Slide 1

Venezuelan Equine Encephalitis

Peste Loca
Venezuelan Encephalitis
Venezuelan Equine Fever

Slide 2

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control
- Actions to Take

In today's presentation we will cover information regarding the agent that causes Venezuelan equine encephalomyelitis and its epidemiology. We will also talk about the history of this diseases, how it is transmitted, species that it affects, and clinical signs seen in humans and animals. Finally, we will address prevention and control measures, as well as actions to take if Venezuelan equine encephalomyelitis is suspected.

[Photo: Horses in field. Source: U.S. Department of Agriculture]

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THE ORGANISM

Slide 4

The Virus

- Venezuelan equine encephalomyelitis virus
  - Family Togaviridae
  - Genus *Alphavirus*
- Six subtypes
  - Epizootic and enzootic
- Mosquito-borne
- Disease
  - Encephalitis in humans and horses

Venezuelan equine encephalomyelitis (VEE) results from infection by the respectively named virus in the genus *Alphavirus* (family Togaviridae). The VEE complex contains at least six viral subtypes, I to VI. VEE complex viruses are divided into epizootic (or epidemic) and enzootic (or endemic) groups. VEE is a mosquito-borne, viral infection that can cause severe encephalitis in horses and humans.

[Photo: Electron micrograph of the Eastern equine encephalitis virus. Source: Dr. Fred Murphy and Sylvia Whitfield/CDC Public Health Image Library]

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Viral Strains

Subtype	Cycle	Pathogenic
I-A I-B I-C	Epizootic/ Epidemic	Highly virulent for equines
I-D II I-E III I-F IV V VI	Enzootic/ Endemic	Not for horses Limited cases in humans

Venezuelan equine encephalomyelitis (VEE) virus has a complex classification system due to its large number of subtypes. Subtype I includes six variants, three of which are epidemic variants. The distinction is important from an epidemiological standpoint as some subtypes cause severe disease and epidemics. Variants A,B, and C of subtype I (i.e., I-A, I-B, and I-C) are considered epizootic (or epidemic) strains and are highly virulent to equines. Subtype I-A originated in donkeys in Trinidad; I-B originated in humans in Honduras. [Note: These two subtypes are usually referred to as I-AB because of their almost identical fingerprints.] I-C originated in horses in Venezuela. The variants D, E, and F of subtype I (i.e., I-D, I-E, and

I-F) and subtypes II, III, IV, V, VI are considered enzootic (or endemic) strains and are not pathogenic for equines. There have been infrequent limited outbreaks from these strains in humans. Enzootic (endemic) strains have a wide geographic distribution in the Americas, but the pathogenic form has not been seen in the United States since 1971. VEE viruses have been classified into six subtypes based on antigenic analysis: subtypes I-D, I-E, and I-F; subtype II (Everglades virus - which was the only subtype found in the United States); subtype III (Mucambo virus A,B,C); subtype IV (Pixuna virus); subtype V (Cabassou virus); and subtype VI (AGso-663 virus).

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Viral Strains

- Epizootic/Epidemic
  - I-A, I-B, and I-C
  - Disease in humans and horses
  - Transmission by many mosquito species
  - Natural reservoir unknown
  - Horses and donkeys act as amplifiers
- Enzootic/Endemic
  - Disease in humans
  - Transmission mainly by *Culex* (*Melanoconion*) species
  - Natural reservoir is rodents living in swamps and forests

The epidemic strains of VEE (i.e., I-A, I-B, and I-C) cause disease in humans and horses, while the enzootic strains (i.e., I-D, I-E, I-F, II, III, IV, V, VI) only cause intermittent disease in humans. Enzootic strains have been isolated from mosquitoes, whereas epidemic strains have not been identified since 1973, questioning whether they are still present in nature. Epidemic strains utilize a large number of mosquito species as a means to spread disease; vertebrates, primarily horses and donkeys amplify the virus. The natural reservoir is unknown. Enzootic strains have a wide geographic distribution in the Americas and are maintained in wild animals, specifically rodents living in rain forests and swamps. They are transmitted by fewer mosquito vectors, mainly *Culex* (*Melanoconion*) species.

