West Nile Virus

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02/11/15
History And Description of the WNV...

- While doing research on yellow fever, West Nile Virus was isolated from the blood of a febrile patient in the West Nile district of northern Uganda in 1937 Edward. T (pg 133).

- According to MCP article, WNV is a mosquito-borne and is the etiologic agent of West Nile encephalitis and “their pathogenic mechanisms depend on complex virus-cell interactions” and the “clinical manifestations of West Nile Virus infection are diverse.” (MCP, 2009).

- According to Theresa L. Smith, WNV is spherical shaped virus of 45-50 nm in diameter; single stranded RNA is 11,000-12,000 nucleotides long which encodes for 7 nonstructural and 3 structural proteins; its RNA is enclosed in an “icosahedral nucleocapsid made of 12kDa capsid protein building blocks [which in ] turn the capsid lies within a host-derived membrane envelope altered by two viral membrane glycoproteins, E, and prM.” (Edward.T, 2006)
History and Description continued..
In the book, Immunology and Microbiology by George Valiakos et.al, When WNV was introduced in North America in 1999, it became a public health concern. (Valiakos et.al).

Just before this Romania recorded one of the first and largest outbreak of West Nile neuroinvasive disease in Europe (1996) and there were 393 confirmed cases (Valiakos et.al).

After that outbreaks of WNV and Encephalitis were seen in regions throughout the world which included America, Europe, and Middle East, which caused animal and human deaths (Valiakos et.al).
In 2010 and 2011, there were a great number of infections that (WNV) occurred in Greece.

There were 363 laboratory confirmed cases and 44 deaths.

“WNV lineage 2 strains were first detected from pools of *Culex* mosquitoes (strain Nea Santa-Greece-2010) and a Eurasian magpie (strain magpie-Greece/10) at the epicenter of the outbreak.” (Valiakos.G, et.al).

(Valiakos.G, et.al)
Replication Cycle of WNV

- Can replicate in various cell cultures (mammal, amphibian, insects, and avian). In the first step, the E protein binds to a cellular molecule-receptor. (Valiakos G. et.al)

- “The virion is attached to the cellular membrane of the host cell via the cellular receptors, and the envelope fuses with the membrane. The viral RNA is released by the nucleocapsid with a yet unknown mechanism and serves as mRNA for translation of all viral proteins and as template during RNA replication. Virion assembly and release of them to the extracellular milieu complete the replication cycle.” (Valiakos. G, et.al).
Replication Cycle
Virulence And Transmission

- The factor contributing to the virulence of West Nile Virus is its ability to infect target cells and invade immune system through the arrangement of envelope proteins on the surface of the virus (N-linked glycosylation of the E. proteins).

- Also warm temperatures could be another Virulence factors since mosquitoes tend to like warm climates.

- “Mutations at the Envelope protein at residues 154 to 156, which abolished the N-linked glycosylation motif (N-Y-S/T) was proved to attenuate virus pathogenicity in mouse models; these mutations seem to alter the protein such that it cannot be recognized by oligosaccharyl-transferase, thus glycan loss is caused. This glycosylation motif has been recognized to various flaviviruses and spatially is located in close proximity to the center of the fusion peptide of DII of E protein, and thus is considered to increase the stability of the protein to a fusion-active form even at high temperatures.” (Valiakos.G, et.al).
Transmission

- Most commonly transmitted to humans by mosquitoes while other means include; blood transfusions, exposure in lab settings, organ transplant, etc.

- When mosquitoes bite an infected bird, the virus enters the mosquitoes blood stream which moves to its salivary glands. When the mosquito bites a human, it releases it into the humans or animals (host).

- The incubation period ranges from 3 to 14 days. (Mayoclinic).
West Nile Virus Transmission Cycle

In nature, West Nile virus cycles between mosquitoes (especially Culex species) and birds. Some infected birds can develop high levels of the virus in their bloodstream and mosquitoes can become infected by biting these infected birds. After about a week, infected mosquitoes can pass the virus to more birds when they bite.

Mosquitoes with West Nile virus also bite and infect people, horses and other mammals. However, humans, horses and other mammals are not good hosts. This means that they do not develop high levels of virus in their bloodstream, and cannot pass the virus on to other biting mosquitoes.
Pathophysiology

- After an infected mosquito bite, WNV infects keratinocytes and langerhans cells, which then migrates to lymph nodes which results in primary Viremia (refers to the initial spread of virus in the blood from the first site of infection). Valiakos. G, et.al.

