Togaviridae

Latin word Toga - Cloak or **mantle**

Western Equine Encephalomyelitis (WEE)
Eastern Equine Encephalomyelitis (EEE)
Venezuelan Equine Encephalomyelitis (VEE)

Group A Arboviruses
Group IV: ssRNA positive-strand viruses
Family: ***Togaviridae***
Genus Alphaviruses:

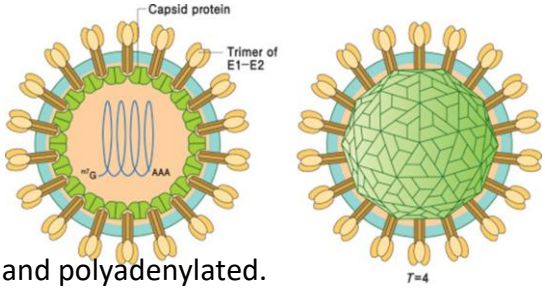
- Arthritis,
- Chikungunya disease
- **Encephalitis**
  - Eastern equine encephalitis virus (EEE)
  - Western equine encephalitis virus (WEE)
  - Venezuelan equine encephalitis virus (VEE)

Equine encephalitis is a viral disorders, usually transmitted by mosquitoes or other blood-feeding insects, involve central nervous system dysfunction and moderate to high mortality with zoonotic importance causing permanent neural impairment in human.

NATURAL HOSTS Human, mammals, marsupials, birds, mosquitoes.

TRANSMISSION
Alphaviruses: Zoonosis, arthropod bite
Within the family, the *Alphavirus* genus includes a large number of species that are mostly mosquito-borne and pathogenic in their vertebrate hosts. Many are important human and veterinary pathogens (e.g. **chikungunya virus, eastern equine encephalitis virus**). Before April 2019 the family also contained the genus *Rubivirus* that has now been moved to the family *Matonaviridae.*

Alpha: from Greek letter α., originally group A arboviruses.
Chikungunya virus: *chikungunya* derives from a word in the Kimakonde/Makonde language, meaning "to become contorted", and describes the stooped appearance of sufferers with joint pain (arthralgia).



Eastern equine encephalitis virus (EEE)

Properties of virus
Enveloped, spherical, capsid icosahedral symmetry,
Size of virus: 65-70nm in diameter.
The envelope contains 80 trimer spikes.
Genome: **ssRNA positive-strand.** The genome is capped and polyadenylated.
Replication: Cytoplasmic

- Unstable at room temperature.
- Stable at -20 degree C to
- Inactivated at 56 degree for 30 minutes
- Readily inactivated by formalin

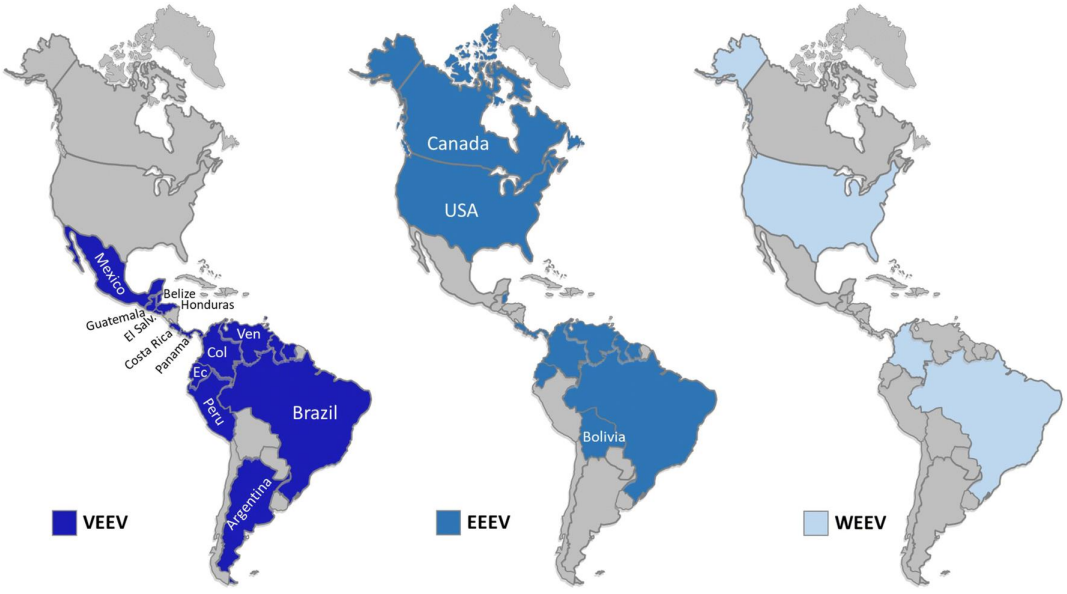
Host

- Birds and rodents are the primary reservoirs, but unvaccinated horses are particularly susceptible and often serve as sentinels.
- **Zoonotic**, infecting humans, and are a public health concern.