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HISTORY

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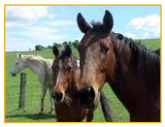
VEE History

- 1938
  - Isolated from horse brain
- 1962-1964
  - Outbreak in Venezuela
    - 23,000 human cases
- 1967
  - Outbreak in Colombia
    - 220,000 human cases
    - Over 67,000 horse deaths



Outbreaks of VEE-type diseases have occurred in the Western Hemisphere since the 1920s, and the virus was finally isolated in 1938 from a horse brain. Annual outbreaks occurred throughout the 1960s in Colombia and Venezuela. A long standing epidemic from 1962 to 1964 in Venezuela caused more than 23,000 human cases of VEE with a case-fatality rate of 0.6%. In 1967, a major epidemic hit Colombia, causing 220,000 human cases and over 67,000 horse deaths.

[Photo: Horses. Source: U.S. Department of Agriculture]

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VEE History

- 1969-1971
  - Largest recorded outbreak
  - Covered area from Costa Rica to Rio Grande Valley in Texas
  - Thousands of human encephalitis cases
  - Over 100,000 horses died
- 1995
  - Venezuela and Colombia
  - Over 90,000 human cases

The largest recorded outbreak of VEE began in 1969 in Guatemala and covered a geographic region from Costa Rica to the Rio Grande Valley of Texas. Human cases of encephalitis were in the thousands, and over 100,000 horses died as a result of VEE. Small, occasional outbreaks have occurred in Peru and Mexico, but in fall of 1995 there were over 90,000 human cases in Venezuela and Colombia.

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Countries with Confirmed VEE, 2007-2012

This slide shows the countries reporting confirmed VEE cases in horses between 2007-2012.
Source: OIE World Animal Health Information Database and USDA FAD PReP Venezuelan equine encephalomyelitis standard operating procedures.

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TRANSMISSION

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Epizootic Transmission

Primary Vector
multiple mosquito species

Other species naturally infected but not amplifiers

Dead-end hosts
Humans

Vertebrate Host
Horses

Epizootic strains of VEE virus can be transmitted by a large number of mosquito species, such as *Mansonia titillans, M. indubitans, Psorophora confinnis, Ps. discolor, Deinocerites pseudes, Aedes thelcter, Ae. sollicitans, Ae. taeniarhynchus, Ae. scapularis,* and *Ae. aegypti*. Horses and donkeys are the principal amplifying hosts for VEE, while humans are dead-end hosts. There are other domestic species of animals that have been naturally infected with the virus, such as cattle, swine, dogs, and chickens, but there is not enough evidence to suggest they are silent amplifiers or reservoirs of disease. Wild species, such as cotton rats, opossums, gray foxes, bats, and wild birds, have been isolated as carriers of the virus in an outbreak, but again their role is unclear as amplifiers or maintainers of VEE.

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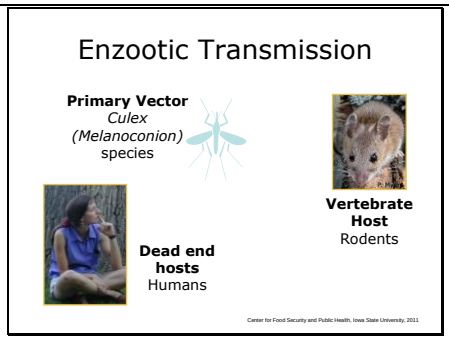

Enzootic transmission of VEE occurs between mosquitoes (primarily *Culex [Melanoconion]* species) and rodents who live in or near swamps and rain forests. Humans are dead-end hosts for VEE.

