Lesson S03: PreAnesthetic Assessment of the Patient Infected With West Nile Virus

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Needs assessment

The West Nile Virus (WNV), endemic in Africa, was first isolated in the United States in 1999 when a cluster of encephalitis cases were identified in New York City. Seven deaths were reported in the region. Active surveillance for human cases and infected birds has been established throughout the United States. Such information enables rapid identification of localities susceptible to outbreaks and implementation of effective control measures. The virus causes encephalitis which may result in hysteria. Anesthetists should be aware of the clinical presentation of this disease and potential complications in patient management.

Objectives

At the end of the lesson, the participant will be able to:

1. Identify vertebrate hosts for WNV.
2. Describe the life cycle of WNV in the mosquito.
3. List geographic locations for WNV infection.
4. Describe the symptoms of encephalitis.
5. Compare commonly used repellents.
6. Inform patients about prevention techniques.
7. Define WNV infection.
8. List the differential diagnoses.
9. Discuss the pharmacology of DEET.
10. List public health measures to control WNV infection.
11. Discuss the likelihood of WNV transmission, morbidity and mortality.
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Case Presentation

An elderly man was brought into the emergency room of an inner city hospital during a period of warm and humid weather. He had been found wandering in a park near a river where he regularly sought shelter under a bridge. He was disoriented to time and place. He was unkempt, severely undernourished and had been reportedly behaving “funny” for a few days. Physical examination revealed several insect bite marks on his arms and legs and a gangrenous left foot for which a surgical consultant recommended disarticulation. Shortly after admission, the patient vomited and became unresponsive.

History of West Nile Virus Infection

The West Nile virus (WNV) was first isolated in 1937 from a woman in the West Nile district of Uganda. Closer examination of the relationship between the organism and the environment was performed in Egypt in the 1950’s. In 1957, WNV was isolated as the cause of an outbreak of severe meningoencephalitis in elderly patients in Israel. Transmission to horses was identified in Egypt and France in the early 1960’s. The virus has been isolated in Africa, Europe and the Middle East, as well as in western and central Asia. Outbreaks of WNV encephalitis in humans have been recorded in Algeria in 1994, in Romania in 1996-1997, the Czech Republic in 1997, the Congo in 1998 and Russia in 1999. Major breakouts were recorded in horses in Morocco in 1996 and in Italy in 1998. The virus was first identified in the United States in 1999 as the cause of encephalitis in both humans and in horses. There were seven human deaths recorded and 62 cases of severe human encephalitis. The virus spread rapidly across the US with human disease documented in 39 states and the District of Columbia by 2003. Equine disease was first identified in Long Island, NY - eastern New York - and spread throughout the country.

Definition and Causation

West Nile virus is part of the group of flaviviruses that also includes the causative organisms of St Louis encephalitis, dengue, Japanese encephalitis, tick borne encephalitis and yellow fever. The viruses all share a common size (40-60nm), symmetry (enveloped, icosahedral nucleocapsid), nucleic acid (positive-sense, single stranded RNA, approximately 10,000-11,000 bases) and appearance in the electron microscope. The virus found in New York was initially identified as being genetically related to WNV (West Nile–like virus). Subsequent genetic sequencing positively identified the virus as WNV.

Arthropod-borne viruses, or arboviruses such as WNV, perpetuate by transmission to non-human vertebrate hosts through the blood feeding habits of arthropods (e.g., mosquitoes, sand flies, ticks, and ceratopogonids). All arboviral encephalitides are zoonotic with a complex life cycle involving a non-human primary vertebrate host and a primary arthropod vector. Humans are not an integral part of the life cycle. They become incidental targets when human populations encroach on natural reservoirs of infection or when the virus is inadvertently carried to human populations by a secondary vector.

West Nile virus multiplies by ongoing transmission between adult mosquito vectors feeding on the blood of bird reservoir hosts. The cycle begins when infected mosquitoes carrying the virus in their salivary glands inject the virus into susceptible birds while acquiring blood. The injected bird becomes a reservoir of infection and can sustain an infectious viremia for 1 - 4 days after exposure. New mosquito vectors feed on viremic host birds and acquire the virus in their blood meal. Following an
incubation period of 10 – 14 days, the virus is stored in the salivary glands of the mosquito and may be readily transmitted to other susceptible hosts to create additional reservoirs of infection.

