Hemorrhagic Disease 2012 - One for the Record Books?

Based on early reports of suspected hemorrhagic disease (HD) activity, we recommended “increased vigilance for deer mortality due to HD” in the last issue of the SCWDS BRIEFS. From the HD samples we received for testing this year, it is apparent that our readers took this request to heart. This is an exceptional year for HD in both the eastern and midwestern United States, and 2012 may be one for the record books.

Our first HD case was confirmed on July 18th when we isolated epizootic hemorrhagic disease virus (EHDV) serotype-2 from samples from a white-tailed deer from North Carolina. So far this year, we have isolated and identified nearly 200 EHD and bluetongue (BT) viruses from wild ungulates in 27 states. The distribution of these isolates is shown on the map. All of the North American EHDV serotypes were isolated and all were widely distributed. All three EHDV subtypes were confirmed in deer in three states (Missouri, Indiana, and Michigan). We also isolated BTV-10,
-11, and -13, but only a few confirmed cases were observed.

As in previous years, most of the viruses isolated in 2012 were EHDV-2; however, this is the first year that EHDV-6 represented a predominant serotype. EHDV-6 was first detected in 2006 in Indiana and Illinois. It subsequently was detected in 2007 (Missouri), 2008 (Texas and Kansas), 2009 (Michigan), and 2010 (Arkansas) with 1-6 viruses isolated each year. During 2012, EHDV-6 clearly demonstrated that it is here to stay with over 50 isolations from 12 states. This serotype was the predominant virus that we isolated from deer in Arkansas, Florida, Louisiana, Michigan, and Wisconsin.

Two other observations related to HD activity in 2012 are noteworthy. As in 2007, much of the reported HD activity was in northern states that historically reported HD on rare occasions or not at all. Since 2007, we have confirmed recurring activity in many of these areas. For example, from 2007 to 2012, EHDV was isolated during most years in Michigan (4 years), Indiana (4 years), Pennsylvania (3 years), and New Jersey (4 years). The causes for this apparent northern expansion are not known, but this trend deserves future attention.

The second interesting observation relates to EHDV in cattle. During 2012, there were multiple cases of EHDV causing disease in cattle herds and other species, such as captive yaks in Colorado and alpacas in Pennsylvania. The details of these outbreaks are not fully characterized, but EHDV-2 was isolated in numerous cases. Disease associated with EHDV-2 has been reported in cattle during previous HD outbreaks, but it currently is not considered to be a significant cattle pathogen. As with the apparent range expansion of these viruses in the United States, the potential significance of EHDV infections in cattle deserves additional attention.

We are very grateful for the support and samples we receive from state wildlife and agriculture agencies throughout the country, as well as the information provided through the annual HD questionnaire. This annual surveillance would not be possible without your help, and we plan to continue this collaboration in the years to come. (Prepared by David Stallknecht and Jamie Phillips)

A Big Year for West Nile Virus

This fall marked the 13-year anniversary of the first detection of West Nile virus (WNV) in the United States. Human infections have occurred every year since then and reached their peak in 2003, when more than 9,000 cases were reported to the U.S. Centers for Disease Control and Prevention (CDC). However, CDC officials suggest that the number of human cases and deaths reported in 2012 could top the numbers reported in 2003.

Federal officials have said that the number of WNV cases reported through the last week in September in 2012 is the highest since 2003. Through November 27, 2012, there were 5,245 human cases reported, with 70% of them occurring in just eight states: California, Illinois, Louisiana, Michigan, Mississippi, Oklahoma, South Dakota, and Texas. In fact, Texas accounts for more than 1/3 of the country’s cases. There have been 236 fatal cases this year. In 2003, there were 264 deaths reported in the United States.

West Nile virus continues to be a cause of mortality in wild birds. The virus has been detected in 65,963 dead wild birds since 1999. During 2012, WNV has been found in 2,430 dead wild birds. This number is up from recent years (906 in 2011 and 700 in 2010) but is considerably lower than in 2003, when WNV was confirmed in more than 11,000 dead wild birds. The decreased number of WNV-positive dead wild birds since the 2003 transmission season most likely is due to a combination of factors including decreased funding for testing, shifting WNV surveillance priorities, apathy or complacency in reporting dead birds, decreased numbers of susceptible wild birds, and decreased media attention. The increase in numbers detected in 2012 compared to 2011 and 2010 probably is related to increased wild bird testing in response to the high numbers of human cases, as well as the increased coverage of WNV in the media.

