



衛生防護中心
Centre for Health Protection

Scientific Committee on Vector-borne Diseases

Enhancing Preparedness for West Nile Virus in Hong Kong

Purpose

West Nile Virus (WNV) infections have long been discovered in Africa and the Middle East. It was usually only associated with mild disease and isolated outbreaks until the 1990's when it started to cause larger and more frequent outbreaks of severe human disease. It has caused more than 15,000 infections and 648 deaths since its dramatic emergence in the United States of America (USA) in 1999^{1,2}, prompting different countries to review their risk and enhance their preparedness for the disease.

2. On July 23, 2005, the Scientific Committee on Vector-borne Diseases discussed a paper (SCVBD 6/2005) reviewing the public health strategies in safeguarding against the emergence of West Nile Virus in the local community. Views from members have been consolidated in this revised paper to propose recommendations on enhancing surveillance and response capacities in Hong Kong.

West Nile Virus in Nature

3. WNV is a small, single stranded RNA virus of the family Flaviviridae and genus Flavivirus. It is a member of the Japanese encephalitis virus antigenic complex, which also includes Murray Valley Encephalitis and St Louis Encephalitis viruses, and Kunjin (a subtype of WNV) There are two genetic lineages of WNV, lineage I and II. Members of lineage I WNV are more widely distributed, responsible for the recent large outbreaks, and have been associated with clinical human encephalitis; while lineage II are maintained in enzootic foci in Africa and have not been associated with clinical **human encephalitis**^{3,4}. **All**



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North American strains were closely related to phylogenetic lineage I⁵. This has led to the suggestion that lineage I was more virulent, although neuroinvasive strains have been shown in both lineages in animal models. In the temperate and subtropical zones, human WNV infections occur primarily in the late summer or early fall. In the tropics, it was postulated that the incidence would be greatest during the rainy season when mosquitoes are abundant, although little published literature is available regarding the epidemiology in the tropics. In southern climates where temperatures are milder, the virus can be transmitted all year round^{1,6}.

4. Wild birds are the primary hosts of WNV although mammals, reptiles, and amphibians can also be infected. Birds are considered amplifying hosts as they can develop a high and sustained viraemia, sufficient to infect the key vector species. Human and most mammals rarely develop a viraemia sufficient to infect vectors and therefore are described as dead-end or incidental hosts. WNV has been documented in at least 146 species of birds^{4,7}. Members of the order Passeriformes (jays, blackbirds, finches, warblers, sparrows, crows) seemed to be important in maintaining the virus in nature. Infection in birds may be rapidly fatal or mildly symptomatic, depending on the species. Most infected birds survive although some, particularly those of the Corvidae family (crows and jays) can become ill or die^{4,8}.

5. Mosquitoes are the principal vectors for maintaining the transmission among birds. Although at least 75 species of mosquitoes in 11 genera have been found infected with WNV, those in the genus *Culex* is by far the most important for being able to replicate and transmit the virus⁹. Mosquitoes become infected with WNV when they feed on a bird carrying the virus in its blood. Within 10–14 days of exposure, a mosquito can transmit the virus in its saliva to another bird or animal. The biting preference of different species of mosquitoes and the relative abundance of hosts affect the epidemiology of the disease⁵. Overwintering of the *Culex* species was thought to have mediated the survival of the virus through winter and contributed to rapid spread of the disease, as witnessed in the US outbreak¹. WNV has also been isolated from ticks but their potential role as vectors of WNV are uncertain¹⁰.

WNV in human population

6. WNV infection is first recognized in human in 1937 when it was isolated in the blood of a febrile woman in the West Nile district of Uganda.¹ Since its isolation, the virus has caused infrequent outbreaks in humans, the most notable being those occurring in Israel (1951-54 and 1957) and South Africa (1974). Outbreaks of WNV in Israel during the early 1950s were characterized by benign febrile illness in young adults. In a later outbreak in 1957, the association of WNV infection with severe meningoencephalitis in human was first noted^{7,11}. Subsequent outbreaks in Israel and Africa were mild

and consisted of a flu-like illness only. The epidemic in South Africa in 1974, although having caused 18,000 human infections, did not lead to any death^{8,12}.