![West Nile Virus Transmission Cycle](image)

**Fig. 1: West Nile Virus Transmission Cycle. From CDC Division of Vector-Borne Infectious Diseases**

Crows are most commonly infected, although 20 native bird species in the United States and bats have tested positive for virus by reverse transcriptase-polymerase chain reaction. Wild birds and domestic geese can die or become ill. Humans are not effective reservoirs of infection because levels of viremia are low-grade and transient.

**Role of the Mosquito in Causation of WNV**

Mosquitoes are two-winged insects that belong to the order of Diptera and are ubiquitous throughout the world with the exception of polar environments such as Antarctica. Bites to humans are usually from insects of the genera *Anopheles*, *Culex* and *Aedes*. In North America, there are about 170 species of mosquitoes. The *Culex* species – primarily responsible for transmission of WNV - can survive through the winter in the adult stage.

Two hundred and ten isolates of WNV were obtained from 17 mosquito species in six genera in statewide surveillance conducted in Connecticut from June through October, 1999-2003. The most likely vectors of WNV were identified as *Culex pipiens* (86), *Culex salinarius* (32), *Culex restuans* (26), *Culiseta melanura* (32), and *Aedes vexans* (12). *Culex pipiens* was isolated from July through September and is probably involved in early season enzootic transmission and late season epizootic amplification of the virus in wild bird populations. The prevalence of *Culex restuans* in June and July and isolates of WNV in early July suggest that this species may play an important role as an enzootic vector involved in early amplification of WNV virus among wild birds. Its involvement as a bridge vector to humans is unlikely. *Culex salinarius* was the most frequently captured *Culex* species and was
found mainly in August and September when virus activity was highest. Frequent isolations of WNV from this species in September when the majority of human cases were reported, combined with its abundance at this time of the year, demonstrates vector competence and broad feeding habits. Thus, *Culex salinarius* is a likely bridge vector to humans, horses and other mammals. WNV was collected from *Cs. melanura* in more rural locales in late August and September, which suggests that this predominant avian feeder may play a significant role in epizootic amplification of the virus among wild bird populations in these environs. *Aedes vexans* was the only species of *Aedes* or *Ochlerotatus* from which multiple isolations of WNV were made throughout the season. Its aggressive mammalian and human biting behavior makes it a likely bridge vector to humans and horses. In Connecticut, the principal foci of WNV activity were identified as densely populated residential communities in coastal Fairfield and New Haven Counties (>3,000 people/mi²). The incidence of human cases closely parallels the number of virus isolations made from mosquitoes with both peaks falling in early September. The risk of human infection extends from early August through the end of October. However, the virus may survive with the mosquito, indicating that surveillance is necessary throughout the entire year.

**Life Cycle of the Mosquito**

Standing water is essential to the life cycle of the mosquito. The insect can live in salt or fresh water, and in the stagnant water found in discarded rubber tires or in holes of trees. There are four stages to the life cycle – eggs, larvae, pupae, adults. The female mosquito lays several hundred eggs on the surface of standing water or in an area that is prone to flooding. Desiccated eggs can remain viable until the right conditions for hatching develop. The eggs of most species hatch in 2–3 days and the larvae feed on organic matter in the water for about a week and change into pupae. The pupae continue to live in the water for another 2–3 days and then metamorphose into adult mosquitoes. Male mosquitoes feed on flower nectar and do not require blood meals. Only the females require blood to produce eggs. Feeding occurs approximately every three days and usually occurs at twilight, although some insects will feed during the day. A female mosquito will typically consume its own weight in blood.

Zoophilic mosquitoes have a preference for feeding on animals while anthropophilic mosquitoes prefer humans. In some species, seasonal switching allows for the proliferation of the virus in animal hosts. Mosquitoes are efficient vectors for a number of viruses and protozoa. However, they are not able to carry and transmit *all* blood-borne viruses. Human Immunodeficiency Virus (HIV) does not survive or replicate in mosquitoes and the blood extracted during a blood meal is not injected into the next person during subsequent feedings. Although mosquito bites in the United States are usually considered a simple irritation or annoyance at backyard barbeques, it has been estimated that mosquitoes transmit disease to more than 700,000,000 people annually. Malaria, a protozoan infection carried by mosquitoes, is responsible for about 3 million deaths annually. Also transmitted are the arboviruses responsible for yellow fever, epidemic polyarthritis and several forms of encephalitis. Bancroftian filariasis, a disease of tropical and sub-tropical areas of the world, is caused by a nematode that is spread by mosquitoes.

