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THE DEVASTATING WEST NILE VIRUS (WNV) AND ITS PREVENTION

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ABSTRACT

West Nile virus (WNV) is an infectious disease that first appeared in the United States in 1999. Infected mosquitoes spread the virus that causes it. People who get WNV usually have no symptoms or mild symptoms. The symptoms include a fever, headache, body aches, skin rash, and swollen lymph glands. They can last a few days to several weeks, and usually go away on their own. If West Nile virus enters the brain, however, it can be life-threatening. It may cause inflammation of the brain, called encephalitis, or inflammation of the tissue that surrounds the brain and spinal cord, called meningitis. A physical exam, medical history, and laboratory tests can diagnose it. West Nile virus was first identified in 1937 in Uganda in eastern Africa. It was first discovered in the United States in the summer of 1999 in New York. Since then, the virus has spread throughout the US. Researchers believe West Nile virus is spread when a mosquito bites an infected bird and then bites a person. West Nile virus (WNV) infection is a mosquito-borne zoonosis that is endemo-epidemic in Europe. The disease affects countries in southern, eastern and western Europe. About 2,000 people have died of West Nile virus in the United States since it was first detected in New York City in 1999.

KEYWORDS: arbovirus, disease control, eastern equine encephalitis virus, Lyme disease, predictive model, public health, vector index.

INTRODUCTION

West Nile virus (WNV) is a single-stranded RNA virus that causes West Nile fever. It is a member of the family Flaviviridae, specifically from the genus Flavivirus, which also contains the Zika virus, dengue virus, and yellow fever virus. West Nile virus is primarily transmitted by mosquitoes, mostly species of Culex. The primary hosts of WNV are birds, so that the virus remains within a "bird–mosquito–bird" transmission cycle.[1]

Virus classification

Table-1: Taxonomy of WNV.

Realm:	*Riboviria*
Kingdom:	*Orthornavirae*
Phylum:	*Kitrinoviricota*
Class:	*Flasuviricetes*
Order:	*Amarillovirales*
Family:	*Flaviviridae*
Genus:	*Flavivirus*
Species:	*West Nile virus*

Structure: The composition of the virus has some surprising similarities to a peanut M&M. First we find the outer layer of the virus, which is a lipid bilayer known as an envelope. We can compare this to the chocolate layer in our M&M. However, instead of a smooth candy surface, on the virus we would see spiky glycoproteins projecting out from the envelope. These proteins will help the virus bind to the cells of its host. Like the prized peanut hidden in our M&M, tucked safely in the center of the virus is the core, which is called the nucleocapsid. The nucleocapsid is made up of two parts.[2]

- First is the protein shell, known as the capsid. Like a treasure chest, this structure protects the precious cargo inside.
- The second part of the nucleocapsid is genetic information in the form of single-stranded RNA.

Looking closer at the capsid, we see that it is not simply a round bubble which holds the RNA. This protein shell is quite an advanced structure, known as an icosahedron. For those of you who are not geometry buffs, an icosahedron is an object with twenty flat faces. Perhaps a unique structure, it serves.

Genome: The West Nile virus genome. WNV is a positive-sense, single-stranded RNA virus. Its genome is approximately 11,000 nucleotides long and is flanked by 5' and 3' non-coding stem loop structures. The coding region of the genome codes for three structural proteins and seven nonstructural (NS) proteins, proteins that are not incorporated into the structure of new viruses. The WNV genome is first translated into a polyprotein and later cleaved by virus and host proteases into separate proteins (i.e. NS1, C, and E). to allow for plenty of room for the all-important RNA.[3]

