



## West Nile Fever: An Overview

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### Abstract

West Nile fever is caused by flavivirus of the family *Flaviviridae* which is composed of single stranded RNA. It is a vector borne disease usually transmitted through culex mosquito which also causes elephantitis in humans. Apart from humans the virus can also infect some animals like horse. The name west nile fever is coined so because it was first found in west nile district of Uganda. Viral meningo encephalitis was the manifestation of the infection which attracted scientists for doing research on west nile virus. The world wide spread of virus was possibly through migration of infected birds or by illegally transported birds. Presence of IgM and IgG antibodies confirms the presence of virus in blood. Use of antivirals like ribavirin, interferons and immunoglobulins can control the infections, however mosquito control is the best method to keep west nile fever at bay. Vaccine till today is available only for horses and can not be used by humans.

**Keywords:** West Nile virus, Meningo encephalitis, Culex, Interferons

### Introduction

West Nile virus (or WNV) is a virus of the family *Flaviviridae*. Part of the Japanese encephalitis (JE) antigenic complex of viruses, it is found in both tropical and temperate regions. It mainly infects birds, but is known to infect humans, horses, dogs, cats, bats, chipmunks, skunks, squirrels and domestic rabbits. The main route of human infection is through the bite of an infected mosquito. Image reconstructions and cryoelectron microscopy reveal a 45–50 nm virion covered with a relatively smooth protein surface. This structure is similar to the dengue fever virus; both belong to the genus *Flavivirus* within the family *Flaviviridae*. The genetic material of WNV is a positive-sense, single strand of RNA, which is between 11,000 and 12,000 nucleotides long; these genes encode seven non-structural proteins and three structural proteins. The RNA strand is held within a nucleocapsid formed from 12 kDa protein blocks; the capsid is contained within a host-derived membrane altered by two viral glycoproteins.[1]

### History

Studies of phylogenetic lineages have determined that WNV emerged as a distinct virus around 1000 years ago. This initial

virus developed into two distinct lineages, Lineage 1 and its multiple profiles is the source of the epidemic transmission in Africa and throughout the world, while Lineage 2 remains as an African zoonosis. WNV has been posited as one of the possible causes of Alexander the Great's early death based on reports of avian deaths before his illness period. [2, 3, 4]

### Epidemiology

Since its first isolation in the West Nile district in Uganda in 1937, WNV has become endemic throughout Africa and areas of the Middle East, where the prevalence of WNV antibody among children was 3.5% to 8% [5]. Since the mid-1990s and numerous epidemics have also occurred in Europe. WNV was first recognized in the Western hemisphere in August 1999 when a report of 62 patients with meningoencephalitis, sometimes associated with weakness, was published in New York. An exponential increase in WNV activity in the United States was observed, with at least 3737 cases and 201 fatalities in 2002. Since its introduction, the virus has spread West and South to involve the majority of the continental United States. The virus is amplified in birds and is transmitted to humans most commonly

**Table 1: History of West Nile Fever**

1937	WNV was first isolated from a feverish 37 year old woman at Omogo in the West Nile District of Uganda during research on yellow fever virus
1939	A series of serosurveys in central Africa found anti-WNV positive results ranging from 1.4% (Congo) to 46.4% (White Nile region, Sudan).
1942	It was subsequently identified in Egypt
1950	Serosurvey in Egypt found 90% of those over 40 years in age had WNV antibodies.
1953	It was subsequently identified in India.
1953	The ecology was characterized with studies in Egypt and Israel
1957	The virus became recognized as a cause of severe human meningoencephalitis in elderly patients during an outbreak in Israel
1960	The disease was first noted in horses in Egypt and France in the early and found to be widespread in southern Europe, southwest Asia and Australia.
1998	The US virus was very closely related to a lineage 1 strain found in Israel
1999	The first appearance of West Nile virus in the Western hemisphere was with encephalitis reported in humans, dogs, cats and horses and the subsequent spread in the United States may be an important milestone in the evolving history of this virus. Since the first North American cases in 1999, the virus has been reported throughout the United States, Canada, Mexico, the Caribbean and Central America. There have been human cases and horse cases and many birds are infected. The Barbary Macaque, <i>Macaca sylvanus</i> was the first non-human primate to contract West Nile Virus
2001/ 2002	A high level of media coverage through 2001/2002 raised public awareness of West Nile virus. This coverage was most likely the result of successive appearances of the virus in new areas and had the unintended effect of increasing funding for research on this virus and related arthropod-borne viruses. Such research has expanded our understanding of viruses transmitted by mosquitoes.

