

Eastern Equine Encephalomyelitis

Agent: Eastern Equine Encephalomyelitis virus (EEE) is a mosquito-borne alphavirus of the family Togaviridae. Other members of this family of viruses include Venezuelan Equine Encephalomyelitis (VEE), Western Equine Encephalomyelitis (WEE), and Highlands J Virus. Of the two antigenic variants of EEE, the North American variant is more pathogenic. EEE can be found in eastern Canada, the United States east of the Mississippi River, Arkansas, Texas, and along the Gulf Coast. Rare cases have also been reported in other inland states. The less pathogenic South American variant is found in South and Central America.

Brief Description: EEE virus causes encephalitis in horses, and rarely, in some avian species, swine, and other equids. Georgia typically has less than 10 laboratory confirmed cases of EEE annually; however, 2003 had a record breaking 83 cases. The number of confirmed EEE cases dropped to 7 in 2004, and rose again in 2005 with 21 confirmed cases. There were 4 confirmed cases in 2006 and 6 confirmed cases in 2007. In horses, the initial clinical signs are usually fever, anorexia, and depression. Progressive neurological signs may include involuntary muscle movements, impaired vision, hyperexcitability, aimless wandering, head pressing, circling, inability to swallow, ataxia, paresis, paralysis, convulsions, lateral recumbency, and death. The mortality rate in horses may range from 75-90%. Subclinical infections may occur.

From 2003-2007, only 4 human EEE cases were reported to the Georgia Division of Public Health. EEE can be transmitted from infected birds to humans via mosquitoes. Equine epizootics are often precursors to human disease, although sick horses cannot directly spread EEE to humans. Because of the high case fatality rate of 30-50% in symptomatic cases, it is classified as the most severe mosquito-borne disease of humans in the United States. Symptoms range from mild flu-like illness to encephalitis (inflammation of the brain), coma, and death. The elderly and children are most susceptible to developing severe disease. Permanent neurological deficits can occur in survivors.

The clinical signs may vary according to the species infected. Birds are often infected asymptotically; however, EEE virus infections have been reported to cause high mortality in captive-raised game birds (primarily pheasants, chukar partridges, and quail).

Differential Diagnoses:

- Rabies and Other Viral Encephalitides such as WEE, VEE, and West Nile Virus (WNV), Aujeszky's disease, Borna disease, Equine Herpes Virus 1 (EHV1)
- Equine Protozoal Myeloencephalitis (EPM)
- Verminous Encephalitis (Visceral Larval Migrants)
- Cervical Vertebral Myelopathy (CVM, Wobbler)
- Equine Degenerative Myelopathy (EDM)
- Cranial Trauma
- Toxicosis
- Botulism
- Bacterial Meningitis
- Listeriosis
- Hepatoencephalopathy
- Leukoencephalomalacia

Reservoir/Host Species: Birds are the natural hosts. Other susceptible animals include horses, donkeys, mules, poultry, game birds, ratites, whooping cranes, swine, bats, reptiles, amphibians, forest-dwelling marsupials, and rodents.

Mode of Transmission: The major route of transmission occurs via the bites of infected mosquitoes. Under natural conditions, the EEE virus cycles between birds and *Culiseta melanura*, a mosquito frequently found in swampy areas. It is believed that birds and other species of mosquitoes, acting as bridge vectors, spread the virus out of the enzootic foci usually found in swamps to horses and humans. Direct transmission can occur between birds from feather picking and cannibalism. In the mosquito population, vertical transmission from the infected female to the offspring through the eggs can occur. Both horses and humans are dead-end hosts for the virus in that they do not produce a significant viremia to contribute to the transmission cycle.

Incubation Period: The incubation period is 1-8 days.

Case Definition:

Clinical signs must include ataxia (including stumbling, staggering, wobbly gait, or incoordination) or at least 2 of the following: circling, hind limb weakness, inability to stand, multiple limb paralysis, muscle fasciculations, proprioceptive deficits, blindness, lip droop/paralysis, teeth grinding, or death. Laboratory confirmation of at least one of the following is necessary in addition to clinical signs:

- Isolation of virus from or a Polymerase Chain Reaction (PCR) positive for viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or
- Fourfold or greater change in serum antibody titer of EEE over WEE, or
- Positive IgM capture ELISA for EEE in a nonvaccinate.