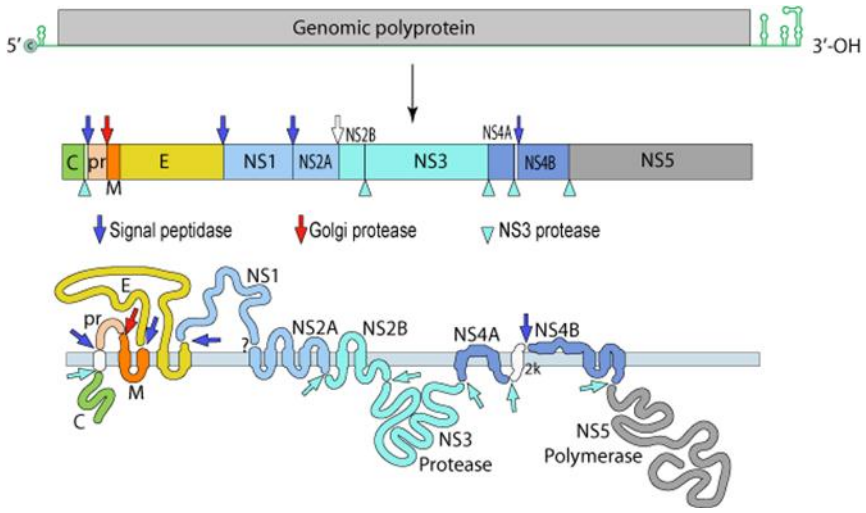

Figure-1: WNV Genome code.

Structural proteins: Structural proteins (C, prM/M, E) are capsid, precursor membrane proteins, and envelope proteins, respectively. The structural proteins are located at the 5' end of the genome and are cleaved into mature proteins by both host and viral proteases.[4]

Nonstructural proteins: Nonstructural proteins consist of NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. These proteins mainly assist with viral replication or act as proteases. The nonstructural proteins are located near the 3' end of the genome.

C: Capsid protein; encloses the RNA genome, packages RNA into immature virions.

prM/M: Viruses with M protein are infectious: the presence of M protein allows for the activation of proteins involved in viral entry into the cell. prM (precursor membrane) protein is present on immature virions, by further cleavage by furin to M protein, the virions become infectious.

E: A glycoprotein that forms the viral envelope, binds to receptors on the host cell surface in order to enter the cell.[5]

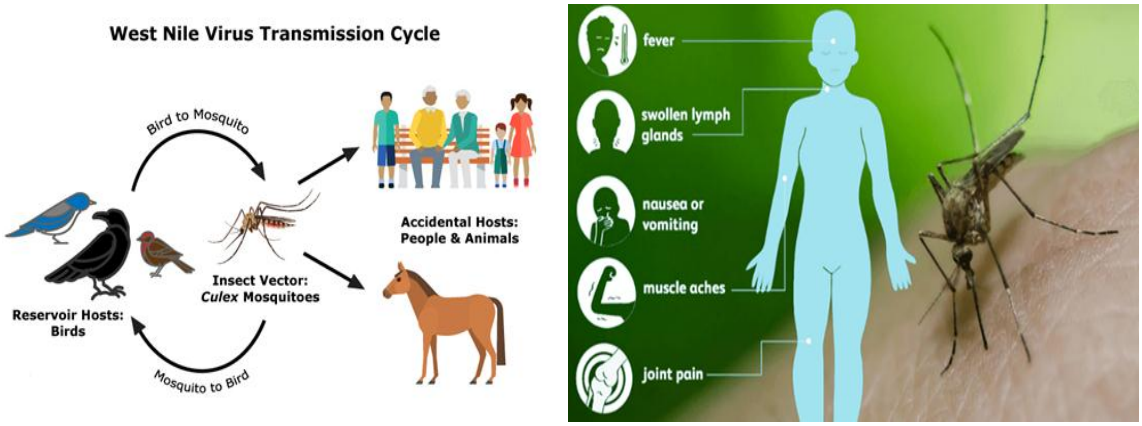

Figure-2: Life cycle.

Life cycle: Once WNV has successfully entered the bloodstream of a host animal, the envelope protein, E, binds to attachment factors called glycosaminoglycans on the host cell. These attachment factors aid entry into the cell, however, binding to primary receptors is also necessary. Primary receptors include DC-SIGN, DC-SIGN-R, and the integrin αvβ3. By binding to these primary receptors, WNV enters the cell through clathrin-mediated endocytosis. As a result of endocytosis, WNV enters the cell within an endosome.[6]

The acidity of the endosome catalyzes the fusion of the endosomal and viral membranes, allowing the genome to be released into the cytoplasm. Translation of the positive-sense single-stranded RNA occurs at the endoplasmic reticulum; the RNA is translated into a polyprotein which is then cleaved by viral proteases NS2B-N23 to produce mature proteins. In order to replicate its genome, NS5, an RNA polymerase, forms a replication complex with other nonstructural proteins to produce an intermediary negative-sense single-stranded RNA; the negative-sense strand serves as a template for synthesis of the final positive-sense RNA. Once the positive-sense RNA has been synthesized, the capsid protein, C, encloses the RNA strands into immature virions. The rest of the virus is assembled along the endoplasmic reticulum and through the Golgi apparatus, and results in non-infectious immature virions. The E protein is then glycosylated and prM is cleaved by furin, a host cell protease, into the M protein, thereby producing an infectious mature virion. The mature viruses are then secreted out of the cell.[7]