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DISEASE IN HUMANS

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VEE in Humans

- Incubation period: 1 to 6 days
- Usually acute, mild, systemic disease
- Clinical signs
  - Fever, chills, headache, myalgia
  - Coughing, vomiting, diarrhea
  - CNS signs
    - Encephalitis occurs in 4% of children
    - Less than 1% of symptomatic adults
- Death is rare

In humans, VEE is usually an acute, often mild, systemic illness. The clinical signs may include fever, chills, generalized malaise, severe headache, photophobia and myalgia particularly in the legs and lumbosacral region. Coughing, sore throat, nausea, vomiting and diarrhea may also be seen. Approximately 4% of children develop mild to severe encephalitis; neurologic disease occurs in less than 1% of symptomatic adults. VEE usually resolves within two weeks, with acute symptoms subsiding after 4 to 6 days, and deaths are rare.

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VEE in Humans

- Pregnant women
  - Fetal encephalitis, placental damage, abortion/stillbirth, congenital disease
- Diagnosis
  - Paired sera with rising titer
  - ELISA IgG or IgM
- Treatment
  - Supportive care
- No vaccine available

In pregnant women, this disease can affect the fetus; fetal encephalitis, placental damage, abortion/ stillbirth or severe congenital neurologic anomalies may be seen. Diagnosis is difficult but involves paired serum samples for rising antibody titer, or ELISA monitoring IgG or IgM. Treatment involves supportive care; there is no vaccine available.

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DISEASE IN ANIMALS

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VEE in Horses

- Incubation period: 1 to 5 days
- Horses most susceptible
  - Fever, anorexia, depression, flaccid lips, droopy eyelids and ears, incoordination, and blindness
  - Death 5 to 14 days after clinical onset
- Case-fatality rate: 50 to 90%
- In utero transmission results in abortion, stillbirth

Incubation period in animals is 1 to 5 days, and horses are the most susceptible to epidemic VEE viral infection. Clinical signs include fever, anorexia, depression, flaccid lips, droopy eyelids and ears, head pressing, circling, incoordination, and blindness. Death usually occurs 5 to 14 days after clinical onset, and case-fatality rate ranges from 50 to 90%. In utero transmission can occur, leading to dead or stillborn foals.

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VEE in Animals

- Most domestic animals do not show clinical signs or amplify the virus
- Experimentally
  - Infected rabbits and dogs die after inoculation
  - Laboratory animals susceptible
    - Act as sentinels
    - Guinea pigs, mice, hamsters
- Enzootic strains do not cause disease in animals

Most other domestic animals, including swine, cattle, and chickens, have not shown clinical signs after natural infection, but rabbits and dogs that were experimentally infected died shortly after inoculation. Laboratory animals vary in their response to the disease, but many are susceptible and act as sentinels for disease prevalence. While guinea pigs experience fever and fatalities without central nervous system signs, mice will experience meningoencephalomyelitis and death. Enzootic strains only cause disease in humans.

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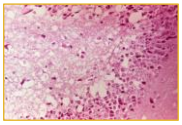
VEE in Animals

- Diagnosis
  - Virus isolation
  - Serology
    - Paired sera with rising titer
    - ELISA IgG or IgM
- Treatment
  - Supportive care
- Vaccine available for horses



VEE can be diagnosed by virus isolation or serology. VEE virus can often be recovered from the blood during the early, febrile stage of disease, but animals with neurologic signs are not usually viremic. Diagnosis is made via serial serum samples monitoring a rise in antibody titer, or by using ELISA for IgG or IgM. Because of the nature of the CNS signs, treatment involves supportive care. Prevention is a better option, and a vaccine is available in the U.S. for horses.

