WEST NILE VIRUS

Animal Group(s) Affected	Transmission	Clinical Signs	Severity	Treatment	Prevention and Control	Zoonotic
Avian Equids Squirrels Other mammals, Alligators	Primarily via mosquito bite, possibly ticks; less efficient means include ingestion of virus via infected carcasses or contaminated fluids (feces, urine, oral or cloacal); occupational exposure, blood transfusion, organ transplant, and maternal transmission	Range: asymptomatic to non-specific (e.g., anorexia, weight loss, dehydration) to neurologic (e.g., ataxia, lethargy, paresis, paralysis, convulsions, seizures, death)	High fatality in some avian species (especially corvids and some raptors); 10-30% of equine clinical cases are fatal; <1% of human cases are severe (i.e., West Nile neuroinvasive disease)	Supportive care, immunoglobulin therapy	Mosquito control; avoiding mosquito bites (repellant, screens, clothing, staying indoors at dawn and dusk); vaccination licensed for horses	Yes

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Susceptible animal groups: Many avian species serve as amplifying hosts for WNV. American robins, house finches, house sparrows, and other species are considered high amplification hosts due to high proportions of WNV-positive mosquito blood meals. Several species of mammals (squirrels, chipmunks, and rabbits), a reptile (alligators), and an amphibian (lake frogs) may also serve as amplifying hosts for West Nile virus (WNV), although viremia titers are relatively low in these species as compared to birds, and the duration of infectious viremia is short (e.g., approximately 1 day). Most mammals are incidental (i.e., dead-end) hosts.

WNV has been reported in at least 326 species of birds in North America and over 1,300 avian species worldwide. All bird species are likely susceptible to WNV infection, although most infections are likely subclinical. North American birds that are of particularly high susceptibility to WNV-associated morbidity and mortality are the American crow as well as other corvids (e.g., blue jays, black- and yellow-billed magpies, fish crows, and others), and to a lesser extent, other passerine species (e.g., common grackles, house sparrows, house finches), as well as raptors (owls, eagles, falcons, hawks). Species of special concern due to apparently high rates of susceptibility and conservation status include California condors, Florida scrub jays, greater sage grouse, and native Hawaiian birds. High rates of death were observed in free-ranging, juvenile American white pelicans in nesting colonies, captive lesser scaup ducklings, and experimentally-infected and free-ranging greater sage grouse. Other birds have been documented with WNV infection, including flamingos, penguins, emus, wild turkeys, cormorants, bronze-winged ducks, sandhill cranes, common coots, and red-legged partridges, and others. A variety of psittacine species housed in outdoor aviaries, many of which were of Australian origin, had clinical WNV disease. Reports of WNV disease and death in New World psittacines are

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relatively rare.
WNV-associated disease in mammals is most severe in equids and can also be significant in squirrels. It has rarely been reported in alpacas, sheep, reindeer, harbor seals, Indian rhinoceroses, a polar bear, a wolf and several domestic canids, a Barbary macaque, white-tailed deer and a killer whale. Antibodies to WNV have been detected in a variety of mammals including cattle, dogs, cats, goats, rabbits, raccoons, Virginia opossums, coyotes, striped skunks, bats, black bears, wild boar, red foxes and killer whales, indicating prior infection.
Some reptiles and amphibians are susceptible to experimental infection, including the American alligator, Nile crocodile, green iguana, crocodile monitor, garter snake, various chelonians, lake frog and North American bullfrog. Among these, alligators had clinical (neurologic) signs.
Very young and old animals are likely most susceptible.

Causative organism: West Nile virus is a single-stranded, enveloped, RNA virus of the Japanese Encephalitis antigenic group, genus *Flavivirus* and Family Flaviviridae. It is an arthropod-borne virus ("arbovirus") transmitted by mosquitoes. *Culex* spp. and *Aedes* spp. are primary vector species. *Culex pipiens*, in particular, is an important bridge vector from avian hosts to humans.

Zoonotic potential: Yes. Transmission to humans is predominantly via mosquito bite but risk is also present during handling tissues and fluids, as transmission can occur via inhalation, mucous membrane contact, open cuts and puncture wounds from a needle stick or contaminated equipment. Gloves should be worn when handling suspect animals and bedding.

Distribution: Worldwide

Incubation period: Approximately 3-15 days in horses, 2-14 days in humans, and 4-14 days in birds. Some birds become detectably viremic by 1 day post-inoculation.