7. Since the mid-1990s, new epidemiologic trends have developed. There was an increasing number of outbreaks in humans and horses, an apparent increase in severe human disease, and high avian death rates accompanying human cases³. Severe outbreaks were reported from Romania, Russia and Israel. The outbreak in Romania in 1996 marked the first major WNV epidemic in Europe, causing 393 confirmed cases of central nervous system (CNS) infection and 17 deaths (case-fatality ratio 4.3%)¹². In 1999, an outbreak of severe encephalitic disease occurred in the Volgograd region in Russia, which was estimated to have caused 480 suspected overt cases of WNV infection.¹³ In 2000, an outbreak occurred in Israel, causing 417 cases, 326 hospitalisations, and 33 deaths¹¹.

8. The disease was first documented in the North America in 1999¹⁴. New York City, on the East Coast of the USA, reported 83 human cases in 1999-2000. Rapid spread of the disease westward had been noted in the subsequent years and by 2004, it was affecting people in most states in the USA. A total of 4156 cases of infection with 284 deaths and 9858 new cases and 262 deaths were recorded in 2002 and 2003 respectively¹.

9. The spread of WNV across continents from Europe and Africa to the Americas has attracted major attention. There is no proven mechanism for such spread although the close genetic relationship between WNV isolates from Israel and New York suggested that the virus was imported from the Middle East to the USA^{3, 15}. Possible mechanisms include importation or migration of infected birds or mosquitoes and international travel of infected persons¹⁶. Other factors like population growth, urbanization, increased international travel; changing agricultural practices and climate change have all been postulated as the cause of recent geographical spread and increased epidemic activity^{17, 18, 19}.

Clinical Features of WNV Infection

10. There are no pathognomonic clinical features. Most persons infected with WNV are asymptomatic, and about 20% develop an influenza-like illness termed “West Nile Fever”. Symptoms include sudden onset of high fever, headache, tiredness, and body aches. In earlier epidemics in which WN fever cases predominated, up to half of the patients had a generalized rash. By contrast, in more recent epidemics where WN meningoencephalitis predominated, skin rash was present in no more than 22% of patients. The incubation period is usually 2 to 15 days, and symptoms typically last a few days^{1,6}.

11. A small proportion (1 in 150) of those infected will develop

neuroinvasive disease, such as encephalitis, meningitis, or meningoencephalitis^{1,2}. In certain areas such as the United States, WNV infection is an important differential diagnosis for acute poliomyelitis-like syndrome characterized by acute flaccid paralysis without sensory involvement^{7,20}. Other syndromes that have been reported include movement disorders, Parkinsonism, and rhabdomyolysis⁷. Age is an important prognostic indicator. Younger patients are more likely to develop West Nile fever alone but symptomatic, severe disease and death are more common in older patients¹.

12. There is no specific treatment for WNV infection. In patients with severe disease, intensive supportive therapy may be indicated. Overall case fatality rate reported in recent WNV outbreaks was about 4-14%⁶. There is currently no licensed human WNV vaccine and research is still in progress.

13. WNV has rarely been isolated from patients' serum or CSF. Diagnosis is usually confirmed by demonstration of a four-fold rise in neutralizing antibody titres between acute- and convalescent-phase phases of illness. Ideally, specimens should be taken on the first day of illness, and again 3 weeks later and tested using plaque-reduction neutralization assay⁶. A battery of other flaviviruses should be included in the assay for comparison.

14. Detection of IgM antibodies to WNV using ELISA, in serum or CSF collected within 8 days of illness onset can also provide supportive evidence of infection²¹. As IgM does not cross the blood-brain barrier, IgM antibody in CSF strongly suggests CNS infection.²² However, results need to be interpreted carefully as IgM antibody may persist for 6 months or longer in blood and up to 16 months in CSF, such that positive results may not necessarily relate to current illness⁶. Also, false positives may occur in those who have been recently vaccinated against or infected with related flaviviruses (yellow fever, Japanese encephalitis, and dengue)²³. Negative IgM tests of specimens collected less than 14 days after illness should be reconfirmed by tests of a later specimen⁶.