- Then the virus spreads to the peripheral viceral organs such as the kidneys and spleen where there is a new replication (happening in epithelium cells and macrophages). Valiakos.G,et.al.

- Depending on the level of virus, the virus may cross the blood brain barrier and enter the central nervous system causing meningo encephalitis. Valiakos. G, et.al.
WNV infects the neurons in the CNS causing degeneration and cell death. Infectious virus could persist for 4 months! (Valiakos.G. et, al).
Most common signs and symptoms of WNV are

- Fever, headaches, body aches, fatigue, skin rash, eye pain, and swollen lymph nodes.
- Some serious signs of the infection are neurological infections (encephalitis or meningoencephalitis), inflammation of the spinal cord, and acute flaccid paralysis.
- The signs and symptoms for West Nile fever can last a few days but signs of encephalitis and meningitis can linger for a while.
According to the MMWR weekly, in August of 2002, a microbiologist working in U.S laboratory “was performing a necropsy on a blue jay submitted as part of a state’s WNV surveillance program.”

He lacerated a thumb while using a scalpel while removing the bird’s brain. The wound was cleansed and bandaged.

After four days, the microbiologists had acute symptoms: headaches, myalgias and malaise with chills, sweats, dysesthesias, recurring hot flashes, swelling of post-auricular lymph nodes, and anorexia.
Two days later noted a rash that began on his face and then appeared over his trunk, arms, and legs during the next 3 days and disappeared overtime.

On the third day (7 days post injury), the microbiologist goes to see a physician. He did not report any history of mosquito bites, prolonged outdoor activities, or recent blood transfusion.

On physical examination, microbiologist was feverish with redness of the skin due to inflammation on the cheeks.
Serial serum samples were taken and tested by the CDC for WNV infection, which revealed that he had an acute WNV. The initial specimen (collected 3 days after illness) was negative for neutralizing antibodies, but specimen collected 13 and 21 days after illness were both positive WNV-IgM antibody.

According to case report, the brain of the blue Jay tested positive for WNV RNA by real-time polymerase chain reaction using two primer/probe sets.
The Doctor may perform Lab tests—a blood test shows a rising level of antibodies to the West Nile Virus. A positive RNA test for the WNV is also an indicator that you have the virus.

Lumbar puncture/Spinal tap is done to diagnose meningitis by analyzing the cerebrospinal fluid surrounding the brain which may show elevated amounts of white cell count.

Brain tests such as EEG can be done to test the brains activity level and an MRI can help detect brain inflammation.

(Mayoclinic)
Methods of Prevention and Treatment

- People can recover from West Nile Virus without a treatment but exceptions go to the ones that are serious.

- Scientists are investigating on the interferon therapy—type of immune cell therapy—to treat encephalitis (Mayo Clinic)
Prevention

- Eliminate standing water from your environment as it is a breeding ground for mosquitoes.
- Avoid outdoor activities when mosquitoes are very prevalent or apply anti mosquito repellent when you know there is mosquitoes around.
- Wear long sleeve shirt and pants especially during night times since mosquitoes love to come out at night.

(Mayoclinic)
According to the CDC, as of January 13, 2015, “a total of a total of 47 states and the District of Columbia have reported West Nile virus infections in people, birds, or mosquitoes in 2014. Overall, 2,122 cases of West Nile virus disease in people have been reported to CDC. Of these, 1,283 (60%) were classified as neuroinvasive disease (such as meningitis or encephalitis) and 839 (40%) were classified as non-neuroinvasive disease.” (CDC).
Statistics (CDC)
So why study West Nile Virus......

- We as citizens should do as much as we can to prevent ourselves from getting this infection. As we can see that it's not fun to be sick; not fun to have inflammation of our brains which can lead to a lot of problems such as not thinking clearly, pain, suffering, and encephalitis and meningitis.

- The main reason, is that it can lead to death!
Spherical virus of 45–50 nm in diameter, with positive-sense, single-stranded RNA is 11000–12,000 nucleotides long. It encodes for 7 nonstructural and 3 structural proteins.
Transmission Cycle of the West Nile Virus

1. Crow-to-crow transmission has been demonstrated in caged birds.

2. Typical WNV transmission cycle: bird ↔ mosquito
   Mosquitoes become infected when they bite birds infected with WNV.

3. "Dead-end" carriers: The virus in mammals generally is not sufficient to be transmitted back to the mosquito, thereby ending the transmission cycle.

