Complete Summary

GUIDELINE TITLE

Epidemic/epizootic West Nile virus in the United States: guidelines for surveillance, prevention, and control.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Epidemic/epizootic West Nile Virus in the United States: guidelines for surveillance, prevention, and control. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2003. 75 p. [77 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Epidemic/epizootic West Nile Virus in the United States: revised guidelines for surveillance, prevention, and control. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2001 Apr. 104 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

West Nile virus infection, including West Nile encephalitis or meningitis

GUIDELINE CATEGORY

Diagnosis
Prevention

CLINICAL SPECIALTY

Infectious Diseases
Pathology
Preventive Medicine

INTENDED USERS

Clinical Laboratory Personnel
Pathology Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To present national, state, and local public health recommendations for West Nile virus surveillance, prevention, and control

TARGET POPULATION

Humans, horses and other mammals, birds, and mosquitoes in the United States

INTERVENTIONS AND PRACTICES CONSIDERED

1. Surveillance
    - Ecologic surveillance
        - Avian surveillance (avian morbidity/mortality; captive sentinel surveillance; free-ranging bird surveillance)
        - Equine surveillance
        - Mosquito surveillance
    - Human surveillance
        - Monitoring of relevant clinical syndromes
        - Passive and active surveillance activities and projects
        - Collections of specimens of cerebrospinal fluid, serum, tissues
        - Use of surveillance case definitions and a surveillance system
    - Geography and timing issues
2. Laboratory Diagnosis of West Nile Virus
    - Biocontainment measures (laboratory safety issues, shipping/transport of West Nile virus and clinical specimens)
    - Serologic laboratory diagnosis in humans and animals
        - Immunoglobulin M and immunoglobulin G enzyme-linked immunosorbent assay
        - Hemagglutination inhibition and direct immunofluorescence assay testing
        - Plaque-reduction neutralization test antibody titer
    - Virologic laboratory diagnosis
        - Isolation of virus (indirect immunofluorescence assay using virus-specific monoclonal antibodies, nucleic acid detection methods, or virus neutralization assays)
        - Virus detection in tissues through antigenic analysis or nucleic acid analysis

3. Prevention and Control
    - Surveillance (mosquito and virus)
    - Source reduction (elimination of mosquito larvae habitat)
        - Sanitation measures
        - Water management
    - Chemical control (larviciding, adulticiding)
    - Insecticide resistance management
    - Biological control
    - Continuing education of mosquito control workers
    - Health education, public information, and behavior change programs
        - Key prevention messages
        - Targeted prevention
4. Setting up appropriate health department infrastructure on both state and local levels
5. Interjurisdictional data sharing and national reporting of human cases

MAJOR OUTCOMES CONSIDERED

- Rates of individuals or groups of individuals reported to, sampled by, or tested by a state's West Nile virus surveillance system, by county or similar jurisdiction within states
- Rates of confirmed or suspected West Nile virus infection in individual mosquito pools, sentinel species, dead birds, ill or dead humans, horses, or other species as determined by laboratory-confirmatory, probable, or equivocal test results

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

To assess the implications of the West Nile virus (WNV) introduction into the U.S. and to develop a comprehensive national response plan, the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA) co-sponsored a meeting of arbovirologists, epidemiologists, laboratorians, vector-control specialists, wildlife biologists, and state and local health and agriculture officials in Fort Collins, Colorado, on November 8-9, 1999.

Since 1999, the CDC and a variety of other U.S. governmental agencies and partners have sponsored yearly national meetings of arbovirologists, epidemiologists, laboratorians, ecologists, vector-control specialists, wildlife biologists, communication experts, and state and local health and agriculture officials to assess the implications of the West Nile virus introduction into the U.S. and to refine the comprehensive national response plan. Recommendations from these meetings have been used to develop and to update these guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: The 2002 West Nile virus (WNV) epidemic was the largest recognized arboviral meningoencephalitis epidemic in the Western Hemisphere and the largest WN meningoencephalitis epidemic ever recorded. Significant human disease activity was recorded in Canada for the first time, and WNV activity was also documented in the Caribbean basin and Mexico. In 2002, 4 novel routes of WNV transmission to humans were documented for the first time: 1) blood transfusion, 2) organ transplantation, 3) transplacental transfer, and 4) breast-feeding.

