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THE MOSQUITO BORNE WEST NILE VIRUS INFECTION: IS IT THREATING TO EGYPT OR A NEGLECTED ENDEMIC DISEASE?

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Abstract

West Nile virus (WNV) is a mosquito-borne zoonotic arbovirus belonging to the genus Flavivirus in the family Flaviviridae. The virus is found in temperate and tropical regions worldwide, but first identified in the West Nile sub-region in the East African nation of Uganda in 1937. Prior to the mid-1990s WNV infection was sporadically and considered a minor risk for humans, until an outbreak in Algeria in 1994, with cases of WNV-caused encephalitis, and the first large outbreak in Romania in 1996, with a high number of cases with neuroinvasive disease. WNV has now spread globally to Europe beyond the Mediterranean Basin and the United States, is now considered to be an endemic pathogen in worldwide especially in Africa

The WNV transmission is mainly by various mosquitoes species, also ticks were incriminated The birds especially passerines are the most commonly infected animal and serving as the prime reservoir host

In Egypt more than 110 mosquito species and subspecies and more than 32 genera of ticks were identified. Besides, not less than 150 species of migratory birds visit Egypt annually in addition to 350 resident ones.

This review provided an overview of the current understanding flaviviruses mainly WNFV. Primary care physician and senior nurse should be able to include the disaster diseases in differential diagnosis of various clinical conditions. They should take a thorough history to request specific dependable laboratory test(s) as soon as possible, and positive patient should be transferred to the fever hospital.

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Introduction

West Nile virus (WNV) is a mosquito-borne zoonotic arbovirus belonging to the genus Flavivirus in the family *Flaviviridae*. This flavivirus is found in the temperate and tropical regions of the world. It was first identified in the West Nile sub-region in the East African nation of Uganda in 1937. Prior to the mid1990s, WNV disease occurred

only sporadically and was considered a minor risk for humans, until an outbreak in Algeria in 1994, with cases of WNV-caused encephalitis, and the first large outbreak in Romania in 1996, with a high number of cases with neuroinvasive disease (Khairallah *et al*, 2012). WNV has now spread globally, with the first case in the Western Hemisphere being identified in New York City in 1999over the next 5 years, the virus spread across the continental United States, north into Canada, and southward into the Caribbean Islands and Latin America. WNV also spread to Europe, beyond the Mediterranean Basin [a new strain of the virus was recently (2012) identified in Italy]. WNV is now considered to be an endemic pathogen in Africa, Asia, Australia, the Middle East, and Europe and in the United States, which in 2012 has experienced one of its worst epidemics (Schmidt-Chanasit *et al,* 2012).

WNV, a member of the Japanese encephalitis virus antigenic complex, was first isolated in a blood sample in a patient from the West Nile province of Uganda in 1937. This RNA virus was initially considered of minor public health importance (Gubler, 2007). It emerged from obscurity in 1999 when the first incursion of the virus into North America caused 62 cases of encephalitis and seven deaths in New York. Since that time, the virus has dramatically spread, and WN virus activity has now been detected in all 48 continental states, the District of Columbia, and Puerto Rico. The WN virus causes both sporadic infection and outbreaks that may be associated with severe neurologic disease (Petersen and Hayes, 2008).

WN virus is one of the most widely distributed of all arboviruses with an extensive distribution in the Old World, throughout Africa, the Middle East, parts of Europe and the former Soviet Union, South Asia, and Australia. The virus had not been detected in the Americas before the 1999 New York City outbreak. It is unknown how WN virus got to the United States; however, the circulating strain is nearly genetically identical to a virus identified in Israel, suggesting importation from the Middle East (Lanciotti *et al*, 1999).

Since the first discovery of WN virus, infrequent human outbreaks were mostly reported in groups of soldiers, children, and healthy adults in Israel and Africa (Zeller and Schuffenecker, 2004). These outbreaks were associated with only minor illness in the majority of patients; some case fatalities were associated with increasing age. In one of the largest outbreaks reported, thousands of self-limited and relatively mild clinical cases, consisting of fever, rash, and polyarthralgias occurred in South Africa, resulting in an epidemic attack rate of 55% (McIntosh *et al*, 1970).

However, since the mid-1990s, outbreaks of WN virus infection associated with severe neurologic disease have occurred in Algeria (1994, 1997), Tunisia (1997), Romania (1996), Russia (1999), Israel (2000), the United States of America (1999, 2002-2007), the Sudan (2002), and Canada (2002, 2003, 2007). In these outbreaks, mor-

tality among the patients with meningitis and encephalitis was approximately 10% and occurred more often in elderly patients (Drebo *et al*, 2003).

In the United States- Since 2000, the Arbo-NET national surveillance system has tracked the WN virus in the United States. West Nile fever cases are considerably underreported since most patients do not seek medical care and routine diagnostic testing for uncomplicated West Nile fever cases is not recommended. Thus, the most accurate trend data derive from monitoring cases of invasive neurologic disease. Only 19 human cases of WN neuroinvasive disease were reported in the United States in 2000 and 64 in 2001. However, in 2002, the multistate outbreak throughout the Midwest involved 2946 neuroinvasive disease cases. At the peak of the outbreak in 2003, WN virus was reported in all but three states in the continental United States, with a total of 2866 with neuroinvasive disease. From 2005 through 2008, 670 to 1500 cases of neuroinvasive disease have been reported annually, with the highest incidence in states in the Midwest and West (Lindsey*et al*, 2008).

Weingartl *et al*. (2003) evaluated six tests for the detection of West Nile virus (WNV) antibodies in the serum of experimentally infected chickens found that sera gave positive results in the ELISAs and then could be tested by the micro-PRNT to determine the specificity of antibodies to WNV.

