# Togaviridae

**Latin : Toga - Cloak** or **mantle**

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

# Togaviridae



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)

**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.*

# Togaviridae

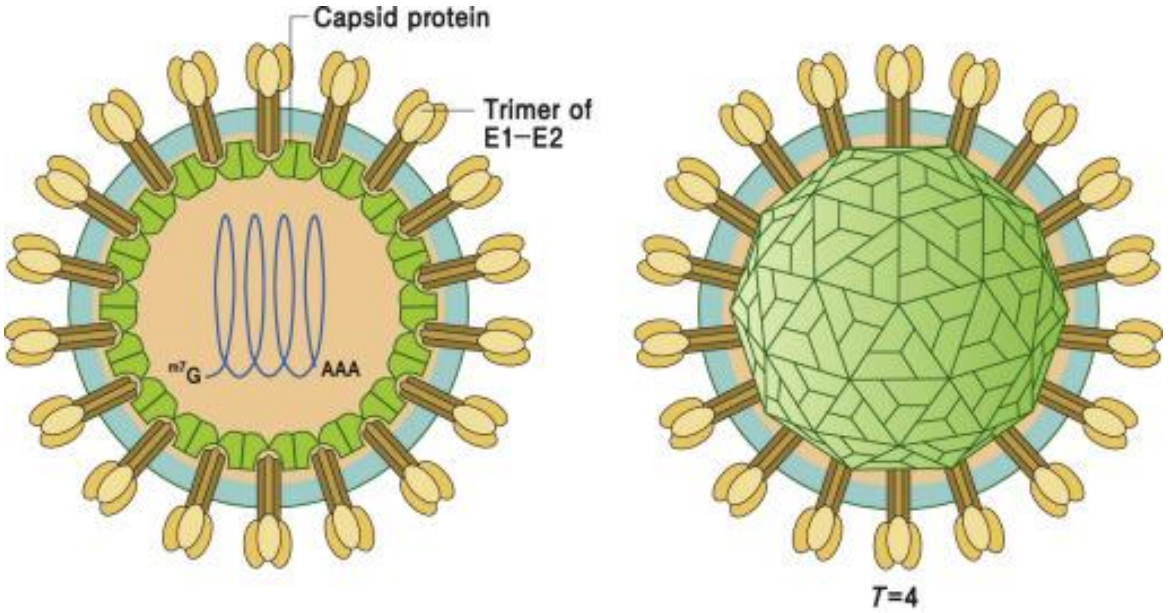
***Alpha***: from Greek letter α., originally group A arboviruses.

**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).

# Togaviridae

# EEV

**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



# Equine encephalomyelitis virus

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

# Host & Occurrence

## 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.

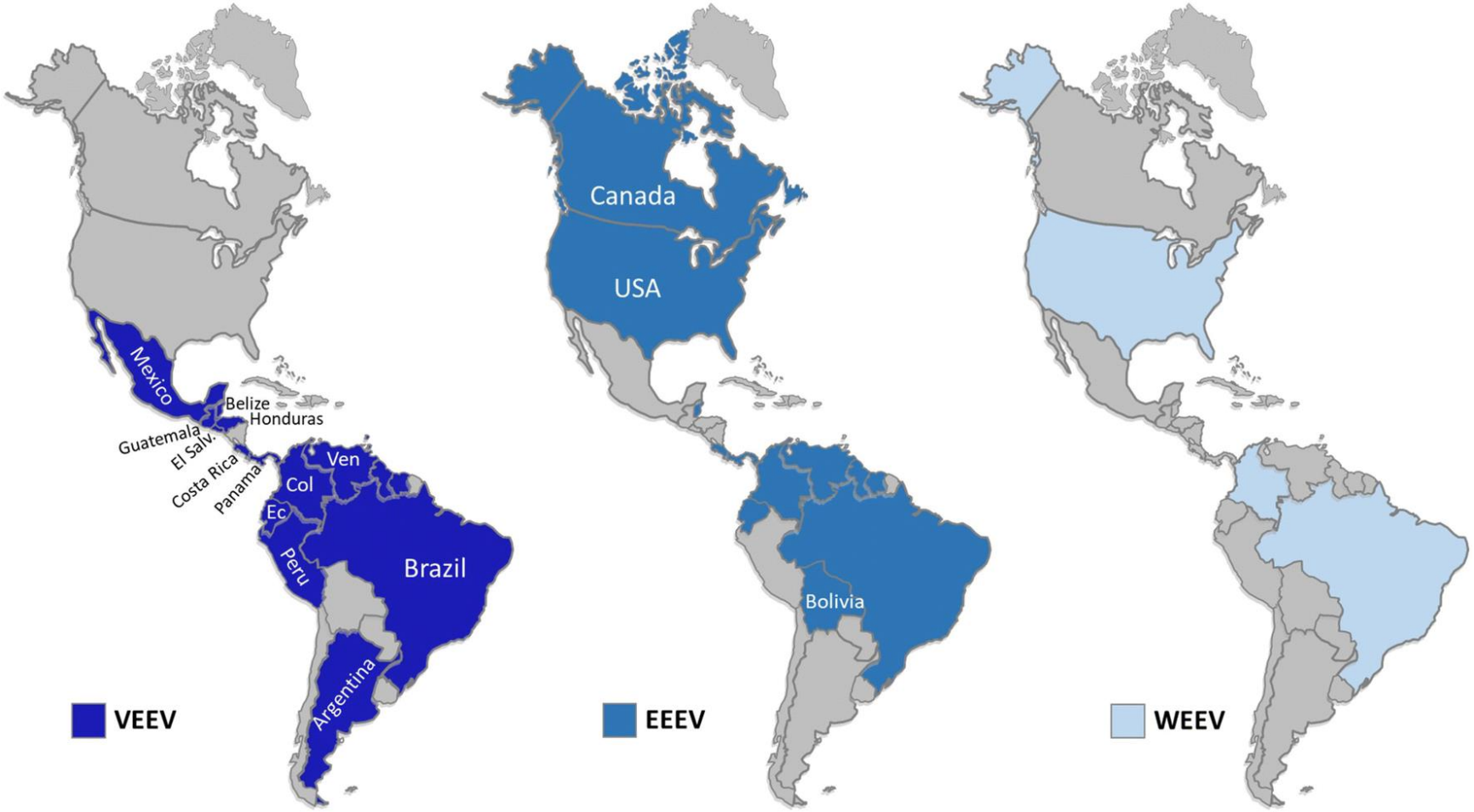
## Occurrence:

**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**.

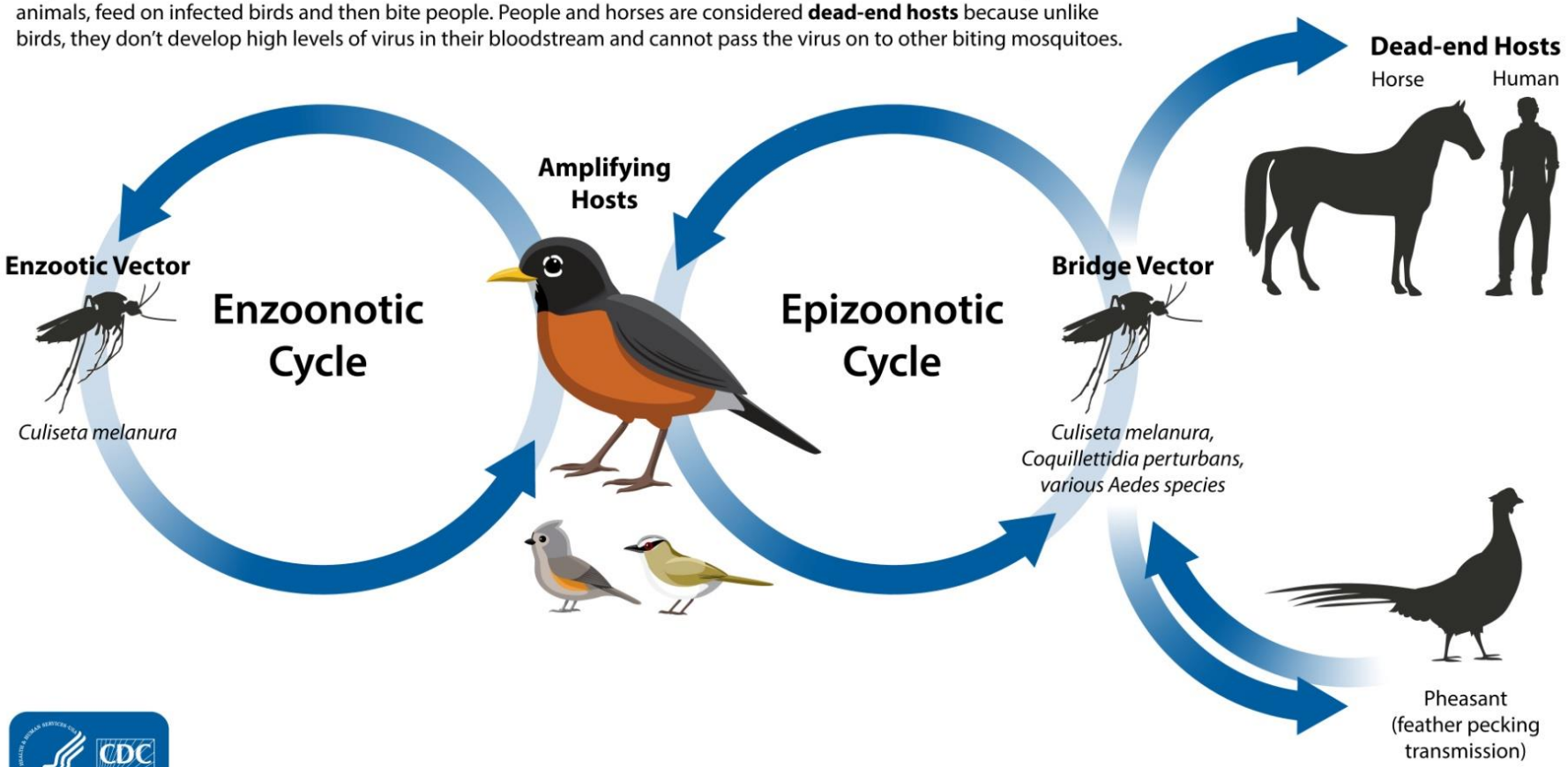
# Geographical distribution of the equine encephalitis in the Americas. **a** VEEV. **b** EEEV. **c** WEEV



