



Pan American
Health
Organization



World Health
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REGIONAL OFFICE FOR THE
Americas

Epidemiological update Western Equine Encephalitis in the Region of the Americas 10 January 2024

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). From that date until 9 January 2024, 374 additional outbreaks¹ in animals were reported (338 in Argentina and 36 in Uruguay) and 21 human cases, all of them in Argentina (2,3,4,5,6).

Cases in animals

In **Argentina**, from 25 November 2023 to 9 January 2024, the National Food Safety and Quality Service (SENASA as per its acronym in Spanish) confirmed 1,258 outbreaks¹ (40 diagnosed by laboratory and 1,218 by clinical and epidemiology) which are registered in 15 provinces: Buenos Aires, Catamarca, Chaco, Corrientes, Córdoba, Entre Ríos, Formosa, La Pampa, La Rioja, Mendoza, Río Negro, Santa Fe, San Luis, Santiago del Estero and Salta. The highest proportion of cases in animals was recorded in the province of Buenos Aires, which accounts for 60% of confirmed cases (2,6).

In **Uruguay**, from 5 December 2023 to 9 January 2024, the Ministry of Livestock, Agriculture and Fisheries (MGAP as per its acronym in Spanish) confirmed 56 cases in equines in 15 departments of the country: Artigas, Canelones, Durazno, Flores, Lavalleja, Montevideo, Paysandú, Río Negro, Rivera, Rocha, Salto, San José, Soriano, Tacuarembó and Treinta y Tres. The highest proportion of cases was recorded in the department of Paysandú, which accounts for 23% of confirmed cases (4).

Human WEE cases

In **Argentina**, a human case of western equine encephalitis was reported in the country on 20 December 2023, after more than two decades without reported cases. The case corresponds to a 32-year-old man, a rural worker, resident of the province of Santa Fe, who presented the onset of symptoms on 19 November (headache, myalgia, dizziness, disorientation, and sudden onset fever). On 24 November, he received medical attention at a public health facility in the province. He required intensive care and mechanical ventilation for 12 days and was discharged on 20 December 2023 (3,5,7).

In addition, and as a result of the active search up to epidemiological week (EW) 52, 91 suspected cases were reported in 11 provinces, of which 21 were laboratory-confirmed, including one death. The confirmed cases come from the provinces of Buenos Aires (n=11), Santa Fé (n=8), Entre Ríos (n=1) and Santiago del Estero (n=1) (**Figure 1 and Figure 2**) (5, 7).

¹ Equine outbreak: occurrence of one or more cases of WEE in equines (7).

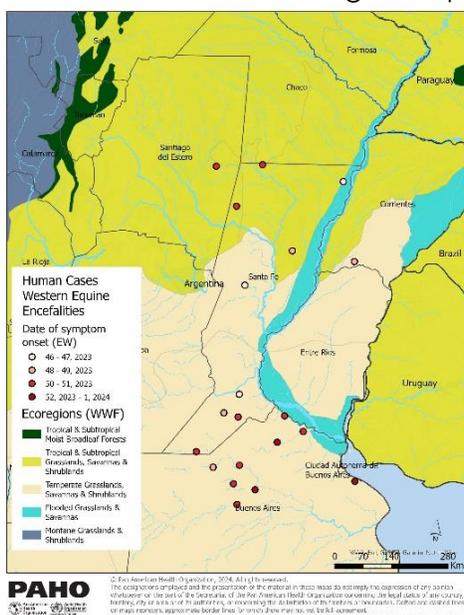
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Figure 1. Human cases of Western equine encephalitis by probable place of infection (province), up to EW 52, 2023, Argentina.