Human-to-human transmission

15. In North America where extensive human infections have occurred, iatrogenic, perinatal and laboratory-acquired infections have been reported.

Iatrogenic WNV infection

16. WNV infection has occurred in recipients of blood transfusion and organ transplantation. In 2002, 23 blood-transfusion-acquired cases of WNV infection were reported in the USA, involving blood components from 16 blood donors. Of the 23 recipients, 10 were immunocompromised and 8 were older than 70²⁴. Thirteen of the blood-transfusion-acquired cases

developed WN meningoencephalitis and 2 had WN fever. Immunocompromised recipients tended to have longer incubation periods than non-immunocompromised recipients and infected persons in mosquito-borne community outbreaks.

17. These cases were identified either because they developed WNV-associated illness after blood transfusion or were actively traced for having received WNV-infected blood products. One other case was found because of transmitting the disease through organ donation²⁵. This case acquired the infection through blood transfusion during aggressive resuscitation for an accident. She subsequently died and donated her organs, transmitting the infection to four transplant recipients. Apart from this case, 6 other cases died, although the causes were unclear because of their underlying medical conditions.

18. Among the 16 donors, 9 reported viral symptoms before or after donation, 5 were asymptomatic, 2 were lost to follow-up and all were negative for West Nile virus-specific IgM antibody at the time of donation²⁴.

19. To minimize the risk of WNV transmission through blood transfusion, the Food and Drug Administration (FDA) recommended deferring donors reporting fever with headache in the week before donation. Apart from clinical screening, blood-collection agencies (BCAs) screen all blood donations and identify potentially infectious donations for quarantine and retrieval since 1 June 2003²⁶.

Perinatal transmission

20. Following the first documented case of transplacental transmission in 2002, a registry was established to follow birth outcomes of women with WNV illness in pregnancy and since then over 70 women had been identified to have acquired WNV during pregnancy¹. The first documented case involved a mother who suffered from WN meningoencephalitis at 27th week of gestation. She delivered a live infant at 38 weeks gestation. The presence of WNV-specific IgM in the infant's serum and CSF confirmed intrauterine infection. Although the infant had evidence of congenital abnormalities including bilateral chorioretinitis and cerebral destruction, the causal relationship between these abnormalities and the infection was not proven²⁷. In 2003, one infant had laboratory evidence of intrauterine infection without apparent abnormalities. Another three had WNV infection that could have been acquired *in utero* but unconfirmed due to the timing of specimens. One of these infants died of lissencephaly and superimposed WNV infection while the others had neonatal rash and neuroinvasive disease respectively²⁸. Further research is necessary to study the effect of maternal infection on the developing fetus.

21. A possible case of WNV transmission through breastfeeding had been reported in the US in 2002. The mother contracted the disease via blood transfusion shortly after giving birth. She breastfed her infant and 3 weeks later, the infant was tested positive for infection, despite being asymptomatic¹.

Laboratory-acquired infection

22. In 2002, the CDC documented two laboratory-acquired WNV cases. One acquired infection as a result of a wound sustained from a scalpel while removing the brain from a blue jay and the other acquired infection through a needle-stick injury to the finger when harvesting WNV-infected mouse brains. Illnesses in both laboratory workers were mild and self-limited but these cases suggest that laboratory workers are at risk for occupationally acquired WNV infection²⁹.

Potential Impact of WNV to Hong Kong

23. International travel, importation of birds and mosquitoes, and migration of birds are risk factors for the international spread of WNV.

24. Several species of mosquitoes including *Culex quinquefasciatus*, *Culex pipiens*, *Aedes albopictus*, and *Aedes vexans* which are known to be WNV vectors overseas are common in Hong Kong³⁰. Moreover, Hong Kong has 465 bird species and it is on the East Asian-Australasian flyway which more than 4 million migratory water birds use. The birds spend spring and summer in northern Asia and pass through this area between August to November on their way south for the winter. They return through Hong Kong from February to May³¹.