Host range and transmission: *Culex pipiens* mosquitoes are a vector for WNV. The natural hosts for WNV are birds and mosquitoes. Over 300 different species of bird have been shown to be infected with the virus. Some birds, including the American crow (*Corvus brachyrhynchos*), blue jay (*Cyanocitta cristata*) and greater sage-grouse (*Centrocercus*

urophasianus), are killed by the infection, but others survive. The American robin (*Turdus migratorius*) and house sparrow (*Passer domesticus*) are thought to be among the most important reservoir species in N. American and European cities. Brown thrashers (*Toxostoma rufum*), gray catbirds (*Dumetella carolinensis*), northern cardinals (*Cardinalis cardinalis*), northern mockingbirds (*Mimus polyglottos*), wood thrushes (*Hylocichla mustelina*) and the dove family are among the other common N. American birds in which high levels of antibodies against WNV have been found.[8]

WNV has been demonstrated in a large number of mosquito species, but the most significant for viral transmission are Culex species that feed on birds, including *Culex pipiens*, *C. restuans*, *C. salinarius*, *C. quinquefasciatus*, *C. nigripalpus*, *C. erraticus* and *C. tarsalis*. Experimental infection has also been demonstrated with soft tick vectors, but is unlikely to be important in natural transmission. WNV has a broad host range, and is also known to be able to infect at least 30 mammalian species, including humans, some non-human primates, horses, dogs and cats. Some infected humans and horses experience disease but dogs and cats rarely show symptoms. Reptiles and amphibians can also be infected, including some species of crocodiles, alligators, snakes, lizards and frogs. Mammals are considered incidental or dead-end hosts for the virus: they do not usually develop a high enough level of virus in the blood (viremia) to infect another mosquito feeding on them and carry on the transmission cycle; some birds are also dead-end hosts. In the normal rural or enzootic transmission cycle, the virus alternates between the bird reservoir and the mosquito vector. It can also be transmitted between birds via direct contact, by eating an infected bird carcass or by drinking infected water. Vertical transmission between female and offspring is possible in mosquitoes, and might potentially be important in overwintering. In the urban or spillover cycle, infected mosquitoes that have fed on infected birds transmit the virus to humans. This requires mosquito species that bite both birds and humans, which are termed bridge vectors. The virus can also rarely be spread through blood transfusions, organ transplants, or from mother to baby during pregnancy, delivery, or breastfeeding. Unlike in birds, it does not otherwise spread directly between people.[9]

History: The virus was discovered in Uganda in 1937 and was first detected in North America in 1999. West Nile Virus has been reported in Europe, Africa, Asia, Australia, and North America. In the United States thousands of cases are reported a year, with most

occurring in August and September. It can occur in outbreaks of disease. A surveillance system in birds is useful for early detection of a potential human outbreak.[10]

Epidemiology: According to the Center for Disease Control, infection with West Nile Virus is seasonal in temperate zones. Climates that are temperate, such as those in the United States and Europe, see peak season from July to October. Peak season changes depending on geographic region and warmer and humid climates can see longer peak seasons. All ages are equally likely to be infected but there is a higher amount of death and neuroinvasive West Nile Virus in people 60-89 years old. People of older age are more likely to have adverse effects of being infected. There are several modes of transmission but the most common cause of infection in humans is by being bitten by an infected mosquito. Other modes of transmission include blood transfusion, organ transplantation, breast-feeding, transplacental transmission, and laboratory acquisition. These alternative modes of transmission are extremely rare.[11]

Diagnosis: West Nile virus can be diagnosed by a number of different tests:

- IgG antibody sero-conversion (or significant increase in antibody titers) in two serial specimens collected at a one-week interval by enzyme-linked immunosorbent assay (ELISA);
- IgM antibody capture enzyme-linked immunosorbent assay (ELISA);
- neutralization assays;
- viral detection by reverse transcription polymerase chain reaction (RT-PCR) assay, and
- Virus isolation by cell culture.

IgM can be detected in nearly all cerebrospinal fluid (CSF) and serum specimens received from WNV infected patients at the time of their clinical presentation. Serum IgM antibody may persist for more than a year.