Case Classification:

- **Confirmed:** a clinically compatible case that is laboratory confirmed
- **Suspect:** a clinically compatible case occurring during a period when arboviral transmission is likely with an IgM capture ELISA positive and recent vaccination (within 6 weeks). A suspect case may also arise if there are suggestive clinical signs, a negative IgM capture ELISA and a high EEE Serum neutralization titer coupled with a low or negative WEE titer.

Diagnosis: A definitive diagnosis can only be made by virus isolation or detecting an increase in antibody titer between paired and convalescent sera. EEE induces a transient viremia in horses, but virus isolation from the blood is not possible by the time neurologic signs are observed. The virus may be isolated from the cerebrospinal fluid of animals with acute infections. Preferably, brain specimens should be kept refrigerated or on ice, neither frozen nor chemically fixed. If brain samples will not arrive at the laboratory within 48 hours of collection, then freeze and send on dry ice. It is recommended that half the brain be sent separately to the appropriate laboratory for rabies diagnosis. The brain should be examined microscopically for the presence of nonsuppurative meningoencephalitis. Appropriate protective gear should be used when extracting specimens for laboratory submission to reduce exposure to potentially infectious material. Virus isolation and a polymerase chain reaction (PCR) for viral antigen should also be attempted from the brain of dead animals. Serologic tests for acute and convalescent sera consist of Hemagglutination Inhibition, Complement Fixation, Virus Neutralization, and antibody capture Enzyme-linked Immunosorbent Assay (ELISA) for IgM. Serum samples should be submitted on ice packs and via courier (ex. FedEx, UPS) within 24 hours of collection. Samples should be kept cold, but not frozen. IgM ELISA tests are set up on Mondays and Wednesdays in Tifton with test results available in 2 days. Serum neutralization tests are set up on Tuesdays and Fridays and require 3 – 5 days to complete. If the brain is submitted for Rabies testing, then the remaining samples will be held until completion of Rabies testing. Hemagglutination Inhibition antibody cross-reacts between EEE, WEE, and VEE. See page 5: “Decision Tree for Diagnosis of Eastern Equine Encephalomyelitis (EEE)”

Suggestive Necropsy Findings: No gross lesions are characteristically seen in association with EEE.

Prevention Measures/Control: Control mosquitoes around stables and keep horses vaccinated for EEE as recommended in the sections that follow. EEE virus does not survive outside of the host.

Environment:

- Aerate or drain standing water to reduce mosquito breeding habitats.
- When draining standing water is impractical, consider using Mosquito Dunks containing (BTI) *Bacillus thuringiensis israeliensis* or *Bacillus sphaericus*, mosquito larvicides. Follow label directions carefully. <http://www.ent.uga.edu/pubs/protectinsects.htm>

Equine:

- Vaccinate horses with a licensed EEE vaccine in accordance with the label instructions and veterinary recommendations.
- Thoroughly clean watering troughs every 3-4 days. Use either Mosquito Dunks or mosquito eating fish in water tanks that are impractical to drain.
- Stable your horse from dawn to dusk and use window screens and fans to reduce mosquitoes feeding on horses.
- Numerous insecticides and repellents are labeled for use on horses and/or barns. Using insect repellants may help decrease exposure of horses to adult mosquitoes. Synthetic pyrethroid compounds (such as permethrin) kill as well as repel mosquitoes. Use repellants and other pesticides according to label instructions. <http://www.ent.uga.edu/pubs/homeipm.htm#mosquitoes>

Humans:

- Apply insect repellants containing DEET or Picaridin being careful to follow the label instructions. http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm
<http://www.cdc.gov/ncidod/dvbid/westnile/RepellentUpdates.htm>
- Consider staying indoors during peak exposure times of dawn, dusk, and the early evening. If outdoors during peak exposure times, wear long sleeved shirts and long pants sprayed with a permethrin product.
- Install or repair window and door screens to reduce indoor mosquitoes.