However, the serologic surveys and extrapolations from blood donor screening data indicate that neuroinvasive disease following infection is infrequent, with estimates ranging from 1 in 140 to 1 in 256 infections resulting in meningitis or encephalitis (Busch *et al*, 2006). By extrapolation, the nearly 12,000 cases of invasive neurologic disease reported in the United States through 2008 would imply that from 1.6 to 3.1 million persons have been infected. Serological surveys indicate that even in areas experiencing outbreaks, less than 10% of the population is infected with WN virus.

The human illness peaks in late summer or early fall. Sporadic cases occur throughout the year in southern states. The seasonal variation is due to the fact that mosquitoes emerge in the spring in temperate climates, which begins viral amplification in the bird-mosquito-bird cycle. Viral amplification peaks in early fall; the risk of infection then decreases in humans when female mosquitoes begin diapause and infrequently bite (Schellenberg *et al*, 2006).

The epidemiology and ecology of WN virus in Canada reflects that of the northern United States. The first human cases were reported in 2002, with 414 reported illnesses and deaths reported from Quebec and Ontario. In 2003, a total of 1481 cases were reported, of whom 217 had neuroinvasive disease and ten died. In 2004 to 2006, less than 50 cases of neuroinvasive disease were reported each year, only to be followed by a large outbreak in Alberta, Saskatchewan, and Manitoba in 2007 with 2338 cases reported, including the 130 cases with neuroinvasive disease.

The WNF virus was the first time de-

tected south of the United States borders in 2001, when a resident of the Cayman Islands developed WNV encephalitis. Subsequently, serologic studies in birds and horses suggested that WN virus has circulated in Argentina (2006), Colombia (2004), Cuba (2004), Dominican Republic (2002), El Salvador (2005), Guadeloupe (2002), Guatemala (2003), Haiti (2004), Jamaica (2002), Mexico (2002), Puerto-Rico (2002), and Venezuela (2004) (Go to; Dupuis *et al*, 2005; Pupo *et al*, 2006).

However, viral isolations have been infrequent and documented avian, equine, and human morbidity are scant (Morales *et al*, 2006). Documented human infections have been limited to a few patients in the Cayman Islands, Cuba, Haiti, and northern Mexico.

The reasons for the discrepancy between the serologic evidence indicating widespread WN virus circulation in the Caribbean, Central and South America, and Mexico and the lack of substantial avian, equine, or human morbidity remain a mystery (Beatty *et al*, 2007).

Nearly all human infections of WN virus are due to mosquito bites. Birds are the primary amplifying hosts, and the virus is maintained in a bird-mosquito-bird cycle. Humans, horses, and many other vertebrates serve as incidental hosts and are not felt to be important for transmission since viremia is both short-lived and low-grade (Kilpatrick *et al*, 2006).

Mosquitoes that transmit WN virus are usually of the *Culex* species, which vary by geographic area. The major mosquito-vectors in Africa and in the Middle East are *Cx. univittatus* and *Cx. pipiens molestus,* and in Asia, *Cx. tritaeniorhynchus*. The WNV was recovered from ticks in Russia, but wasunclear what role they play in maintaining or disseminating the virus (Busch *et al*, 2005).

The surveillance identified 64 mosquito species infected with the WN virus in North America. However, WN and the St. Louis encephalitis viruses appear to share the same maintenance vectors. *Cx. pipiens pipiens* (northern house mosquito) is an important maintenance vector in the northern United States and Canada, while *Cx. pipiens quinquefasciatus* (southern house mosquito) was important in the southern United States, and *Cx. tarsalis* is important in the western United States and Canada, respectively. The relative proportion of human infections caused by each mosquito species is difficult to discern, but likely varies geographically (Turell *et al*, 2001).

Wild birds develop prolonged high levels of viremia and serve as amplifying hosts but generally remain asymptomatic (Komar *et al*, 2003). Nevertheless, dead bird surveillance has noted more than 320 species of native and captive birds in the United States. Significant avian mortality has only been noted in Israel, the United States, and Canada, in which similar strains of the virus have circulated (Swayne *et al*, 2001). High mortality has been noted among American crows and other North American corves (ravens, jays, and other crows). A single nucleotide change in the NS3 gene appears re-

sponsible for the increased mortality in American crows (Brault *et al*, 2007).

Crows are amplifying hosts and also herald disease activity in humans. As West Nile virus spread across the United States, a higher incidence of West Nile infection was noted in residents of high crow-mortality areas relative to those outside of these areas and clusters of dead crows predicted an increased risk for one to two weeks prior to appearance of human cases. However, decreasing susceptible bird populations and waning interest in avian mortality surveillance have decreased the value of dead crow sightings as an indicator of virus activity in recent years (Johnson *et al*, 2006).

Malkinson and Banet (2002) reported that surveys on wild birds conducted during the last two decades in Europe, notably Poland and the Czech Republic, showed that some species of seropositive birds were non-migratory while others were hatchlings of migrating species. Persistently infected avian reservoirs are potential sources of viruses for mosquitoes that multiply in the temperate European zone in hot, wet summers. With the reappearance of epidemic WN fever in European countries, interest has been focused once again on the African origin of the causal agent carried by migrating wild birds. Isolates from human cases or mosquitoes and only serologic evidence for infection was available from domestic and wild bird populations. They added that unique susceptibility of young domestic geese in Israel in 1997-2000 to WN virus and the isolation of similar strains from migrating the white storks in Israel and Egypt suggested that the isolates were more pathogenic for certain avian species and that migrating birds do play a crucial role in geographical spread of the virus.