**Epidemiology of Human Infection**

West Nile virus is the leading cause of arboviral encephalitis in the United States. The Centers for Disease Control and Prevention together with the US Geographical Survey, USDA Animal and Plant Health Inspection Service, State wildlife agencies, and State and local health and vector control agencies track WNV on a daily basis. WNV infections in humans, birds, mosquitoes, and nonhuman
mammals are reported to CDC through ArboNET, an internet-based arbovirus surveillance system managed by state health departments and the CDC.

Since its discovery in New York City in 1999, WNV has caused seasonal epidemics of febrile illness and severe neurologic disease, usually during the months of July and August. From 1999 through 2004, more than 16,600 cases of WNV-related illnesses were reported in the United States, of which >7,000 were neuroinvasive disease and >600 were fatal. In 2005, a total of 2,744 cases of WNV disease in humans were reported, an increase from 2,359 cases reported in 2004. During 2005, WNV transmission to humans or animals expanded into 21 counties that had not previously reported transmission and recurred in 1,196 counties where transmission had been reported in previous years. Reported case numbers for 2008 indicate the lowest incidence of disease since 2001, according to the CDC (Table 1) with a total of 833 cases.

**Signs and Symptoms**

Thorough examination of North American epidemics has enhanced understanding of the clinical spectrum of symptomatic WNV infection in humans. About 80% of human infections are asymptomatic. Of those persons in whom symptoms develop, most have self-limited West Nile fever (WNF), characterized by the acute onset of fever, headache, fatigue, malaise, muscle pain, and weakness. Gastrointestinal symptoms and a transient macular rash on the trunk and extremities are sometimes reported. Patients have frequently reported difficulty concentrating and neck pain or stiffness, and that fatigue and muscle weakness often lasted for more than 1 month.

Other nonneurologic clinical manifestations that may rarely occur during WNV infection include hepatitis, pancreatitis, myocarditis, rhabdomyolysis, orchitis, and ocular manifestations. A study in Tunisia found that 69% of 29 patients hospitalized with WNV disease had chorioretinitis. Cardiac dysrhythmias have been observed in some North American patients.  

Of patients who are bitten by an infected mosquito, only 1 of 5 become infected. Approximately one in 150 WNV infections results in severe neuroinvasive illness such as meningitis, encephalitis and paralysis. Signs can include stupor, disorientation, tremors, seizures, coma and even death as the virus replicates in the human body and crosses the blood brain barrier. The proportion of reported cases that are neuroinvasive disease is higher because neuroinvasive disease is more likely to be reported than WNF or asymptomatic infections.

Acute, asymmetric flaccid paralysis - similar to that seen with poliomyelitis – occurs in approximately 13% of patients with neuroinvasive disease where WNV infects spinal motor neurons (anterior horn cells). Infection of the brainstem and high cervical spinal cord may cause diaphragmatic and intercostal muscle paralysis with resulting respiratory failure and sometimes death. Guillain-Barré syndrome has been infrequently reported.

Diagnosis depends on viral isolation and serologic tests. Testing for IgM antibody to WNV in serum or cerebrospinal fluid (samples from the acute and convalescent phases, submitted at least two weeks apart) is the most common diagnostic method. Local or state health departments usually can perform the test within 24 to 36 hours of submission.
Table 1: 2008 West Nile Virus Activity in the United States (Reported to CDC as of October 21, 2008)

<table>
<thead>
<tr>
<th>State</th>
<th>Encephalitis /</th>
<th>Fever</th>
<th>Other Clinical /</th>
<th>Total</th>
<th>Fatalities</th>
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<td><strong>580</strong></td>
<td><strong>41</strong></td>
<td><strong>1141</strong></td>
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</table>

Universal blood screening for WNV has not been shown to be cost effective. The risk of transmitting WNV during transfusion of fresh frozen plasma and platelets is extremely small. National blood donor screening for WNV RNA using minipool nucleic acid amplification testing (MP-NAT) was implemented in the United States in July 2003. WNV donor screening yielded 944 confirmed viremic donors. MP-NAT yield peaked in August of that year with >0.5% of donations positive for WNV RNA in 4 states. Peak IgM seroprevalence for North Dakota was 5.2% in late September. The average time viremia is detectable by MP-NAT was 6.9 days (95% confidence interval [CI] 3.0-10.7). An estimated 735,000 (95% CI 322,000-1,147,000) infections occurred in 2003, with 256 (95% CI 112-401) infections per
neuroinvasive case. In addition to preventing transfusion-transmitted WNV infection, donor screening can serve as a tool to monitor seasonal incidence in the general population.