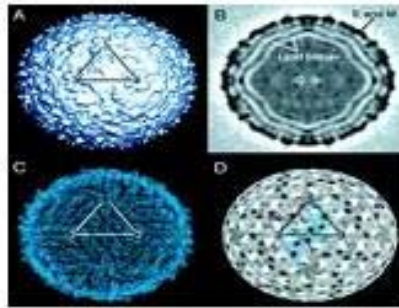
through infected *Culex* mosquito bites [6]. Transmission through blood transfusion, organ transplantation and breast-feeding has also been reported. Fortunately, most of the WNV seroconversions are subclinical, with overt clinical illness affecting 1 in 100 to 1 in 150 patients. The peak incidence of infection is in August and September. Elderly men are most susceptible to severe disease, with the median age of hospitalized patients in the seventh or eighth decade and a male-to-female ratio of 3:1. Patients seldom recall a specific mosquito bite, but they are often self-reported active persons with significant outdoor and therefore mosquito exposures. [7]

#### Genomic Structure

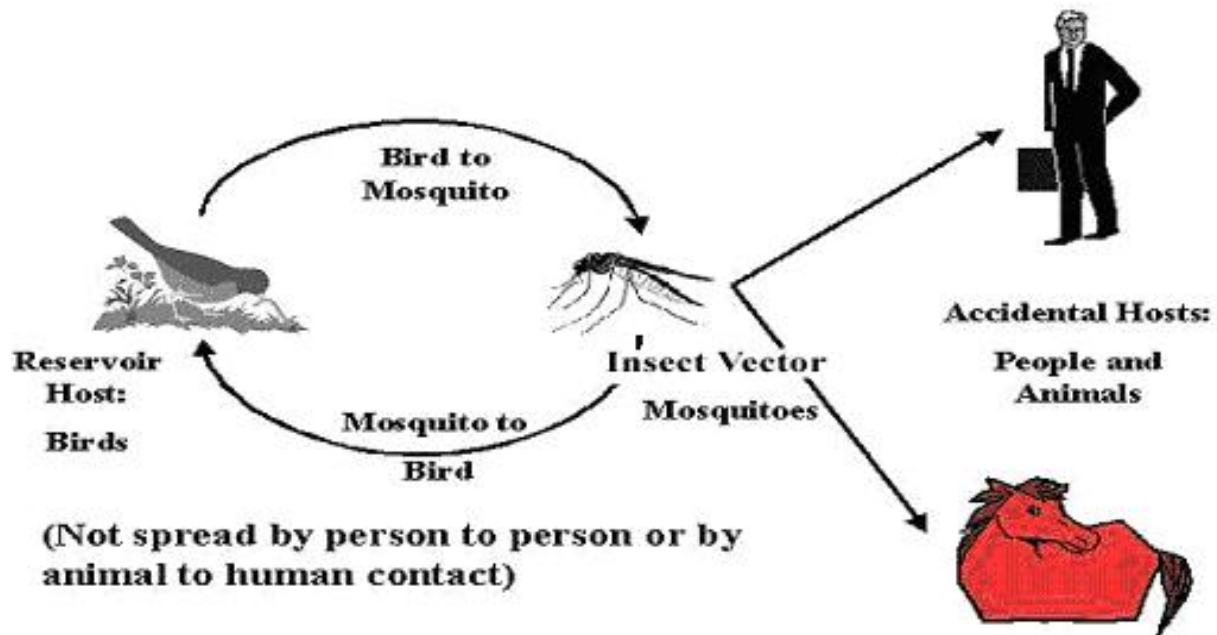
A 17 Å structure of West Nile virus determined by cryo-EM. (A) A surface shaded view of the virus with one

asymmetric unit of the icosahedrons shown by the triangle. The 5-fold and 3-fold icosahedral symmetry axes are labeled. (B) A central cross section showing the concentric layers of density. (C) The arrangement of the homology modeled WNV E protein (C $\alpha$ -backbone is shown in blue). Residues 307 and 330, which bind neutralizing monoclonal antibodies, are shown in green. Residue Asn, which is glycosylated, is shown in pink. (D) A difference density map between dengue virus and WNV shown at a radius 248 Å. Positive density (from dengue virus) is shown in black and negative density (from WNV) is shown in white. The outlines for a set of three E homodimers are indicated by the blue lines. [8]

Birds act both as carriers and amplifying hosts of WN virus in nature. Ornithophilic