Occurrence:

- **Eastern equine encephalitis** is the most common of the three and is found widely in several regions of the United States (especially in areas of high mosquito populations).
- **Western equine encephalitis** occurs infrequently, but circulates in wildlife.
- **Venezuelan equine encephalitis** is a Foreign Animal Disease
- **EEE** has been reported in **North and South America**.
- **WEE** have been recorded more commonly in the **Western US**.
- **VEE** causes outbreaks in horses in Central America, South America, Mexico and occasionally in the southern US.

Transmission of EEE/WEE/VEE is by **primarily mosquitoes**, and infrequently by other insects, ticks, or nasal secretion. Although vaccination has reduced the size and number of outbreaks of EEE, WEE and VEE in horses, the impact of these diseases **is still significant because of the high mortality rate**.

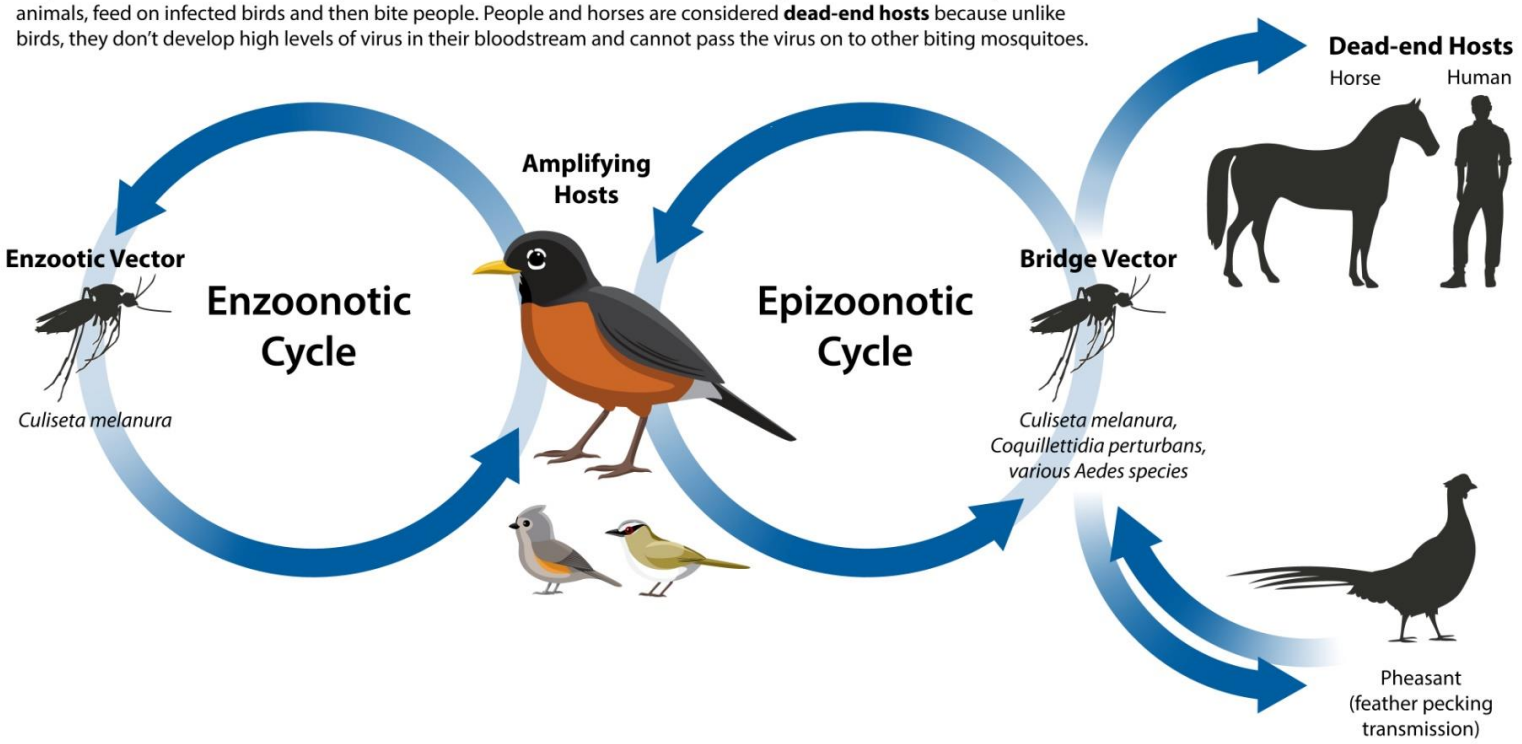


Geographical distribution of the equine encephalitis in the Americas. **a** VEEV. **b** EEEV. **c** WEEV

Eastern Equine Encephalitis Transmission

The Eastern equine encephalitis virus **cycles between mosquitoes and birds**. The *Culiseta melanura* mosquito, which primarily bites birds, is responsible for spreading the virus among birds. The virus then multiplies in the birds' bloodstream.

People and other animals, like horses, become infected with the virus when mosquito species that feed on many kinds animals, feed on infected birds and then bite people. People and horses are considered **dead-end hosts** because unlike birds, they don't develop high levels of virus in their bloodstream and cannot pass the virus on to other biting mosquitoes.



Pathogenesis- EEE, WEE, and VEE

- **Birds are the primary reservoir** for EEE, WEE, and VEE. Transfer of infection depends on an interplay between migratory bird patterns and vector seasonal population fluctuations. EEE may be found year-round in the southeastern United States. Small rodents can harbor VEE.
- **Virus replication occurs within arthropod vector** (mosquitoes *Culex*, *Aedes*, *Anopheles*, and *Culiseta*).
- After inoculation into the equine host, local replication occurs in the subcutaneous tissue at the site of inoculation.
- **Lymphatic spread** to the spleen and liver.