Transmission has also been described via transfused blood, red blood cells, platelets, and fresh frozen plasma. However, universal screening of the US and Canadian blood supplies has nearly eliminated the risk of transfusion-transmitted WNV infection (Petersen and Epstein, 2005). Nevertheless, a small residual risk remains from donations with low viremia not detected by nucleic acid detection tests (NAT) tested in the minipool format used by blood centers. Transmission has also been documented by transplanted organs (Iwamoto *et al*, 2003), transplacental transmission, occupational transmission via percutaneous exposure, conjunctival exposure, and in a dialysis center by unidentified means. Transmission via breast milk is also likely (Fonseca *et al*, 2005).

In 2002, transmission via donated organs was first documented when four recipients of organs from a common donor developed WN virus infection. Serum from the day of organ harvest was positive for WN virus by NAT and culture. The second transmission occurred in 2005 in which three of four organ recipients developed WN virus infection. Serum from the day of organ harvesting was positive for WN virus-specific IgG and IgM antibodies, but was negative for WN virus RNA, suggesting that transmission occurred from WN virus sequestered in organs in the

absence of detected viremia in serum. But, the pathogenesis of severe infection with WN virus was not well understood at that time.

During feeding, the mosquito injects virus-laden saliva into the host. Initial WN virus replication is thought to occur in skin Langerhans dendritic cells. These cells migrate to regional lymph nodes, where virus replication produces a viremia that seeds various organs and tissues, such as liver and kidney. In animal models, the primary viremia is cleared in approximately one week, at which time virus levels in the central nervous system infection increase and neurological symptoms become clinically manifest. The mechanisms by which WN virus enters the CNS are not precisely known, but likely include (Gea-Banacloche *et al*, 2004): Hematogenous spread infection or passive transport through endothelium or choroid plexus epithelial cells Transport by infected immune cells that traffic to the CNS Direct axonal retrograde transport from infected peripheral neurons

Humoral and cellular immunity: As with other flaviviruses, humoral immunity is critical for protection from WN virus. Mice genetically deficient in B cells had increased WN viral loads in the CNS, and the infection was lethal at lower doses of virus than in controls. The presence of neutralizing antibody correlates with protection from flaviviruses and passive transfer of IgG antibody can protect against WN challenge. T cell responses are also critical for protection from WN virus, as demonstrated in animal models and extreme susceptibility to infection in persons with certain immunocompromising conditions (Samuel *et al*, 2007).

Interferons likely play a critical role in control of initial WN virus infection. Mice lacking type 1 interferon (IFN-alpha and IFN-beta) receptor had uncontrolled viral replication, rapid dissemination to the CNS, and enhanced lethality. Mice deficient in type 2 interferon (IFN-gamma) also showed greater viral burden, early CNS entry, and increased mortality.

Toll-like receptors help cells to recognize and respond to infections by RNA viruses. Mice deficient in toll-like receptor 3 have decreased viral RNA production and inflammation in the CNS with subsequent decreased neuronal injury compared to mice with wild-type receptors.

Other mechanisms are also important in modulating the early WN viremia. Complement is required for protection from lethal infection in mice and an immunomodulatory function has been demonstrated for WN virus nonstructural protein (NS)-1, which binds and recruits the complement regulatory protein factor H. This may lower the ability of the immune system to target WN virus by decreasing complement-mediated recognition of infected cells. Macrophage depletion led to higher levels of viremia and accelerated development of encephalitis and death compared to control mice.

In a study of 23 patients who died from WN encephalomyelitis, glial nodules with variable loss of neurons and perivascular cuffing by mononuclear cells was observed in all patients. Mo-

nonuclear infiltration and loss of neurons were most prominent in the gray matter of the medulla, pons, and midbrain. Inflammation of the spinal cord was universally present, particularly in the anterior horns (Tobler *et al*, 2008).

In a review of WN virus encephalitis in 11 solid organ transplant recipients, the clinical presentation and laboratory findings were similar to those in immuno-competent patients, but the degree of neurologic damage was at the severe end of the spectrum. Other reports, based upon a small number of cases and extrapolation to a larger population, suggest that neuroinvasive disease is approximately 40 times more likely to develop in transplant recipients than in the general population (Kumar *et al*, 2004).

Case reports suggest that certain cancers, particularly hematological malignancies, increase the risk of severe disease after infection. The case-control study showed that cancer and chemotherapy increased at least six-fold the risk of developing neuroinvasive disease. Eleven percent of patients inoculated with WN virus as a cancer treatment in the 1950s developed encephalitis, particularly among patients with hematological malignancies. Host genetic factors, such as CCR5 deficiency, may increase the risk of severe disease. Advanced age is the most important risk factor for severe neurological disease, although the mechanism for increased susceptibility is unknown (Patnaik *et al*, 2006).

Besides, Piţigoi *et al*. (1998) reported that WNV is present in Egypt, Israel, India and is widespread in parts of Africa, the northern Mediterranean area and Western Asia. The first major West Nile fever epidemic in Europe occurred in Romania, in 1996, with a high rate of neurological infections. 393 patients with serologically confirmed or probable the WN fever infection (352 had acute central-nervous-system infections) were identified, but the mild cases could not be estimated. WN virus was recovered from *Cx. pipiens* mosquitoes. The virus is not transmitted through direct human contact; probably the infected mosquitoes transmit the virus throughout their life. The viremia is essential for vector infection and occurs during early clinical illness in humans. Susceptibility appears to be general, in both the males and females, throughout life, and that unapparent infections and the mild disease could be common.

De-Filette *et al*. (2012) stated that since the mid-1990s, outbreaks of WN fever and encephalitis have occurred throughout the world and WNV is now endemic in Africa, Asia, Australia, the Middle East, Europe and the Unites States. They reviewed the molecular virology, epidemiology, pathogenesis, and highlights recent progress regarding diagnosis and vaccination against WNV infections.