**Figure 1: Genomic Structure of West Nile Virus**



**Figure 2- Life Cycle of WNV**

mosquitoes belonging mainly to *Culex* species act as vectors for transmission of infection from viraemic birds to a large spectrum of vertebrate hosts. *Cx. Univittatus* complex (South Africa, Israel), *Cx. modestus* (France), *Cx. vishnui* complex (India and Pakistan), *Cx. pipiens pipiens* (Romania, USA) act as major vectors of WN virus. There is no evidence to suggest person to person or animal, or animal to animal or person transmission [9]. The virus multiplies in mosquito vectors and after an extrinsic incubation period of about 2 weeks, the vector becomes infective for active

transmission to a susceptible host. Hibernating mosquitoes can carry the virus and vertical transmission of the virus to the infected female to her progeny has been reported. Migratory birds play a major role in the WN virus dissemination. However, virus dissemination through infected mosquitoes or by illegally imported infected pet birds should also be considered a possibility. [10]

**Etiological agent**

West Nile virus is a single stranded RNA virus of the family *Flaviviridae*, genus *Flavivirus*. It is a member of the Japanese encephalitis virus serocomplex, which contains several medically important viruses

associated with human encephalitis: Japanese encephalitis, St. Louis encephalitis, Murray Valley encephalitis and Kunjin virus (an Australian subtype of West Nile virus) [11]. The close antigenic relationship of the flaviviruses, particularly those belonging to the Japanese encephalitis complex, accounts for the serologic cross reactions observed in the diagnostic laboratory.[12]

### **Pathophysiology**

WNV is a member of the Japanese encephalitis complex of viruses that also includes the Japanese encephalitis virus and St. Louis encephalitis virus, which accounts for cross-reactivity in serologic testing. [13] This virus group belongs to the Flaviviridae, a family of single-stranded RNA viruses transmitted by arthropods, mostly *Culex* mosquitoes in the case of WNV. After a phase of initial replication and seeding of the reticuloendothelial system, a secondary viremia occurs with seeding of the central nervous system (CNS). Viremia is usually a transient phenomenon that precedes onset of symptoms and disappears with development of specific immunoglobulin (Ig) G and IgM antibodies. The presence of intact B cells plays a critical early role in the development of IgM antibodies and thus the defense against disseminated infection, a fact that explains prolonged periods of viremia (up to 1 month) and more severe CNS disease and delays in the seroconversion of WNV-infected immunosuppressed patients. Clinical symptoms develop in less than 1% of cases [14]. This appears to be due to the strength of the host immune system but could partly be due to the difference in severity of neurovirulence among different WNV strains. Risk factors for increased mortality include host characteristics such as older age (>75 years), diabetes mellitus and level of immuno suppression, as well as measures of disease severity such as decreased level of consciousness, neuro

imaging abnormalities and the development of limb weakness.

WNV shares with the other Japanese encephalitis complex viruses a tendency to cause encephalitis and, less often, aseptic meningitis and paralytic poliomyelitis. Those Flavivirus, including WNV, infect neurons throughout the CNS, but more severely in certain sites appropriate for the different clinical syndromes [15]. More severe infections of the basal ganglia and thalamus, as suggested by neuroimaging were found in patients with prominent Parkinsonism and movement disorders. Prominent inflammation of the brainstem was pathologically confirmed in patients with bulbar and ophthalmoplegic symptoms. Acute flaccid paralysis observed in WNV was correlated in multiple studies with perivascular lymphocytic infiltration and neuronophagia of the anterior horn cell region, similar to poliomyelitis. Although the presence of specific viral receptors on motor neurons explains the anterior horn cell neurotropism with polioviruses, the pathogenesis of the preferential rostral and anterior horn cell infection with WNV remains poorly understood. The pathologic changes are illustrated in figure 3 and 4. Rarely, peripheral demyelination or axonal losses have been postulated. [16]

### **Transmission**

The proboscis of an *Aedes albopictus* mosquito feeding on human blood. Under experimental conditions, the *Aedes albopictus* mosquito (also known as the Asian Tiger Mosquito) has been found to be a vector of West Nile Virus. The virus is transmitted through mosquito vectors, which bite and infect birds[17]. The birds are amplifying hosts, developing sufficient viral levels to transmit the infection to other biting mosquitoes which go on to infect other birds (in the Western hemisphere the American robin and the American crow are the most common carriers) and also humans.