Province	Confirmed cases	Probable cases	Suspected cases	Suspected cases not conclusive	Total
Buenos Aires	11	2	14	19	46
Chaco				2	2
Córdoba			1	1	2
Corrientes				2	2
Entre Ríos	1		7	1	9
Formosa				1	1
La Pampa				2	2
Mendoza			2		2
Santa Fe	8		11	4	23
Santiago del Estero	1			1	2
Total	21	2	35	33	91

Source: Adapted from the Ministry of Health of the Argentine Republic. National Epidemiological Bulletin, epidemiological week 52. Western Equine Encephalitis (WEE) Update. Number 685. January 2024. Buenos Aires: MSAL; 2024. Available in Spanish from: <https://bancos.salud.gob.ar/recurso/boletin-epidemiologico-nacional-n-685-se-52-2023>

Figure 2. Geographic distribution by locality of exposure of confirmed cases of WEE in humans Argentina by symptom onset EW* and eco-regions, up to EW 1 of 2024

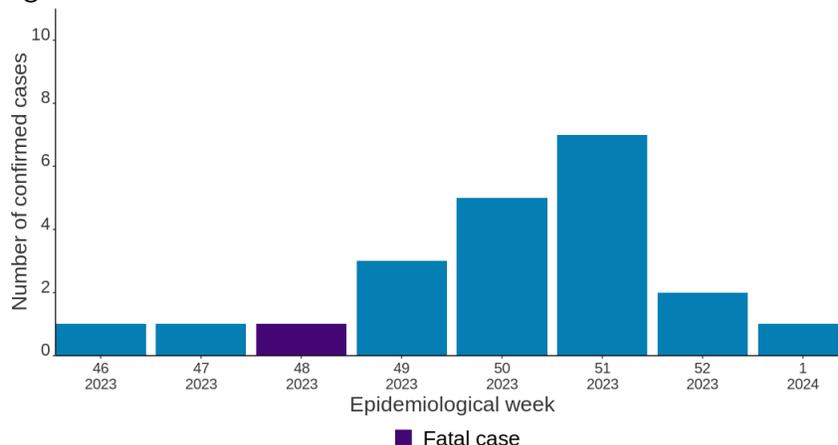


*For three of the cases, the date of notification was used because the date of symptom onset was not available

Source: Adapted from the information provided by the Argentina International Health Regulations (IHR) National Focal Point (NFP). Communications received on 9 January 2024 via email. Buenos Aires; January. Unpublished.

Regarding the distribution of cases by epidemiological week, 71% of cases occurred between EW 49 and 51 of 2023. The first case occurred in EW 46, with one fatal case in EW 48 (Figure 3) (7).

Figure 3. Distribution of confirmed cases of WEE by EW of symptom onset*. EW 46 of 2023 to EW 1 of 2024, Argentina

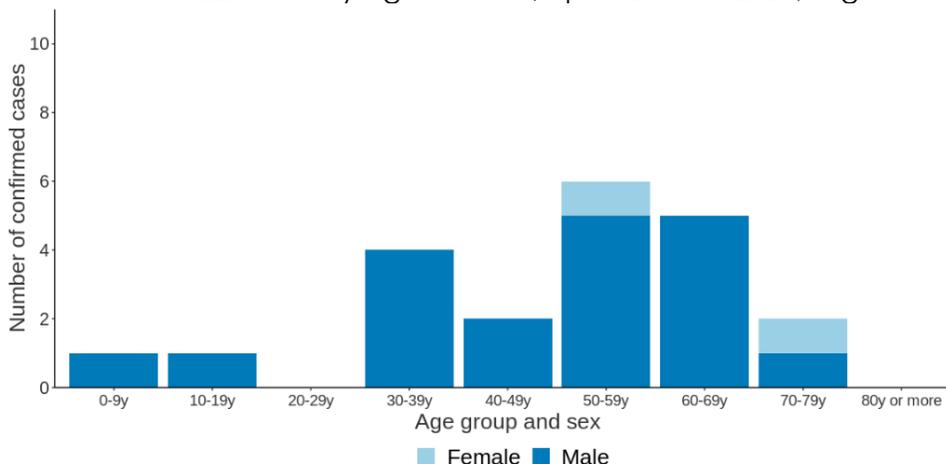


*For three of the cases, the date of notification was used because the date of symptom onset was not available

Source: Adapted from the information provided by the Argentina International Health Regulations (IHR) National Focal Point (NFP). Communications received on 9 January 2024 via email. Buenos Aires; January. Unpublished.