Vaccine: There is a killed vaccine against EEE available for horses, other equids, and some birds. In unvaccinated adult horses, an initial vaccination is given before mosquito season with a booster dose given 4-6 weeks later. For previously vaccinated pregnant mares, a booster dose 3-4 weeks prepartum is recommended. For foals in Georgia, a series of 4 vaccinations is recommended starting at 3-4 months of age with the initial 3 vaccines given at 4 week intervals and the fourth dose at 10-12 months of age. After the initial series, vaccination is usually annually or biannually depending on the horse's exposure risk. http://www.aaep.org/eee_wee.htm

Zoonotic Risk: The enzootic (animal-based) transmission cycle is most common to coastal areas and freshwater swamps. Human cases occur relatively infrequently, largely because the primary transmission cycle takes place in swampy areas where populations tend to be limited. Both humans and horses are dead-end hosts for EEE.

Potential as Biothreat Agent in Humans/Animals: EEE is on the High Consequence Livestock Pathogens and Toxins/Select Agents List (USDA/HHS Overlap Agents) and the OIE list of potential biothreat agents.

Reporting Requirements

- **Any person who makes a laboratory confirmation of Eastern Equine Encephalomyelitis (EEE) in an animal shall report it by the close of the next business day** to the State Veterinarian's office at (404) 656-3667 or (404) 656-3671 in Atlanta, or 1-800-282-5852 outside of Atlanta, or to the USDA Area Veterinarian in Charge at (770) 922-7860.
- **A clinical diagnosis or laboratory confirmation of Eastern Equine Encephalitis (EEE) in humans is immediately reportable** to the Georgia Division of Public Health, Notifiable Disease

Section. For more information, or to contact the Georgia Division of Public Health, call (404)-657-2588 or go to <http://health.state.ga.us/epi/disease/index.asp>

Electronic References:

American Association of Equine Practitioners. Core Vaccination Guidelines: Eastern/Western Equine Encephalomyelitis

http://www.aaep.org/eee_wee.htm

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http://www.cfsph.iastate.edu/Factsheets/pdfs/easter_wester_venezuelan_equine_encephalomyelitis.pdf

Centers for Disease Control and Prevention (CDC). Eastern Equine Encephalitis Fact Sheet.

<http://www.cdc.gov/ncidod/dvbid/arboreeefact.htm>

Franklin RP, Kinde H, Jay MT, Kramer LD, Green EN, Chiles RE, et al. Eastern Equine Encephalomyelitis Virus Infection In a Horse from California. *Emerging Infectious Diseases* 2002 March; 8: 283-8.

<http://www.cdc.gov/ncidod/EID/vol8no3/01-0199.htm#Figure1>

The Georgia Division of Public Health. Arboviral Fact Sheet.

<http://www.health.state.ga.us/pdfs/epi/notifiable/arboviral.fs.02.pdf>

The Georgia Division of Public Health. Arboviral Infection Q & A.

<http://www.health.state.ga.us/pdfs/epi/notifiable/arboviral.qa.02.pdf>

The Georgia Division of Public Health. Eastern Equine Encephalitis Frequently Asked Questions.

<http://www.health.state.ga.us/pdfs/epi/vbd/eeefaq.02.pdf>

The Georgia Division of Public Health. Online Analytical Statistical Information System (OASIS). OASIS Arboviral Surveillance Tool.

<http://oasis.state.ga.us/index.asp>

The Merck Veterinary Manual, 50th Anniversary edition.

<http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/100900.htm>

Office International des Epizooties (OIE) – Manual of Standards for Diagnostic Tests and Vaccines for Terrestrial Animals 2004. *Eastern Equine Encephalomyelitis*.

http://www.oie.int/fr/normes/mmanual/A_00081.htm

USDA-APHIS Animal Health Factsheets. Eastern Equine Encephalomyelitis.

http://www.aphis.usda.gov/lpa/pubs/fsheet_faq_notice/fs_aheasterne.html

USDA-APHIS, Animal Health Monitoring & Surveillance. Eastern and Western Equine Encephalitis.

<http://www.aphis.usda.gov/vs/nahss/equine/ee/>

Other References:

Chin J, ed. Arthropod-borne Viral Encephalitides. In *Control of Communicable Diseases Manual*. 17th ed. Washington DC: American Public Health Association, 2000: 39-43

Decision Tree for Diagnosis of Eastern Equine Encephalomyelitis (EEE)

