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A Comprehensive Overview of Eastern Equine Encephalitis (EEE)

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ABSTRACT

Eastern Equine Encephalitis (EEE) is a rare but serious mosquito-borne viral infection affecting humans, horses and certain birds in North America. The virus is primarily transmitted by *Culiseta melanura* mosquitoes, which feed on infected wild birds. Humans and horses are considered dead-end hosts, they do not contribute to the transmission cycle. While infections in humans are uncommon, they can lead to severe neurological disease, with symptoms ranging from fever and head ache to encephalitis, seizures and coma. EEE has a high mortality rate in humans, with survivors often experiencing long-term neurological damage. No specific treatments or vaccines exists for human infection, making prevention through mosquito control and personal protective measures critical. This overview provides insight into the history, etiology, epidemiology, transmission, symptoms, diagnosis and prevention of EEE.

Keywords: Encephalitis, North America, EEEV, arbovirus, *Culiseta melanura*.

INTRODUCTION

Eastern equine encephalomyelitis is a mosquito-borne viral disease of all equine species such as horses, asses, and zebras. After infection, equines may suddenly die or show progressive central nervous system disorders. The equine mortality rate due to EEE ranges from 75 to 90 percent. Humans can also contract this disease. Healthy adults who become infected by the virus may experience flu-like symptoms such as high fevers and headaches. The young, the elderly, and people with weakened immune system can become severely ill or die from this disease.

HISTORY

Eastern equine encephalitis virus (EEEV) is thought to have been the cause of EEE in North American horses since 1831. However, the virus itself may have been present in its endemic form long before that. The virus did not receive its name until a major outbreak occurred in horses in coastal areas of Delaware, Maryland, New Jersey, and Virginia in 1933.

Additional outbreaks occurred in Virginia and North Carolina in 1935 respectively. Mosquitoes were first determined to be potential carriers of EEEV in 1934. Since then, a number of studies have shown that various mosquito species of Aedes and Culex could become infected with and transmit EEEV from one vertebrae to another.

It was during the 1935 outbreak that birds were considered to be a possible reservoir host for the virus, but it was not until 1950 that the first virus isolation was made from a wild bird proving that to be true. Subsequent studies have shown that many birds, including all passerine species (warblers, finches, and sparrows), are susceptible to EEEV infection.

Because outbreaks of EEE are infrequent, the disease has a significant economic and social impact once a specific area has been identified. When the disease appears in an area for the first time, there is a loss of horses and poultry. The area may also experience an increase in human morbidity and mortality.

ETIOLOGY OF EEE

Eastern equine encephalitis virus (EEEV) is an arbovirus from the *Togaviridae* family, genus alphavirus. Maintained by a cycle between birds and predominantly *Culiseta melanura* mosquitoes associated with freshwater hardwood swamps. Eastern equine

encephalitis virus has a single-stranded, positive-sense RNA genome. The virus particles are spherical and have a diameter of 60–65 nm.

There are four lineages of the eastern equine encephalitis virus antigenic complex.

- Group I consists of only eastern equine encephalitis virus and is endemic in North America and the Caribbean and causes most human disease cases.

- The other three groups (IIA, IIB, and III) are caused by related Madariaga virus (formerly known as South American eastern equine encephalitis virus) and cause primarily equine illness in Central and South America.

Recent data suggest other mosquitoes species also involved in EEBV transmission include *Coquillettidia perturbans*, *Aedes cinereus*, and *Aedes canadensis*. The mosquitoes get infected and transmit EEV during blood feeding to passerine (tree-perching) birds and opportunistic mammals, reptiles, or amphibians. This virus can escape its usual reservoir to infect dead-end hosts (humans, swine, equids, pheasants). Humans are described as dead-end hosts since viremia levels are not usually reached to a level to allow the transmission to the feeding mosquitoes. This cross-transmission happens unpredictably, but changes in weather and global warming may have an effect on this rising incidence. Other factors include environmental perturbations, movement of birds, and human interaction with the environment. In 2017, EEEV transmission was reported for the first time via organ transplantation.