Surveillance

Appropriate and timely response to surveillance data is the key to preventing human and animal disease associated with WNV and other arboviruses. That response must include effective mosquito control and public education without delay, if an increasing intensity of virus activity is detected by bird- or mosquito-based surveillance systems. See the Centers of Disease Control and Prevention (CDC) "Guidelines for Arbovirus Surveillance Programs in the United States" for more information.

A. Ecologic Surveillance

Detection of WNV in bird and mosquito populations helps health officials predict and prevent human and domestic animal infections. Surveillance to detect WNV should focus on the avian and mosquito components of the enzootic transmission cycle. Non-human mammals, particularly equines, may also serve as effective sentinels because a high intensity of mosquito exposure makes them more likely to be infected than people. Descriptions of the avian-, mosquito-, and nonhuman mammal-based surveillance strategies follow.

1. Avian

a. Avian morbidity/mortality surveillance appears to be the most sensitive early detection system for WNV activity, and should be a component of every state's arbovirus surveillance program.

Protocols and specimens:

- The level of effort involved in this surveillance activity will depend on a risk assessment in each jurisdiction. Generally, avian surveillance should be initiated when local adult mosquito activity begins in the spring. A database should be established to record and analyze dead bird sightings with the following suggested data: caller identification and call-back number, date observed, location geocoded to the highest feasible resolution, species, and condition. Samples from birds in good condition (unscavenged and without obvious decomposition or maggot infestation) may be submitted for laboratory testing. As with all dead animals, carcasses should be handled carefully, avoiding direct contact with skin. For greatest sensitivity, a variety of

bird species should be tested, but corvids should be emphasized (Eidson et al., "Crow deaths," 2001). The number of bird specimens tested will be dependent upon resources and whether WNV-infected birds have been found in the area; triage of specimens may be necessary on the basis of sensitive species (such as corvids) and geographic location. Many jurisdictions may limit (or even stop) avian mortality surveillance once WNV is confirmed in their region. It is suggested that avian mortality surveillance be continued in each region as long as it remains necessary to know whether local transmission persists, because dead-bird-based surveillance is the most sensitive method for detection of WNV activity in most regions.

- A single organ specimen from each bird is sufficient to detect WNV or viral ribonucleic acid (RNA). Kidneys, brains, or hearts are preferable (Guptil et al., 2003, Julian et al., 2002, Mostashari et al., 2003). Oral swabs from corvids have been validated as a sensitive alternative to organ samples, and because fewer resources are necessary to acquire them, oral swabs are the preferred specimen from corvid carcasses (Steele et al., 2000) Testing involves isolation of infectious virus, specific RNA detection by reverse transcription-polymerase chain reaction (RT-PCR) (Panella et al., 2000), or antigen detection (Kramer & Bernard, 2001, Komar et al., 2002), and will generally be positive within 1 to 2 weeks after specimen submission.

Refer to the original guideline document for detailed information on recent experience, advantages, and disadvantages of avian morbidity/mortality surveillance.

b. Live-bird surveillance has been used traditionally both to detect and monitor arbovirus transmission (e.g., for St. Louis encephalitis [SLE], eastern equine encephalitis [EEE], and western equine encephalitis [WEE] viruses). Two approaches are captive sentinel surveillance (typically using chickens, but other species have been used as well), and free-ranging bird surveillance (Nasci et al., 2002). Both depend on serological testing, which generally requires at least 3 weeks to detect and confirm an infection. Successful application of these approaches requires extensive knowledge of local transmission dynamics. It is recommended that further research be done before relying on sentinel birds as a primary means of WNV surveillance. Use of sentinel birds may require institutional animal use and care protocols and other authorization permits.
    1. Captive sentinel surveillance

       Although an ideal captive avian sentinel for WNV--or any other arbovirus--may not exist, such a species would meet the following criteria: 1) is universally susceptible

to infection, 2) has a 100% survival rate from infection and universally develops easily detectable antibodies, 3) poses no risk of infection to handlers, and 4) never develops viremia sufficient to infect vector mosquitoes (CDC, 1993). Captive sentinel flocks should be placed in likely transmission foci (e.g., near vector breeding sites or adult mosquito congregation sites) and presented appropriately to allow feeding by enzootic WNV vectors. Alternatively, pre-existing captive birds (e.g., domestic poultry or pigeons, or zoo birds) may be used as sentinels.