Treatment and vaccine: Treatment is supportive for patients with neuro-invasive West Nile virus, often involving hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections. No vaccine is available for humans.[12]

Figure-3: Nile river.

Vector and animal hosts: WN virus is maintained in nature in a mosquito-bird-mosquito transmission cycle. Mosquitoes of the genus Culex are generally considered the principal vectors of WNV, in particular Cx. Pipiens. WNV is maintained in mosquito populations through vertical transmission (adults to eggs). Birds are the reservoir hosts of WNV. In Europe, Africa, Middle East and Asia, mortality in birds associated with WNV infection is rare. In striking contrast, the virus is highly pathogenic for birds in the Americas. Members of the crow family (Corvidae) are particularly susceptible, but virus has been detected in dead and dying birds of more than 250 species. Birds can be infected by a variety of routes other than mosquito bites, and different species may have different potential for maintaining the transmission cycle.

Horses, just like humans, are "dead-end" hosts, meaning that while they become infected, they do not spread the infection. Symptomatic infections in horses are also rare and generally mild, but can cause neurologic disease, including fatal encephalomyelitis.[13]

Figure-4: Mosquito bite & Vaccination for WNV.

Prevention: Preventing transmission in horses:

Since WNV outbreaks in animals precede human cases, the establishment of an active animal health surveillance system to detect new cases in birds and horses is essential in providing early warning for veterinary and human public health authorities. In the Americas, it is important to help the community by reporting dead birds to local authorities.

Vaccines have been developed for horses. Treatment is supportive and consistent with standard veterinary practices for animals infected with a viral agent.

Reducing the risk of infection in people: In the absence of a vaccine, the only way to reduce infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus.[14]

Public health educational messages should focus on the following: Reducing the risk of mosquito transmission. Efforts to prevent transmission should first focus on personal and community protection against mosquito bites through the use of mosquito nets, personal insect repellent, by wearing light coloured clothing (long-sleeved shirts and trousers) and by avoiding outdoor activity at peak biting times. In addition community programmes should encourage communities to destroy mosquito breeding sites in residential areas.

Reducing the risk of animal-to-human transmission. Gloves and other protective clothing should be worn while handling sick animals or their tissues, and during slaughtering and culling procedures.

Reducing the risk of transmission through blood transfusion and organ transplant. Blood and organ donation restrictions and laboratory testing should be considered at the time of the outbreak in the affected areas after assessing the local/regional epidemiological situation.[15]

Vector Control: Effective prevention of human WNV infections depends on the development of comprehensive, integrated mosquito surveillance and control programmes in areas where the virus occurs. Studies should identify local mosquito species that play a role in WNV transmission, including those that might serve as a “bridge” from birds to human beings. Emphasis should be on integrated control measures including source reduction (with community participation), water management, chemicals, and biological control methods.[16]