- Short-lived viremia ensues in the majority of infected animals. Viremia of EEE and WEE is too low to infect vectors, so the horse is a dead-end host. However, VEE titers are sufficient to infect vectors.
- In a small number of infected horses, the **blood-brain barrier is crossed** and encephalomyelitis results.
- Infected EEE and WEE horses do not cause direct or indirect lateral spread.
- Widespread neuronal necrosis throughout the central nervous system, especially the cerebrum.

Pathogenesis - Equine encephalomyelitis

1. Entry of virus through mosquito bite
2. **Viscerotropic** and **neurotropic** virus
3. Initially multiply in the muscles, myeloid, lymphoreticular tissue
4. First phase of viraemia 2-3 days
5. Fever returns to normal
6. After 6-7 days Second viraemia followed by invasion to CNS with virus replication and destruction of neurons-Nerve cell degeneration.
7. Leading to **encephalitis**.
8. Mortality:

   EEE – 75-100 %
   WEE-10-40%
   VEE40-70%

Clinical Signs - Equine encephalomyelitis

- Anorexia
- First phase of viraemia 2-3 days - Fever
- Fever returns to normal in 72 hours
- After 6-7 days Second viraemia – Fever
- Symptoms of CNS involvement- Paralysis of lips and pharynx, drooping of eyelids, incoordination develops-This stage is fatal.
- **Eastern equine encephalitis** and **Western equine encephalitis-** Lesions are present in brain stem and changes are neuronophagia, perivascular cuffing and gliosis
- **Venezulean Equine encephalitis**- necrotic foci in visceral organs-in spleen and lymph nodes.

Clinical signs not pathognomonic

- Biphasic Fever associated with viremia in majority of infected horses
- Initial hyperexcitability, progressing to depression and recumbency
- Blindness , Head pressing, Ataxia
- Compulsive walking, circling, Seizure activity
- Permanent neurologic deficits may occur in survivors
- Early neurologic signs reflect diffuse, multifocal cortical disease
- **Mortality ranges from 75% to 90% for EEE, 19% to 50% for WEE, and 40% to 90% for VEE**

Immunity

Animal recovered from infection usually **acquires solid immunity**.
CF and NA appear in the circulation of infected and recovered horses.

Diagnosis

Material collection:

- Unclotted blood during pyrexia
- Brain tissue- Cerebrum, brain stem
- Spleen, lung, liver, kidney. Lymph node, paired sera samples.