EPIDEMIOLOGY

The first identification of Eastern equine encephalitis virus in humans dates from 1938 during an important outbreak affecting Massachusetts, U.S. As previously described, humans do not usually participate in the natural cycle but rather get affected sporadically in the geographic region along the Atlantic, and Gulf coasts of the U.S. The largest EEEV outbreak recorded is from 1959 in New Jersey, U.S., and involved 32 cases during 8 weeks. EEE is now a nationally notifiable condition and is monitor through ArboNET, a national arboviral disease surveillance disease system since 2003. The latest data reflects EEEV was present in 20 states. Massachusetts, Florida, and New Hampshire as the states with more reported cases nationwide, but new states have been now included in this list, such as Arkansas, Connecticut, Maine, Tennessee, North Carolina, and Vermont showing a larger geographic range affected by this viral encephalitis. Annual incidence reflects a mean of 8 cases in the U.S. Neuroinvassive disease is 2 times higher among males. The incidence of EEEV also has shown a bimodal presentation with the highest risk among the population less than 5 years of age and above 60 years of age. Data from Lindsey et al. also described a fatality rate as high as 41%, with 50% of long-term neurological sequelae.

As per ArboNET reports, non-human active areas are much greater than what human data suggests. Some researchers hypothesize this is likely due to the lack of necessary conditions for the EEBV to escape the enzootic cycle (non-human animal endemic) and then enter the epizootic cycle (non-human animal epidemic). It could also be related to surveillance and/or testing biases.

TRANSMISSION

Eastern equine encephalitis virus is maintained in a cycle between *Culiseta melanura* mosquitoes and avian hosts in freshwater hardwood swamps. *Cs. melanura* is not considered to be an important vector of eastern equine encephalitis virus to humans because it feeds almost exclusively on birds. Transmission to people requires another mosquito species to create a "bridge" between infected birds and uninfected mammals, such as people or horses. Most of the bridge species are within the *Aedes*, *Coquillettidia*, and *Culex* genera. Eastern equine encephalitis virus has been documented to be transmitted through solid organ transplantation, with one organ donor transmitting the infection to three organ transplant recipients.

Horses are susceptible to eastern equine encephalitis virus infection and many cases are fatal. Eastern equine encephalitis virus infections in horses, however, do not increase risk for human infections because horses (like humans) are considered to be “dead-end” hosts for the virus (i.e., the concentration of virus in their bloodstreams is usually insufficient to infect mosquitoes). There is a vaccine to prevent eastern equine encephalitis virus infection in horses.

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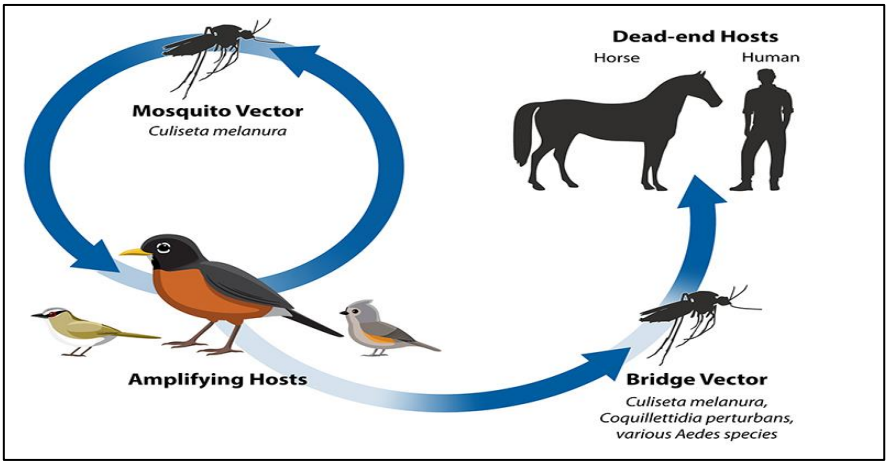

Fig.1 Eastern Equine Encephalitis Transmission

Source: Centers for Disease Control and Prevention (U.S.)

CLINICAL SYMPTOMS

The symptoms usually appear 4 to 10 days after a bite from an infected mosquito (incubation period). The type of symptoms usually depends on the age of the person. People over age 50 and younger than age 15 are at greatest risk for developing severe disease. Severe cases of EEE infection begin with the sudden onset of head ache, high fever, chills and vomiting that may progress into disorientation, seizures, encephalitis (inflammation of the brain), and coma. Equines infected with EEE may show one or more of the following signs: Chills, Fever, Joint pain, Muscle pain, Depression, Loss of appetite, Vomiting, Weakness, Diarrhea, Drowsiness.

HUMAN CASES

EEE is a rare but very serious disease that involves inflammation and swelling of the brain. Fortunately, only 5% of human EEEV infections result in EEE. However, one out of three people who develop EEE will die, and many survivors have mild to severe brain damage.