**Figure 3, 4-Pathophysiology**

The infected mosquito species vary according to geographical area; in the US *Culex pipiens* (Eastern US), *Culex tarsalis* (Midwest and West) and *Culex quinquefasciatus* (Southeast) are the main sources. In mammals the virus does not multiply as readily (i.e. does not develop high viremia during infection) and it is believed that mosquitoes biting infected mammals do not ingest sufficient virus to become infected, making mammals so-called dead-end infections [18]. *Culex pipiens* mosquitoes existed in two populations in Europe, one which bites birds and one which bites humans. In North America 40% of *Culex pipiens* were found to be hybrids of the two types which bite both birds and humans, providing a vector for West Nile virus. This is argued to provide an explanation of why the West Nile disease has spread more quickly in North America than Europe.<sup>[13]</sup> However, these conclusions have been disputed.[19]

#### **Mortality rate**

The United States in 2007; "A total of 3,630 cases of WNV neuroinvasive disease (WNND) and 124 deaths were reported." This means that of extremely serious infections of WNV, 3.4% were fatal and the general total mortality rate was likely much less than 4% as most cases are not severe.[20]

#### **Overwintering mechanism**

Vertical transmission of West Nile Virus from female *Culex pipiens* mosquitoes to their progeny has been demonstrated in the laboratory. It has been suggested that vertically infected *Culex* could survive the winter to initiate a WNV amplification cycle the following spring. *Culex* mosquitoes spend the winter hibernating in protected structures such as root cellars, bank barns, caves, abandoned tunnels and other subterranean locations. The first overwintering adult mosquitoes to test positive for WNV were collected in New York, 2000. Since then, positive samples have been identified in New Jersey, 2003 and in Pennsylvania, 2003, 2004 and 2005. [21]

#### **Disease Scenario:**

##### **Global Scenario:**

WNV is recognized as the most widespread virus among flaviviruses. It was first isolated during 1937 in the West Nile district of Uganda from a patient suffering from mild illness [22]. WNV has been reported from Algeria, Russia, Azerbaijan, Botswana, Central African Republic and Cote d'Ivoire, Cyprus, Democratic Republic of Congo, Egypt, Ethiopia, Israel, Kazakhstan, Madagascar, Morocco, Mozambique, Nigeria, Pakistan, Senegal, South Africa, Tajikistan, Turkmenia, Uganda and Uzbekistan. Several epidemics have been reported from middle

East, Africa and Israel and the WNV is endemic in Middle East, Africa and Southwest Asia [23]. WNV specific neutralizing antibodies have been detected in Armenia, Borneo, China, Georgia, Iraq, Uganda, Kenya, Lebanon, Malaysia, Philippines, Sri Lanka, Syria, Thailand, Tunisia, Turkey Belgian Congo and Sudan. Recently, the virus has been recognized in New York, America. [24]

### **Indian Scenario**

In India, presence of West Nile antibodies in humans was first reported from Bombay (now Mumbai) by Banker in 1952[36]. Smithburn *et al* [25] confirmed the report by detecting the WNV neutralizing antibodies. During a post sero-epidemiological study, Risbud *et al*, detected WNV neutralizing antibodies among humans at South Arcot district of Tamil Nadu. WNV has been isolated from sporadic cases of encephalitis and mosquitoes. Work postulated a hypothesis of a zoogeographical interface of Japanese encephalitis and West Nile virus. The hypothesis proposed the intermingling distribution of JEV and WNV at the south Indian peninsular region. The relative prevalence of JEV and WNV needs to be studied in India. From the available data, it is evident that different viruses may predominate in different years since in South Arcot District of Tamil Nadu, Risbud *et al* [26] observed a higher prevalence of neutralizing antibodies to WNV than JEV during a post encephalitis outbreak survey in 1982, whereas in the same area, during 1989 and 1990, Gajanana *et al* [27] found a low prevalence of WNV.

### **Occurrence and Distribution**

Today, the West Nile Virus is widely distributed throughout Africa, the Middle East, Europe, Asia, Canada, Central America, Mexico, the USA and the Caribbean. A variety of WNV, the Kunjin virus has been isolated in Australia and Southeast Asia [28].

### **Causes**

The West Nile virus is a type of virus known as a flavivirus. Researchers believe West Nile virus is spread when a mosquito bites an infected bird and then bites a person. Mosquito's carry the highest amounts of virus in the early fall, which is why the rate of the disease increases in late August to early September. The risk of disease decreases as the weather becomes colder and mosquito's die off. Although many people are bitten by mosquito's that carry West Nile virus, most do not know they've been exposed. Few people develop severe disease or even notice any symptoms at all. Mild, flu-like illness is often called West Nile fever. More severe forms of disease, which can be life threatening, may be called West Nile encephalitis or West Nile meningitis, depending on what part of the body is affected. Risk factors for developing a more severe form of West Nile virus include: Conditions that weaken the immune system, such as HIV, organ transplants and recent chemotherapy older age, Pregnancy. West Nile virus may also be spread through blood transfusions and organ transplants. It is possible for an infected mother to spread the virus to her child through breast milk. [36]