The factors that facilitated the 2012 resurgence of WNV during the summer are unknown, and the high case numbers have taken a lot of health professionals and medical entomologists by surprise. It is possible that the extended drought and high temperatures over much of the United States created ideal conditions for mosquitoes and increased WNV transmission. This seems to
be counter intuitive because immature mosquitoes develop in aquatic environments. However, the drought may have brought the mosquitoes and the virus amplifying hosts (wild birds) together in higher concentrations at the limited available water sources, thereby increasing opportunities for virus transmission. Higher ambient temperatures may have resulted in a shorter time interval between the acquisition of WNV by the vectors and their ability to transmit WNV to other susceptible vertebrate hosts, including humans.

Because WNV and St. Louis encephalitis virus (endemic in many parts of the United States) have similar transmission cycles, it was thought that future WNV outbreaks would mirror what we see with St. Louis encephalitis virus: sporadic yearly activity and infrequent outbreaks that occur in a limited geographic area. Obviously, this has not been the case with WNV in 2012.

The CDC offers these suggestions for protecting yourself from WNV: Use mosquito repellent with DEET; dress in long pants and long sleeves; be especially careful at dusk and dawn; and drain any standing water, such as unused kiddie pools or bird baths, where mosquitoes like to breed. (Prepared by Danny Mead)

A New Tick-Borne Virus in Missouri?

In June 2009, two men from different locations in northwest Missouri were hospitalized after developing fever, fatigue, anorexia, and diarrhea. Both lived in areas with deciduous forest and agricultural fields, and both had removed one or more ticks from themselves in the week prior to becoming sick. Blood work done on both patients revealed leukopenia (low white blood cell counts), neutropenia (low neutrophils), thrombocytopenia (low platelets), and liver damage. Although the men recovered, they suffered fatigue, short-term memory deficits, and anorexia for weeks to months after 7-10 day hospitalizations.

Initially, physicians suspected these patients had ehrlichiosis, a tick-borne bacterial disease caused by *Ehrlichia chaffeensis* or *E. ewingii*, but both patients were culture- and PCR-negative for *Ehrlichia* and failed to respond to antibiotic therapy. However, a virus was isolated from the white blood cells of both patients, and genetic analysis indicated that the isolates represent a novel virus that has been named Heartland virus (for Heartland Regional Medical Center in St. Joseph, Missouri, where both patients were hospitalized).

Heartland virus is a member of the genus *Phlebovirus* in the family *Bunyaviridae*. The closest relative of Heartland virus is the severe fever with thrombocytopenia syndrome virus (SFTSV) that was identified recently in China. Similar to Heartland virus, SFTSV causes fever, thrombocytopenia, gastrointestinal signs, and leukopenia. However, SFTSV has a relatively high case fatality rate (12%) and some SFTSV patients developed blood clotting problems that were not observed in the two Heartland virus patients. Currently, Heartland virus and SFTSV are the only tick-borne phleboviruses known to infect humans. Because the symptoms of Heartland virus infection are vague and are similar to ehrlichiosis, additional human cases may have gone undiagnosed.

The lone star tick (*Amblyomma americanum*) is a common tick that feeds on people and is found throughout Missouri in high densities. The lone star tick is one of the most common ticks in the southeastern United States, and in recent years it has increased its range into the upper Midwest and Northeast. All three mobile stages of the lone star tick feed on white-tailed deer, the primary host; however, the ticks will feed on a wide range of wildlife (e.g., turkeys, raccoons, coyotes, fox) and domestic animals (e.g., dogs, cats, horses, and cattle). Lone star ticks can transmit many zoonotic agents including the causative agents of ehrlichiosis (*E. chaffeensis*, *E. ewingii*, and the *Ehrlichia* sp. that causes Panola Mountain ehrlichiosis), as well as *Francisella tularensis* (tularemia), *Rickettsia* spp., and possibly an unknown pathogen that is thought to cause a Lyme disease-like illness called southern tick-associated rash illness (STARI).