[Photo: A photomicrograph of mouse brain tissue after dying of Venezuelan encephalitis. It reveals neural necrosis and edema. Source: CDC Public Health Image Library]

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VEE as a Biological Weapon

- Aerosolized VEE
- Human and equine disease occur simultaneously
- Flu-like symptoms in humans
- Possible neurological signs in horses
- Large number of cases in a given geographic area

If a bioterrorism attack were to occur using a viral encephalitis agent, experts feel the most likely agent for weaponization would be Venezuelan equine encephalomyelitis virus. The virus particles would be aerosolized and disseminated, with human disease as the primary event. Equines would also be susceptible, but disease would most likely occur simultaneously, without animals acting as sentinels. Disease symptoms in humans would resemble the flu and be hard to distinguish, so basis of an outbreak would likely be a large number of sick individuals and horses in a given geographic area. Horses may or may not exhibit neurological signs, depending on how the virus was weaponized.

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PREVENTION AND CONTROL

Slide 23

Management of Mosquito-Borne Diseases

- Source reduction
- Surveillance
- Biological control
- Chemical control
  - Larvicide
  - Adulticide
- Educating the public
  - How to protect themselves

Prevention and control of mosquito-borne diseases involves source reduction, surveillance, biological control, chemical control (larvicides and adulticides), and educating the public on how to protect themselves.

[Photo: *Culeseta* mosquito. Source: Wikimedia Commons]

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Source Reduction

- Mosquito habitats
  - Make unavailable or unsuitable for egg laying and larval development
- Minimize irrigation and lawn watering
- Punch holes in old tires
- Fill tree holes with cement
- Clean bird baths, outside waterers, fountains

By trying to eliminate the source of mosquitoes, humans and animals can decrease their risk of exposure. Efforts should be concentrated on making habitats for egg laying and larval development unsuitable. Less irrigation should be utilized or ditches managed so that water does not sit undisturbed for more than 2 days. Other actions include punching holes in old tires to encourage drainage, filling tree holes with cement, and cleaning bird baths and outside animal waterers at least once a week.

[Photo: Domestic mosquitoes are often found breeding in old discarded tires. Source: CDC Public Health Image Library]

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Source Reduction Cont'd

- Drain or fill temporary pools with dirt
- Keep swimming pools treated and circulating
  - Avoid stagnant water
- Open marsh water management
  - Connect to deep water habitats and flood occasionally
  - Fish access

Further source reductions include draining or filling temporary pools with dirt and keeping swimming pools treated and circulating to avoid stagnant water; eliminating puddles in gutters, around faucets, air conditioners, and septic tanks; and managing open marshes by connecting mosquito areas and shallow ditches to deep water habitats that allow drainage or fish access.

[Photo: Domestic mosquitoes are seen here breeding in jars of rainwater. Source: CDC Public Health Image Library]

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Surveillance

- Mosquito trapping and testing for viral presence
- Record keeping
  - Weather data, mosquito larval populations, adult flight patterns
- Sentinel chicken flocks
  - Blood test and ELISA to monitor seroconversion

Many states and local governments utilize surveillance programs when there are established risk factors for human disease present. This may include mosquito trapping and testing for viral presence in a given area. When established mosquito larval and adult threshold populations are exceeded, control activities can be initiated. For example, heavy winter snow fall followed by heavy spring rains can lead to flooding and more standing water for mosquitoes to lay eggs upon. Seasonal weather patterns and historical records are kept to predict mosquito larval occurrence and adult flights. Instituting surveillance programs using sentinel chicken flocks and mosquito

trapping and testing are ways to monitor disease prevalence in a given area. Blood testing birds, either wild or young, unexposed chickens, and monitoring viral seroconversion or antibody titer allows authorities time to alert the general public if there is concern. These are common practices for EEE.