### **Symptoms**

West Nile Virus (WNV) has three different effects on humans. The first is an asymptomatic infection; the second is a mild febrile syndrome termed West Nile Fever; the third is a neuroinvasive disease termed West Nile meningitis or encephalitis. In many infected individuals the ratio between the three states is roughly 110:30:1.[37] The second, febrile stage has an incubation period of 2 to 8 days followed by fever, headache, chills, diaphoresis (excessive sweating), weakness, lymphadenopathy (swollen lymph nodes), drowsiness, pain in the joints and symptoms like those of influenza or the flu. Occasionally there is a short-lived truncal rash and some patients



**Figure 5- Occurrence and Distribution of WNV**

**Reported deaths in WN virus** [29, 30, 31]

**Table 2: Reported deaths in WN virus**

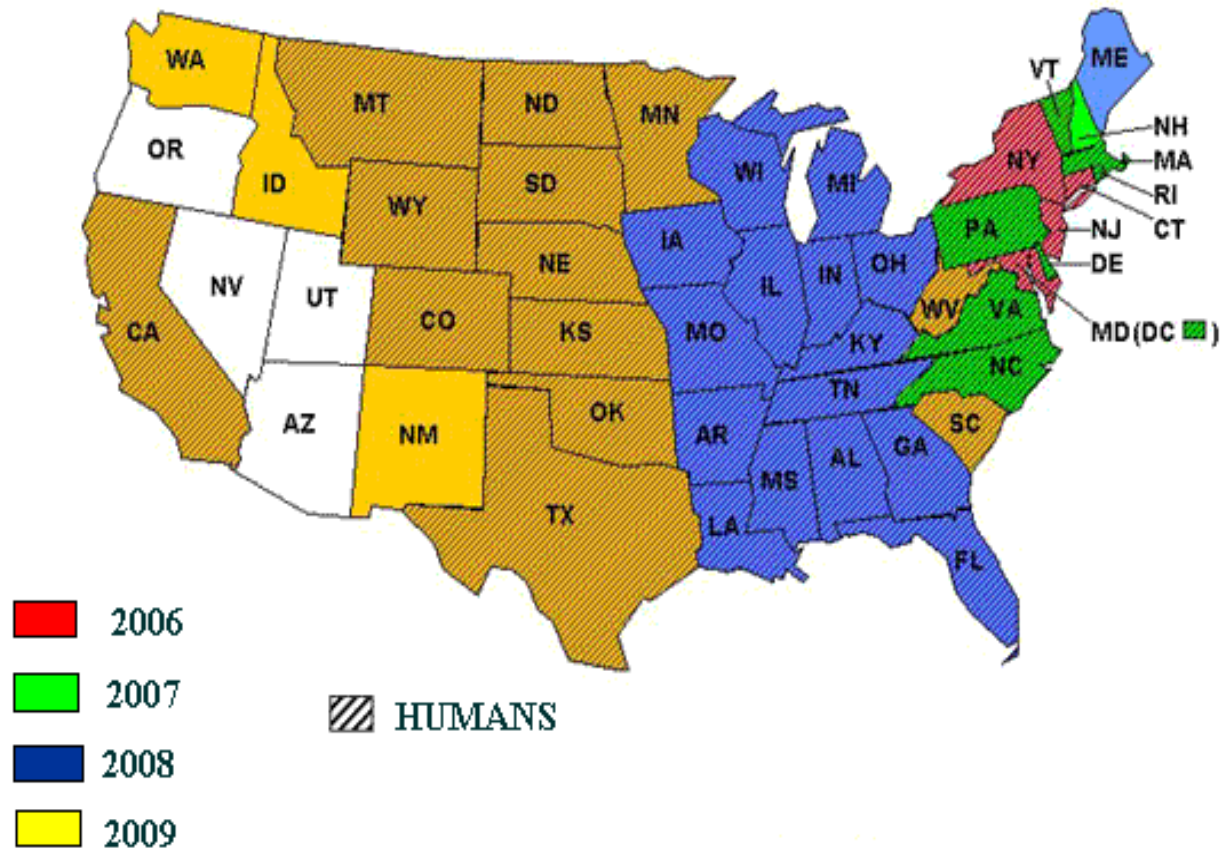
Year	Location	No. cases studied	Deaths (%)
1994	Algeria	13	13.3 <sup>a</sup>
1996	South Romania	393	4.3
1999	New York	61	11.5
1999	South Russia	1,000	4.0
2000	New York, New Jersey	19 <sup>b</sup>	10.5
2000	Israel	417	8.4
2001	Mexico	312	4.7
2001	Azerbaijan	123	3.2
2003	Uganda	987 <sup>b</sup>	12.7
2005	India	543	9.5 <sup>a</sup>
2008	Kenya	323	5.1
2009	USA	156	3.2