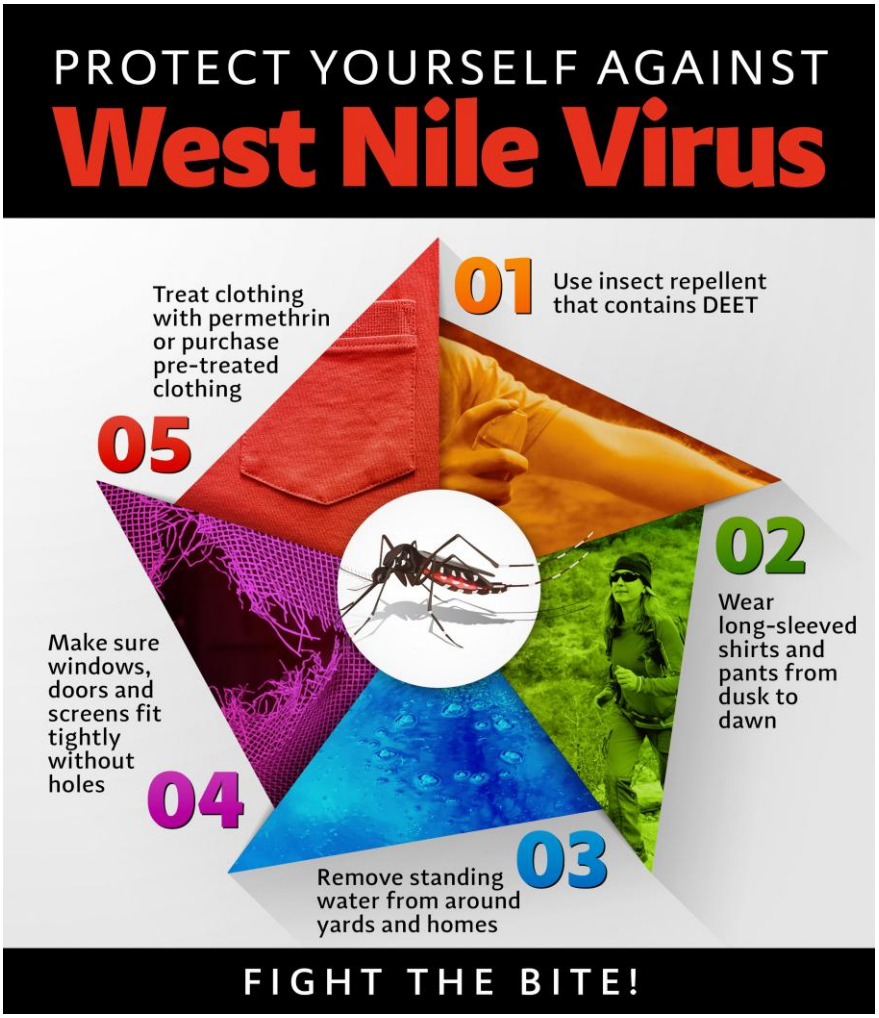

Figure-5: Fight the WNV carrier bite.

Preventing infection in health-care settings: Health-care workers caring for patients with suspected or confirmed WNV infection, or handling specimens from them, should implement standard infection control precautions. Samples taken from people and animals with suspected WNV infection should be handled by trained staff working in suitably equipped laboratories.[17]

Figure-6: Diagnosis and treatment.

Ecology: West Nile virus is a single-stranded RNA virus that is maintained in a bird-mosquito-bird cycle. In early spring in Canada, adult mosquitoes emerge from their aquatic stages and begin infecting birds. Both wild and domestic birds, particularly corvine species, such as ravens, jays, and crows, can serve as viral reservoirs.[18]

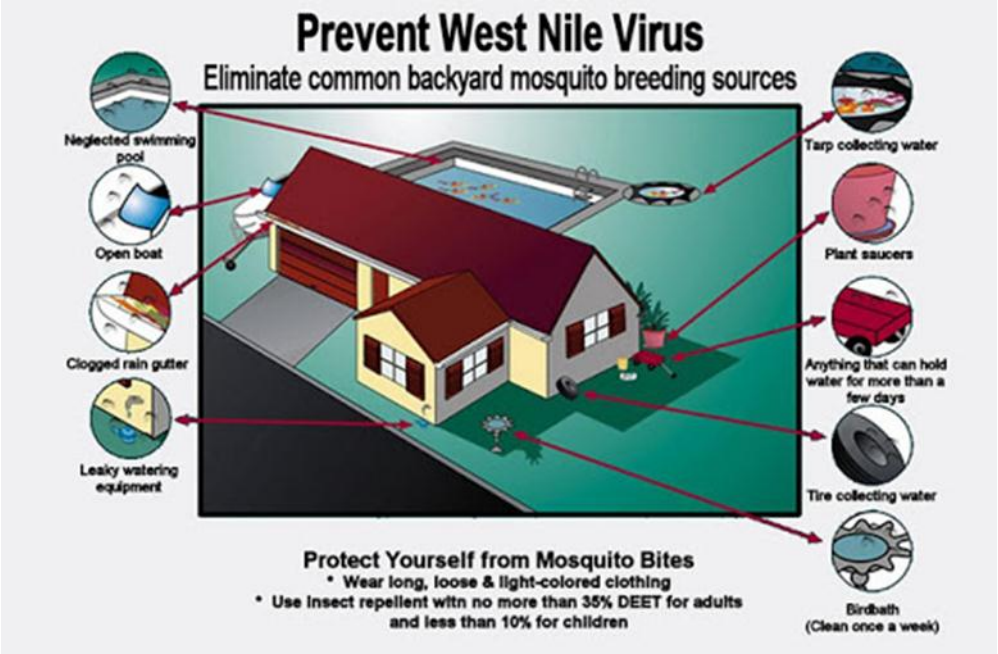

Figure-7: No to mosquito and Yes to health.