As of December 11, 2012, 48 of United States have reported WNF infections in people, birds, or mosquitoes. A total of 5,387 cases of WNF disease in people, including 243 deaths, have been reported to CDC.

What about Egypt?

Mohammed *et al*. (1970) examined acute blood samples from 120 children, attending the fever hospital in Alexandria and complaining of fever for the hemagglutination-inhibiting (HAI) and the complement-fixing (CF) antibodies against arbovirus antigens; Sindbis, West Nile (WN), Yellow fever, Dengue 1, Sand-fly fever, Quaranfil, Chenuda and Nyamanini. Positive reactions were only detected against Sindbis (4.3%) and WN (4.3%) antigens. The convalescent sera obtained from 48 of these children showed a pronounced HAI titer against WN antigen in 14.6% of them. The same sera showed a lower titer against yellow fever antigen (Asibi strain) which is due to cross-reaction between the two viruses. None of the acute or the convalescent sera showed CF antibodies against Quaranfil, Chenuda or Nyamanini antigens. They suggested that of the known arboviruses in Egypt, WN is the most important from the public health point of view.

Darwish*et al*. (1987) stated that fever and myalgia are non-specific clinical manifestations of illness which commonly occur in patients with arboviral disease. In Egypt, such illness is often mis-diagnosed as "influenza". They examined sera samples of 55 patients with fever and myalgia, acute and convalescent in ImbabaFever Hospital, Giza. Based on viral isolation, and clinically, 4 patients (7%) had acute arboviral infections. Hemagglutination inhibition and IFA tests showed that one had WNV infection, 2 had sand-fly fever virus-Naples (SFN), and 1 had sand-fly fever virus-Sicilian (SFS) infection. SFN was isolated from the acute serum sample of 1 of the 2 patients with SFN infection.

Corwin *et al*. (1992) estimated the prevalence of selected arboviral, rickettsial, and Hantaan viral antibody in a sample of schoolchildren (8- 14 years) from 4 villages in the Bilbeis district of the River Nile Delta. The enzyme immunoassay testing indicated that the antibody prevalence was 9% (21/223) for Sicilian sand-fly fever, 4% (8/223) for RVF, 3% (15/437) for WNV and 9% (28/315) for Hantaan (HTN) virus. Antibody was demonstrated among 22% (93/418) of the same study subjects against *Coxiella burnetti*, 53% (199/373) against *Rickettsia typhi*, and 37% (137/371) against *R. conorii.*

Corwin *et al*. (1993) also examined blood samples from a total 915 persons representing 190 study households. Enzyme immunoassay testing showed that the overall prevalence of IgG antibody was 4% to sand fly fever Sicilian (SFS), 2% to sand-fly fever Naples (SFN), 15% to RVF, 20% to the WN, and 4% to Hantaan (HTN) viruses. Antibody was demonstrated among 32% of the same study subjects to *Coxiella-burnetii*, 58% to *Rickettsia typhi*, and 32% to *R. conorii*. They did not detect antibodies in population less than seven years of age and in only 3% of those 7-12 years old. In contrast, 26% of the study population 13-19 years old, who were young children and infants at the time of the outbreak, Geometric mean titers (GMT) ranged from 139 for C. *burnetii* to 1,305 for RVF, and did not vary significantly by age, except for high titers for RVF in the 20-49-year-old age group. A significant upward

trend in GMT was also noted when antibody was detected in the specimen for more than one phlebovirus.

Abbassy *et al*. (1993) reported experimentally that WN virus was detected for three and four days after feeding in *A. persicus* and *A. hermanni*, respectively, and decreased to undetectable levels in both species. When the infective dose was increased to 10 (6.2), virus was detected until days 6 and 8, respectively. In *A. arboreus*, virus titers in whole tick homogenates reached a peak of 10 (4.0) on the 4th day post-feeding and remained constant at 10(3.0) after day 6 throughout the 20- or 50-day observation periods. No evidence of transstadial transmission from nymph to adult was detected. Larvae from experimentally infected females successfully transmitted virus to clean chicks and virus was recovered from F1 larvae. Virus was present in coxal fluids secreted by infected females after infective meals. They concluded the demonstration of the WN virus infection in experimentally infected *A. arboreus* ticks and documents horizontal and vertical transmission.

Darwish*et al*. (1996) evaluated three serologic tests for WNV detection. ELISA showed 45% while HI and IFT indicated 37.6 and 26.4% positive sera among the tested 178 sera taken from the flooded village, respectively. The positive predictive values for the 3 tests were more than 80% while the negative predictive ones were different for these tests: 66.7% for ELISA, 44.1% and 37% for HI and IFT, respectively. They concluded that for screening of population in an endemic area, started with ELISA (the more sensitive) followed by HI and/or IFT.

El-Esnawy (2001) examined Egyptian workers at sewage treatment plants (STPs) work and lives in areas, which are highly infested with arthropods. Most of these diseases cause, febrile, influenza like illness, headache, backache, abdominal pain, and fatigue. To determine arboviral etiology in those workers, 264 serum samples were obtained from the workers in four STPs during January and October 1999. ELISA was performed for IgG & IgM, to detect the WN, Sindbis (SIN), Rift Valley fever (RVF), Sand-fly Naples (SFN) and Sand-fly Sicilian (SFS) viruses. The results showed that (WN) has the highest prevalence (143/264, 54.14%), followed by (SFN) (58/264, 21.97%) then (RVF) (23/264, 7.95%), while, only one recent infection for each of RVF, SFS and SFN (1/264, 0.38%) and 3 persons for SIN viruses. Out of the four STPs Helwan workers' exhibited the highest infection rate for most of the studied arboviruses WN, SFN, SIN and SFS.