<sup>a</sup>Patients were mainly young children,

<sup>b</sup>Hospitalized patients only.

experience gastrointestinal symptoms including nausea, vomiting, loss of appetite, or diarrhea. All symptoms are resolved within 7 to 10 days, although fatigue can last for some weeks and lymphadenopathy can take up to two months to resolve. The first signs are swelling [38]. The more dangerous encephalitis is characterized by similar early symptoms but also a decreased level of consciousness, sometimes approaching near-coma. Deep tendon reflexes are hyperactive at first, later diminished. There are also extrapyramidal disorders. Recovery is marked by a long convalescence with fatigue. More recent outbreaks have resulted in a deeper study of the disease and other, rarer, outcomes have been identified. The spinal cord may be infected, marked by anterior myelitis with or without encephalitis. WNV-associated Guillain-Barré syndrome has been identified and other rare effects include multifocal chorioretinitis (which has 100% specificity for identifying WNV infection in patients with possible WNV encephalitis), hepatitis,

## WEST NILE FEVER IN UNITED STATES 2006-2009



**Figure 6: Distribution of West Nile Fever in USA 2006-2009**

myocarditis, nephritis, pancreatitis and splenomegaly. [39]

### Exams and Tests (Diagnosis)

Signs of West Nile virus infection are similar to those of other viral infections. There may be no specific findings on a physical examination to diagnose West Nile virus infection. About 20 - 50% of patients may have a rash. Muscle weakness with other related symptoms are signs of a West Nile virus infection.

### Tests to diagnose West Nile virus include:

- Complete blood count (CBC)
- Head CT scan
- Head MRI scan
- Lumbar puncture and cerebrospinal fluid (CSF) testing.

The most accurate way to diagnose this infection is with a serology test, which checks a blood or CSF sample for antibodies against the virus. Rarely, a sample of blood or CSF may be sent to a lab to be cultured for the presence of West Nile virus. The virus can also be identified in body fluids using a technique called polymerase chain reaction (PCR). However, these methods



**Reported Cases and Death (Human Cases of USA from 2006-2009)****Table 3: 2006 West Nile Virus Activity in the United States** [32]

State	Encephalitis /Meningitis	Fever	Clinical / Unspecified	Total	Fatalities
Alabama	8	0	0	8	0
Arizona	65	77	8	150	11
Arkansas	24	5	0	29	4
California	81	186	11	278	7
Colorado	66	279	0	345	7
Connecticut	7	2	0	9	1
District of Columbia	0	2	0	2	0
Florida	3	0	0	3	0
Georgia	2	5	1	8	1
Idaho	115	827	54	996	21
Illinois	122	69	24	215	10
Indiana	27	8	45	80	5
Iowa	21	13	3	37	0
Kansas	17	13	0	30	4
Kentucky	5	1	0	6	1
Louisiana	91	89	0	180	9
Maryland	9	1	1	11	1
Massachusetts	2	1	0	3	0
Michigan	43	10	2	55	7
Minnesota	31	34	0	65	3
Mississippi	89	94	0	183	14
Missouri	50	11	1	62	5
Montana	12	21	1	34	0
Nebraska	45	219	0	264	1
Nevada	34	76	14	124	1
New Jersey	2	2	1	5	0
New Mexico	3	5	0	8	1
New York	16	8	0	24	4
North Carolina	1	0	0	1	0
North Dakota	20	117	0	137	1
Ohio	36	12	0	48	4
Oklahoma	26	21	1	48	6
Oregon	7	50	12	69	2
Pennsylvania	8	1	0	9	2
South Carolina	1	0	0	1	0
South Dakota	38	75	0	113	3
Tennessee	16	6	0	22	1

Texas	233	121	0	354	32
Utah	56	102	0	158	5
Virginia	0	0	5	5	0
Washington	0	3	0	3	0
West Virginia	1	0	0	1	0
Wisconsin	11	10	0	21	1
Wyoming	15	40	10	65	2
<b>Totals</b>	<b>1459</b>	<b>2616</b>	<b>194</b>	<b>4269</b>	<b>177</b>