Infected birds give the virus an opportunity to amplify, resulting in spread of infection to large numbers of bridge vectors. These bridge vectors include mosquitoes that bite both humans and birds, enabling the virus to pass from bird hosts to humans without direct contact between humans and birds. While the Culex genus of mosquito is the principal vector, bites from other mosquitos can lead to human infection also. Many birds are found dead in a region shortly before human cases develop there.[19]

Climate change: Infectious disease transmission is sensitive to local, small-scale differences in weather, human modification of the landscape, the diversity of animal hosts, and human behavior affects vector-human contact, among other factors. Climate change affects human health in various forms. The impacts of climate change are complex, vary in scale and timing and depend on environmental conditions and human vulnerability. Climate change influences the emergence of the vector-borne disease West Nile Virus. Climate change alters disease rates, ranges, seasonality and affects the distribution of WNV, Climate change is a major environmental factor that influences the epidemiology of the disease. Projected changes in

flood frequency and severity can bring new challenges in flood risk management. For urban areas in particular, flooding impacts critical infrastructure in ways that are difficult to foresee and can result in interconnected and cascading failures. Weather conditions affected by climate change including temperature, precipitation and wind may affect the survival and reproduction rates of mosquitoes, suitable habitats, distribution, and abundance. Ambient temperatures drive mosquito replication rates and transmission of WNV by affecting the peak season of mosquitoes and geographic variations. For example, increased temperatures can affect the rate of virus replication, speed up the virus evolution rate, and viral transmission efficiency. Furthermore, higher winter temperatures and warmer spring may lead to larger summer mosquito populations, increasing the risk for WNV. Similarly, rainfall may also drive mosquito replication rates and affect the seasonality and geographic variations of the virus. Studies show an association between heavy precipitation and higher incidence of reported WNV. Likewise, wind is another environmental factor that serves as a dispersal mechanism for mosquitoes.[20]

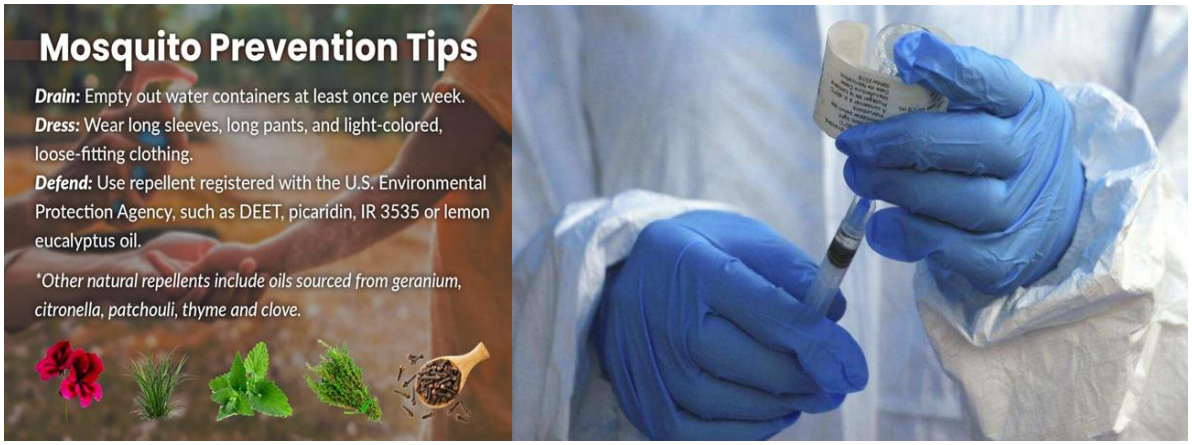

Figure-8: Prevention from WNV.

Global Distribution of West Nile Virus CDC: Mosquitoes have extremely wide environmental tolerances and a nearly ubiquitous geographical distribution, being present on all major land masses except Antarctica and Iceland. Nevertheless, changes in climate and land use on ecological timescales can variously expand or fragment their distribution patterns, raising consequent concerns for human health.

CONCLUSION

Infections of WNV have resulted in pronounced human and economic losses since WNV first appeared in the United States in 1999. The year 2002 saw a dramatic increase in the number

of cases, widening geographic distribution, and an increase in the period when cases occurred. Also, several new modes of transmission and new clinical presentations were recognized. The illness causes substantial morbidity in elderly persons, immunosuppressed persons, and pregnant women. These groups should take special precautions against mosquito bites. Management consists of supportive care; no specific treatment or vaccine is currently available.

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