

### Summary of the situation

On 19 December 2023, the Pan American Health Organization / World Health Organization (PAHO/WHO), warned about the risk to human health associated with the circulation of the Western Equine Encephalitis virus (WEE) (1) and published an update on 10 January 2024 (2). This epidemiological update provides new information on the WEE cases in the Americas, as well as surveillance guidance and the case definition for WEE in humans.

As of 9 January 2024, there were 1,314 outbreaks<sup>1</sup> in animals (1,258 in Argentina and 56 in Uruguay) reported and 21 cases of this virus in humans had been confirmed, including one death, all in Argentina (2, 3).

As of 5 February 2024, there were 2,438 outbreaks in animals (1,419 in Argentina, 1,018 in Uruguay, and one in Brazil) and 58 confirmed cases in humans (56 in Argentina and two in Uruguay) (4).

#### Western Equine Encephalitis (WEE) cases in animals

In **Argentina**, between 25 November 2023 and 5 February 2024, the National Food Safety and Quality Service (SENASA per its acronym in Spanish) confirmed 1,419 cases in equines (45 diagnosed by laboratory and 1,374 by clinical and epidemiological link). The cases (including confirmed, suspected, discarded, and negative) are reported in 20 provinces: Buenos Aires, Catamarca, Chaco, Córdoba, Corrientes, Entre Ríos, Formosa, Jujuy, La Pampa, La Rioja, Mendoza, Misiones, Neuquén, Río Negro, Salta, San Juan, San Luis, Santa Fe, Santiago del Estero y Tucumán. The greatest proportion was reported in the province of Buenos Aires, accounting for 29% of laboratory confirmed cases in equines (n=13) (5).

In **Uruguay**, between 2 December 2023 and 6 February 2024, the Ministry of Livestock, Agriculture and Fisheries (MGAP per its acronym in Spanish) confirmed 1,018 suspected cases in equines (77 confirmed by laboratory). The cases with positive laboratory results have been identified in 16 departments of the country: Artigas, Canelones, Cerro Largo, Durazno, Flores, Lavalleja, Montevideo, Paysandú, Río Negro, Rivera, Rocha, Salto, San José, Soriano, Tacuarembó, Treinta y tres. The greatest proportion was reported in the department of San José, accounting for 30% of laboratory confirmed cases in equines (n=23) (6).

In **Brazil**, on 26 January 2024, the Secretariat of Agriculture, Livestock, Sustainable Production and Irrigation (Seapi per its acronym in Portuguese) of the state of Rio Grande do Sul, reported a confirmed WEE equine case in the municipality of Barra do Quaraí, on the western border of the state of Rio Grande do Sul. The Federal Agricultural Defense Laboratory of Minas Gerais

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<sup>1</sup> Outbreak: means the occurrence of one or more cases in an epidemiological unit.

(LFDA/MG per its acronym in Portuguese) confirmed the WEE diagnosis following receipt of the sample collected on 15 December 2023 (7).

### Human cases of Western Equine Encephalitis

In **Argentina**, since the first human case of Western Equine Encephalitis (WEE) was reported (8) in the country on 20 December 2023, and up to epidemiological week (EW) 4 of 2024, 279 suspected human cases have been reported among 15 provinces. Of these, 56 have been laboratory confirmed and are reported in the provinces of Buenos Aires (n=31), Santa Fe (n=13), Entre Ríos (n=5), Córdoba (n=4), the Autonomous City of Buenos Aires (n=2), and Santiago del Estero (1). In addition, 20 cases were categorized as probable in the provinces of Buenos Aires (n=13), Córdoba (n=1), and Santa Fe (n=6) (**Table 1; Figure 1**). Confirmed cases are identified in all age groups with a median age of 58.5 years, a maximum of 81 years and a minimum of 4 months; 57% of the cases were in the age group of 50 to 69 years. Males account for 82% of the cases and females 18% (**Figure 2**) (9).