Protocols and specimens

Whole blood can be collected and centrifuged for serum. Serum is screened by either hemagglutination inhibition (HI), enzyme-linked immunosorbent assay (ELISA) or plaque-reduction neutralization test (PRNT) (Guptil et al., 2003). It is important to note that the extraction of avian serum samples to remove nonspecific inhibitors of hemagglutination for use in the HI test follows procedures different from those used in tests of human serum samples (Mostashari et al., 2003). Positive tests must be confirmed by neutralization to rule out false positives and cross-reactions due to infection with related flaviviruses (e.g., SLE virus).

Refer to the original guideline document for detailed information on recent experience, advantages, and disadvantages of captive sentinel surveillance.

c. Free-ranging bird surveillance

Free-ranging birds provide the opportunity for sampling important reservoir host species and may be used both for early detection and for monitoring virus activity. This type of surveillance has been used effectively for SLE, EEE, and WEE virus surveillance in several states. In each geographic area, the optimal free-ranging bird species to be monitored should be determined by serosurveys. The best species for serologic surveillance are those in which infection is rarely, if ever, fatal, and population replacement rates are high, ensuring a high proportion of uninfected individuals.

Protocols and specimens

The use of free-ranging birds requires differentiation of recent infection from infections acquired in previous years. For most species, assays for detection of immunoglobulin M (IgM) antibody will not be available and other tests such as IgG (IgY)-detection ELISAs (Komar et al., "Serologic evidence for West Nile virus infection in birds in the New York City vicinity," 2001; Komar et al., "Serologic evidence for West Nile virus infection in birds in Staten Island," 2001) and the PRNT (Guptil et al., 2003) must be used to detect WNV-specific antibody. Antibody-positive birds less than 1 year old may be presumed to have been infected recently (during current transmission season). Weak

seropositivity in very young birds (less than 1 month old) may be due to maternal transfer of antibody. Seroconversion in older birds is also evidence of recent transmission but requires frequent recapture for acquisition of multiple specimens from uniquely banded individuals during the course of the transmission season. WNV seropositivity among after-hatch-year birds, when determined from a single serum specimen, should not be interpreted or reported as evidence of recent infection. State and federal permits are required for capture and banding of federally-protected migratory birds.

> Refer to the original guideline document for detailed information on recent experience, advantages, and disadvantages of free-ranging bird surveillance.

2. **Equine**

Equines appear to be important sentinels of WNV epizootic activity and human risk, at least in some geographic regions. In addition, equine health is an important economic issue. Therefore, surveillance for equine WNV disease should be conducted in jurisdictions where equines are present. Veterinarians, veterinary service societies/agencies, and state agriculture departments are essential partners in any surveillance activities involving equine WNV disease. A working surveillance case definition of clinical WNV infection in equines is presented in Appendix B in the original guideline document.

Protocols and Specimens

- Serum and cerebrospinal fluid (CSF) for antibody testing. Because an equine WNV vaccine is now in widespread use, a complete vaccination history should accompany all specimens submitted for antibody testing.
- Necropsy tissues (especially brain and spinal cord) for gross pathology, histopathology, RT-PCR, virus isolation, and immunohistochemistry. The differential diagnosis of equine encephalitis includes, but is not limited to, the other arboviral encephalitides and rabies.

Refer to the original guideline document for detailed information on recent experience, advantages, disadvantages and minimal components of an equine surveillance program.

3. **Mosquito**

While dead-bird-based surveillance has proven to be the most sensitive method of detecting WNV presence in an area, mosquito-based surveillance remains the primary tool for quantifying the intensity of virus transmission in an area and should be a mainstay in most surveillance programs for WNV and other arboviruses.

Protocols and specimens

- Adult mosquitoes are collected using a variety of trapping techniques and are used to identify the mosquito species and primary vector species present in an area and the relative density of those species. When coupled with virus detection protocols, mosquito collections can be screened for the presence of virus and provide a quantifiable index of WNV activity. Adequate sampling requires trapping regularly at representative sites throughout a community and rapid testing of collections of sufficient size to detect low infection rates in the vector population. Minimally, adult mosquito density (number collected per trap night) and infection rate (number of individual mosquitoes estimated containing WNV per 1,000 specimens tested) should be recorded for each area to provide a basis for tracking mosquito density and virus incidence.
- Larval mosquitoes are collected by taking dip samples from a variety of habitats to identify species present in the area and to identify mosquito sources. Thorough mapping of larval habitats will facilitate larval control or source reduction activities. In addition, where larval management is not feasible, quantitative estimates of larval densities will permit anticipation of new adult emergences. Minimally, the number of larvae collected per dip and location where collected should be recorded to provide a basis for tracking larval production and association of larval density with resulting adult mosquito population density.