Turell *et al*. (2002) collected mosquitoes in villages with known RVF viral activity. A total of 33 virus isolates was made from 36,024 mosquitoes. Viruses were initially identified by indirect fluorescent antibody testing and consisted of 30 flaviviruses (all members of the Japanese encephalitis complex, most probably WN virus and three alphaviruses (all members of western equine encephalitis complex, most probably Sindbis). The identity of selected viruses was confirmed by reverse transcriptase-PCR and sequencing. *Cx. an-*

tennatus and *Cx. perexiguus* accounted for five (17%) and 23 (77%) of the WN virus isolations, respectively, RVF virus was not isolated from these mosquitoes.. They concluded, that one must remember, that even during a known arbovirus outbreak, other arboviruses might still be circulating and causing disease.

Soliman *et al,* (2010) demonstrates that WNV was actively circulating during the study period in different areas in Egypt and causing febrile illness in a considerable proportion of individuals in the study sites.

Kropman *et al*. (2012) in the Netherlands reported a 44-year-old female presented with fever and a flaccid paresis of the left leg, following a holiday in Egypt. The laboratory investigation demonstrated an acute West Nile virus (WNV) infection, after which the diagnosis 'WNV poliomyelitis' was made.

Regarding the resident and migratory birds in Egypt: Morsy *et al*. (1999) studied the role played by birds in the distribution of various bacterial, viral and parasitic infections is increasingly from year to year, taking into consideration the flying ability of birds and their migration for food and vital processes. They added that commonest Egyptian resident birds were house sparrow (*Passer d. niloticus*) and laughing dove (*Streptopelia s. aegyptiaca*).

Mazyad *et al*. (1999) reported that Egypt is one of the most important countries of migratory birds. Not less than 300 species of birds visit Egypt annually from all-over the world. They recovered mite fauna of two migratory birds (quail or Simmaan) in North Sinai Governorate and Suez Canal Zone (starling or zarzuur).

Khalil *et al*. (2011) stated that Egypt includes many desert and rural areas. The small uptown fertile areas are placed under illegal enormous pressure of existing resources, where intensive agricultural practices are performed in combination with high population densities. The brown necked ravens (*Corvus ruficollis*) are attracted in huge numbers to such areas from Saudi Arabia. The birds are omnivorous, very aggressive pest and seriously affect the human welfare.

Prevalence and distribution of huge species mosquitoes allover Egypt was reported (Morsy *et al*, 2004; El-Bashier *et al*, 2006; Mikhail *et al*, 2009; Shoukry and Morsy, 2011; Morsy, 2012; Abdel-Hamid, 2012)

What about neighboring countries?

The Sudan:

Watts *et al*. (1994) determined whether arboviruses were associated with human illness during a fever outbreak. Prevalence of IgG antibody was 59% for WNV, 53% for Sand-fly fever Sicilian (SFS), 32% for Sand-fly fever Naples (SFN), 39% for Yellow fever (YF), 24% for dengue-2 (DEN-2), 23% for Rift Valley fever, 12% for Chikungunya (CHIK) and 5% for Crimean-CHF viruses. Antibody prevalence increased with age for WNV& YFV. Antibody rates were about the same for males and females for most tested viruses. Prevalence of IgM antibody to SFN was 24% and reciprocal IgM titer exceeded 12,800 for some individuals

suggesting that this virus was the cause of recent infection. Prevalence of IgM antibody for other viruses did not exceed 5%. They stated that several arboviruses were endemic and some of them caused human disease in the Northern Province of Sudan.

McCarthy *et al*. (1996) following severe flooding in Khartoum, Sudan 1988 examined 200 patients with acute febrile illness and 100 afebrile controls at the Omdurman Military Hospital, Khartoum, Sudan. Sera were tested for IgM and IgG antibodies to six arthropod-borne viruses by ELISA, and for similar antibodies to Lassa fever, Crimean-Congo hemorrhagic fever, and Ebola and Marburg viruses by an indirect fluorescence assay, and thick and thin blood smears for malaria parasites, and fecal and blood specimens for bacteria by standard culture methods. Among the acute and convalescent 67 febrile patients, five cases were caused by sand-fly fever Sicilian (SFS), six by sand-fly fever Naples (SFN), and 12 by unidentified phleboviruses. Of 233 remaining unpaired, acute-phase sera collected from cases and controls, 49 (21%) had IgM antibodies to SFS or SFN, RVF, WNV, and Chikungunya (CHIK) viruses. Forty-three (22%) of 192 febrile cases and two of the 100 afebrile controls were positive for Plasmodium falciparum, and bacterial enteropathogens were associated with 25 (13%) cases and four controls. They concluded that phleboviruses and to a lesser extent, WN, *P. falciparum*, and enterobacterial pathogens were causes of acute febrile illnesses.

Depoortere *et al.* (2004) reported outbreak of WNV causing severe neurological involvement in children, Nuba. They used ELISA and neutralization tests for laboratory diagnosis identified 31 cases (median age was 36 months) with encephalitis, four of whom died. They concluded that the unique aspects of WNW outbreak in Sudan, i.e. disease occurrence solely among children and the clinical domination of encephalitis, involving severe neurological sequelae showing the continuing evolution of WNV virulence, and spreading to other countries could not be excluded.

Kuwait and Saudi Arabia:

Cope *et al.* (1996) collected a total of 1,556 arthropods from 12 areas of Kuwait and Saudi Arabia during the Persian Gulf during Operations Desert Shield and Desert Storm. The vectors of leishmaniasis, sand fly fever, WNF, RVF and CCHF were identified; lacked arboviruses or leishmaniasis data neither among specimens nor rodents that was attributed to insecticides and repellents, and deployment of most ground troops to open desert during cooler, winter conditions least favorable for arthropod-borne diseases transmission.