25. The United Kingdom's (UK) experience shows that even when the mosquito densities were low, transfer of WNV from migratory birds to the local resident birds has occurred³². Given the abundant migratory birds and mosquito vectors in Hong Kong, there is a potential for the transmission cycle to be established if the virus is introduced into Hong Kong. It is therefore crucial for Hong Kong to review and enhance its preparedness for the emergence of WNV infection.

Public health control strategies for WNV

26. Targeting the different modes of transmission, strategies for prevention of WNV include: the surveillance of animals, mosquitoes, and humans; implementation of measures to prevent blood-borne transmissions; enhancing laboratory safety; and the prevention of perinatal transmission.

Surveillance

27. A review of international experience revealed that both passive and active surveillance strategies have been used, targeting at mosquitoes, birds, human and other animals. In the USA, for instance, surveillance strategies have been developed to target at:

- assessing the potential threat to human;
- detecting the first human and/or animal cases;
- guiding implementation of control measures; and
- monitoring the progress of outbreaks.

Human surveillance

28. Passive human surveillance by testing for WNV infection in hospitalized cases of encephalitis is undertaken in the USA and in some European countries. A high clinical suspicion for arboviral encephalitis is encouraged among health care providers. When the diagnosis is in doubt, appropriate clinical specimens are submitted to the laboratory capable of performing reliable WNV tests. Active human surveillance is considered in areas with known WNV activity. It involves contacting physicians in relevant specialties and hospital infection control personnel on a regular basis for potential cases of arboviral infections, and/or implementing laboratory-based surveillance to test for WNV in CSF specimens meeting certain non-specific but sensitive criteria for arboviral infections¹⁶.

29. In Hong Kong, the Public Health Laboratory Services Branch of the Centre for Health Protection provides support for virology testing for suspected cases in both public and private sectors. Medical practitioners are encouraged to report to the CHP any unusual cases and diagnostic tests are arranged depending on investigation findings. Moreover, the presentation of neuroinvasive WNV infection is similar to Japanese encephalitis which is a notifiable disease, and any specimen positive for JE on initial haemagglutination inhibition testing will also be screened for WNV. Confirmation tests would be carried out as necessary. So far, there is no human case identified in Hong Kong. Any confirmed positive cases will trigger responses and control actions targeted at WNV.

Mosquito surveillance

30. Mosquito surveillance program involves collecting adult mosquitoes regularly at representative sites such as locales with aggregation of migratory birds by trapping techniques. The purposes are to construct the distribution of mosquito species and its abundance. It is the primary tool for quantifying the intensity of virus transmission in an area. Attempts have been made to use infection rates in mosquitoes to identify high risk geographic areas for strategic interventions. However, tested infection rates are generally very low even when transmission rates are high. WNV was only isolated in 1.7% of mosquito pools tested in Egypt's study, isolation rates has been similar in the US, despite selectively capturing large numbers of older female mosquitoes

that have taken at least one blood meal⁸. Nevertheless, the mosquitoes collected through the surveillance programme are suggested to be examined for the presence of the WNV.

31. In Hong Kong, the Food and Environmental Hygiene Department (FEHD) currently conducts specific surveys for mosquito vectors of malaria, dengue fever and Japanese encephalitis³⁰ covering the mosquito species *Anopheles minimus*, *Anopheles jeyporiensis*, *Aedes albopictus*, *Aedes aegypti* and *Culex tritaeniorhynchus*. While these species could also be vectors for WNV transmission, these data do not routinely cover key WNV vectors like *Culex quinquefasciatus*, *Culex pipiens*, and *Aedes vexans*. Although past surveys have indicated that important WN vectors such as *Culex quinquefasciatus* are widely distributed in Hong Kong, it would still be useful to conduct a WNV-specific vector survey for baseline identification of high risk areas and to guide the development of control strategies in the event of positive detection of animal or human cases.

Bird surveillance

32. Strategies for WNV surveillance using birds may be divided into three groups (1) dead wild birds; (2) trapped wild birds (3) captive sentinel birds/domestic poultry.