1. Isolation and identification of virus
2. Intracerebral inoculation in 1-3 day old mice –FAT, CFT
3. Cell cluture-Mouse embryo fibroblast or CEF
4. Test to identify the virus
5. HI titre 1: 40 and above, CFT (In unvaccinated animals)

Alphavirus Diagnosis

. Clinical signs are usually not useful for diagnosis.

•**Serologic testing with a four-fold rise in antibody titers is diagnostic**. However, a four-fold rise may not be detected as antibody levels rise rapidly after infection and a delay in taking the acute sample frequently results in sampling during the peak antibody titer. Another problem frequently encountered with serologic testing is that horses with EEE often do not live long enough for comparison of paired samples.

•High immunoglobulin M (IgM) titers suggest recent exposure to EEE virus and may be detected with an antibody-capture enzyme linked immunosorbent assay (ELISA).

•**Definitive ante-mortem diagnosis** can also be made based on **viral isolation** or **identification of viral nucleic acid by reverse transcriptase-polymerase chain reaction** (RT-PCR).

EEE, WEE or VEE viruses can be isolated from brain tissue of infected horses via **Vero-cell culture or mouse**. Virus isolation from serum is usually unsuccessful.

RT-PCR is a sensitive and specific test for detection of viral nucleic acid in CNS tissue or CSF.

•Other non-specific findings are peripheral leukocytosis and increased cellularity and elevated protein concentration of CSF.

Equine Encephalomyelitis

Prevention and Control

- Control of vector population: Vectors play an important role in spread of disease.
- Cell culture propagated Inactivated trivalent (EEE,WEE,VEE) vaccines

Vaccines and Vaccination – EEE,WEE,VEE

Vaccines for all three diseases are available as **killed** products and were shown to be highly efficacious in protecting against clinical disease.

Vaccination Schedules

Immunization for EEE/WEE are core vaccines for all horses residing and traveling within the United States. Immunization for VEE is risk-based. The schedules presented here apply to **bivalent** and **multivalent vaccines**.

Adult Horses

Adult horses previously vaccinated against EEE/WEE: **Annual revaccination** must be completed **prior to vector season in the spring**. In animals of high risk or with limited immunity, more frequent vaccination or appropriately timed vaccination is recommended in order to induce protective immunity during periods of likely exposure.

Adult horses, previously unvaccinated against EEE/WEE or of unknown vaccine history: Administer a **primary series of 2 doses with a 3- to 6-week interval between** doses as per product label. **Revaccinate prior to the onset of the next vector season** and **annually** thereafter.

Pregnant Horses

Pregnant mares, previously vaccinated against EEE/WEE: Vaccinate **4 to 6 weeks before foaling**.
Pregnant mares, unvaccinated : Immediately begin a 2-dose primary series with a 3 to 6-week interval between doses as per product label. Booster at 4 to 6 weeks before foaling or prior to the onset of the next vector season—whichever occurs first.

Foals

Foals of mares vaccinated/unvaccinated against EEE/WEE in the pre-partum period: Administer a primary 2-dose series beginning at 4 to 6 months of age. A 4- to 6-week interval between the first and second doses is recommended. A third dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

Vaccination – EEE,WEV

Eastern/Western Equine Encephalomyelitis (EEE/WEE) **3-dose series:** 1st dose at 4 - 6 months of age 2nd dose 4 - 6 weeks after the 1st dose 3rd dose at 10 - 12 months of age Note: Primary vaccination series scheduling may be amended with vaccinations administered earlier to younger foals that are at increased disease risk due to the presence of vectors. * Foals in the Southeastern USA: The primary vaccination series can be initiated with an additional dose at 2-3 months of age due to early seasonal vector presence	**Eastern / Western Equine Encephalo- myelitis (EEE/WEE)** Previously vaccinated: Annual, 4 - 6 weeks pre-partum Previously unvaccinated or having unknown vaccination history: **2-dose series** 2-dose series 2nd dose 4 weeks after 1st dose. Revaccinate 4-6 weeks pre-partum. Annual – spring, prior to onset of vector season. Booster at time of penetrating injury or prior to surgery if last dose was administered over 6 months previously.

Vaccine and Vaccination

EEE,WEE,VEE

- Vaccination against a foreign animal disease may confound testing in the event of an outbreak.
- An IgM capture ELISA (as we do with EEE, WEE, and WNV) would be used to confirm the diagnosis in a clinical animal. This can differentiate vaccinated (IgG only) versus virulent virus (IgM).
- There is some evidence that **vaccination against EEE/WEE may also result in cross-protection to VEE** -based on one study

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