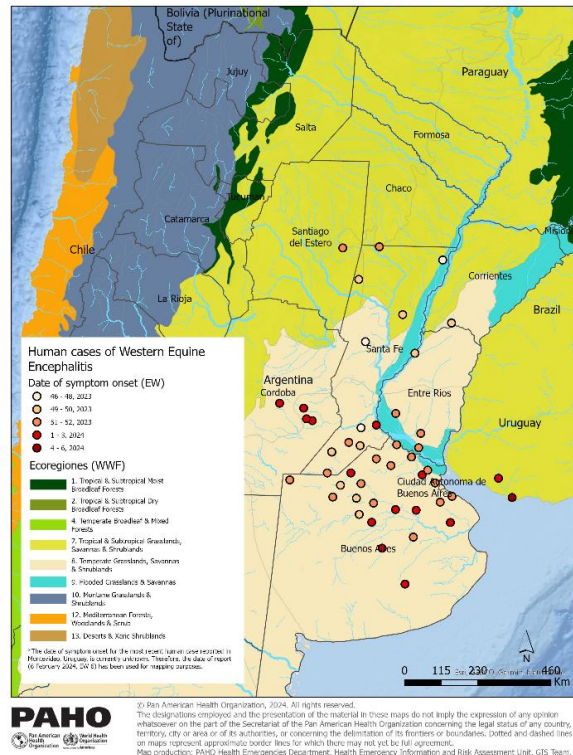
Among the cases, seven deaths were reported in the provinces of Buenos Aires (n=3), Santa Fe (n=2), Córdoba (n=1), and Entre Ríos (n=1) (**Table 1**). Among the fatal cases (five male and two female), six had reported having lived, worked, or visited a rural area and the epidemiological history is not yet available for one of the fatal cases. Six of seven fatal cases had a history of underlying pathological conditions (diabetes, oncological disease, high blood pressure, among others). The fatal cases were between 36 and 74 years of age (9,10).

**Figure 1.** Human cases of Western Equine Encephalitis by probable place of infection (province), up to EW 4 of 2024, Argentina.

Province	Confirmed cases	Probable Cases	Suspected Cases	Deaths
Buenos Aires	31	13	53	3
Santa Fe	13	6	17	2
Entre Ríos	5	0	11	1
Córdoba	4	1	3	1
CABA	2	0	1	0
Mendoza	0	0	1	0
San Juan	0	0	1	0
San Luis	0	0	1	0
Chaco	0	0	0	0
Santiago del Estero	1	0	0	0
<b>Total</b>	<b>56</b>	<b>20</b>	<b>88</b>	<b>7</b>

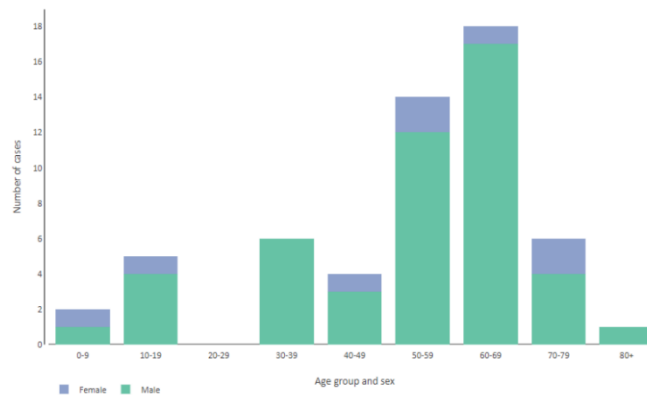
**Source:** Adapted from the Argentina Ministry of Health. National Epidemiological Bulletin, epidemiological week 4 of 2024. Western Equine Encephalitis (WEE) Update. Number 689. February 2024. Buenos Aires: MSAL; 2024. Available in Spanish from: <https://bancos.salud.gob.ar/recurso/boletin-epidemiologico-nacional-n-689-se-4-2024>

**Figure 1.** Geographic distribution by locality of exposure of confirmed human cases of WEE by symptom onset EW and eco-regions, up to EW 6 of 2024, Argentina and Uruguay.