United Arab Emirate:

Alfaresi and Elkoush (2008) reported WNV in the blood donors in the UAE.

Lebanon:

Gallian *et al*. (2010) reported WNV in the blood donors at Hôtel-Dieu de France, Beirut, Lebanon.

Israel:

Giladi *et al*. (2001) reported WN

virus. Rogers *et al*. (2009) reported the imported WNV encephalitis in an Israeli tourist. Aboutaleb *et al*. (2010) reported WNV in German travelers returning from Israel.

Kopel *et al*. (2011) in Israel presented the findings of 2005-2010 of human WNV infection in Tel Aviv district. They added that104 patients (age ranged 15 to 95 years), 79 with WNV neuroinvasive and 25 with WNV non-neuroinvasive disease were reported. Fifty-three of these patients had encephalitis, 14 had acute flaccid paralysis, and 12 had meningitis, with case-fatality rate of 8%. They concluded data were concordant with previous data, at the national level, published in Israel and the United States.

Conclusion

The main mode of the WNV transmission is via various species of mosquitoes, the main vector, with birds being the most commonly infected animal and serving as the prime reservoir host-especially passerines which are of the largest order (Passeriformes) of birds. WNV has been found in various species of ticks, but current research suggested that they are not important vectors. The WNV also infects various mammal species, including humans, and identified in reptilian species, including alligators and crocodiles, and also in amphibians. Not all animal species that are susceptible to WNV infection-humans included, and not all bird species develop sufficient viral levels to transmit the disease to uninfected mosquitoes, and are thus not considered major factors in the WNV transmission.

Approximately 80% of the WNV infections in man are subclinical, without any symptom. In symptoms cases the termed West Nile fever in cases without neurological disease is used. The incubation period takes 2 to 15 days. Symptoms may include fever, headaches, fatigue, muscle pain or aches, malaise, nausea, anorexia, vomiting, myalgias and rash. Less than 1% of cases is severe and result in neurological disease when the CNS is affected. The old aged population, the very young, or those with immunosuppression, either medically induced, such as those on immunosuppressive drugs, or due to a pre-existing medical condition such as HIV infection, are most susceptible. The specific neurological diseases are the West Nile encephalitis that causes inflammation of the brain, West Nile meningitis, West Nile meningoencephalitis, and West Nile poliomyelitis-spinal cord inflammation with a syndrome similar to the polio causingthe acute flaccid paralysis.

Recommendations

Egypt is the cross road of many nations. The present of many arthropod-borne diseases and the resident and migratory birds as well the climatic and environmental conditions favor introduction and spreading of much disaster mosquito-borne infectious diseases.

The prevention including the public health measures to reduce the number of mosquitoes and personal protection remains the mainstay for arthropod vector disease control.

It is hoped to stimulate the awareness of the Public Health, Veterinarian and Agricultural Authorities not only concerning the reviewed West Nile fever virus but also for all mosquitoes and ticks borne zoonotic diseases.

References

Abbassy, MM, Osman, M, Marzouk, AS, 1993: West Nile virus (Flaviviridae: Flavivirus) in experimentally infected Argas ticks (Acari:Argasidae). Am. J. Trop. Med. Hyg. 48, 5:726-37.

Abdel-Hamid, YM, 2012: The association among mosquito species in the northern part of Egypt. Egypt. Acad. J. Biol. Sci. 4, 1:13-9.

Aboutaleb, N, Beersma, MF, Wunderink, HF, Vossen, AC, Visser, LG, 2010: Israel. Euro Surreall. 15, 34: 19649

Alfaresi, M, Elkoush, A, 2008: West Nile virus in the blood donors in UAE. Indian J. Med. Microbiol. 26, 1:92-3.

Beatty, ME, Hunsperger, E, Long, E, *et al*, 2007: Mosquito-borne infections after Hurricane Jeanne, Haiti, 2004. Emerg. Infect. Dis. 13:308-14.

Brault, AC, Huang, CY, Langevin, SA, *et al*, 2007: A single positively selected West Nile viral mutation confers increased virogenesis in American crows. Nat. Genet. 39:1162-8.

Busch, MP, Caglioti, S, Robertson, EF, *et al*, 2005: Screening the blood supply for West Nile virus RNA by nucleic acid amplification testing. N. Engl. J. Med. 353:460-6.

Busch, MP, Wright, DJ, Custer, B, *et al*, 2006: The West Nile virus infections projected from blood donor screening data, United States, 2003. Emerg. Infect. Dis. 12:395.

CDC 2012: West Nile Virus Update: Go to: home page.

Cope, SE, Schultz, GW, Richards, A L, Savage, HM, Smith, GC, 1996: Assessment of arthropod vectors of infectious diseases in areas of U.S. troop deployment in the Persian Gulf. Am. J. Trop. Med. Hyg. 54, 1:49-53.

Corwin, A, Habib, M, Olson, J, Scott, D, Ksiazek, T, 1992: Prevalence of arboviral, rickettsial, and Hantaan-like viral antibody among schoolchildren in the Nile river delta of Egypt. Trans. R. Soc. Trop. Med. Hyg. 86, 6:677-9.

Corwin, A, Habib, M, Watts, D, Darwish, M, Olson, J, *et al*, 1993: Community-based prevalence profile of arboviral, rickettsial, and Hantaan-like viral antibody in the Nile River Delta of Egypt. Am. J. Trop. Med. Hyg. 48, 6:776-83.

Darwish, MA, Feinsod, FM, Scott, R M, Ksiazek, TG, Botros, BA, 1987: Arboviral causes of non-specific fever and myalgia in a fever hospital patient population in Cairo, Egypt. Trans. Roy. Soc. Trop. Med. Hyg. 81, 6:1001-3.