Currently, there is no commercially available test to diagnose Heartland virus; however, infection should be considered in patients with suspected ehrlichiosis, especially those that fail to respond to antibiotic treatment. Increased awareness among physicians and diagnostic testing may result in increased case reports. Surveys for potential vectors and reservoir hosts of this newly recognized virus are underway. (Prepared by Laura Martin, College of Veterinary Medicine and Biomedical Sciences, Colorado State University)
EEE Virus in 2012

Although summer has come and gone, the numbers of mosquito-borne disease cases continue to rise in humans and equines. West Nile virus is not the only mosquito-borne virus causing disease and deaths in humans and animals in the United States. One we typically hear little about in the Southeast is eastern equine encephalitis virus (EEEV), because it is a relatively rare cause of human disease. Through November, there have been 12 human and 212 equine cases confirmed this year in the United States. Both of these numbers represent increases over the long term averages of annual human and equine cases.

The EEE virus is an Alphavirus in the Togaviridae family. It first was isolated from infected horse brains in 1933, and the first confirmed human cases were identified in 1938, when thirty children died of encephalitis in the northeastern United States. Although most persons (<10%) infected with EEEV show no signs or symptoms, the development of clinical neurological disease can be deadly: In humans the fatality rate in clinical cases is approximately 33% and permanent brain damage may occur in those who survive. In non-vaccinated horses, the case fatality rate approaches 90%.

The EEE virus is maintained through a wild bird-mosquito cycle. The primary endemic vector, Culiseta melanura, typically is found near freshwater, hardwood swamps; however, this species is not considered an important vector of EEEV for humans or horses, because it feeds almost exclusively on birds. Transmission from infected birds to uninfected mammals requires "bridge" vectors, such as some mosquito species in the Aedes, Coquillettidia, and Culex genera. Infected horses and humans do not develop a level of viremia sufficient for infecting additional mosquitoes.

The historic distribution of EEEV was restricted to states along the Atlantic and Gulf coasts. However, the current distribution now includes regions in the upper midwestern states of Indiana, Michigan and Wisconsin. The geographic distribution and risk of exposure to EEEV vary from year-to-year with changes in the distribution of the insect vectors and wild avian reservoirs important in the ecology of the virus. In the United States, human infections due to EEEV usually are sporadic, with low numbers of cases reported each summer.

In Georgia, EEEV is endemic and SCWDS routinely detects the virus in samples that are submitted by local agencies for mosquito-borne virus testing. We also detect EEEV in clinical cases submitted to our diagnostic service by our cooperating states. In 2005, we reported the first fatal case of EEEV infection in white-tailed deer (SCWDS BRIEFS Vol. 21, No. 3).

Although there is no specific treatment for EEEV infection, there are things you can do to protect your horses and yourself. Vaccinate susceptible animals, avoid being outside in the morning and evening when mosquitoes are most active, use mosquito repellent, drain standing water where mosquitoes breed, and wear clothing that covers the majority of your skin. (Prepared by Danny Mead)

Hantavirus Outbreak – Yosemite National Park

An outbreak of hantavirus infection in campers visiting Yosemite National Park in California this past summer caught the nation by surprise. On August 19, the California Department of Public Health first reported two cases of hantavirus in campers that had recently visited Yosemite National Park, and an additional case quickly prompted the National Park Service to publish a notice of the outbreak on August 27. The highly publicized outbreak, involving ten cases and three deaths as of November 5, has many again concerned about this emerging infectious disease. Hantavirus was first identified in the United States in 1993 when Sin Nombre virus caused an outbreak of rapidly progressing respiratory illness in persons in the Four Corners region in the Southwest. However, hantaviruses have been found in nearly every corner of the globe. Hantaviruses are RNA viruses belonging to the family Bunyaviridae. Rodents are the primary reservoirs of hantaviruses. There are many strains of hantavirus throughout the world, and most strains are uniquely adapted to a single rodent reservoir species. Hantavirus strains in the Eastern hemisphere, often referred to as the Old World hantaviruses, are numerous and include Puumala virus in bank voles and Seoul virus in
Hantavirus infections in their rodent hosts are asymptomatic and are maintained in reservoir populations through inhalation of infectious virus from aerosolized urine or feces, or through bite wounds. Rodent hosts remain infected for the duration of their lives, and may intermittently shed virus.

