several months even years in a percentage of affected individuals (Boughton 1996). Whereas infection with Ross River virus is commonly encountered in horses in many areas of Australia, especially in the northern tropical regions where there is year-round virus activity (Russell 2002), the overall clinical attack rate would appear to be low (Azuolas 1998).

Aetiology
Ross River virus is a single-stranded, positive sense RNA virus with quasi-species structure belonging to the genus Alphavirus, family Togaviridae. It is classified in the Semliki Forest complex along with Semliki Forest, Bebaru, Getah, Chikungunya, O’nyong-nyong, Una and Mayaro viruses and belongs to the Getah virus serogroup of agents (van Regenmortel et al. 2000). Considerable sequence homology exists between the genomes of Ross River and Getah viruses (Strauss and Strauss 1994), with evidence of geographic variability among isolates of Ross River virus (Lindsay et al. 1993). Ross River virus is primarily a mosquito-borne infection and an important human pathogen.

Epidemiology
As previously indicated, Ross River virus is arthropod-borne, and infection principally results from the bite of an infected mosquito (Russell 1994, 1996 and 2002). Different mosquito species are involved as vectors in various regions of Australia or wherever the virus is found. The species vary depending on different climatic and environmental conditions, with mosquitoes belonging to the genera Culex, Aedes (Ochlerotatus), Anopheles, Coquillettidia and Mansonia implicated in transmission under field or experimental circumstances (Aaskov 1997; Russell...
2002). Notwithstanding the wide range of mosquito species that can serve as potential vectors of Ross River virus, only a small number are of primary importance in transmission in coastal or inland, urban or rural settings. Principal vectors in coastal situations are the northern saltmarsh mosquito, *Ae. vigilax* and the southern saltmarsh mosquito, *Ae. camptorhynchus*, whereas in inland areas, *Cx. annulirostris* is the major vector. Similar to Getah virus, and many other arboviruses, Ross River virus is maintained in a mosquito-vertebrate-mosquito host cycle. Vertical transmission of the virus has been confirmed in species of culicine mosquitoes (Dhileepan et al. 1996).

The natural vertebrate hosts of Ross River virus are considered to be nonmigratory native macropodids e.g. kangaroos and wallabies. Other marsupials may also serve as possible reservoir hosts (Russell 2002). Kangaroos and wallabies are assumed to be the most important amplifying hosts. In the area around Brisbane, marsupials (brushtail possums and Macropods), flying foxes and horses were identified as the most important host species (Kay et al. 2007). In the latter study, mosquitoes collected in the Brisbane area were analysed for host blood meals. The most commonly identified blood meal was dog blood (average of 37.4% of all identified blood meals), followed by bird (18.4%), horse (16.8%), brushtail possum (13.3%), human (11.6%), cat (1.7%), flying fox (0.7%) and macropod (0.2%). Since horses infected with Ross River virus may develop high-level viraemias of up to $10^{6.3}$ suckling mouse intracerebral LD$_{50}$/ml (Kay et al. 1987), they serve as an important source of infection for mosquitoes and may well play a role in disseminating and perhaps maintaining the virus in certain areas/regions of the country. There is some evidence to suggest that horses may not necessarily be efficient amplifying hosts (Kay et al. 1987). The prevalence of Ross River virus infection in horses is high in endemic areas of Australia. In Queensland (an area believed to have year-round mosquito activity), the seropositivity rate was approximately 80%, compared to 50% in the region of the Gippsland Lakes in southern Australia (an area with seasonal mosquito activity) (Azuolas 1998). In a serological survey of vertebrate sera (1706 samples) obtained from 5 animal species in the area around Brisbane, sera from dogs and horses were most commonly found positive for antibodies to Ross River virus, with antibodies present in 22.5% and 25.5% of samples, respectively.