**Risk Factors**

The risk of complications and increased severity of disease from WNV infection is highest for those of advanced age or those with compromised immune systems.

Case fatality rates among patients hospitalized during major outbreaks have ranged from 4% in Romania (1996) to 12% in New York (1999) and 14% in Israel (2000)\(^2,6\) with those of advanced age having the highest mortality risk. For hospitalized persons older than 70 years of age, case fatality rates were 15% in Romania and 29% in Israel. In New York, persons 75 years of age and older were nearly nine times more likely to die than younger persons.\(^2,6\) Other risk factors associated with increased risk of mortality were encephalitis with severe muscle weakness and change in the level of consciousness. There is no evidence that pregnant women are at any greater risk of complication from the infection.

A retrospective study from Texas examined 172 confirmed WNV cases hospitalized in Houston between 2002 and 2004. There were 113 cases of encephalitis, 47 cases of meningitis, 12 fever cases and 17 deaths. Sixty seven percent were male. Homeless patients were more likely to be hospitalized from WNV compared to the general population. A multiple logistic regression model identified age [odds ratio (OR) 1.1, \(P<0.001\)], history of hypertension (including patients taking hypertension-inducing drugs) [OR 2.9, \(P=0.012\)], and history of cardiovascular disease [OR 3.5, \(P=0.061\)] as independent risk factors for developing encephalitis from WNV infection. After adjusting for age, race/ethnicity (i.e., being black) [OR 12.0, \(P<0.001\)], chronic renal disease [OR 10.6, \(P<0.001\)], hepatitis C virus [OR 23.1, \(P=0.0013\)], and immunosuppression [OR 3.9, \(P=0.033\)] were identified as risk factors for death from WNV infection.\(^{13}\)

A review of demographic characteristics and data from medical records of 221 patients hospitalized in 2003 in 4 Colorado counties also indicated that cardiovascular problems might play a role in outcome from WNV infection. Univariate and multivariate analyses were used to identify factors associated with West Nile encephalitis (WNE), limb weakness, or death by comparing factors among persons with and without the outcome of interest. In the patient sample, 103 were diagnosed with West Nile meningitis, 65 had WNE, and 53 had West Nile fever. Respiratory failure, limb weakness, and cardiac arrhythmia occurred in all groups, with significantly more cases of each in the WNE group. Age, alcohol abuse, and diabetes were associated with WNE. Age and WNE were associated with limb weakness. The mortality rate in the WNE group was 18%; age, immunosuppression, requirement of mechanical ventilation, and history of stroke were associated with death. Only 21% of patients with WNE who survived returned to a prehospital level of function. The estimated incidence of West Nile fever cases that required hospitalization was 6.0 cases per 100,000 persons; West Nile fever was associated with arrhythmia, limb weakness, and respiratory failure.\(^{14}\)

**Diagnosis**

Diagnosis of WNV infection is based on a high index of clinical suspicion and obtaining specific laboratory tests. WNV, or other arboviral diseases such as St. Louis encephalitis, should be strongly considered in adults >50 years who develop unexplained encephalitis or meningitis in summer or early fall. Year-round transmission is possible in some areas. Therefore, WNV should be considered in all
persons with unexplained encephalitis and meningitis. If local health authorities are reporting outbreaks, the index of suspicion should be raised. Obtaining a recent travel history is also important.

West Nile virus (WNV) testing for patients with encephalitis, meningitis, or other serious central nervous system infections can be obtained through local or state health departments. The most conclusive diagnostic method to identify persons with WNV infection of the central nervous system (CNS) is detecting WNV-specific IgM antibody in CSF using MAC-ELISA. This can be done with a CSF specimen obtained during initial clinical presentation. Because IgM antibody does not readily cross the blood-brain barrier, IgM antibody in CSF strongly suggests acute CNS infection. Because serum IgM antibody may persist for more than a year, physicians must determine whether or not the antibody is the result of a WNV infection in the previous year and unrelated to the current clinical presentation.