# 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.




CDC

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# 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.

# Equine encephalomyelitis - Pathogenicity

- Entry of virus through mosquito bite
- **Viscerotropic** and neurotropic virus
- Initially multiply in the muscles, myeloid, lymphoreticular tissue
- First phase of viraemia 2-3 days
- Fever returns to normal.
- After 6-7 days Second viraemia followed by invasion to CNS with virus replication n destruction of neurons-Nerve cell degenration.
- Leading to **encephalitis**.
- Mortality:
  - EEE – 75-100 %
  - WEE-10-40%
  - VEE40-70%

# Equine encephalomyelitis – Clinical signs

- 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 - Horses

## 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.

# Equine Encephalitis - Laboratory 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**

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.

# Vaccines and Vaccination – EEE,WEE,VEE

***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

# Human Perception

# Eastern Equine Encephalomyelitis

EEE was first isolated from horse brain in 1933 and from human brain during the Massachusetts epidemic of 1938. The EEE zoonosis is maintained by **passerine birds and *Culiseta melanura* mosquitoes** in forested marshes. These mosquitoes feed mainly on birds; *Aedes* and *Culex* mosquitoes account for transmission of EEE to horses or humans.

After an incubation period of 5–10 days, fever, malaise, headache, photophobia, and vomiting rapidly evolve into meningismus with fulminant deterioration in consciousness. In many cases, coma with paralysis has developed by the second or third day of illness. Initial leukopenia is followed by the development of leukocytosis.

The **fatality rate for EEE ranges from 20% to 70% across all age groups**, but it is 75% in infants and is also high in the elderly. A majority of survivors manifest significant neurological injury with intellectual impairment, personality changes, or spastic paralysis. Permanent abnormalities of this sort occur as a result of EEE in 70–90% of infants. The overall risk for epilepsy is 14–37%.

# Western Equine Encephalomyelitis

- WEE is closely related to EEE, but it has a lower case fatality rate: approximately 10%. As with EEE, it is a summertime disease, but WEE is found in states west of the Mississippi River and in some western Canadian provinces.
- It is also maintained by a bird-mosquito-bird life cycle, with its primary vector the mosquito ***Culex tarsalis***.
- The worst outbreak recorded was 3336 human cases in 1941.

- The isolation of WEE from **equine brain** in California in 1930 was the first isolation of an encephalitogenic arbovirus in the United States. The virus was recovered from the brain of a child in 1938.
- WEE is **less neurovirulent for humans** than for horses. WEE is harbored in birds and wild herds of western horses.
- The vectors for humans and horses are principally ***Culex tarsalis*** and ***Culex melanura*** mosquitoes. Most human and equine cases of WEE occur in the summer, especially in June and July or slightly later in Canada.

# Western Equine Encephalomyelitis

Young children and infants are at greatest risk for severe infections or death, and among those who recover, there is great risk for epilepsy (focal or generalized convulsive) and other forms of significant permanent neurological impairment.

The case fatality rate is 6–8% for WEE, with the highest rates in elderly patients. **Permanent motor signs or intellectual difficulties** are found in approximately 13% of the cases.