**Source:** Adapted from the Pan American Health Organization / World Health Organization. Dashboard on Western Equine Encephalitis in the Region of the Americas. Washington, D.C.: PAHO/WHO; 2024. [cited 6 February 2024]. Available from: <https://shiny.paho-phe.org/encephalitis/>

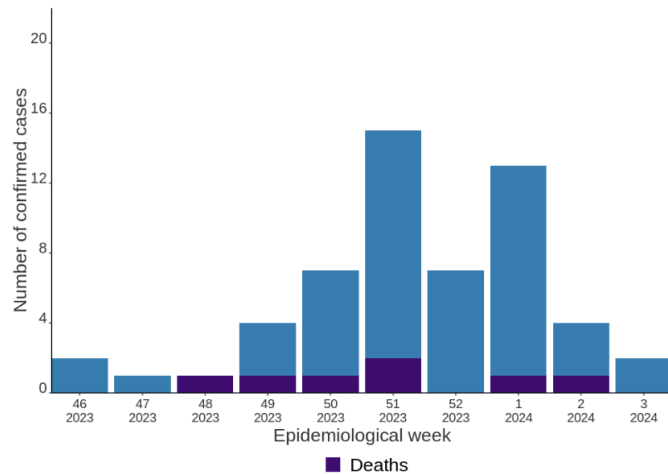
**Figure 2.** Distribution of confirmed human cases of WEE by age group and sex, up to EW 4 of 2024, Argentina.



**Source:** Pan American Health Organization / World Health Organization. Dashboard on Western Equine Encephalitis in the Region of the Americas. Washington, D.C.: PAHO/WHO; 2024. [cited 2 February 2024]. Available from: <https://shiny.paho-phe.org/encephalitis/>

For the distribution of cases by epidemiological week (EW), 63% (n=35) of cases occurred between EW 51 of 2023 and EW 1 of 2024. The first case occurred in EW 46, with seven fatal cases as of EW 4 of 2024 (**Figure 3**) (9).

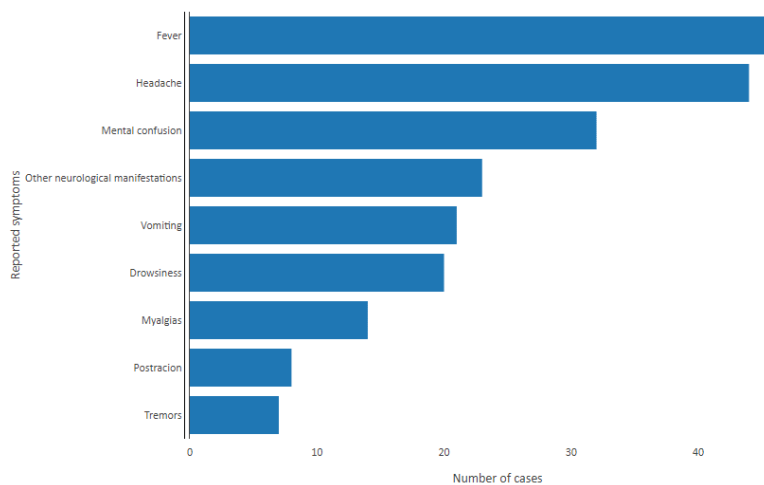
**Figure 3.** Confirmed human cases of WEE by EW of symptom onset. EW 46 of 2023 to EW 4 of 2024, Argentina.



**Source:** Adapted from the Pan American Health Organization / World Health Organization. Dashboard on Western Equine Encephalitis in the Region of the Americas. Washington, D.C.: PAHO/WHO; 2024. [cited 2 February 2024]. Available from: <https://shiny.paho-phe.org/encephalitis/>

Among the symptoms reported by the confirmed human cases, 82% presented with sudden onset of fever (n=46), 79% headache (n=44), 57% mental confusion (n=32), 41% other neurological manifestations (n=23), 38% vomiting (n=21), 36% drowsiness (n=20), 25% myalgia (n=14), 14% presented prostration (n=8), and 13% tremors (n=7) (**Figure 4**) (9).