Darwish, M, el-Khashaab, TH, Mostafa, A, Hamid, TA, Shope, R, 1996: A comparative study of serological techniques for detection of West Nile virus antibodies. J. Egypt. Pub. Hlth Assoc. 71, 3/4:201-11.

De Filette, M, Ulbert, S, Diamond, M, Sanders, NN, 2012: Recent progress in West Nile virus diagnosis and the vaccination. Vet. Res. 43, 1:16-22.

Depoortere, E, Kavle, J, Keus, K,

Zeller, H, Murri, S, *et al*, 2004: Outbreak of West Nile virus causing severe neurological involvement in children, Nuba Mountains, Sudan, 2002. Trop. Med. Int. Hlth. 29, 6:730-6.

Drebot, MA, Lindsay, R, Barker, IK, *et al*, 2003: West Nile virus surveillance and diagnostics: A Canadian perspective. Can. J. Infect. Dis. 14:105-10.

Dupuis AP, 2nd, Marra, PP, Reitsma, R, *et al*, 2005: Serologic evidence for West Nile virus transmission in Puerto Rico and Cuba. Am. J. Trop. Med. Hyg. 73:474-80.

El-Bashier, ZM, Hassan, MI, Mangoud, AM, Morsy, TA, Mohammad, KA, 2006: A preliminary pilot survey (*Culexpipiens*), Sharkia G., Egypt. J. Egypt. Soc. Parasitol. 36, 1:81-92.

El-Esnawy, NA, 2001: Infection by certain arboviruses among workers potentially at risk of infection. J. Egypt. Pub. Hlth. Assoc. 76, 3/4:169-82.

Fonseca, K, Prince, GD, Bratvold, J, *et al*, 2005: West Nile virus infection and conjunctival exposure. Emerg. Infect. Dis. 11:1648.

Gallian, P, de Micco, P, Ghorra, P, 2010: Sero-prevalence of West Nile virus in blood donors at Hôtel-Dieu de France, Beirut, Lebanon. Transfusion 50, 5:1156-8.

Gea-Banacloche, J, Johnson, RT, Bagic, A, *et al*, 2004: West Nile virus: pathogenesis and therapeutic options. Ann. Int. Med. 140:545-54.

Giladi, M, Metzkor-Cotter, E, Martin, DA, *et al*, 2001: West Nile encephphalitis in Israel1999: the New York connection. Emerg. Infect. Dis. 7:659.

Glass, WG, McDermott, DH, Lim, JK, *et al*, 2006: CCR5 deficiency increases risk of symptomatic West Nile virus infection. J. Exp. Med. 203:35.

Gubler, DJ, 2007: The continuing spread of West Nile virus in the western hemisphere. Clin. Infect. Dis. 45: 1039-44.

Iwamoto, M, Jernigan, DB, Guasch, A, *et al*, 2003: Transmission of West Nile virus from an organ donor to four transplant recipients. N. Engl. J. Med. 348:2196-204.

Johnson, GD, Eidson, M, Schmit, K, *et al*, 2006: Geographic prediction of human onset of West Nile virus using dead crow clusters: an evaluation of year 2002 data in New York State. Am. J. Epidemiol. 163:171-8.

Khairallah, M, Kahloun, R, Ben Yahia, S, Jelliti, B, Messaoud, R, 2012: New infectious etiologies for posterior uveitis. Ophthalmic Res. 49, 2:66-72.

Khalil, MF, Shoukry, NM, Morsy, T A, 2011: *Corvus R. ruficollis* (Desert or Brown necked raven): A reservoir host for zoonotic parasites in Egypt J. Egypt .Soc. Parasitol. 41, 3:753-64.

Kilpatrick, AM, Daszak, P, Jones, M J, *et al*, 2006: Host heterogeneity dominates West Nile virus transmission. Proc. Biol. Sci. 273:2327.

Komar, O, Robbins, MB, Klenk, K, *et al*, 2003: West Nile virus transmission in resident birds, Dominican Republic. Emerg. Infect. Dis. 9:1299-306.

Kopel, E, Amitai, Z, Bin, H, Shulman, LM, Mendelson, E, *et al,* 2011:

Surveillance of West Nile virusdisease: Tel Aviv district, Israel, 2005 to 2010. Euro Surveill. 16, 25: pii: 19894.

Kropman, E, Bakke, LJ, de Sonnaville, JJ, Koopmans, MP, Raaphorst, J, *et al*, 2012: West Nile virus poliomyelitis after a holiday in Egypt. Ned. Tijdschr.Geneeskd. 155, 35:A4333.

Kumar, D, Drebot, MA, Wong, SJ, *et al*, 2004: A sero-prevalence study of West Nile virus infection in solid organ transplant recipients. Am. J. Transplant. 4:1883-90.

Lanciotti, RS, Roehrig, JT, Deubel, V, *et al*, 1999: Origin of the West Nile virus responsible for an outbreak of encephalitis in the northeastern United States. Science 286:2333-42.

Lindsey, NP, Kuhn, S, Campbell, GL, Hayes, EB, 2008: West Nile virus neuroinvasive disease incidence in the United States, 2002-2006. Vector Bor. Zoonotic Dis. 8:35-42.

Malkinson, M, Banet, C, 2002: The role of birds in the ecology of West Nile virus in Europe and Africa. Curr. Trop. Microbiol, Immunol. 267:309-22.

Mazyad, SA, Morsy, TA, Fekry, AA, Farrag, AM, 1999: Mites infesting two migratorybirds, *Coturnix c. coturnix* (quail or Simmaan) and *Sturnus v. vulgaris* (starling or zarzuur) with reference to avian zoonosis. J. Egypt. Soc. Parasitol. 29, 3:745-61.