[Photo: Sentinel chicken flock. Source: Danelle Bickett-Weddle/CFSPH]

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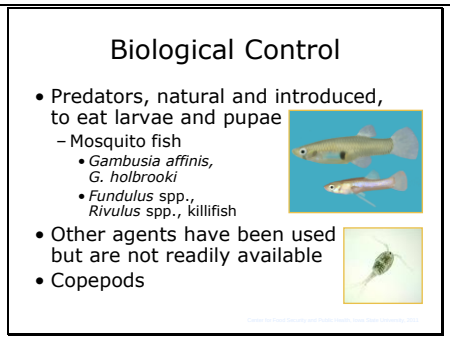

Biological control involves using different predators that eat mosquito larvae and pupae. The mosquito fish, *Gambusia affinis* and *G. holbrooki* are the most commonly used supplemental control because they are easily reared. They are indiscriminate feeders, though, and may eat other things, such as tadpoles, zooplankton, aquatic insects and other fish eggs. Some naturally occurring fish, such as *Fundulus* spp., *Rivulus* spp., and killifish, play an important role in controlling mosquitoes in open marsh water and rotational impoundment management. There are other agents, such as fungi, protozoa, and nematodes, that have been tried but are not readily available. A predacious copepod, *Mesocyclops longisetus*, preys on mosquito larvae and is a candidate for local rearing with *Paramecium* spp. for food. [Note: Copepods are tiny aquatic crustaceans (shrimp, crabs lobster, and relatives) that are widespread in both fresh and salt water habitats.]

[Photo: (Top) *Gambusia holbrooki* (Eastern mosquitofish). Source: Wikimedia Commons; (Bottom) Adult copepod. Source: University of Florida Extension at http://edis.ifas.ufl.edu/in490]

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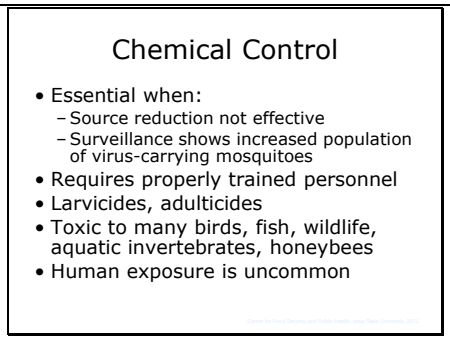

Chemical control is often warranted when source reduction is not enough and surveillance shows an increased population of virus-carrying mosquitoes. All insecticide use requires proper training by the personnel applying it, and can be targeted at the immature (larvicides) or adult (adulticides) mosquitoes. While it is limited, there is a risk of toxic effects on nontarget organisms, such as birds, fish, wildlife, aquatic vertebrates, and honeybees, so low levels of pesticide and proper training of applicators are used. Humans are often concerned with the use of chemicals, but low application rates, ultra low volume (ULV) methods, spraying at night while people are indoors, and notifying the public prior to application all decrease exposure risks.

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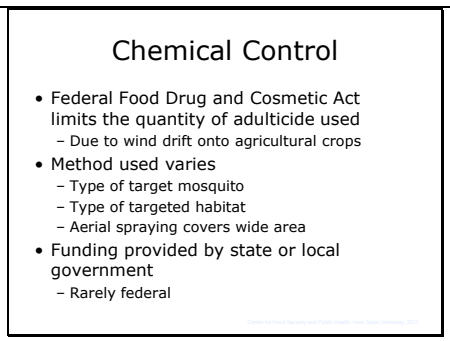

To further prevent human exposure, the Federal Food Drug and Cosmetic Act (FFDCA) limits the quantity of poisonous or deleterious substances added to food, specifically adulticides carried by wind drift over agricultural crops. The method selected depends on the type of mosquitoes that need to be controlled and the targeted habitat. Aerial spraying can cover a wide geographic area to control nuisance mosquitoes in emergency situations. Costs for such application are often covered by state or local emergency funds, and rarely by federal funds unless a natural disaster has occurred.

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Larvicides

- Use when source reduction and biological control not feasible
- More effective and target-specific
- Less controversial than adulticides
- Applied to smaller geographic areas
  - Larvae concentrate in specific locations

Larvicides are used when immature mosquito populations become larger than source reduction can manage or biological control can handle. They are often more effective and target-specific than adulticides, making them less controversial. They can be applied to smaller geographic areas than adulticides because larvae are often concentrated in specific locations, such as standing water.