**Figure 4.** Distribution of symptoms reported in confirmed WEE cases in humans, up to EW 4 of 2024, Argentina.



**Source:** Adapted from the Pan American Health Organization / World Health Organization. Dashboard on Western Equine Encephalitis in the Region of the Americas. Washington, D.C.: PAHO/WHO; 2024. [cited 2 February 2024]. Available from: <https://shiny.paho-phe.org/encephalitis/>

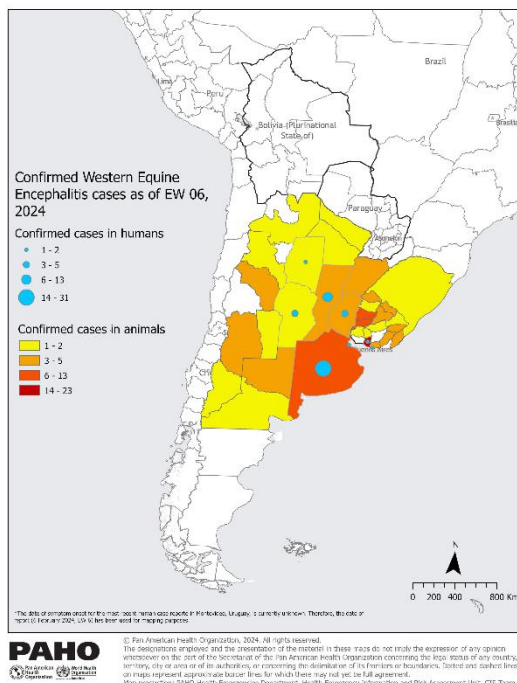
In **Uruguay**, as of 6 February 2024, two WEE human cases have been identified in San José and Montevideo Departments. Currently a total of 15 suspected cases are under investigation in the departments of Canelones, Montevideo, Paysandú, Río Negro, Rocha, San José y Soriano (11).

The first case of WEE was identified in the Department of San José and was reported on 30 January 2024 by the Uruguay International Health Regulations (IHR) National Focal Point (NFP). The case is a 42-year-old male with onset of symptoms on 1 January 2024 and no recent history of international travel. The case reported the following symptoms, retro-orbital headache, fever, photophobia, and vomiting. During the clinical course, he then presented with deterioration of consciousness, imaging studies were compatible with encephalitis, and he was admitted to the intensive care unit (ICU) for a few days; the patient is now under regular care.

Based on the patient's evolution, cerebrospinal fluid (CSF) studies were performed for analysis in accordance with the protocol and the supplies available in the region at that time. The initial CSF sample was processed by the Uruguay Ministry of Health National Laboratory, the Department Public Health Laboratory, initially obtaining a negative result by PCR technique. The patient's evolution required several lumbar punctures for medical indication, which were analysed and detected specific neutralizing antibodies for the WEE virus; on 30 January 2024, a positive WEE result was obtained (12, 13).

The second case identified in the department of Montevideo is under clinical follow-up and undergoing epidemiological investigation (11).

**Figure 5.** Geographic distribution of cases of WEE in humans and equines, up to EW 6 of 2024, Argentina, Uruguay, and Brazil.



**Source:** Adapted from the Pan American Health Organization / World Health Organization. Dashboard on Western Equine Encephalitis in the Region of the Americas. Washington, D.C.: PAHO/WHO; 2024. [cited 6 February 2024]. Available from: <https://shiny.paho-phe.org/encephalitis/>

In **Figure 5**, it is highlighted that the distribution of confirmed cases in humans in Argentina and Uruguay coincides with areas showing a higher number of suspected and confirmed cases in equines.

## Recommendations

The Pan American Health Organization/World Health Organization (PAHO/WHO) reminds Member States of the importance of strengthening epidemiological surveillance and diagnosis of equine encephalitis, as well as the importance of intersectoral coordination with the animal health sector and strengthening surveillance and vector control (1).

Following are the proposed case definitions for WEE in humans and a reiteration of the key recommendations for diagnosis, prevention measures, and risk communication.

### Human Case Surveillance

#### Case definitions for WEE in humans (14)

##### **Suspected case**

Patient that:

- 1) present with or previously presented with sudden onset fever, accompanied by headache or myalgia without involvement of the upper airways; and
- 2) presents neurological manifestations (including vomiting, drowsiness, confusion, prostration, tremors), meningitis or encephalitis and without other apparent etiology.

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

##### **Confirmed case**

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

- 1) detection of viral RNA by RT-PCR in any type of sample; or
- 2) detection of IgM anti-WEEV antibodies by ELISA in a cerebrospinal fluid sample; or
- 3) seroconversion of anti-WEEV IgM antibodies by ELISA in paired acute and convalescent samples taken more than 7-10 days apart; or
- 4) seroconversion or increase in neutralizing antibody titer by PRNT (or microneutralization) in paired acute and convalescent samples taken more than 7-10 days apart.

