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Study finds snakes in the wild harbor deadly mosquito-borne EEEV virus through hibernation

Research finds snakes play role in transmission cycle of Eastern Equine Encephalomyelitis Virus, one of the most lethal mosquito-borne viruses affecting horses and humans; opens door to strategy to counter spread of highly pathogenic virus

BURNESS COMMUNICATIONS

Deerfield, IL (October 1, 2012) Snakes in the wild serve as hosts for the deadly mosquito-borne Eastern equine encephalomyelitis Virus (EEEV), possibly acting as a "bridge" to the next season, according to researchers studying endemic areas in the Tuskegee National Forest in Alabama. This sets the stage for mosquitoes feeding on the infected snakes - primarily in the early spring - to become virus carriers. Scientists have been puzzled as to how the virus survived a harsh winter. With this new link established in the transmission cycle, a viable strategy to counter the virus may be at hand. The findings were published today online in the *American Journal of Tropical Medicine and Hygiene* and will be published in the December print issue.

While previous studies demonstrated that snakes experimentally infected with EEEV in laboratories could harbor the virus in their blood through hibernation, this is the first evidence documenting wild-caught snakes with EEEV already circulating in their blood. "This study confirms that the snakes carry the live virus across seasons," said study co-author Thomas R. Unnasch, Ph.D., of the University of South Florida's Global Health Infectious Disease Research Program. "So after hibernating all winter, when they emerge in the sun in the spring, they still have the virus in their blood ready to share with a new crop of mosquitoes which can then spread it on to other animals."

"Triple E is one of the most deadly viruses that's endemic to the United States and what this result allows us to do is to start thinking about early season interventions to basically eliminate the virus transmission early in the season and interrupt it before it gets going, before it will be a threat to human beings later on in the season," he said.

EEEV has been detected in Central, South and in North America, along the Atlantic and Gulf coasts of the U.S. as well as Michigan and Ohio. Most human cases have occurred in Florida, Georgia, New Jersey, New York and Massachusetts. Currently, in Massachusetts public health officials have confirmed that at least seven residents have contracted the virus commonly called "Triple E" (EEE) and two of them have died from the disease. The number of cases in the state alone has already reached the average number of EEE cases reported annually nationwide.

EEEV - Deadly to Horses and Humans

EEEV is transmitted through the bite of an infected mosquito. The virus can be passed to a wide range of animals including birds, reptiles, amphibians and mammals. But once infected, horses and humans appear to suffer the most adverse effects. For horses with EEE there's a 90 percent chance of death. And although there is a vaccine available, hundreds of horses go unvaccinated. According to the U.S. Department of Agriculture (USDA), on average 200 EEE horse cases were reported annually over the past five years. For humans EEE is rare, with approximately five to ten cases reported annually in the U.S., according to the Centers for Disease Control and Prevention (CDC). About 35% of the people who contract the disease will die and among those who survive, 35% will have long term severe neurological damage. In severe cases of the virus (involving encephalitis, an inflammation of the brain) symptoms include the sudden onset of headache, high fever, chills and vomiting. The illness may then progress into disorientation, seizures or coma. There is no cure for EEEV and care is based on symptoms. There is currently no vaccine approved for human use.

EEEV Breeding grounds

Freshwater hardwood swamps in the Northeast are hotbeds for EEEV and the virus is maintained through a cycle of *Culiseta melanura* mosquitoes which primarily get their blood meals from birds. As infection rates rise among more mosquitoes feeding on their avian hosts, the birds spread the virus rapidly and broadly but it takes a mosquito species (*Aedes*, *Coquillettidia* and *Culex*) capable of bridging the infection from infected birds to uninfected mammals for the virus to be transmitted.

Until now, the mystery of how the virus survived the winter has been an outstanding question because the virus has appeared in the same locations in several Northeastern U.S. states from year to year. "There are no mosquitoes there in the winter and not many birds and there's never been evidence that mosquitoes can carry the virus over the winter," Unnasch said.

Snake Wrangling

For their research for this study, scientists from the University of South Florida and Auburn University wrangled snakes for blood samples from an area in the Tuskegee National Forest where EEEV has circulated for years. They found that the infected snakes, mostly cottonmouths, hibernate the virus in their blood during winter. They also discovered that the virus in snakes peaked in April and September. Unnasch said when the major transmission agents, migratory birds, leave the area in the fall the mosquitoes turn to the snakes -- feeding through the eye membranes of the vipers, not their tough skin -- which is why infection rates peak in September. He added that there is no research on whether the virus can be transmitted by a snake bite, but they plan to use defanged snakes in their next experiments."

Prevention

Unnasch and his colleagues believe that the virus can be stopped before it becomes a threat. Further study could prove whether early season interventions could be really useful in eliminating infections in the summer, which may involve humans. "We'd like to test this experimentally by doing some early season insecticide treatments for mosquitoes in Florida," said Unnasch, adding that according to the CDC his home state has far more cases of Triple E virus than any other.

"This study not only offers insight into the ways to prevent the outbreaks of deadly mosquito-borne viruses like EEEV and West Nile Virus, it also provides a path toward finding cures and vaccines that will save lives and money," said James W. Kazura, MD, President of the American Society of Tropical Medicine and Hygiene, which publishes the journal, and director of the Center for Global Health and Diseases at Case Western Reserve University. "We must never forget that the lives of real people are at stake here. Each year, through the generosity of the Labell family, ASTMH's American Committee on Arthropod-Borne Viruses awards a \$2000 grant to a graduate student conducting research on EEEV or other mosquito-borne diseases in the name of their daughter, Kelly, a New Hampshire teenager who died tragically in 2005 from EEEV. This research is another step closer to preventing tragedy for another family."

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The study was supported by a grant from the National Institute of Allergy and Infectious Diseases.

About the American Society of Tropical Medicine and Hygiene

ASTMH, founded in 1903, is a worldwide organization of scientists, clinicians and program professionals whose mission is to promote global health through the prevention and control of infectious and other diseases that disproportionately afflict the global poor.

About the American Journal of Tropical Medicine and Hygiene

Continuously published since 1921, *AJTMH* is the peer-reviewed journal of the American Society of Tropical Medicine and Hygiene, and the world's leading voice in the fields of tropical medicine and global health. *AJTMH* disseminates new knowledge in fundamental, translational, clinical and public health sciences focusing on improving global health.

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Media Contact

Bridget DeSimone
301-280-5735
bdesimone@burnesscommunications.com

Preeti Singh
301-280-5722
psingh@burnesscommunications.com

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