Dead bird surveillance

33. In countries where outbreaks of WNV have occurred, high bird mortality has been found to correlate strongly with WNV activity and has indicated where human disease was likely to occur. It was reported that as early as the end of June 1999, an unusual number of dead and dying crows were noted in New York City, preceding the earliest human cases occurring in the first week of August³³. Therefore, if established before a WNV outbreak, surveillance of bird deaths may provide a sensitive method of detecting WNV. In 2002, 56% of the 589 counties reporting human WN meningoencephalitis cases detected WNV-infected dead birds as the first positive surveillance event, preceding human illness onset by a median of 38.5 days (range 2-252 days)¹⁶.

34. Dead bird surveillance has two components: reporting of sightings of dead birds and the testing of samples of dead birds for WNV. This approach relies on public participation in the timely reporting of dead bird sightings and the submission of selected individual birds for WNV testing. One important limitation of this type of surveillance is that the public may not participate equally in all areas of the region or at all times.

Trapped wild birds surveillance

35. Free-living birds can move around, increasing the probability that they will come into contact with the virus. This surveillance may be used for

early detection and monitoring of virus activity. Free-living wild birds are captured and their blood samples tested for WNV antibody. Individual bird would be given a leg-band before being released for identification for recapture and testing of changes in antibody titres. The best species for serologic surveillance are those in which infection is rarely fatal and population replacement rates are high to ensure the replenishment of the susceptible population. The limitations of this surveillance approach are that free-living birds are seldom recaptured and seroconversion could not be confirmed, and the time of infection of seropositive birds could not be ascertained, though seropositive young birds may mean recent infection. A much greater effort is required for this type of surveillance, and in general, it has not been consistently used in the USA or elsewhere.

Sentinel bird surveillance

36. The goal of such surveillance is to detect seroconversion in birds as an indicator of WNV activity. Live captive birds (usually chickens or rock pigeons) have been used as sentinels in WNV surveillance programmes in a number of countries. Chickens and rock pigeons are considered suitable species for captive bird surveillance program because they develop antibodies after infection without becoming highly infectious to mosquito vectors. Important considerations in the use of captive sentinel birds, in addition to the species chosen, are location, type and positioning of cage, the number of birds and any other factor that may render the sentinels more or less attractive to the vector. One alternate approach is using domestic poultry as sentinel bird. Domestic poultry can overcome some problems in wild birds surveillance because the birds' age is known, their initial serological status can easily be checked and they can be widespread in a given geographical area. However, experience from the USA found that seroconversions were detected in captive sentinel birds but they were rarely the earliest indicators of WNV activity. The US Centers for Disease Control and Prevention (US CDC) recommended further research before relying on this strategy as a primary means of WNV surveillance.

37. The Agriculture, Fisheries and Conservation Department (AFCD) undertakes routine passive surveillance of dead birds, captive birds and chickens including taking samples for serology. Any evidence of multiple mortalities in birds is investigated immediately due to concerns with avian influenza. Bird cadavers collected and submitted to the laboratory are routinely examined for histological evidence of viral encephalitis. If gross pathologic or histopathologic findings were suggestive of WNV viral infection, specimens may be sent to overseas laboratories for confirmatory tests. From January 2003 to February 2005, a total of 318 wild birds, 46 captive birds and 315 chickens have been submitted to AFCD's laboratory and no WNV has been detected so far³⁵.

Surveillance of horses and other animals

38. WNV infection in horses can cause equine viral encephalomyelitis but most do not become ill. The passive reporting and testing of dead (or sick) horses has been used for WNV surveillance in the USA. However, disease in horses was the first indication of WNV activity in only 16% of counties where there were reported human cases of WNV in 2002. A significant difference between the US horse population and the local one is that US horses are routinely vaccinated against WNV.

39. The risk of WNV being brought into the Hong Kong through horses is extremely remote as horses are considered 'dead end' hosts. Even so, all horses imported are accompanied by veterinary health certificates and checked by AFCD. WNV is one in a list of 27 diseases included in the health information document for importation³⁶.

Blood product screening

40. Following the reporting of WNV infections related to blood transfusions in 2002, the US Food and Drug Administration recommended using WNV nucleic acid amplification tests (RT-PCR) to screen all blood donations. This screening was performed on approximately 6 million units during June-December 2003, resulting in the removal of at least 818 viremic blood donations. However, 6 cases of WNV transfusion-associated transmission still occurred due to the low viral load being below the detection levels^{24, 26}.

