

A MOSQUITO - BORNE VIRAL DISEASE IN INDIA

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ABSTRACT

West Nile Virus is an arthropod born viruses that transmit mainly through mosquito bites. The virus was first isolated from the West Nile district of Northern Uganda in 1937. After that the virus gradually spread all over the world. WNV outbreaks observed in the various parts of the world including Israel, Egypt, India, France, South Africa, North America etc. 80% of the WNV infection is asymptomatic while 20% shows flu-like symptoms including fever, headache, malaise, nausea etc. As of today no treatment is available for WNV infection and the infection is managed by supportive cares. Mosquito control is the cornerstone of controlling West Nile Virus outbreaks and preventing future ones as there are no antiviral drugs or a vaccine for WNV.

Keywords: Arbovirus, Mosquitoes, West Nile Virus, WNV.

A REVIEW ON WEST NILE VIRUS

West Nile Virus is a positive stranded RNA arboviruses (arthropod borne viruses) belongs to the family Flaviviridae, which includes other human pathogens such as dengue, yellow fever and Japanese encephalitis viruses. The virus was first isolated from the blood of a woman patient from the West Nile district of Northern Uganda in 1937^{1,2}, hence the name West Nile Virus.

Virus characteristics

The structure of WNV particles have been elucidated by Mukhopadhyay et al³. Structurally the WNV virion is a ~50nm icosahedral particle, surrounded by a lipid bilayer. It has a single stranded RNA genome of approximately 11kb, containing 10 genes flanked by 5' and 3' noncoding region (NCR) with no polyadenylation tail at the 3' end. The NCRs of the WNV genome form stem loop structures essential for viral replication.

Epidemiology

West Nile Virus was first isolated from Uganda in 1937. After that WNV outbreaks observed in the various parts of the world including Israel, Egypt, India, France, South Africa, North America etc.. The time line showing the outbreak of WNV in various parts across the world is shown in Table 1.

Transmission

WNV can be transmitted through the bites of infected mosquitoes and ticks, primarily to mammals (E.g. humans, horses, dogs, cats or squirrels) and other hosts (E.g. birds, chickens, or turkeys). The three principal vectors of WNV detected in US are *Culex pipiens*, *Cx quinquefasciatus* and *Cx tarsalis*⁵. During viral entry, the E protein interacts with one or more cell surface receptor(s). It is not completely clear which cellular receptors are involved in WNV binding. DC-SIGN (Dendritic Cell Specific Intercellular adhesion molecule-3-Grabbing Non-integrin), alphaVbeta3 integrin and laminin-binding protein have been reported as potential receptors for WNV binding. After binding to the cell, the virus is taken up via clathrin-mediated endocytosis and in the acidified endosome the E protein undergoes conformational changes resulting in fusion between the viral and cellular membranes. After the fusion event the positive stranded RNA genome is released into the cytoplasm of the cell. The viral RNA is translated into a single polyprotein, which is proteolytically processed to yield three structural proteins: capsid (C); Pre-M/Membrane (prM/M); and Envelope (E); and 7 nonstructural (NS) proteins: NS1; NS2A; NS2B; NS3; NS4A; NS4B; and NS5⁴. Whereas the cleavages at the host signal peptidase located within the lumen of the endoplasmic reticulum, the remaining peptide bonds are cleaved by the virus encoded NS3 protease. Flaviviruses

replication requires the viral protein NS, which then serves as a template for the synthesis of many new copies of the infectious positive strand RNA genome.

WNV has complex host, host amplification and transmission requirements. When an appropriate bird host is infected by the bite of a

mosquito carrying the virus, the virus will amplify in the bird, then an uninfected mosquito can then acquire the virus by biting the viremic bird; both infected mosquitoes can transmit the infection to humans or other hosts by its bite⁵. The life cycle of WNF was shown in Figure 1.