McCarthy, MC, Haberberger, RL, Salib, AW, Soliman, BA, El-Tigani, A, *et al,* 1996: Evaluation of arthropod-borne viruses and other infectious disease pathogens as the causes of febrile illnesses in the Khartoum Province of Sudan. J. Med. Virol. 48, 2:141-6.

McIntosh, BM, Jupp, PG, Dos Santos, I, *et al*, 1970: Epidemics of West Nile and Sindbis viruses in South Africa with *Culex (Culex) univittatus* Theobold as vector. S. Afr. J. Sci. 72:295.

Mikhail, MW, Al-Bursheed, KhM, AbdEl-Halim, AS, Morsy, TA, 2009: Studies on mosquito borne diseases in Egypt and Qatar. J. Egypt. Soc. Parasitol. 39, 3:745-56.

Mohammed, YS, Gresiková, M, Adamyová, K, Ragib, AH, el-Dawala, K, 1970: Studies on arboviruses in Egypt. II. Contribution of arboviruses to the aetiology of undiagnosed fever among children. J. Hyg, (Lond). 68, 3:491-5.

Morales, MA, Barrandeguy, M, Fabbri, C, *et al*, 2006: West Nile virus isolation from equines in Argentina, 2006. Emerg. Infect. Dis. 12:1559.

Morsy, TA, 2012: Insect bites and what is eating you? J. Egypt .Soc. Parasitol. 42, 2:291-308.

Morsy, TA, Mazyad, SA, Younis, M S, 1999: Feather and nest mites of two common resident birds in two ecologically different Egyptian governorates. J. Egypt. Soc. Parasitol. 29, 2:417-30.

Morsy, TA, Khalil, NM, Habib, FS, El-Laboudy, N, 2004: Seasonal distribution of culicini larvae in greater Cairo. J. Egypt. Soc. Parasitol. 34, 1:143-52.

Patnaik, JL, Harmon, H, Vogt, RL, 2006: Follow-up of 2003 human West Nile virus infections, Denver, Colorado. Emerg. Infect. Dis. 12:1129-34.

Petersen, LR, Epstein, JS, 2005: Pro-

blem solved? the WNV and transfusion safety. N. Engl. J. Med. 353:516-22.

Petersen, LR, Hayes, EB, 2008: West Nile virus in the Americas. Med. Clin. North Am, 92:1307-12.

Piţigoi, D, Popa, MI, Streinu-Cercel, A, 1998: The epidemiological process of WNV infection. Bacteriol. Virusol. Parazitol. Epidemiol. 43, 4:281-8.

Pupo, M, Guzman, MG, Fernandez, R, *et al*, 2006: West Nile virus infection in humans and horses, Cuba. Emerg. Infect. Dis. 12:1022-9.

Rogers, BA, Hueston, L, Ratnam, I, 2009: Imported West Nile virus encephalitis in an Israeli tourist. Med. J. Aust. 191, 4:232-4.

Samuel, MA, Wang, H, Siddharthan, V, *et al*, 2007: Axonal transport mediates West Nile virus entry into the central nervous system and induces acute flaccid paralysis. Proc. Natl. Acad. Sci. USA 104:17140.

Schellenberg, TL, Anderson, ME, Drebot, MA, *et al*, 2006: Seroprevalence of West Nile virus in Saskatchewan's Five Hills Health Region, 2003. Can. J. Pub. Hlth. 97:369-74.

Schmidt-Chanasit, J, Schmiedel, S, Fleischer, B, Burchard, GD, 2012: Viruses acquired abroad: what does the primary care physician need to know? Dtsch. Arztebl. Int. 109, 41:681-92.

Shoukry, NM, Morsy, TA, 2011: Arthropod borne diseases at Toshka, Upper Egypt. World J. Zool. 6, 2:126-33.

Soliman, A, Mohareb, E, Salman, D, Saad, M, Salama, S, *et al*, 2010: Studies on West Nile virus infection in Egypt. J. Infect. Publ. Hlth. 3, 2:54-9.

Swayne, DE, Beck, JR, Smith, CS, *et al*, 2001: Fatal encephalitis and myocarditis in young domestic geese (*Anseranser domesticus*) caused by West Nile virus. Emerg. Infect. Dis. 27:751.

Tobler, LH, Cameron,MJ, Lanteri, MC, *et al*, 2008: Interferon and interferon-induced chemokine expression is associated with control of acute viremia in West Nile Virus-infected blood donors. J. Infect. Dis. 198:979-82.

Turell, MJ, Sardelis, MR, Dohm, DJ, O'Guinn, ML, 2001: Potential North American vectors of West Nile virus. Ann. N Y Acad. Sci. 951:317-20.

Turell, MJ, Morrill, JC, Rossi, CA, Gad, AM, Cope, SE, *et al*, 2002: Isolation of west Nile and Sindbis viruses from mosquitoes collected in the Nile Valley of Egypt during an outbreak of Rift Valley fever. J. Med. Entomol. 39, 1:248-50.

Watts, DM, el-Tigani, A, Botros, BA, Salib, AW, Olson, JG, *et al*, 1994: Arthropod-borne viral infections associated with a fever outbreak in the northern province of Sudan. J. Trop. Med. Hyg. 97, 4:228-30.

Weingartl, HM, Drebot, MA, Hubálek, Z, Halouzka, J, Andonova, M, *et al*, 2003: Comparison of assays for the detection of West Nile virus antibodies in chicken serum. Can. J. Vet. Res. 67, 2:128-32.

Zeller, HG, Schuffenecker, I, 2004: West Nile virus: an overview of its spread in Europe and the Mediterranean Basin in contrast to its spread in the Americas. Eur. J. Clin. Microbiol. Infect. Dis. 23:147.