Clinical signs:
People**:** The majority of infected people are asymptomatic, although some have mild, non-specific symptoms ("West Nile fever," involving fever, headache, fatigue and/or myalgia/arthralgia; skin rash is also possible), and rarely (<1% of those diagnosed with WNV) experience severe, neurological symptoms ("West Nile neuroinvasive disease," involving encephalitis, meningitis, and/or paralysis), leading to death in geriatric patients.
Birds**:** Clinical signs vary and can include depression, ruffled feathers, anorexia, rapid weight loss, decreased activity to lethargy, torticollis, opisthotonos, nystagmus, ataxia, diarrhea, nasal discharge, drooping wings, labored breathing, and sudden death. Most affected birds deteriorate rapidly following the onset of clinical signs; however, there are several reports of captive birds exhibiting clinical signs for weeks or months.
Equids*:* About 10% of horses develop clinical disease that may include anorexia, depression, ataxia, paresis, paralysis, teeth grinding, aimless wandering, convulsions, circling, tremors of facial and neck muscles, cranial nerve deficits, difficulty swallowing, hyperesthesia, apprehension, hyperexcitability, facial edema, coma, impaired vision, conjunctivitis, abdominal pain, colic, urinary dysfunction, fever, and head pressing. Injuries and secondary pulmonary infections due to prolonged recumbency can also occur. Horses that recover usually show improvement within 7 days of onset of signs. About 10-20 % of recovered horses have residual effects, such as neurologic deficits.
Squirrels**:** Head tilt, tremors, paralysis, and ataxia.
Reptiles (alligators): Anorexia, weakness, tremors, slow reflexes, heat tilt, anisocoria, opisthotonos, circling, and lymphohistiocytic proliferative cutaneous lesions.

Post mortem, gross, or histologic findings: Lesions are variable among species and there or no pathognomonic findings.
Birds**:** Gross lesions are often absent, but can be non-specific, including white-tan mottling or streaking of the myocardium, splenomegaly, congested cerebral vessels, and poor nutritional condition. Histologic lesions can be minimal to severe, and can include heterophilic to lymphoplasmacytic myocarditis, encephalitis,

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ganglionitis, hepatitis, and nephritis. Vasculitis can also occur.
Equids**:** Gross lesions are usually absent. When gross lesions are present, they are most often in the CNS: submeningeal edema and hemorrhage of spinal cord, brain stem, and midbrain. Histologic findings: nonsuppurative encephalitis or encephalomyelitis.
Squirrels**:** No gross lesions. Histologic findings: lymphoplasmacytic encephalitis or meningoencephalitis with multifocal microglial nodules, perivascular and meningeal infiltrates of neutrophils, neuronal necrosis, and neuronophagia.
Other mammals*:* Few reports of gross lesions. Histologic lesions similar to equids.
Reptiles**:** Fluid in coelomic cavity; mottled enlarged liver, spleen, and myocardium. Intracellular heterophilic infiltrates in epithelial cells and cellular necrosis.

Diagnosis
Serology**:** Increase in WNV-specific antibodies in acute and convalescent sera, IgM in CSF, or IgM in serum (suggestive). ELISA, with confirmation of results by plaque reduction neutralization test.
Virus isolation, or antigen or RNA detection: Infectious virus (virus isolation) or viral components can be detected in serum, CSF, tissues (brain, heart, kidneys and spleen), oral/cloacal swabs, and/or urine of some animals. The period in which virus can be detected in live animals is limited, and can be especially difficult in animals with low viremia titers (e.g., horses). RT-PCR can be more sensitive than virus isolation.

Material required for laboratory analysis: Bodily fluids such as blood (centrifuged for separation of serum or plasma), CSF, urine, saliva, or swabs of body cavities (oropharyngeal or cloacal cavities, rectum), or tissues (heart, kidney, and spleen have been consistently useful for virus isolation and PCR testing in birds and can also be useful for immunohistochemistry [IHC] in birds); feather pulp, nonvascular feathers, brain, eye, spinal cord, liver, and others; tissues can be pooled to possibly increase sensitivity. Testing maggots from carcasses for RNA may be useful in decomposed birds.

Relevant diagnostic laboratories: Most state public health laboratories conduct WNV testing; however, virus isolation and plaque reduction neutralization tests are time and labor intensive and require BSL-3 conditions.