Table 1: Time line showing the outbreak of WNV in various parts across the world

1937	First isolation of WNV from Uganda.
1951	ISRAEL - first recognised epidemic of WNV. During this outbreak the various clinical features associated with infection were first described in detail.
1951-1954	EGYPT - further understanding of ecology, epidemiology and clinical characteristics of WNV.
1957	ISRAEL - severe neurologic manifestations among a group of elderly nursing home residents became the first reports of such neurologic events among human.
1962	FRANCE - patients developed meningitis or encephalitis.
1974	SOUTH AFRICA - thousands of febrile illness cases were documented, with onle one case of encephalitis noted.
1970-1980	RUSSIA, SPAIN, SOUTH AFRICA, INDIA - large outbreaks of WNV were very infrequent.
1981	INDIA – first pediatric fatalities from WN neurological disease were reported.
1996	ROMANIA (Southeastern European Country) - epidemiology and clinical spectrum of WNV appeared to change. it was the first outbreak to be centered in a predominantly urban area, and it was the first outbreak of the virus in which the preponderance of symptomatic cases involved CNS infection. MOROCCO (North Africa) - a high rates of CNS infection were observed.
1997	TUNISIAN OUTBREAK - 173 patients were hospitalized with meningitis or meningoencephalitis and 8 deaths occurred.
1998	ITALY & ISRAEL - these large outbreaks were associated with higher rates of severe CNS diseases and higher fatality rates.
1999	NORTH AMERICA - the virus was first detected in North America. VOLGOGRAD REGION OF RUSSIA - a large outbreak of WNV was observed.
2000	US - progressive spread of WNV through the US. FRANCE
2001	Expanded its geographic range from Mississippi river area to Pacafic Coast.
2002	The number of WNV cases in North America was unprecedented. this was the largest outbreak of WN Meningoencephalitis ever recorded anywhere, and also the largest outbreak of arboviral meningoencephalitis ever documented in the Western hemisphere.
2003	The virus was endemic to continental USA.
2004	INDIA – coinfection with JEV (Japanese encephalitis virus) was observed.
2004-2010	Although most states in US reported cases and fatalities between 2004-2010, these were generally more sporadic.
2010	INDIA – WNV in Tamil Nadu state was associated with ocular disease, an infrequently reported WNV complication.
2012	Outbreak is on track to be one of the worst West Nile season in North America.
2013	CHINA – the first confirmed human cases of WNV in China were reported in 2013.

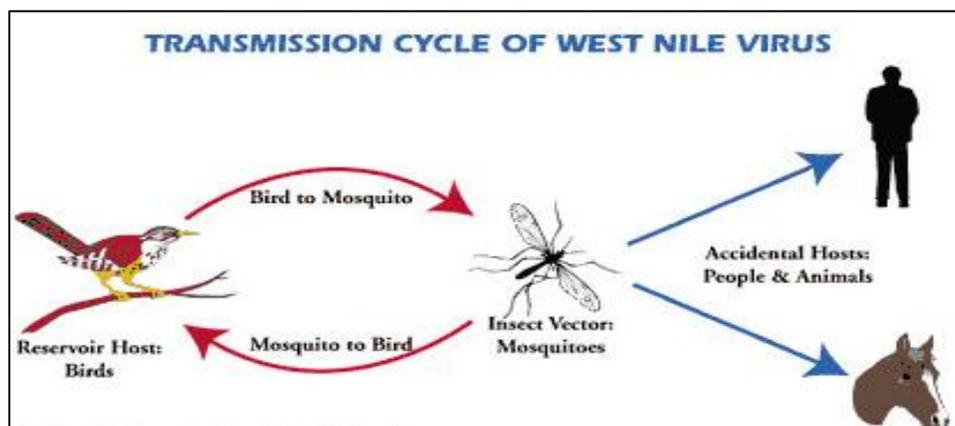


Fig. 1: Life cycle of West Nile Virus

Signs and symptoms

The majority of WNV infections are asymptomatic. Symptomatic infections are primarily a mild, self-limiting febrile illness. However, approximately 1% of infected persons develop neurologic infections and disease. Most symptomatic patients exhibit mild illness with fever, sometimes associated with headache, myalgia, nausea and vomiting and chills. Approximately 5% of patients with symptomatic WNV infection develop neurologic disease including meningitis, encephalitis and poliomyelitis like disease, presented as acute flaccid paralysis^{1,5}.

Diagnosis²

- Nucleic acid based tests for WNV.
- Serologic diagnosis of WNV infections.
- WNV antigen detection.

Treatment

Till now, no cure or specific treatments are available for WNV infection. Supportive care is the only option for caring patients infected with WNV. For mild cases, supportive care includes over the counter medications for fever control and pain relief. In severe cases, patients may require hospitalization for IV fluid administration, medication to control fever and pain, and possibly respiratory support. For patients with meningitis, encephalitis, or flaccid paralysis secondary to infection, treatment is based on guidelines for managing those disorders.

Prevention

As WNV is transmitted mainly through mosquito bites, the best way to avoid WNV is to prevent mosquito bites. The possible precautions that avoid mosquito bites includes,

- ✓ Use insect repellent.
- ✓ Get rid of mosquito breeding sites by emptying standing water from flower pots, buckets or barrels.
- ✓ Stay indoors between dusk and dawn, when mosquitoes are most active.
- ✓ Use screens on windows to keep mosquitoes out.
- ✓ Wear loose, long sleeved shirts and long pants when outdoors.
- ✓ As mosquitoes are thought to be attracted to warm bodies, avoid getting too hot.
- ✓ Use mosquito swatter.

Recent outbreak of WNV

Most recently, two WNV cases are reported in Kozhikode district of Kerala state, India. One case is confirmed by National Institute of Virology (NIV) in Pune and one is suspected case. A woman aged 24 years with confirmed WNV infection is admitted in the Intensive Care Unit in Govt. Medical College, Kozhikode. Further details about the WNV cases are not available^{16,17}.