Refer to the original guideline document for detailed information on recent experience, advantages, disadvantages, and minimal components of an entomological surveillance program.

B. Surveillance for Human Cases

Because the primary public health objective of surveillance systems for neurotropic arboviruses is prevention of human infections and disease, human case surveillance alone should not be used for the detection of arbovirus activity, except in jurisdictions where arbovirus activity is rare or resources to support avian-based and/or mosquito-based arbovirus surveillance are unavailable. Refer to the original guideline document for information on recent experience.

1. Types of Surveillance

a. Clinical syndromes to monitor

Monitoring of encephalitis cases is the highest priority. Monitoring milder illnesses (e.g., aseptic meningitis, Guillain-Barre syndrome, acute flaccid paralysis, and brachial plexopathy, and fever or rash illnesses) is resource-dependent and should be of lower priority.

b. Types of human surveillance

1. Enhanced passive surveillance

In the absence of known WNV activity in an area, passive surveillance (enhanced by general alerts to key health care personnel such as primary care providers, infectious disease physicians, neurologists, hospital infection control personnel, and diagnostic laboratories) for hospitalized cases of encephalitis (and milder clinical syndromes as resources allow), and for patients who have IgM antibodies to either WN or SLE virus in tests conducted in diagnostic or reference laboratories, should be employed.

Note: While human infections with neurotropic arboviruses are usually clinically inapparent, most clinically apparent infections are associated with fever, with or without neurologic manifestations, which can range from mild aseptic meningitis to fulminant and fatal encephalitis. Signs and symptoms may include fever, headache, stiff neck, confusion or other mental status changes, nausea, vomiting, meningismus, cranial nerve abnormalities, paresis or paralysis, sensory deficits, altered reflexes, abnormal movements, convulsions, and coma of varying severity. Arboviral meningitis or encephalitis cannot reliably be clinically distinguished from other central nervous system infections.

A high clinical suspicion for arboviral encephalitis should be encouraged among health care providers. When the diagnosis is in doubt, appropriate clinical specimens should be submitted to CDC or another laboratory capable of performing reliable serologic testing for antibodies to domestic arboviruses. Testing of CSF and paired acute- and convalescent-phase serum samples should be strongly encouraged to maximize the accuracy of serologic results.

2. Active surveillance

   Active surveillance should be strongly considered in areas with known WNV activity. In general, one or both of the following approaches should be taken:

   - Contact physicians in appropriate specialties (i.e., infectious diseases, neurology, and critical care) and hospital infection control personnel on a regular basis to inquire about patients with potential arboviral infections.
   - Implement laboratory-based surveillance to identify CSF specimens meeting sensitive but nonspecific criteria for arboviral infections (e.g., mild to moderate pleocytosis and negative tests for the presence of nonarboviral agents such as bacteria, fungi, herpesviruses, and enteroviruses) and test them for evidence of WNV infection.

3. Special surveillance projects

Special projects may be used to enhance arboviral disease surveillance. Such projects include the Emerging Infections Network of the Infectious Diseases Society of America (IDSA EIN), Emergency Department Sentinel Network for Emerging Infections (EMERGEncy ID NET), Unexplained Deaths and Critical Illnesses Surveillance of the Emerging Infections Programs (EIP), and the Global Emerging Infections Sentinel Network of the International Society of Travel Medicine (GeoSentinel). In some areas, syndromic surveillance systems may be considered. "Piggy-backing" surveillance for West Nile meningoencephalitis (WNME) and milder clinical forms of WN viral infection, such as fever with rash or lymphadenopathy, onto existing syndromic surveillance systems, especially those involving large health maintenance organizations, may be considered. Real-time computerized syndromic surveillance in emergency departments, and special surveillance projects to identify WNV disease in pediatric populations, may be useful.