41. In the UK, the Blood Transfusion Services in 2003 stopped people who have travelled to the USA and Canada during the transmission season (between 1 June and 30 November) from giving blood for 28 days after they left. In 2004, for donors fulfilling the travel risk criterion, blood can be donated and as samples would be tested for WNV (in the US) prior to the donated blood being used for patients³⁷.

42. Since June 2003, the Hong Kong Red Cross Blood Transfusion Service (BTS) has implemented guidelines for the prevention of acquiring WNV through blood transfusions. Between June and November each year, prospective blood donors who had been to North America 2 weeks prior to the date of blood donation would be deferred from donation for 14 days, while those who, at the same time, suffered flu-like symptoms would be deferred for 28 days. Donors are also reminded to inform the BTS at the earliest instance if they have symptoms of WNV infection after blood donation so that the BTS can trace the donated blood for follow-up^{38, 39}.

Laboratory safety

43. Laboratory workers should use every precaution to minimize their risk for exposure to materials potentially infected with WNV. The Subcommittee on Arbovirus Laboratory Safety of the American Committee on Arthropod-Borne Viruses recommended that laboratory investigations that involve handling of live WNV should be conducted under BSL-3 containment. However, to enable timely detection of WNV infections, BSL-2 facilities with modest modifications of procedures, could achieve acceptable level of safety for routine diagnostic procedures involving live WNV, including bird necropsies.

44. In Hong Kong, the neutralization test which involves live virus would be performed in BSL-3 facility while other serological tests and PCR would be performed in BSL-2 facility.

Perinatal transmission

45. Although no conclusive evidence exists for a causal relationship between intrauterine infection of WNV and fetal abnormalities, the US CDC advises pregnant women to take precautions to reduce their risk of WNV during pregnancy by avoiding mosquitoes, using protective clothing, the using repellents containing DEET. Pregnant women who became ill should seek medical advice and undergo appropriate diagnostic testing. Although there was a documented case of possible transmission through breastfeeding, the risk of WNV transmission through breast-feeding is unknown.

Conclusions and Recommendations

46. Hong Kong is considered receptive to WNV, given the abundance of migratory birds and the wide existence of the right mosquito vectors. Although there is currently no evidence suggestive of WNV infection in mosquitoes, birds or human in Hong Kong, we lack a complete understanding of the relevant local vectors and host ecology and further risk assessment based on enhanced surveillance is required. Past experience in the USA has shown that once virus transmission has occurred in the resident bird population it is almost impossible to eliminate human cases of infection. Bird surveillance is therefore the fundamental strategy for monitoring and preventing the emergence of the disease in Hong Kong.

47. The overriding objective of our surveillance would be to detect the earliest possible indication of virus introduction to prevent it from gaining footholds in Hong Kong. The objectives of such surveillance would therefore include:

- (a) Early detection of WNV epidemics in birds;
- (b) Early detection of first human cases;
- (c) Prompt interruption of the transmission when local sources of

infection are identified.

48. Against this background, specific recommendations for enhancing our preparedness and response against WNV are listed as follows:

1. To set up a routine bird surveillance system in Hong Kong which encompasses the following components:
 - (a) Enhanced mechanisms for dead bird surveillance through inter-departmental and public participation;
 - (b) Strengthened testing capacity at the veterinary laboratories for detection of WNV in dead birds
2. To develop vector surveillance and control strategies in response to positive detections in birds;
3. To enhance human surveillance
 - (a) To develop guidelines on surveillance case definitions, clinical features, and testing strategies and make available to medical practitioners;
 - (b) To maintain vigilance on laboratory diagnosis of WNV infection among clinical specimens submitted for testing;
4. To develop information dissemination mechanisms for raising public awareness especially for those who may travel to areas with known WNV outbreaks;
5. To protect the public from iatrogenic, perinatal and laboratory-acquired infections through maintaining awareness among the local Blood Transfusion Services, Obstetric and Paediatrics specialists, and Pathologists and Microbiologists regarding the latest situation assessment on WNV.

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