4. Mammals bitten by infected mosquitoes may test positive for WNV, although some mammals will not get ill.

Infected mosquitoes transmit the virus to birds. Birds of some species get ill and die while others become infected but do not show signs of the disease.
References

Edward, T. (December, 2006). *Emerging Viruses in Human Populations Volume 16*. Elsevier Science Technology. (The details on West Nile Virus are on pages 133-135 and a link is given below to excess it online as long as you have username and password.


(This particular source above is taken from Cleveland Clinic website. Just follow the link which will take you to what I used in the presentation).


(Just follow the link and it will take you the Ochsner Journal and there you will find the information about West Nile Virus)
References

  www.cdc.gov/mmwr/preview/mmwrhtml/mm5150a2.htm
  (Follow the link and it will take you to the spot where I took the case studies from. If you go to CDC website, and type in the search box; history of West Nile Virus, it will show you a list of choices and you have to click the one that says Laboratory-Acquired West Nile Virus infections---United..., otherwise follow the link)

  (http://www.intechopen.com/books/viral-replication)
  (Just follow the link and it will take you to the book site. Click on Chapter 2 to get to the site that I used for West Nile Virus)
(follow the link and it will take you to CDC website. Then click on Transmission and Statistics & Maps to go to the site where I found information on West Nile Virus)

Mayoclinic. Diseases and Conditions: West Nile Virus-Definition, symptoms, Treatment, prevention, diagnosis and Treatment. © 1998-2015 Mayo Foundation for Medical Education and Research. All rights reserved.
http://www.mayoclinic.org/diseases-conditions/west-nile-virus/basics/definition/con-20023076
(Just follow the link to go to the Mayoclinic Website that is specifically on West Nile virus. Then click on the arrows to look at the symptoms, risk factors, prevention, and treatment)
Some of the pictures were already used in the sources above. Below are the separate pictures that I took from other website and the links are given below:


- https://www.google.com/search?q=pictures+of+west+nile+viruses&rlz=1C1_____enUS524US524&esvpx=2&biw=1366&bih=653&tbm=isch&imgil=EbLsCxDGw9cvqM%253A%253BBbQQPhWcg-2P_wM%253Bhttp%25252F%25252Fwww.austincc.edu%25252Fmicrobio%25252F2704s%25252F2704Fwn1.html&m&source=iu&pf=m&fir=EbLsCxDGw9cvqM%253A%253CbQQPhWcg-2P_wM%253C &usg=___nYCFafebgf3DSII1cVjEgh_w%3D&ved=0CDEQyjc&ei=WSPcVID-BcSzogSl3oHgCQ#imgdii= &imgrc=E8GxSG0CHSLTtM%253A%253BHWPoiVHAhODT%252Bhttp%25253A%25252F252F252Fwwy.bayequest.info%25252Fhorsetalk%25252F252FImages%25252Fwestnile.jpg%3Bhttp%25252F%25252F252F252Fwww.bayequest.info%25252Fhorsetalk%25252F252Fwestnilevirus1.htm%3B530%3B429 (Date: 2/11/15)

- https://www.google.com/search?q=pictures+of+west+nile+viruses&rlz=1C1_____enUS524US524&esvpx=2&biw=1366&bih=653&tbm=isch&imgil=EbLsCxDGw9cvqM%253A%253BBbQQPhWcg-2P_wM%253Bhttp%25252F%25252Fwww.austincc.edu%25252Fmicrobio%25252F2704s%25252F2704Fwn1.html&m&source=iu&pf=m&fir=EbLsCxDGw9cvqM%253A%253CbQQPhWcg-2P_wM%253C &usg=___nYCFafebgf3DSII1cVjEgh_w%3D&ved=0CDEQyjc&ei=WSPcVID-BcSzogSl3oHgCQ#imgdii= &imgrc=noXTIA7Y7lyudM%253A%253BWrAg-dCuN1PeM%253Bhttp%25253A%25252F252F252Fwww.cdc.gov%25252Fwestnile%25252FImages%25252F252F13_240124_west_nile_lifecycle_birds_plainlanguage_508.jpg%3Bhttp%25253A%25252F%25252F252Fwww.cdc.gov%25252Fwestnile%25252Ftransmission%25252F252F%3B550%3B425 (Date: 2/11/15)