**Table 4: 2007 West Nile Virus Activity in the United States**<sup>[33]</sup>

State	Encephalitis / Meningitis	Fever	Clinical / Unspecified	Total	Fatalities
Alabama	17	7	0	24	3
Arizona	50	45	2	97	6
Arkansas	13	7	0	20	1
California	154	220	6	380	20
Colorado	99	477	0	576	7
Connecticut	2	2	0	4	0
Delaware	1	0	0	1	0
Florida	3	0	0	3	1
Georgia	23	24	3	50	1
Idaho	10	120	2	132	1
Illinois	57	26	18	101	4
Indiana	14	7	3	24	1
Iowa	12	15	3	30	3
Kansas	14	26	0	40	2
Kentucky	4	0	0	4	0
Louisiana	27	13	0	40	2
Maryland	6	3	1	10	0
Massachusetts	3	3	0	6	0
Michigan	14	1	2	17	4
Minnesota	44	57	0	101	2
Mississippi	50	86	0	136	4
Missouri	61	16	0	77	5
Montana	37	164	1	202	4
Nebraska	21	142	0	163	4
Nevada	2	6	4	12	1
New Jersey	1	0	0	1	0
New Mexico	39	21	0	60	3
New York	16	6	0	22	3
North Carolina	4	4	0	8	0
North Dakota	49	320	0	369	3
Ohio	13	9	1	23	3

Oklahoma	59	47	1	107	8
Oregon	7	19	0	26	0
Pennsylvania	5	5	0	10	0
Rhode Island	0	1	0	1	0
South Carolina	3	2	0	5	0
South Dakota	48	160	0	208	6
Tennessee	5	3	3	11	1
Texas	170	90	0	260	16
Utah	28	42	0	70	2
Virginia	3	1	1	5	0
Wisconsin	7	6	0	13	1
Wyoming	22	147	12	181	2
<b>Totals</b>	<b>1217</b>	<b>2350</b>	<b>63</b>	<b>3630</b>	<b>124</b>

**Table 5: 2008 West Nile Virus Activity in the United States** <sup>[34]</sup>

State	Encephalitis / Meningitis	Fever	Clinical / Unspecified	Total	Fatalities
Alabama	11	7	0	18	0
Arizona	62	43	9	114	7
Arkansas	7	2	0	9	0
California	292	149	4	445	15
Colorado	17	54	0	71	1
Connecticut	5	2	1	8	0
Delaware	0	0	1	1	0
District of Columbia	4	1	3	8	0
Florida	3	0	0	3	0
Georgia	4	3	1	8	0
Idaho	2	31	6	39	1
Illinois	12	4	4	20	1
Indiana	3	0	1	4	0
Iowa	3	0	3	6	1
Kansas	14	17	0	31	0
Kentucky	3	0	0	3	0
Louisiana	18	31	0	49	1
Maryland	6	7	1	14	0
Massachusetts	1	0	0	1	0
Michigan	11	4	2	17	0
Minnesota	2	8	0	10	0
Mississippi	22	43	0	65	2
Missouri	12	3	0	15	1
Montana	0	3	2	5	0
Nebraska	7	40	0	47	1

Nevada	9	5	2	16	0
New Jersey	6	4	0	10	2
New Mexico	5	3	0	8	0
New York	32	14	0	46	6
North Carolina	2	0	1	3	0
North Dakota	2	35	0	37	0
Ohio	14	1	0	15	1
Oklahoma	4	5	0	9	0
Oregon	3	13	0	16	0
Pennsylvania	12	2	0	14	1
Rhode Island	1	0	0	1	0
South Carolina	0	1	0	1	0
South Dakota	11	28	0	39	0
Tennessee	12	7	0	19	1
Texas	40	24	0	64	1
Utah	6	18	2	26	0
Virginia	0	0	1	1	0
Washington	2	1	0	3	0
West Virginia	1	0	0	1	0
Wisconsin	4	3	1	8	1
Wyoming	0	8	0	8	0
<b>Totals</b>	<b>687</b>	<b>624</b>	<b>45</b>	<b>1356</b>	<b>44</b>

**Table 6: 2009 West Nile Virus Activity in the United States** <sup>[35]</sup>

State	Encephalitis / Meningitis	Fever	Clinical / Unspecified	Total	Fatalities
Arizona	9	3	0	12	0
Arkansas	1	0	0	1	0
California	9	10	0	19	0
Colorado	3	11	0	14	0
Idaho	1	6	1	8	1
Indiana	1	0	0	1	1
Iowa	0	1	0	1	0
Kansas	0	4	0	4	0
Louisiana	5	5	0	10	0
Minnesota	1	0	0	1	0
Mississippi	17	9	0	26	2
Missouri	1	0	0	1	0
Montana	1	1	0	2	0

Nebraska	1	6	0	7	0
Nevada	7	4	1	12	0
New Mexico	2	1	0	3	1
New York	1	0	0	1	0
Ohio	0	1	0	1	0
Oklahoma	1	0	0	1	0
Pennsylvania	1	0	0	1	0
South Dakota	3	8	0	11	0
Tennessee	1	1	0	2	0
Texas	11	2	0	13	1
Washington	0	0	1	1	0
Wyoming	1	2	0	3	0
<b>Totals</b>	<b>78</b>	<b>75</b>	<b>3</b>	<b>156</b>	<b>6</b>

can provide false negative results and are not commonly used. [40, 41]

### **Prognosis**

In general, the likely outcome of a mild West Nile virus infection is excellent. For patients with severe cases of West Nile virus infection, the outlook is more uncertain.