##### **Probable case**

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

##### **Negative/discarded case**

Any case without IgM anti-WEEV antibodies detectable by ELISA in a single serum sample (no paired sample) taken more than 10 days after symptom onset.

\*Those cases in which there is only a single sample taken within the first 10 days from the onset of symptoms, with a negative result, and where it is not possible to obtain a paired sample, confirmation or discarding of the suspected case will not be possible. Clinical and epidemiological information should be carefully considered for final classification.

In at risk areas or areas with active outbreaks, it is recommended to implement or strengthen surveillance through the search for compatible neurological syndromes that do not have another defined diagnosis, taking into account the incubation period, geographical area and environmental conditions (case definitions as appropriate).

### **Laboratory diagnosis of WEE in humans (14)**

The diagnosis of WEEV infection requires confirmation through laboratory techniques since the clinical presentation is not specific. These laboratory methods include virological (direct) diagnostic methods by nucleic acid amplification or potentially cell culture and serological (indirect) methods, which aim at detecting antibodies produced against the virus. Generally, samples for diagnosis include serum and cerebrospinal fluid (CSF). CSF should only be collected in cases with neurological symptoms and by clinical indication.

### **Biosafety**

Fresh biological samples, of any type, should be considered potentially infectious. Samples should be processed and handled exclusively by trained professionals after a local risk assessment, considering all biosafety indications and appropriate personal protective equipment. Any procedure involving sample manipulation should be conducted in certified Class II biosafety cabinets. The manipulation of extracted RNA does not require biosafety cabinets. Additionally, all necessary precautions should be taken to prevent percutaneous exposure. The manipulation of materials or cultures with high viral load and/or high volume should be considered only after a local risk assessment considering the necessary containment measures is conducted.

### **Virological methods**

The detection of viral RNA can be performed on serum and CSF samples using real-time or endpoint RT-PCR with specific primers (and probes) for WEEV. Generic protocols (pan-alphavirus) can also be used, followed by specific RT-PCR or nucleotide sequencing.

Viral isolation is carried out using the same types of samples as RT-PCR. Mammalian cell lines (e.g., Vero cells) and mosquito cells (e.g., C6/36 cells) are used. In general, viral isolation is not routinely applied nor is it a requirement for diagnostic confirmation. Technical complexity, containment requirements, costs, as well as the need to identify isolated viruses by RT-PCR or immunofluorescence, limit the use and timeliness of the diagnosis by viral isolation.

In fatal cases, RT-PCR (or viral isolation) can also be performed on tissue samples (in particular, nervous system tissue).

A positive result by RT-PCR (or viral isolation) confirms 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 does not rule out infection and, in cases of 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 viruses such as Eastern Equine Encephalitis (EEE) and Venezuelan Equine Encephalitis (VEE) could be considered as well as neurotropic flaviviruses (e.g. West Nile virus, St. Louis encephalitis virus) could be considered (**Figure 6**).

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 the detecting WEEV infections. In an outbreak context with compatible symptoms, detection by RT-PCR in at least one case allows for the identification of the etiological agent.

### **Serological methods**

IgM antibody detection is performed by ELISA using in-house methodologies. Detection can be performed in both serum and CSF. The kinetics of antibody production have not been fully described. However, it is likely that antibody detection can be performed early after the onset of symptoms, particularly neurological ones (**Figure 6**).

Antibody detection may be limited by potential cross-reactivity between WEEV and other alphaviruses; therefore, in cases with clinical and epidemiological suspicion, a positive result for IgM is considered a probable case of WEEV infection. Nevertheless, the specificity of IgM detection is estimated to be relatively high.