Risk factors for human hantavirus infection include activities that expose people to rodents and their excrement, because human infections result from inhalation of infectious aerosols from rodent urine and feces. The majority of Sin Nombre virus cases in the United States occur in rural areas where contact with rodents may be increased, and cases frequently are linked to activities like farming, cleaning rodent-infested dwellings, and rodent trapping. Rodents living in close quarters with humans also pose a significant risk.

Many rodent populations experience cyclical fluctuations in population density, and these trends often correlate with infection rates. Climatic events, particularly those leading to years of abundant host food resources, are closely tied to reservoir abundance and infection rates. Other investigations have demonstrated an effect of species diversity and habitat disturbance on hantavirus prevalence in rodent hosts. Reservoirs of hantaviruses, like deer mice and Norway rats, often are generalist species that thrive in disturbed environments where species diversity is lower.

The hantavirus outbreak in campers visiting the Yosemite National Park in 2012 likely occurred due to an unfortunate confluence of factors favoring transmission, including abundant food resources and a dense host population leading to an active infestation of the well-insulated Curry Village tent cabins. The CDC is working closely with the National Park Service to identify and notify those who may have been exposed and to educate visitors about the risk of hantavirus. The tent cabins at Curry Village have been closed indefinitely.

This outbreak is a powerful reminder to us that hantaviruses and other zoonotic disease agents exist in our environment, even when we do not see evidence of their presence. As we try to better understand the factors that drive hantavirus
infection and try to develop novel interventions to prevent infection and diminish the effects of this disease, we should remember that proper cleaning and disinfection can remove many disease agents from our environment. More information on preventing hantavirus exposure can be found at [http://www.cdc.gov/hantavirus/hps/prevention.html](http://www.cdc.gov/hantavirus/hps/prevention.html) (Prepared by Betsy Elsmo, School of Veterinary Medicine, University of Wisconsin)

**Zebra Virus in Polar Bears**

In 2010, two polar bears at the Wuppertal Zoo in Germany, suffered from seizures. One bear died and was diagnosed with moderate to severe encephalitis on postmortem examination. The other bear recovered with veterinary care. Researchers suspected a viral etiology and polymerase chain reaction (PCR) analysis of affected tissues identified a virus that was most closely related to equine herpesvirus 1 (EHV-1), a virus that affects equids. Through genetic sequencing, researchers determined that the virus was a novel recombination of EHV-1 and EHV-9, a closely related herpesvirus thought to have originated in the plains zebra.

Equine herpesviruses have crossed the species barrier previously. In fact, EHV-9 was discovered when it caused fatal encephalitis in seven gazelles at a Japanese zoo in 1993. Investigators there isolated a previously unknown strain of EHV that was serologically related to EHV-1, but was morphologically and clinically distinct. Zebras housed in a nearby enclosure were identified as the likely source of the infection and the reservoir for the newly described EHV-9. A similar scenario occurred at the San Diego Zoo in 2007, when a polar bear was euthanized due to neurologic signs and EHV-9 was confirmed as the cause. Zebras in an adjacent enclosure were carrying an identical strain of EHV-9, and two had clinical respiratory disease. In 2009, four black bears at one zoo and two gazelles and 18 guinea pigs at another zoo contracted EHV-1 and either died from the disease or were euthanized.

These reports highlight that, while many viruses only infect or cause disease in single or closely related species, these “species barriers” are not necessarily insurmountable. Many factors may slow or stop the evolution of viruses that allows them to jump species. These barriers include behavioral, temporal, or geographic differences that limit interspecies contact. A species may actually be susceptible to infection, but may never come in contact with that virus. Zoos may create conditions in which animals that may not interact in the wild are brought into close proximity to one another, effectively removing one or more of the above barriers.