**Clinical manifestations** are much the same as those of EEE, although they are somewhat milder overall.
After a 10-day incubation, patients manifest malaise, fever, and headache, often with nausea, vomiting, and photophobia. These changes may be followed by obtundation, extremity weakness, hypo- or hyperreflexia, and tone abnormalities alternating between flaccidity and spasticity.
Muscle stretch reflexes may be increased or decreased. Seizures are common

# Venezulean Equine Encephalomyelitis

VEE **was recognized first in Venezuela in 1936**. The etiologic agent, VEEV, has caused explosive equine epizootics and epidemics in many regions of the Americas. The last major epidemic in northern Venezuela and Colombia in 1995 involved approximately **100 000** persons.

**The VEE virus was first isolated in 1938 from an infected horse's brain**. Annual outbreaks in Colombia and Venezuela occurred through the 1960s. An epidemic in Venezuela that took place from 1962 to 1964 caused more than **23,000 human cases of VEE**. In 1967 Columbia suffered a major epidemic, which caused approximately 220,000 human cases and more than **67,000 equine deaths**. **The largest recorded outbreak of VEE originated in Guatemala in 1969** and spread north to Texas over the course of a few years. This event led to the only known epidemic of VEE in the United States in 1971.

# Venezulean Equine Encephalomyelitis

**Clinical Presentation**

Clinical effects typically begin following an incubation period of several days to 2 weeks. However, the incubation period may be shorter (i.e., 1–5 days) with aerosol-acquired infections.

Infection in humans with VEE virus in adults usually leads to **a low-mortality (<1%)**, influenza-like illness. The initial signs, lasting 24–48 h, include **fever, malaise, dizziness, chills, headaches, severe myalgia, arthralgia, nausea, and vomiting. Lethargy and anorexia can continue for 2–3 weeks**. Severe illness in adults comes from **neurological involvement because of swelling in and around the brain**. A small percentage of patients (<15%) actually experience neurological problems such as photophobia, **convulsions, stiff neck, and altered mental status**.

Some patients experience personality changes, fatigue, recurrent headaches, and altered senses; prognosis with the clinical disease is variable. **Children infected by VEE virus experience severe encephalitis**, in which coma and subsequently death is a more likely outcome

# Additional Information

**Alphavirus (Togaviridae) encephalitis of horses**

•*Eastern equine encephalitis* (EEE). There is one EEE virus with two antigenic variants, North American and South American. EEE is recognized primarily in southeastern Canada and most of the United States east of the Mississippi river, although it has been recognized in the Carribean and Central and South America. Enzootic cycles in North America involve a mosquito vector, and passerine birds as an amplifying host. peak incidence in late summer or early fall. Infected horses and humans are regarded as dead end hosts as the viremia that develops is insufficient to infect epizootic hosts.

•***Western equine encephalitis*** (WEE). The WEE complex has seven virus species. WEE occurs throughout most of the Americas and Canada with extensive epizootics in Argentina. The principal enzootic vector is *Culextarsalis* and the epizootic mosquito vector is an *Aedes* species. Equine cases usually precede human cases by several weeks and thus act as a sentinel for humans. Similar to EEE, **humans and horses are regarded as dead-end hosts for WEE infection**.

•***Venezuelan equine encephalitis*** (VEE). The VEE complex **is one virus with six antigenic subtypes (I through VI)**. South America with extension into Central America. However, epizootics have extended as far north as Texas. *Aedes* and *Psorophora* mosquito species transmit epizootic subtypes, high mortality in both humans and horses. Unlike EEE and WEE, horses with VEE develop a sufficient viremia to act as an amplifier of the disease.

**Alphavirus (Togaviridae) encephalitis of horses**

**Clinical signs**

•Infection with alphaviruses is associated with an **initial incubation period of approximately 1 week** in which a **biphasic viremia takes place**, although the first fever spike may not be noticed. Horses with VEE usually have a consistently elevated temperature during the disease.

•Other non-specific signs such as lethargy and stiffness are seen during the viremic phase. As the disease progresses clinical signs of neurological disease become more evident with the severity of signs dependent on the virus involved and the extent of CNS lesions.

•EEE and WEE usually have a similar initial clinical appearance with ataxia, somnolence, conscious proprioceptive deficits, stiff neck and compulsive walking or chewing. EEE typically progresses to severe CNS deficits that occur secondary to diffuse cerebrocortical disease. Signs EEE include apparent blindness and circling, excitement and aggressive behavior, laryngeal, pharyngeal and tongue paralysis and signs of brainstem dysfunction such as head tilt, nystagmus, strabismus and pupil dilation.

•VEE may also cause inapparent infections, signs similar to other encephalitis viruses or produce signs such as epistaxis, pulmonary hemorrhage, oral ulcers and diarrhea that may be unrelated to CNS damage.

•Seizures can occur with any of the alphavirus infections and sudden death .

# THANKS

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