90% of the cases were male (n=19). The age range is from 9 months to 75 years, with the highest proportion of cases in the group over 60 years of age, with 33% (n=7), followed by the group between 50 and 59 years of age with 29% (n=6) (Figure 4) (7).

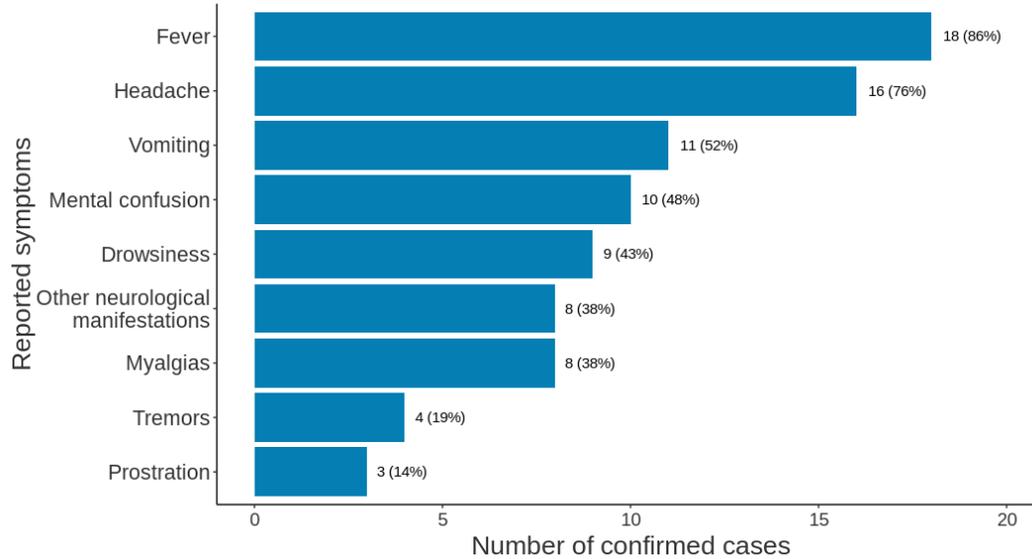
Figure 4. Distribution of WEE cases by age and sex, up to EW 1 of 2024, Argentina.



Source: Adapted from the information provided by the Argentina International Health Regulations (IHR) National Focal Point (NFP). Communications received on 9 January 2024 via email. Buenos Aires; January. Unpublished.

Regarding the reported symptoms, 86% had sudden onset fever (n=18), 76% headache (n=16), 52% vomiting (n=11), 48% mental confusion (n=10), 43% drowsiness (n=9), 38% other neurological manifestations (n=8), 38% myalgias (n=8), 19% tremors (n=4), 14% had prostration (n=3) and 14% reported no symptoms (n=3) (Figure 5) (7).

Figure 5. Distribution of symptoms presented in confirmed cases of WEE in humans, up to EW 1 2024, Argentina.