If CSF is not obtained, acute and convalescent serum samples may be used to make the diagnosis utilizing MAC-ELISA. If the acute sample is IgM-negative, then the illness is unlikely to be an acute WNV infection. If the specimen is IgM-positive and the illness is clinically compatible, then it may be a recent WNV infection. Other reasons for the positive test should be explored such as St. Louis encephalitis (SLE) virus, or recent infection with related flaviviruses (e.g., yellow fever, Japanese encephalitis, and dengue).

Common diagnostic among patients in recent outbreaks are reported in Table 2. In peripheral blood, total leukocyte counts were mostly normal or elevated, with lymphocytopenia and anemia also occurring. Hyponatremia was sometimes present, particularly among patients with encephalitis. Examination of the cerebrospinal fluid (CSF) showed pleocytosis, usually with a predominance of lymphocytes. Protein was universally elevated. Glucose was normal. Computed tomographic scans of the brain mostly did not show evidence of acute disease, but in about one-third of patients, magnetic resonance imaging showed enhancement of the leptomeninges, the periventricular areas, or both.

### Table 2: Common Diagnostic Findings in Patients with WNV

<table>
<thead>
<tr>
<th>Blood</th>
<th>CSF</th>
<th>MRI</th>
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<tbody>
<tr>
<td>Total leukocyte count normal or elevated</td>
<td>Pleocytosis, with predominance of lymphocytes</td>
<td>Enhancement of leptomeninges, or periventricular areas, or both</td>
</tr>
<tr>
<td>Lymphocytopenia</td>
<td>Protein elevated</td>
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<tr>
<td>Anemia</td>
<td>Glucose normal</td>
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<td>Hyponatremia</td>
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**Treatment**

Treatment for WNV infection is supportive consisting mostly of hydration, respiratory support (possibly with controlled ventilation), prevention of secondary infection, and control of hyperthermia. Increase in intracranial pressure can be managed with controlled ventilation, mannitol, furosemide, and mild hypothermia.

Recent studies noted a protective role of several innate immune response elements including alpha/beta interferon (IFN-alpha/beta), immunoglobulin M, gammadelta T cells, and complement. In laboratory mice infected with WNV, a lack of IFN-gamma production or signaling resulted in a rise in mortality from 30% (wild-type mice) to 90% (IFN-gamma(-/-) or IFN-gammaR(-/-) mice) and a decrease in the average survival time. The protective role of IFN-gamma against WNV is likely to be antiviral in
nature and prevents viral dissemination to the CNS. Type I interferon (IFN) has also been shown to have a critical role in controlling WNV replication, spread, and tropism. Mice lacking both the interferon-induced, double-stranded-RNA-activated protein kinase (PKR) and the endoribonuclease of the 2',5'-oligoadenylate synthetase-RNase L system (PKR(-/-) x RL(-/-)) were highly susceptible to subcutaneous WNV infection, with a 90% mortality rate compared to the 30% mortality rate observed in congenic wild-type mice. PKR and RNase L may contribute to IFN-mediated protection in a cell-restricted manner and control WNV infection in peripheral tissues and some neuronal subtypes.  

Clinical trials are under way to examine potential benefits of Alpha-Interferon (Alferon) Therapy for West Nile Meningoencephalitis.  

**Prevention**

As treatment is limited, preventive measures are of paramount importance. Prevention guidelines include the following:

1. When outdoors, wear long sleeved shirts and pants or long skirts.
2. Wear a hat with a shade over the brow.
3. Spray skin and clothing with insect repellent.
4. Restrict outdoor activity at dawn, dusk and during the evening.
5. Use nets to cover babies in strollers.
6. Remove all pools of standing and stagnant water.
7. Keep storm drains free of debris.
8. Drill holes in the bottom of garbage containers to avoid accumulation of rain water.
9. Chlorinate swimming pools.
10. Maintain the integrity of window and door screens.

