Updated, February 5, 2024 [1]

# Context and general considerations

Western Equine Encephalitis is caused by the virus of the same name (WEEV), a member of the *Togaviridae* family, *Alphavirus* genus. Alphaviruses are widely distributed across all continents and are classified into New and Old World alphaviruses according to the first described endemic areas. The two groups are generally associated with notable differences in human infection pathogenesis. Old World alphaviruses such as chikungunya (CHIKV), O'Nyong-Nyong (ONNV), Ross River (RRV), Semliki Forest (SFV) and Sindbis (SINV) viruses primarily cause febrile illnesses with arthritic syndromes. On the other hand, New World alphaviruses like WEEV, Eastern Equine Encephalitis virus (EEEV) and Venezuelan Equine Encephalitis virus (VEEV) generally cause encephalitis in equines, humans and other mammals. Mayaro virus (MAYV), a New World arthralgic alphavirus, is an exception.

WEEV mainly circulates in the western regions of Canada and the United States and in the southern cone. In Argentina, outbreaks in equines, associated with human cases were identified in 1972/73 and 1982/1983. Since late November 2023, an intense circulation of WEEV has been observed with a significant number of outbreaks in horses in Argentina and Uruguay, and the detection of human cases in these two countries (*1, 2*). In addition, a case has also recently been reported in a horse in Brazil (*3*).

## Host, vector and life cycle

WEEV is maintained in a primary enzootic cycle among its natural vertebrate hosts, birds, and mosquitoes, particularly *Culex tarsalis.* A secondary cycle has also been described involving lagomorph mammals and *Aedes melanimon* mosquitoes. Other reservoir (rodents, bats, reptiles) and mosquito species (*Aedes albifasciatus*, as well as *Culex ocossa*, *Psorophora pallescens* and *Anopheles albitarsis*) could potentially contribute to the life cycle, particularly in the southern cone. The involved vectors can also infect equines and humans which are dead-end hosts that do not develop sufficient viremia to infect mosquitoes and maintain the cycle.

## Clinical presentation

The incubation period of the disease is 2 to 10 days. WEEV infection in equines and humans can be asymptomatic. Symptomatic infections are rare, but can be severe, causing conditions such as aseptic meningitis and encephalitis, and leave sequelae. Mortality is estimated at approximately 15-20% and 3-4% in equines and humans, respectively.

[1] This document is an update of the first version published on December 20, 2023. The recommendations presented in this document may be subject to subsequent modifications based on advances in knowledge about the disease and the etiological agent.

In humans, the disease has an acute onset with headache followed by fatigue, chills, fever, myalgia, and general discomfort. These symptoms may worsen the following days, with vomiting, drowsiness, confusion and prostration. The most frequent neurological symptoms include weakness and widespread tremors, especially in the hands, lips and tongue. Improvement generally begins several days after the fevers subsides, typically around 7 to 10 days. There is no human vaccine nor specific antiviral treatment. Management of cases includes rest, adequate hydration, and symptomatic therapy.

## International notification

Disease in equines must be reported to the World Organization for Animal Health. An event involving human infection should be assessed using the "Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern", Annex 2 of the International Health Regulations (2005) (*4*) for reporting through the mechanisms of the Regulations.

## Case definitions

### Suspected case

Patient who:

1) presents or has presented accompanied by a headache; and

2) presents or other (including prostration, tremors, vomiting and somnolence), without another apparent etiology.

Depending on the epidemiological situation, the history of residence in or travel to a place or geographic area with confirmed cases of WEE in animals and/or humans during the 10-15 days prior to the onset of symptoms should be considered.

### Confirmed case

Any suspected case with laboratory confirmation, using any of the following criteria:

1) detection of viral RNA by RT-PCR in any sample type; or

2) detection of anti-WEEV IgM antibodies by ELISA in a cerebrospinal fluid sample; or

3) seroconversion of anti-WEEV IgM antibodies by ELISA in paired acute and convalescent samples collected more than 7-10 days apart; or

4) seroconversion or increase in the titer of neutralizing antibodies by PRNT (or microneutralization) in paired acute and convalescent samples collected more than 7-10 days apart.

### Probable case

Any suspected case with detection of anti-WEEV IgM antibodies by ELISA in a single serum sample (without a paired sample), and who, therefore, does not meet the definition of a confirmed case.

## Negative/discarded case

Any suspected case with no detectable anti-WEEV IgM antibodies by ELISA in a single serum sample (without a paired sample) collected more than 10 days after the onset of symptoms.

A positive result by RT-PCR (or viral isolation) the infection. However, viremia in WEEV infections is low and of short duration. Furthermore, if the case is detected in the neurological phase, the virus is likely no longer present in the blood. Therefore, a negative result infection and, in cases with clinical and epidemiological suspicion, serological methods should be used. Differential diagnosis by molecular methods, particularly for other arboviruses that can cause neurological syndromes, should also be considered. Depending on the epidemiological situation, other equine encephalitis viruses (EEEV and VEEV) as well as neurotropic flaviviruses (e.g. West Nile virus, St. Louis encephalitis virus) could be considered (Figure 1).

While RT-PCR generally has a low sensitivity due to the level and duration of viremia (it may be possible to detect the viral RNA up to 3 days after the onset of symptoms, at most 5 days), its high specificity and fast turnaround make it an important tool in detecting WEEV infections. In the context of an outbreak with compatible symptoms, detection by RT-PCR in at least one case allows for the identification of the

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