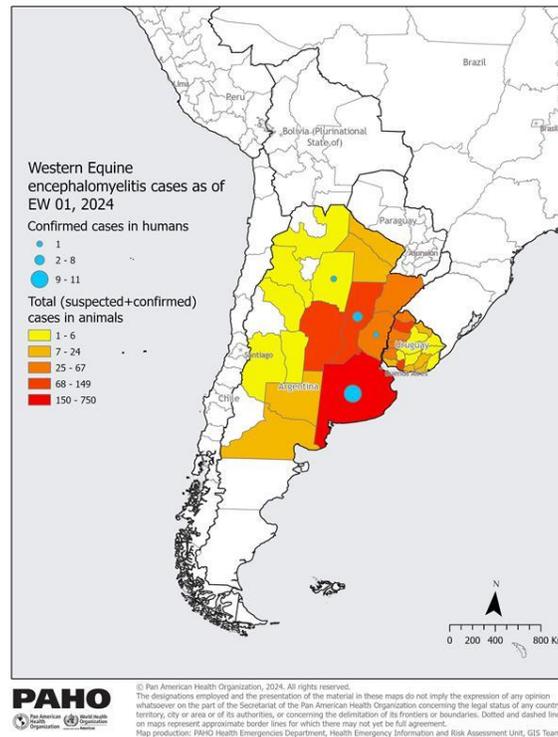
Source: Adapted from the information provided by the Argentina International Health Regulations (IHR) National Focal Point (NFP). Communications received on 9 January 2024 via email. Buenos Aires; January. Unpublished.

In all cases, confirmation was made through specific neutralizing antibodies in serum and cerebrospinal fluid (CSF) samples. All confirmed cases required hospitalization, of these, 8 required care in intensive care unit and 13 in general hospitalization. To date, nine cases have been discharged, 11 remain hospitalized and one has died. The fatal case corresponds to a 66-year-old man, with a previous diagnosis of diabetes, resident of the rural area in the province of Santa Fe, who onset symptoms on 26 November 2023 and died on 22 December 2023 (7).

Regarding the history of exposure, in the cases for which this information is available (n=7), three correspond to people who work as veterinarians, two construction workers, and two reported having carried out outdoor recreational activities (7).

No **human cases** have been reported in **Uruguay** to date. The last human case of WEE reported in Uruguay was in 2009 (8).

Figure 6. Geographic distribution of cases of Western Equine Encephalitis in humans and equines, up to EW 1 2024, Argentina and Uruguay.



Source: Adapted and modified based on the information provided from the Argentina International Health Regulations (IHR) National Focal Point (NFP) (7), Dynamic dashboard with information on ongoing outbreaks, National Food Safety and Quality Service (SENASA as per its acronym in Spanish), Republic of Argentina (2) and Ministry of Livestock, Agriculture and Fisheries (MGAP as per its acronym in Spanish) of the Republic of Uruguay (4).

Figure 6 shows that the distribution of cases in humans is recorded in areas of Argentina with the highest number of suspected and confirmed cases in animals (2,4,6).

Recommendations

On 19 December 2023, the Pan American Health Organization/World Health Organization (PAHO/WHO) issued an epidemiological alert on the risk to human health associated with the circulation of this virus and the high potential for spread to other countries in the Region of the Americas; alerting Member States to the importance of strengthening epidemiological surveillance and diagnosis of equine encephalitis, intersectoral coordination, surveillance and vector control in the Region (1).

Below is a summary of the main recommendations for diagnosis, surveillance, prevention measures, and risk communication.

Laboratory diagnosis of WEE in humans (9)

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 7**).

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 7**).