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Larvicides

Name	Product (Larvae, Pupae, Adult)
Temephos	Abate (L)
Methoprene	Altosid (L)
Oils	BVA, Golden Bear (L, P)
Monomolecular film	Agnique (L, P)
Bacillus thuringiensis israelensis (BTI)	Aquabac, Bactimos, LarvX, Teknar, Dunks (L)
Bacillus sphaericus	VectoLex (L)
Pyrethrins	Pyrenone, Pyronyl (A, L)

This chart depicts the various types of larvicides used in the United States, with their chemical or biological name, as well as the commercial product name. There may be others on the market that this chart does not cover.

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Adulticides

- Necessary when other control measures unsuccessful
- Least efficient
- Proper type and time of application helps efficacy
  - Ultra low volume (ULV) foggers
    - 1 ounce per acre
  - Small droplets contact and kill adults

Despite the efforts listed in previous slides, there are times when the environment prevails or humans are unable to prevent large swarms of mosquitoes. Adulticide use then becomes necessary. It is often the least efficient control program, but ultra low volume spray either on the ground or aerially can reduce the population when the proper type and time of application is followed. Effective adult mosquito control with adulticides requires small droplets that drift through mosquito areas and come in contact with adults to kill them. Large droplets that settle on the ground or vegetation do not contact mosquitoes and may cause undesirable effects on nontargeted organisms. Insecticides are applied in a concentrated form at very low volumes, such as 1 oz (29.6 mL) per acre. Excessive wind and updrafts reduce control, but light wind is necessary for drifting spray droplets.

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Adulticides

Chemical Name	Product
Malathion	Fyfanon, Atrapa, Prentox
Naled	Dibrom, Trumpet
Fenthion	Batex
Permethrin	Permanone, AquaResilin, Biomist, Mosquito Beater
Resmethrin	Scourge
Sumithrin	Anvil

This chart displays the various types of chemicals used as adulticides, namely the organophosphates, malathion, and naled. Natural pyrethrins, fenthion, and synthetic pyrethroids, such as permethrin, resmethrin, and sumithrin, and their product names are also listed.

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Personal Protection

- Stay inside during the evening when mosquitoes are most active
- Wear long pants and sleeves
- Use mosquito repellent when necessary
  - Follow label directions
  - DEET
    - Do not use on pets

Humans can protect themselves in two ways: reduce contact with mosquitoes and reduce the population of infected mosquitoes in the environment. Personal protection involves reducing time outdoors in the early evening hours when mosquitoes are most active, wearing long pants and long sleeved shirts, and applying mosquito repellent containing DEET to exposed skin areas. DEET can be sprayed on clothing, but this is unnecessary because the underlying skin is protected from insect bites by the clothing. **DEET should not be used on pets.** [Photo: Applying mosquito repellant. Source: Radford Davis/CFSPH]

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Personal Protection

- Make sure window and door screens are "bug tight"
- Replace your outdoor lights with yellow "bug" lights
  - Bug zappers are not very effective
- ULV foggers for backyard use
- Keep vegetation and standing water in check around the dwelling

It is important to protect yourself by making sure mosquitoes cannot enter your home. Check window screens for holes and make sure they are bug tight so as not to allow entry. Replacing your outdoor lights with yellow bulbs decreases the attractiveness of many bugs to entry ways. Bug zappers are not specific to mosquitoes and are not much help with control. Ultra low volume foggers can be purchased for backyard use to decrease the mosquito population in the event that people will be outdoors during mosquito feeding hours. Keep vegetation and standing water in check around the dwelling to avoid larval habitats.

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Internet Resources

- CDC Division of Vector Borne Infectious Diseases-Arboviral Encephalitides
  - http://www.cdc.gov/ncidod/dvbid/arbor/

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Acknowledgments

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