Clinical signs

Ross River virus causes a nonfatal infection in horses. Although seroconversion to Ross River virus is common, the majority of horses infected with the virus develop minimal, if any, signs of disease (Kay et al. 1987; Azuolas 1998; Azuolas et al. 2003; El-Hage et al. 2008). Experimental infection of horses with Ross River virus has failed to result in the development of disease. No clinical signs were reported in either of 2 experimental studies comprising a total of 14 horses (Gard et al. 1977). Accepting that variation in pathogenicity probably exists among Ross River virus genotypes (Fraser 1986; Russell 1994), it may be that many virus strains cause only subclinical or inapparent infection. Nonetheless, infection with this virus is considered responsible for musculoskeletal disease in performance horses that has occurred for many years in many riverland and northern regions of Australia (El-Hage et al. 2008), notwithstanding the lack of laboratory confirmation of the disease. Clinical signs associated with Ross River virus infection in horses include pyrexia, inappetence, serous nasal discharge (Fig 1), lethargy (Fig 2), submaxillary lymphadenopathy, distal limb swelling, lameness, stiffness, swollen joints (Fig 3), ataxia, reluctance to move, petechial haemorrhages on the gingival mucous membranes and mild colic (Pascoe et al. 1978; Azuolas 1998; Azuolas et al. 2003; El Hage et al. 2008).
Persistence of certain clinical signs, especially limb soreness and poor performance are believed to occur in a small percentage of affected horses (El-Hage et al. 2008). While seroconversion to Ross River virus is quite common in horses, to date there have been few reports of clinical disease associated with seroconversion or virus isolation (Gard et al. 1977; Pascoe et al. 1978; Azuolas 1998; Azuolas et al. 2003; Studdert et al. 2003). In a recent report, Ross River virus was believed to be the cause of acute illness in 4 horses around the Bellarine peninsula in southwest Victoria, Australia, that were naturally exposed to the virus (El-Hage et al. 2008). The clinical signs exhibited by the affected individuals included petechial haemorrhages, lymphadenopathy, distal limb swelling and reluctance to move. Fibrinogen levels were also elevated in 3 of the 4 horses. Whilst no virus was isolated, serological testing revealed increased IgM titres to the virus in all the horses, confirming recent infection. The outbreak occurred at a time when a known Ross River virus vector, the mosquito *Aedes camptorhynchus* was recorded in very high numbers in the region. Based on the serological finding of IgM antibodies, there is every reason to relate the clinical signs observed in these 4 horses to recent infection with Ross River virus. The signs displayed were consistent with those identified with this virus infection in humans in whom there is targeting of synovial and musculoskeletal tissues. ‘Poor performance’ is a frequently reported outcome in horses suspected of being infected with Ross River virus (Azuolas 1998).

**Diagnosis**

No matter how suggestive the clinical signs exhibited by an affected horse(s) are of infection with Ross River virus, laboratory confirmation of a provisional clinical diagnosis of the disease is essential. Diagnosis is based on detection of the virus in serum or heparinised blood by virus isolation in cell culture or intracerebral inoculation of suckling mice, or by reverse transcription-polymerase chain reaction assay of blood or synovial fluid (Azuolas et al. 2003; Studdert et al. 2003). To optimise the chances of virus isolation, specimens should be collected as early as possible after the onset of clinical signs. Recent exposure to and infection with Ross River virus can also be established by demonstration of a detectable IgM antibody response in a single serum sample or in the acute sample, where paired blood samples taken 2–3 weeks apart are collected from suspect cases of the disease (Azuolas et al. 2003). An IgM antibody response is generally detectable by Day 7–10 after exposure, peaks within 2–3 weeks before declining rapidly and disappearing as IgG antibody levels increase and eventually replace IgM antibodies in the circulation (Azuolas et al. 2003).

**Treatment**

Treatment of horses with suspected Ross River virus infection is supportive and symptomatic, with an emphasis on the use of analgesics and nonsteroidal anti-inflammatory drugs to mitigate the muscle soreness, stiffness in gait and swollen joints.
Prevention

There is no vaccine currently available against Ross River virus infection in horses. Preventing exposure of horses to the virus is dependent primarily on controlling the vector (mosquito) population through reduction of breeding sites and use of larvicides, as well as the natural vertebrate hosts of the virus. The use of topical insect repellents is recommended on horses at risk of infection.

References