West Nile encephalitis or meningitis may lead to brain damage and death.

Approximately 10% of patients with brain inflammation do not survive. [41]

### **Surveillance methods**

West Nile virus can be sampled from the environment by the pooling of trapped mosquitoes, testing avian blood samples drawn from wild birds and dogs and sentinel monkeys, as well as testing brains of dead birds found by various animal control agencies and the public [42]. Testing of the mosquito samples requires the use of RT-PCR to directly amplify and show the presence of virus in the submitted samples. When using the blood sera of wild bird and sentinel chickens, samples must be tested for the presence of West Nile virus antibodies by use of immunohistochemistry (IHC) or Enzyme-Linked Immunosorbent Assay (ELISA). Dead birds, after necropsy, have their various tissues tested for virus by either RT-PCR or immunohistochemistry, where

virus shows up as brown stained tissue because of a substrate-enzyme reaction.[43]

### **Possible Complications**

Complications from mild West Nile virus infection are extremely rare. Complications from severe West Nile virus infection include:

- Permanent brain damage
- Permanent muscle weakness (sometimes similar to polio)
- Death [40,41]

### **Control**

West Nile virus warning sign in Southern California. West Nile control is achieved through mosquito control, by elimination of mosquito breeding sites, larviciding active breeding areas and encouraging personal use of mosquito repellents. The public is also encouraged to spend less time outdoors, wear long covering clothing, apply bug repellent that contains DEET and ensure that mosquitoes cannot enter buildings. Environmentalists have condemned attempts to control the transmitting mosquitoes by spraying pesticide, saying that the detrimental health effects of spraying outweigh the relatively few lives which may be saved and that there are more environmentally friendly ways of controlling mosquitoes. They also question the

effectiveness of insecticide spraying, as they believe mosquitoes that are resting or flying above the level of spraying will not be killed; the most common vector in the northeastern U.S., *Culex pipiens*, is a canopy feeder. An effective horse vaccine was introduced by Fort Dodge Animal Health (Wyeth).[44]

### Treatment

AMD3100, which had been proposed as an antiretroviral drug for HIV, has shown promise against West Nile encephalitis. Morpholino antisense oligos conjugated to cell penetrating peptides have been shown to partially protect mice from WNV disease [45]. There have also been attempts to treat infections using ribavirin, intravenous immunoglobulin, or alpha interferon. GenoMed, a U.S. biotech company, has found that blocking angiotensin II can treat the "cytokine storm" of West Nile virus encephalitis as well as other viruses [46]. In 2007 the World Community Grid launched the Discovering Dengue Drugs – Together project. This uses a distributed network of volunteers' computers via the Berkeley Open Infrastructure for Network Computing (BOINC) to perform computer simulations of interacting molecules. Thousands of small molecules are screened for potential antiviral properties with respect to West Nile and related viruses.[47]

### Vaccination

There is currently no vaccine available to protect humans from the West Nile virus. Scientists are working on this issue and there is hope that a West Nile virus vaccine will become available in the next few years. There is a vaccine licensed for use in horses (known as the equine West Nile vaccine). Some people wonder whether humans should take this vaccine. The answer is no. This vaccine has not been studied in humans and could be harmful. The effectiveness of this vaccine in preventing West Nile virus infections in horses has yet to be fully

evaluated and its effectiveness in humans is completely unknown. Also, veterinary vaccines are not manufactured with the same rigorous quality and purity standards required for human vaccines, nor are they required to undergo the extensive field testing required of human vaccines before they are licensed. For these reasons, veterinary vaccines should never be used in humans. [48]

### Conclusion:

West Nile virus, a member of Japanese encephalitis virus complex, causes serious illness like meningo encephalitis. Cross reactivity in serologic testing is therefore possible. the virus although self controlled can cause deaths in immunocompromised patients, patients on long term chemotherapy, immunosuppressive therapy ,organ transplants ,diabetes mellitus and pregnancy. Small children and old peoples are more prone to the infection and can have massive brain damage. Mosquito control measures are therefore highly needed to prevent infection and further drug borne complications.

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