Of those who contract the EEE virus, the elderly (ages 50 and older) and young (ages 15 and younger) are at the greatest risk of developing encephalitis. An average of 11 human cases of EEE are reported in the United States annually. The chart below shows the cases by year of illness onset from 2003 to 2023. The most cases of EEE were reported in 2019.

EEE is most commonly reported in the eastern and Gulf Coast states, but can also be found in some inland Midwestern states. States that have reported the most cases of EEE include Massachusetts, Michigan, Florida, Georgia, New York, and North Carolina.

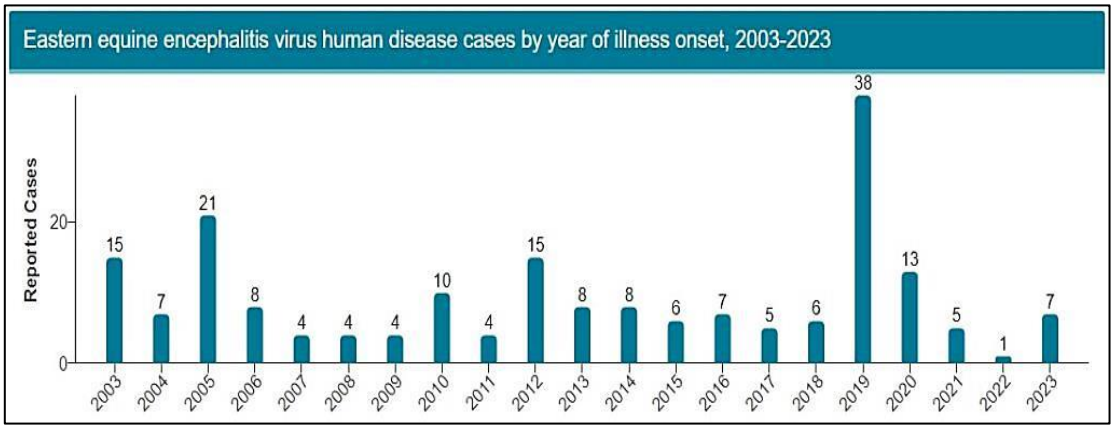

Fig.2 Human disease cases

Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention

DIAGNOSIS AND TREATMENT

Health care provider diagnose EEE based on the patient's clinical symptoms and laboratory diagnosis by testing blood or spinal fluids, which will show if the virus or antibodies against the virus are present in the individual.

There is no specific treatment for EEE. Treatment focuses on supportive therapy, including hospitalization, respiratory support, intravenous fluids and prevention of other infections.

PREVENTION

There is no commercially available human vaccine for EEE and the best protection is to prevent mosquito bites. The following precautions are recommended to reduce the risk of infection from EEE and other mosquito-borne illnesses.

- Consider wearing long sleeves and tucking pants into socks and shirts into pants when outdoors at dusk or dawn, the time of day when mosquitoes are most active.
- Use insect repellents containing DEET. Be sure to follow the insect repellent label directions.
- To reduce the mosquito population around home and property, reduce or remove all standing water.
- Dispose of tins cans, plastic containers, ceramic pots or similar water-holding containers.
- Remove and recycle all discarded tires on property. Used tires are a significant mosquito-breeding site.
- Drill holes in the bottoms of recycling containers that are kept outdoors.
- Make sure roof gutters drains properly and clean clogged gutters in the spring and fall.
- Remove leaf debris from yards and gardens.
- Turn over wading pools and wheelbarrows when not in use.
- Change the water in birdbaths twice weekly.
- Clean vegetation and debris from edges of ponds.
- Clean and chlorinate swimming pools, outdoors saunas, and hot tubs.
- Drain water from pool covers.
- Use landscaping to eliminate standing water that collects on home and property.
- Make sure window and door screens fit properly and are in good condition.

Conclusion

In conclusion, Eastern Equine Encephalitis (EEE) is a rare but severe neuroinvasive disease transmitted to humans through the bite of infected mosquitoes. It primarily affects horses and humans, with humans being accidental hosts. While cases are infrequent, EEE has a high fatality rate in symptomatic individuals, particularly in severe cases involving encephalitis. The disease is prevalent in certain regions, especially in the eastern United States, and tends to occur during warmer months when mosquito activity is high. Prevention focuses on mosquito control and personal protective measures, as no specific antiviral treatment or vaccine available for humans. Awareness and early intervention remain critical in reducing the risk of EEE infection.

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