The possible effects of the novel EHV-1 on other animals is unknown at this time. However, the broader implications are that infection control strategies in artificial environments, such as zoos and menageries, should address the potential for pathogen transmission across species barriers. These strategies should aim to prevent spill-over to captive or free-ranging wild and domestic species, as well as to humans, that may have contact with these captive facilities. Infection control measures may include development and implementation of effective surveillance and outbreak containment protocols, as well as appropriate biosecurity practices and risk mitigating protocols that are based on the results of research and models predicting the potential for cross-species transmission. (Prepared by Annelie Crook, Western College of Veterinary Medicine, University of Saskatchewan)

**A New Virus in Australian Bats**

Researchers from the Australian Animal Health Laboratory and the Queensland Center for Emerging Infectious Diseases have isolated a novel paramyxovirus virus tentatively named Cedar virus. The virus was found during surveillance of fruit bats, and it bears remarkable similarity to Hendra and Nipah viruses, which have been associated with fatal disease in humans and domestic animals in Australia and southeastern Asia, respectively. In contrast to these two highly pathogenic viruses, Cedar virus does not appear to cause observable signs of disease.

Hendra virus, first identified in 1994 in Australia, causes low morbidity but high mortality in horses, and resulted in the deaths of four out of seven infected humans. Nipah virus, which was found four years later in Malaysia, causes high morbidity and low mortality in pigs, but has infected thousands of humans with mortality rates ranging from 40% to 75%. In response to the Nipah virus epidemic, Malaysian authorities ordered the slaughter of approximately 1.1 million pigs at a
cost of several million dollars. Because of their deadly and transmissible nature, Hendra and Nipah viruses are classified as biosafety level (BSL)-4 agents. This classification makes experimental studies difficult and costly, because there are few facilities in which BSL-4 research can be conducted.

Fruit bats of the genus *Pteropus* are the reservoirs for Hendra, Nipah, and Cedar viruses, and routine surveillance is conducted to monitor prevalence. Transmission of Hendra and Nipah viruses is presumed to occur from bats to domestic animals to humans, with human cases often leading to encephalitis, coma, and death. Bats in colonial roosting sites in Asia number into the hundreds of thousands and may forage large distances from these sites. Habitat loss and intensive agricultural practices have compounded the public health risks by increasing opportunities for contact between infected bats, domestic animals, and humans. The public is indifferent to fruit bats in Australia, but they are regarded as pests and are hunted for sport in Malaysia and much of Asia.

The Cedar virus is genetically similar to Hendra and Nipah viruses, but apparently lacks the sequences that encode a protein that is used by other paramyxoviruses to evade the innate immune system. Ferrets and guinea pigs were experimentally inoculated with Cedar virus. Although viral replication and neutralizing antibody production were documented, the animals did not develop clinical disease, as occurs in both species when they are experimentally infected with Hendra and Nipah viruses. The apparently avirulent nature of Cedar virus has resulted in its classification as a BSL-2 agent, which requires much less stringent requirements for experimental work than BSL-4 agents. This classification and the similarity of Cedar virus to the other henipaviruses suggest it could potentially be developed as a useful model for studying the more lethal Hendra and Nipah infections.

Species of the *Henipavirus* genus, now including Cedar virus, Hendra virus, and Nipah virus, are considered emerging infectious disease agents with zoonotic potential. The ecology of their fruit bat reservoirs, combined with increasing interactions between bats, humans, and domestic animals, have facilitated several fatal Hendra and Nipah outbreaks among humans and animals, and have implicated these two viruses as a serious public health concern.

Researchers investigating how Hendra and Nipah viruses spread from domestic animals to humans and why they are so virulent, but progress is slow because of the dangerous nature of these studies. However, with the discovery of the apparently innocuous Cedar virus, an opportunity arises to develop a safe model for *Henipavirus* research, perhaps leading to vaccines or antiviral therapies that could prevent future outbreaks and save lives. (Prepared by Zach Chillig, College of Veterinary Medicine, The University of Georgia)
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Information on SCWDS and recent back issues of the SCWDS BRIEFS can be accessed on the internet at www.scwds.org. If you prefer to read the BRIEFS online, just send an email to Jeanenne Brewton (brewton@uga.edu) or Michael Yabsley (myabsley@uga.edu) and you will be informed each quarter when the latest issue is available.