2. **Specimens**
   a. Cerebrospinal fluid (CSF)

      In WNME cases, WNV-specific IgM antibody commonly can be found in CSF on the day of illness onset using antibody-capture ELISA. Virus also may be isolated (rarely) or detected by RT-PCR (in up to 60% of cases) in acute-phase CSF samples.

   b. Serum

      Paired acute-phase (collected 0-8 days after onset of illness) and convalescent-phase (collected 14-21 days after the acute specimen) serum specimens are useful for demonstration of seroconversion to WNV and other arboviruses by ELISA or neutralization tests. Although tests of a single acute-phase serum specimen may provide evidence of a recent WNV infection, a negative acute-phase specimen is inadequate for ruling out such an infection, underscoring the importance of collecting paired samples. As mentioned previously, antibody synthesis in immunocompromised individuals might be delayed or absent altogether.

   c. Tissues

      When arboviral encephalitis is suspected in a patient who undergoes a brain biopsy or who dies, tissues (especially brain samples, including samples of cortex, midbrain, and brainstem), heart/venous blood, and buffy coat samples should be submitted to CDC or other specialized laboratories for arbovirus and other testing. Tissue specimens should be divided; half should be frozen at -70 degrees C and the other

half fixed in formalin. Available studies include gross pathology, histopathology, RT-PCR tests, virus isolation, and immunohistochemistry.

3. **Surveillance Case Definition**

   The national case definition for arboviral encephalitis (available at www.cdc.gov/epo/dphsi/casedef/encephalitiscurrent.htm) should be used to classify cases as confirmed or probable, once appropriate laboratory results are available (also see Section II in the original guideline document).

4. Minimal components of a human surveillance system include enhanced passive surveillance for hospitalized encephalitis cases of unknown etiology and for patients who have IgM antibodies to either WN or SLE virus in tests conducted in diagnostic or reference laboratories.

C. **Geography and Timing**

In general, the WNV transmission season in the U.S. is longer than that for other domestic arboviruses and requires longer periods of ecologic and human surveillance. Refer to the original guideline document for information on the appropriate timing of surveillance activities by geographic region.

Laboratory Diagnosis

The clinical presentation of most patients with viral encephalitis is similar regardless of the cause. Also, infection by many of the arboviruses that cause encephalitis, including West Nile and St. Louis encephalitis viruses, usually is clinically inapparent or causes a nonspecific viral syndrome in most patients. Definitive diagnosis, therefore, can only be made by laboratory testing using specific reagents. To be successful, active surveillance must have adequate laboratory support.

The basic laboratory diagnostic tests—and how they should be used at the national, state, and local level—are outlined below. The initial designation of reference and regional laboratories that can do all testing will be based on the availability of biosafety level 3 (BSL3) containment facilities. Details of the surveillance case definition for human West Nile virus (WNV) disease and of how the laboratory diagnostic tests are used to support surveillance are presented in Appendix B of the original guideline document.

A. **Biocontainment**

1. **Laboratory Safety Issues**

   a. WNV may be present in blood, serum, tissues, and CSF of infected humans, birds, mammals, and reptiles. The virus has been found in the oral fluids and feces of birds. Parenteral inoculation with contaminated materials poses the greatest hazard; contact exposure of broken skin is a possible risk. Sharps precautions should be strictly adhered to when handling potentially infectious materials. Workers performing necropsies on infected animals may be at high risk of infection.

b. Biosafety Level 2 practices and facilities are recommended for activities for human diagnostic specimens. In some cases it may be advisable to perform initial processing of clinical samples in a biosafety cabinet, particularly if high levels of virus is suspected (such as tissues from fatal human cases). Biosafety Level 2 is recommended for processing field collected mosquito pools. Biosafety Level 3 and Animal Biosafety Level 3 practices, containment equipment, and facilities are recommended, respectively, for all manipulations of West Nile cultures and for experimental animal and vector studies. Containment specifications are available in the Centers for Disease Control and Prevention/National Institutes of Health publication "Biosafety in Microbiological and Biomedical Laboratories (BMBL)" (Blitvich et al., 2003).
c. All bird necropsies should be done in a Class 2 biological safety cabinet.

2. **Shipping of Agents**

Shipping and transport of WNV and clinical specimens should follow current International Air Transport Association (IATA) and Department of Commerce recommendations.

B. Serologic Laboratory Diagnosis

Accurate interpretation of serologic findings requires knowledge of the specimen. For human specimens the following data must accompany specimens submitted for serology before testing can proceed or results can be properly interpreted and reported: 1) symptom onset date (when known); 2) date of sample collection; 3) unusual immunological status of patient (e.g., immunosuppression); 4) state and county of residence; 5) travel history in flavivirus-endemic areas; 6) history of prior vaccination against flavivirus disease (e.g., yellow fever, Japanese encephalitis, or Central European encephalitis); 7) brief clinical summary including clinical diagnosis (e.g., encephalitis, aseptic meningitis).