There is no evidence that WNV is transmitted from infected live or dead birds. Carcasses should be carefully removed and disposed into double plastic bags in accordance with local protocols. Infection in domestic animals is low and there is no evidence linking transmission of WNV by dogs and cats (although the virus was identified in one dead cat in New York). The disease is not spread from one animal to another. While cats or dogs could conceivably become contaminated by eating carcasses of infected birds, such a sequence has not been identified. Infected animals are likely to have a full recovery. Horses vaccinated against eastern equine encephalitis (EEE), western equine encephalitis (WEE), and Venezuelan equine encephalitis are not protected against WNV infection. The extent to which duck and other wild game are susceptible to WNV infection is unknown but surveillance studies continue in collaboration with the US Geological Survey National Wildlife Center, Madison WI.

In conjunction with active surveillance, insecticide spraying programs have been established in several states. The spraying agent Malathion was used early on but was found to induce respiratory difficulties in susceptible individuals. In 2000, a safer synthetic neurotoxin, Anvil®, was employed. Daily schedules of spraying times and areas are circulated to allow the public the opportunity to stay indoors.

Several visual, thermal and olfactory factors stimulate the attraction of mosquitoes to a host. Daytime feeding insects are oriented to the host by dark colored clothing. Such visual stimuli enable flight orientation, especially at far distances. Byproducts of human metabolism (over 100 volatile substances) are present in human breath, with carbon dioxide and lactic acid being most attractive to mosquitoes. Carbon dioxide can be detected by mosquitoes at up to 100 feet. Lactic acid
chemoreceptors on the antennae of the insects may be inhibited by N,N-diethyl-m-toluamide (DEET)-based insect repellents. Other chemoattractants include volatile compounds derived from sebum, eccrine and apocrine sweat and the cutaneous microfloral actions on these secretions. Floral fragrances, perfumes, soaps, lotions and shampoos also can increase the likelihood of being bitten. Skin temperature and moisture are also attractive. Propensity to bite around the head or feet may be due to local temperature and eccrine sweat gland output. Mosquitoes are generally not attracted to anhydrotic individuals.

There seems also to be a gender and age preference as men are bitten more frequently than women, adults more than children (except for the very old), and larger people more often than thinner ones (perhaps because of greater relative heat and carbon dioxide production).

**Insect Repellents**

Repellents have marked species variation and consist solely of topical preparations that may have adverse effects such as skin irritation. Effective repellents have appropriate volatility and maintain an effective vapor concentration on the skin without evaporating too quickly. Factors that contribute to the effectiveness of repellents include the frequency and uniformity of application, organism susceptibility, and the host’s activity and level of attractiveness to the biting insect. Repellents all become less effective in the rain, as the individual sweats, as the temperature rises (10°C rise in temperature causes 50% decrease in effectiveness), and as wind increases.

- **Chemical Repellents**

  The gold standard in chemical repellents is DEET, which was discovered and developed by scientists at the US Department of Agriculture and patented by the US Army in 1946. Registration for use by the public occurred in 1957. Although more than 20,000 compounds have subsequently been tested, none have proven as effective. It is a broad spectrum repellent with a long duration of action. The US Environmental Protection Agency (EPA) estimates that one third of the US population uses this preparation every year and that worldwide use exceeds 200 million annually.

  DEET is available in many formulations and strengths ranging from 5% to 100%. Over the past 40 years, it has been shown to have a remarkable safety profile. Specifically skin irritation is very rare, although contact urticaria in the antecubital fossa has been described. Eye irritation from direct spraying has also been reported. Currently a slow release, polymer-based product containing 35% DEET, which is the formulation provided to US military personnel, is marketed under the brand name of Hour Guard® (Amway Corp, New York). Lower strengths of extended release DEET (6.5% and 10%) are marketed by Minnetonka Brands (Eden Prairie, MN).

  Unfortunately, there is not an “insect repellent factor” that can be appended to drug labels, so the appropriate concentration and times of application are unknown, particularly as mosquitoes vary greatly in their susceptibility to the compound. However, the polymer formulation appears to increase the effectiveness to about 12 hours. The American Academy of Pediatrics has recommended that repellents used for children contain not more than 10% DEET. While DEET does not affect natural fibers, it can damage plastics, synthetic materials, leather and painted or varnished surfaces. It should also be noted that application of DEET in conjunction with a sunscreen preparation will decrease the effectiveness of the latter.
• **Plant Derived Repellents**

Although thousands of plant derived compounds have been tested for repellent activity, none have tested as effective as DEET with regard to duration and broad spectrum activity. Some essential oils that are effective include citronella, cedar, geranium, lavender, rosemary, basil, thyme, allspice, garlic and peppermint. Generally, protection lasts less than 2 hours. Citronella has been used widely in candles as an insect repellent. However, studies have shown an almost equal protective effect from plain candles, perhaps due to the action of the latter as a decoy of warmth, moisture and carbon dioxide.