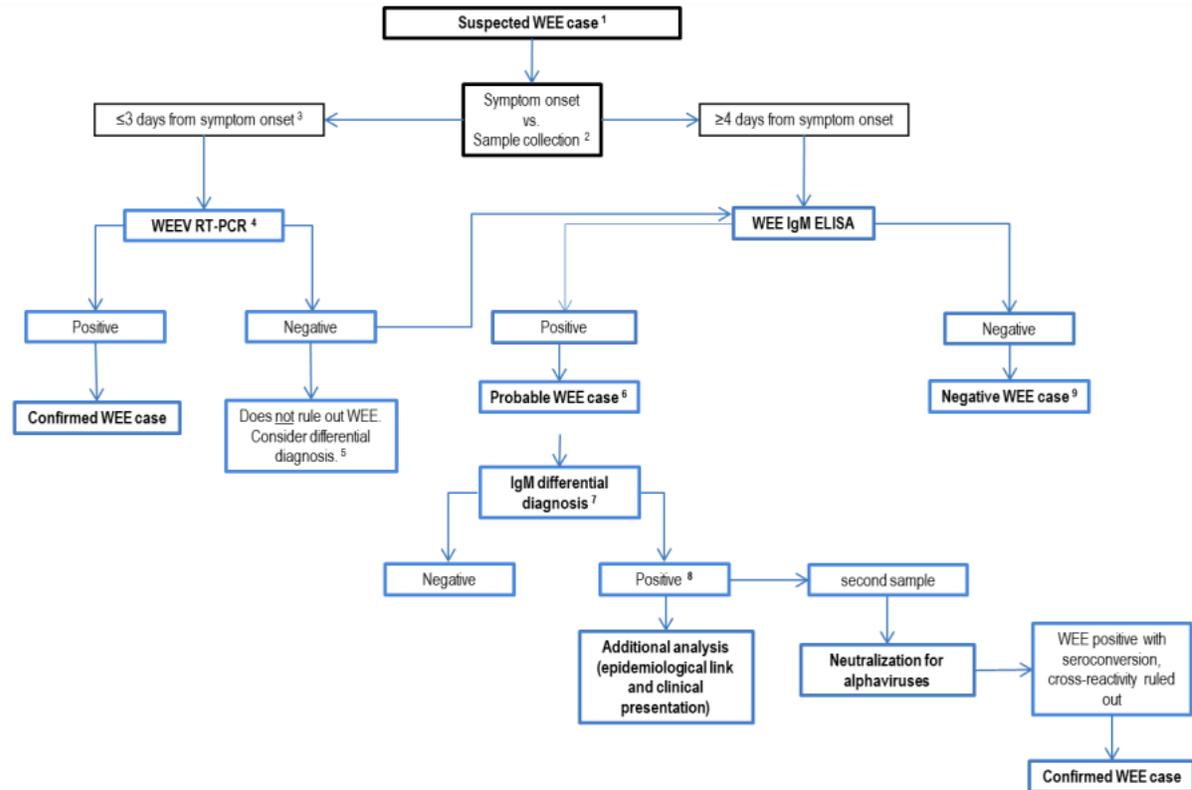
Antibody detection may be limited by potential cross-reactivity between WEEV and other alphaviruses; therefore, in cases with clinical and epidemiological suspicion, a positive result for IgM is considered a probable case of WEEV infection. Nevertheless, the specificity of IgM detection is estimated 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 7**). 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 7. Algorithm for laboratory confirmation of Western Equine Encephalitis (WEE) virus infection.



¹ See case definition.

² 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.

³ 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.

⁴ Generic panalphavirus RT-PCR can also be used, followed by the identification of the etiological agent by sequencing.

⁵ Consider other equine encephalitis viruses, West Nile virus, St. Louis encephalitis virus, and others, depending on the epidemiological situation of the area/country.

⁶ A positive IgM result in a single sample is not confirmatory. Serological cross-reactivity with other alphaviruses might be observed.

⁷ Consider the chikungunya virus and other alphaviruses, according to the epidemiological situation of the area/country.

⁸ 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).

⁹ 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. 20 December 2023. Washington, D.C. Available from: <https://www.paho.org/en/documents/laboratory-guidelines-detection-and-diagnosis-western-equine-encephalitis-virus-human>

Human Case Surveillance

In areas at risk or 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.

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

Managing the Environment

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

- Filling or draining water collections, ponds, or temporary flooding sites that may serve as sites of female oviposition and breeding sites for mosquito larvae.
- Elimination of weeds around the premises to reduce mosquito resting and shelter sites.
- The equids can be protected by sheltering them in barns with mosquito nets, especially at times when mosquitoes are most active.
- Avoid gatherings and movements of horses at fairs, sporting events, and similar activities.
- Despite the fact that the main vectors do not have indoor habits, it is advisable to protect homes with mosquito nets on doors and windows; in this way other arboviruses are also prevented.

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. It is advisable to seek high vaccination coverage in susceptible equids in areas considered at risk and to 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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