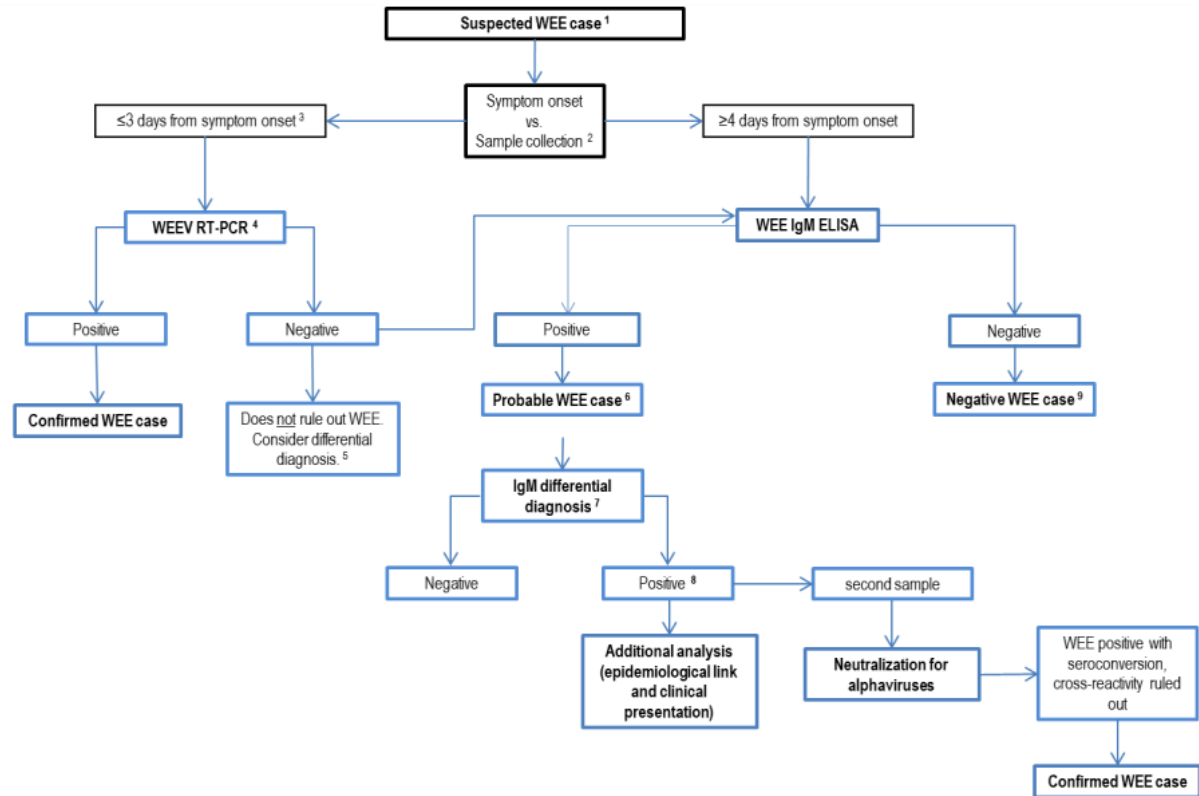
The potential cross-reactivity can be assessed by conducting differential IgM serological tests for other alphaviruses, particularly Chikungunya (CHIKV), always taking into account the epidemiological context. In cases of positivity to more than one alphavirus, additional clinical and epidemiological criteria should be used for the final interpretation of the case. Cases of cross-reactivity can also be evaluated by neutralization assays such as the plaque reduction neutralization test (PRNT) or microneutralization, ideally using paired samples (acute and convalescent samples collected with more than 7-10 days of difference, convalescent sample collected more than 14 days after the onset of symptoms). Depending on the epidemiological situation in the area where the infection likely happened, it is recommended to detect in parallel neutralizing antibodies against WEEV, EEEV, VEEV, CHIKV and Mayaro (MAYV) (**Figure 6**). Finally, the detection of specific antibodies in CSF confirms WEEV infection in a case with neurological manifestations.

### **Sample storage**

- Serum and CSF samples:
  - Keep refrigerated (2 - 8 °C) if processed (or sent to a reference laboratory) within 48 hours.
  - Keep frozen (-10 to -20 °C) if processed after 48 hours or within 7 days.
  - Keep frozen (-70°C or less) if processed more than one week after collection. The sample is adequately preserved at -70 °C for extended periods of time.
- Tissue samples: freeze and ship on dry ice.
- Avoid multiple freeze-thaw cycles.