Pyrethrum is a rapidly acting insecticide that is neurotoxic to the insect. It is derived from the chrysanthemum. Permethrin is a synthetic pyrethroid. The agent is effective against several insects, has low toxicity and is rapidly inactivated by ester hydrolysis. It should be applied directly to clothing or to screens or nets. Potency is maintained for up to 2 weeks.

• **Electronic Devices**

Ultrasonic, handheld devices that are advertised to emit sounds that repel mosquitoes are not effective. Similarly, larger devices that are hung in gardens and back yards (bug zappers) to attract and electrocute insects are ineffective against mosquitoes. Of the insects killed by these instruments, only about 0.1% are female mosquitoes. It has been estimated that 71 billion to 350 billion beneficial insects are killed in this manner annually.

**Management of the Case**

The elderly patient was admitted to the intensive care unit and hydrated with several liters of normal saline solution. His airway was secured and controlled ventilation instituted. He was found to be febrile and a cooling blanket was applied. After blood had been drawn for electrolytes, complete blood count and cultures, antibiotic coverage was started. He was found to be hyponatremic and supplementation was made. Sedation was maintained with small amounts of midazolam (0.5mg/hour). A bispectral analysis (BIS®) monitor was used and after 2 days there was noted to be increased activity. The midazolam was discontinued and after 4 hours, the BIS® reading was 95. The patient was responsive. His trachea was extubated and after another day he was transferred to the operating room where ankle disarticulation was conducted under regional block. Although he recovered within one week, some weakness persisted in his extremities and his discharge was delayed pending contacting family and social service arrangements.

**Summary**

Physicians should consider West Nile virus infection when evaluating febrile patients who have unexplained neurologic symptoms, muscle weakness, or erythematous rash during late spring through early fall, or throughout the year in warm climates. West Nile virus infection has no characteristic findings on routine laboratory tests, although anemia, leukocytosis, or lymphopenia may be present. Testing for IgM antibody to West Nile virus in serum or cerebrospinal fluid (samples from the acute and convalescent phases, submitted at least two weeks apart) is the most common diagnostic method.
References

2. Outbreak of West Nile-Like Viral Encephalitis New York. MMWR. 1999; 48 (38); 845-9.
9. MMWR. 2005; Dec 16; 54(49); 1253-6.


POST-TEST

1. Infection with WNV was first recognized:
   a. In ancient Egypt
   b. After isolation in the US in 1998
   c. Following an outbreak in Romania in 1996
   d. From a single case in Uganda in 1937

2. The most effective host reservoir for WNV is a:
   a. Crow
   b. Horse
   c. Dog
   d. Human

3. Regarding mosquitoes:
   a. They may transmit disease to more than 700 million people annually.
   b. Approximately 170 species have been identified in North America.
   c. The Culex species transmits WNV.
   d. All of the above.

4. The least effective deterrent to mosquito bites is:
   a. DEET spray
   b. Citronella candles
   c. Permethrin
   d. Bug Zappers

5. The following vaccinations protect horses from WNV infection
   a. Western equine encephalitis
   b. Eastern equine encephalitis
   c. Venezuelan equine encephalitis
   d. None of the above
6. Encephalitis associated with WNV infection is due to:
   a. Disruption of the blood brain barrier
   b. Dehydration
   c. Secondary infection
   d. Generalized hemolysis

7. The life cycle of the mosquito:
   a. Requires flowing water
   b. Is very fragile because of lack of adaptation
   c. Involves four cycles
   d. Takes over a month to complete

8. Anthropophilic biting mosquitoes:
   a. Prefer to feed on dogs
   b. Are female
   c. Are not subject to seasonal switching
   d. Easily transmit HIV

9. Human infection with WNV:
   a. May be contracted from domestic animals.
   b. Is rising rapidly.
   c. Usually causes only mild symptoms.
   d. Results in death in 75% of cases.

10. Regarding treatment of WNV:
    a. There is no specific therapy.
    b. Gamma interferon may have an early antiviral role.
    c. Hospitalized patients with encephalitis are likely to remain impaired.
    d. All of the above.