Arbovirus Diagnostic Laboratory, DRA
CDC/DVBID/ADB
3150 Rampart Road
Fort Collins, C0 80521
Phone: (970) 221-6445
http://www.cdc.gov/ncidod/dvbid/misc/arboviral_shipping.htm

Formalin-fixed specimens for immunohistochemistry:
Infectious Disease Pathology Activity
CDC (MS-G32)
1600 Clifton Rd, NE
Atlanta, GA 30333
Phone: 1-800-232-4636

National Wildlife Health Center, USGS
6006 Schroeder Road
Madison, Wisconsin 53711
Phone: (608) 270-2400 Fax: (608) 270-2415

Treatment: Supportive care (i.e., fluids, nutrition, heat or cold) can be provided with the goal of reducing CNS inflammation, preventing injuries, minimizing the effects of prolonged recumbency, and nursing the

animal beyond the severe morbidity that can occur. Morbid birds and horses can have neurologic deficits that range from ataxia to paralysis and seizures, and therefore, padded caging may be necessary to prevent further injury. Long-term (i.e., up to several years) neurologic defects have been observed in some raptors following WNV infection. Immunoglobulin therapy has been used in horses (serum based, Novartis Animal Health and a plasma based product, Lake Immunogenics, Inc.). L-lysine supplement and homeopathic treatments have been used with some success in raptors. Mild cases may resolve without treatment.

Prevention and control: Mosquito control measures should be implemented: screened housing, fans, repellants (10% DEET), avoiding stagnant water, larvicides, and stocking mosquito fish in ponds. Insect repellants listed by the CDC as being EPA-registered and providing long-lasting protection include: DEET, picaridin, natural or synthetic oil of lemon eucalyptus and IR3535 (3-[N-Butyl-N-acetyl]-aminopropionic acid, ethyl ester). Isolation of infected individuals and quarantine of new animals is recommended. Avoid feeding potentially contaminated meat/carcasses.

Four vaccines were developed for use in horses: a killed vaccine (West Nile-Innovator® DNA vaccine, Fort Dodge Animal Health), a recombinant vaccine in a canarypox vector (Recombitek®, Merial Animal Health), a flavivirus chimera vaccine (Equi-Nile™, Intervet), and a recombinant DNA plasmid-pCBWN (CDC/Fort Dodge Animal Health-not yet licensed). Many zoological facilities vaccinate equids and sensitive avian species with available vaccines.

Extra-label use of vaccines or use of vaccines that have not been adequately assessed in the target animal (i.e., controlled challenge studies) should be used with caution and not assumed to be protective. Numerous vaccines have been tested to various degrees in birds (some without challenge) with varied responses. Flamingoes failed to seroconvert after a single vaccination with the killed product. A modified live vaccine was tested in domestic geese in Israel with 75-94% protection. The killed equine vaccine, DNA plasmid vaccine, and recombinant equine vaccine provided partial protection in island scrub jays. Some red-tailed hawks vaccinated with a DNA-plasmid vaccine had partial protection while American robins and California condors vaccinated with the same vaccine seroconverted. Results were variable among adult and juvenile thick-billed parrots vaccinated with the killed equine vaccine. Seroconversion occurred in some penguins following administration of DNA plasmid and killed vaccines. A DNA plasmid vaccine failed to protect greater sage grouse from mortality. Oral vaccines in fish crows were ineffective. The Recombitek vaccine was immunogenic in rhinos.

Suggested disinfectant for housing facilities: As an enveloped virus, WNV does not persist for long periods in the environment. 70% ethanol and bleach are sufficient for general cleaning. Viricides such as Virkon® are highly effective when concern is high but can be damaging to skin and mucus membranes.

Notification: Certain states require veterinary cases to be reported to the state animal health authority.

Measures required under the Animal Disease Surveillance Plan: Laboratory-confirmed positive cases in humans, horses, other mammals, birds and mosquitoes from across the United States are collected by ArboNET (Centers for Disease Control and Prevenation; http://www.cdc.gov/ncidod/dvbid/westnile/usgs_frame.html). Equine cases are usually determined from passive reporting from private practitioners and diagnostic submissions.

Measures required for introducing virus to infected animals: WNV has been spread horizontally shortly after experimental inoculation in some birds that were housed in close captive quarters, as well as in the American alligator. Infected individuals should be isolated. Viremia usually wanes 5-10 days in birds and up to 14 days in alligators. However, experimental infection in hamsters resulted in urine viral shedding for over 300 days and infectious virus persisted in tissues of house sparrows for up to 43 days. Antibodies persist in some previously infected birds for years to life-long.

Conditions for restoring disease-free status after an outbreak: WNV is firmly established in avian and mosquito populations worldwide. The virus is endemic and transmission is reinitiated annually in the summer within temperate areas of North America and Europe. Therefore, animals housed outdoors in endemic or at-risk

areas will be at a continual risk. Seasonal and climatic factors may precipitate outbreaks of disease in wildlife (i.e., wild birds) that may spillover into captive populations and humans. Proper disinfection of housing facilities and equipment after an outbreak is necessary.

Experts who may be consulted:

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