CONCLUSION

As of today West Nile Virus has spread beyond its original known geographic range and caused human disease all over the world. In majority of the cases the infection is asymptomatic. Fever, headache, myalgia, nausea, chill are some clinical presentation during symptomatic infection. In some cases WNV are associated with meningitis or meningoencephalitis that complicate the situation. Mosquito control is the cornerstone of controlling West Nile Virus outbreaks and preventing future ones as there are no antiviral drugs or a vaccine for WNV.

REFERENCES

1. Rossi SL, Ross TM, Evans JD. West Nile Virus. *Clin Lab Med*. 2010 Mar;30(1):47–65.
2. De Filette M, Ulbert S, Diamond M, Sanders NN. Recent progress in West Nile virus diagnosis and vaccination. *Vet Res*. 2012 Mar 1;43:16.
3. Mukhopadhyay S, Kim B-S, Chipman PR, Rossmann MG, Kuhn RJ. Structure of West Nile virus. *Science*. 2003 Oct 10;302(5643):248.
4. Chancey C, Grinev A, Volkova E, Rios M. The Global Ecology and Epidemiology of West Nile Virus [Internet]. *BioMed Research International*. 2015 [cited 2018 Aug 13]. Available from: <https://www.hindawi.com/journals/bmri/2015/376230/>
5. Denman S, Hart AM. Arthropod-borne Disease: West Nile Fever. *J Nurse Pract*. 2015 Jan 1;11(1):27–33.
6. Al-Jabi SW. Global research trends in West Nile virus from 1943 to 2016: a bibliometric analysis. *Glob Health [Internet]*. 2017 Aug 3 [cited 2018 Aug 13];13. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5543434/>
7. Arnold C. West Nile virus bites back. *Lancet Neurol*. 2012 Dec 1;11(12):1023–4.
8. Calisher JSM and CH. Alexander the Great and West Nile Virus Encephalitis - Volume

- 9, Number 12—December 2003 - Emerging Infectious Diseases journal - CDC. [cited 2018 Aug 13]; Available from: https://wwwnc.cdc.gov/eid/article/9/12/03-0288_article
9. Halouzka ZH and J. West Nile Fever—a Reemerging Mosquito-Borne Viral Disease in Europe - Volume 5, Number 5—October 1999 - Emerging Infectious Diseases journal - CDC. [cited 2018 Aug 13]; Available from: https://wwwnc.cdc.gov/eid/article/5/5/99-0505_article
 10. Kozhikode BG. Suspected West Nile fever case in Kozhikode. The Hindu [Internet]. 2018 Aug 3 [cited 2018 Aug 13]; Available from: <https://www.thehindu.com/news/national/kerala/suspected-west-nile-fever-case-in-kozhikode/article24594982.ece>
 11. Rahav G, Hagin M, Maor Y, Yahalom G, Hindiyyeh M, Mendelson E, et al. Primary Versus Nonprimary West Nile Virus Infection: A Cohort Study. *J Infect Dis*. 2016 Mar 1;213(5):755–61.
 12. Sejvar JJ. West Nile Virus: An Historical Overview. *Ochsner J*. 2003;5(3):6–10.
 13. Simon RB. West Nile virus. *Nursing* 2018 Aug;47(8):58.
 14. Soliman A, Mohareb E, Salman D, Saad M, Salama S, Fayez C, et al. Studies on West Nile virus infection in Egypt. *J Infect Public Health*. 2010 Jan 1;3(2):54–9.
 15. 'Symptoms are of West Nile fever'. The Hindu [Internet]. 2006 Oct 3 [cited 2018 Aug 13]; Available from: <https://www.thehindu.com/todays-paper/tp-national/tp-kerala/symptoms-are-of-west-nile-fever/article3055732.ece>.
 16. Kerala: After Nipah, West Nile viral infection suspected in Kozhikode [Internet]. The Indian Express. 2018 [cited 2018 Aug 13]. Available from: <https://indianexpress.com/article/india/suspected-west-nile-fever-case-in-keralas-kozhikode-5290751/>
 17. Two people suspected to have contracted West Nile Virus in Kozhikode [Internet]. The News Minute. 2018 [cited 2018 Aug 13]. Available from: <https://www.thenewsminute.com/article/two-people-suspected-have-contracted-west-nile-virus-kozhikode-85925>
 18. West Nile Virus [Internet]. [cited 2018 Aug 13]. Available from: <https://medlineplus.gov/westnilevirus.html>
 19. West Nile virus [Internet]. World Health Organization. [cited 2018 Aug 13]. Available from: <http://www.who.int/news-room/factsheets/detail/west-nile-virus>
 20. West Nile Virus | NIH: National Institute of Allergy and Infectious Diseases [Internet]. [cited 2018 Aug 13]. Available from: <https://www.niaid.nih.gov/diseases-conditions/west-nile-virus>
 21. West Nile Virus Clinical Presentation: History, Physical, Causes [Internet]. [cited 2018 Aug 13]. Available from: <https://emedicine.medscape.com/article/312210-clinical>.