**Figure 6.** Algorithm for laboratory confirmation of Western Equine Encephalitis (WEE) virus infection (14).



<sup>1</sup> See case definition.  
<sup>2</sup> Laboratories that only have the capacity to perform RT-PCR or IgM ELISA should test samples with the available technique. Results should be interpreted according to the algorithm.  
<sup>3</sup> In the first 3 days (or up to 5) from the onset of symptoms, it is recommended to use RT-PCR although it may have low sensitivity. The presence of viral RNA in the CSF is longer. A positive result confirms the case, however, a negative result does not rule out WEEV infection and additional testing is recommended.  
<sup>4</sup> Generic panalphavirus RT-PCR can also be used, followed by the identification of the etiological agent by sequencing.  
<sup>5</sup> Consider other equine encephalitis viruses, West Nile virus, St. Louis encephalitis virus, and others, depending on the epidemiological situation of the area/country.  
<sup>6</sup> A positive IgM result in a single sample is not confirmatory. Serological cross-reactivity with other alphaviruses might be observed.  
<sup>7</sup> Consider the chikungunya virus and other alphaviruses, according to the epidemiological situation of the area/country.  
<sup>8</sup> In cases of cross-reactivity, the IgM ELISA results do not allow confirmation of the etiological agent. However, this result does not rule out WEEV infection. Additional clinical and epidemiological criteria should be used for the final interpretation of the case. Neutralization can also be performed in a reference laboratory to analyze cross-reactive samples (ideally, in paired acute and convalescent samples).  
<sup>9</sup> IgM levels may be below the limit of detection if the sample was taken early in the acute phase (days 1-3). In these cases, consider collecting a second sample.

CSF: cerebrospinal fluid.

**Source:** Pan American Health Organization/World Health Organization. Laboratory Guidelines for the Detection and Diagnosis of Human Infection with Western Equine Encephalitis Virus. 5 February 2023. Washington, D.C. Available from: <https://www.paho.org/en/documents/laboratory-guidelines-detection-and-diagnosis-western-equine-encephalitis-virus-human>

## Patient Management and Infection Prevention Measures in Health Facilities

There is no specific antiviral treatment. Most infections are characterized by a mild clinical presentation in which treatment is symptomatic. Patients presenting with neurologic symptoms should be evaluated by a specialist and require close monitoring.

## Prevention Measures

The preventive measures listed below should be organized within the framework of One Health, considering the inter-institutional and comprehensive action between animal health, human health, and the environment.

## **Environmental Management**

Considering the ecology and biology of the main vectors of the WEE virus, the main prevention measure is the modification of surroundings and the environmental management, seeking to reduce the number of mosquitoes and their contact with equids and humans. These measures include:

- Filling or draining water collection areas, ponds, or temporary flooding sites that may serve as sites of female oviposition and breeding sites for mosquito larvae.
- Elimination of nuisances around the premises to reduce mosquito resting and shelter sites.
- Protecting equids by sheltering them in barns with mosquito nets, especially at times when mosquitoes are most active.
- Avoiding gatherings and movements of equines at fairs, sporting events, and similar activities.
- While the main vectors do not have indoor habits, homes should be protected with mosquito nets on doors and windows, also preventing other arboviruses.

## **Vector Control**

Vector control measures for WEE should be considered within the framework of Integrated Vector Management (IVM). It is important to consider that the decision to carry out vector control activities with insecticides depends on entomological surveillance data and the variables that may condition an increase in the risk of transmission, including insecticide resistance data.

- Insecticide spraying may be considered as an additional measure and, where technically feasible, in areas of transmission where high mosquito populations are detected. The methodology should be established based on the ecology and behavior of the local vectors.

## **Vaccination for equids**

- Vaccines are available for equids. Achieving high vaccination coverage in susceptible equids in areas considered at risk should be sought and carry out annual vaccination boosters in these equines.

## **Personal Protective Measures**

- Use of clothing that covers the legs and arms, especially in homes where someone is sick.
- Use of repellents containing DEET, IR3535 or Icaridin, which may be applied to exposed skin or clothing; their use must be in strict accordance with the instructions on the product label.
- Use wire mesh/mosquito netting on doors and windows.
- Use of insecticide-treated or non-insecticide nets for daytime sleepers (e.g., pregnant women, infants, bedridden, elderly, and night shift workers).
- During outbreaks, outdoor activities should be avoided during the mosquitoes' peak feeding period (dawn and dusk).

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