1. **Human**
   a. Commercial kits for human serologic diagnosis of WNV infection are currently in development. Until these kits are available, the CDC-defined IgM and IgG ELISA should be the front-line tests for serum and CSF (Roehrig et al., 2003, Mostashari et al., 2001, CDC & National Institutes of Health (NIH), 2000) These ELISA tests are the most sensitive screening assays available. The HI and indirect immunofluorescent antibody (IFA) test may also be used to screen samples for flavivirus antibodies. Laboratories performing HI assays need be aware that the recombinant WNV antigens produced to date are not useful in the HI test; mouse brain source antigen (available from CDC) must be used in HI tests. The recombinant WNV antigen is available from commercial sources.
   b. To date, the prototype WNV strains Eg101 or NY99 strains have performed equally well as antigens in diagnostic tests for WNV in North America.

c. To maintain Clinical Laboratory Improvements Amendments (CLIA) certification, CLIA recommendations for positive and negative ranges should be followed, and laboratories doing WNV testing should participate in a proficiency testing program through experienced reference laboratories; CDC's Division of Vector-Borne Infectious Diseases in Fort Collins, Colorado, and the National Veterinary Services Laboratories in Ames, Iowa, both offer this type of program.
d. Because the ELISA can cross-react between flaviviruses (e.g., SLE, dengue, yellow fever, WN), it should be viewed as a screening test only. Initial serologically positive samples should be confirmed by neutralization test. Specimens submitted for arboviral serology should also be tested against other arboviruses known to be active or be present in the given area (e.g., test against SLE, WN and EEE viruses in Florida).

2. **Animal**
   a. In general, the procedures for animal serology should follow those used with humans cited above.
   b. Plaque-reduction neutralization test (PRNT) and HI assays, although technically more demanding, may be useful because they are species independent.

C. **Virologic Laboratory Diagnosis**

Experience gained in WNV diagnostic testing over the past 4 years has led to the following recommendations:

1. **Virus Isolation**
   a. Virus isolation attempts should be performed in known susceptible mammalian or mosquito cell lines. Mosquito origin cells may not show cytopathic effect and should be screened by immunofluorescence.
   b. Appropriate samples for virus isolation are prioritized as follows:
      1. Clinically ill humans - CSF (serum samples may be useful early in infection)
      2. Human (biopsy or postmortem) - brain tissue
      3. Horses (postmortem) - brain tissue (including brainstem), spinal cord tissue
      4. Birds - kidney, brain, heart
      5. Other mammals - multiple tissues, especially kidney and brain
   c. Confirmation of virus isolate identity can by accomplished by indirect immunofluorescence assay (IFA) using virus-specific monoclonal antibodies, nucleic acid detection, or virus neutralization.
   d. The IFA using well-defined murine monoclonal antibodies (MAbs) is the most efficient, economical, and rapid method to identify flaviviruses. MAbs are available that can differentiate WNV and SLE virus from each other and from other flaviviruses. Flavivirus-grouping MAbs are available for use as positive controls, and MAbs specific for other arboviruses can be used as negative controls. In addition, incorporating MAbs specific

for other arboviruses known to circulate in various regions will increase the rapid diagnostic capacities of state and local laboratories. These reagents are available and should be used.

e. Nucleic acid detection methods including RT-PCR, TaqMan, and nucleic acid sequence based amplification (NASBA) methods may be used to confirm virus isolates as WNV.
f. Virus neutralization assays also may be used to differentiate viruses, by using fourfold or greater titer differences as the diagnostic criterion in paired specimens (acute- and convalescent-phase).

2. **Virus Detection in Tissues**
   a. Antigenic analysis
      1. Immunohistochemistry (IHC) using virus-specific MAbs on brain tissue has been very useful in identifying both human and avian cases of WNV infection. In suspected fatal cases, IHC should be performed on formalin-fixed autopsy, biopsy, and necropsy material, ideally collected from multiple anatomic regions of the brain, including the brainstem, midbrain, and cortex (Panella et al., 2001, Monath et al., 1984).
      2. Well-characterized antigen-capture ELISAs are now available for detection of SLE (Martin et al., 2000, Johnson et al., 2000) and WNV antigen in mosquito pools and avian tissues (Kramer & Bernard, 2001).
   b. Nucleic acid analysis

      A number of nucleic acid detection methods have recently been employed for WNV diagnostic and surveillance purposes. An independent antigen or nucleic acid test is required to confirm detection of WNV nucleic acid with any of these methods.

      1. RT-PCR of tissues, mosquito pools, and CSF has proven to be a useful surveillance tool. RT-nested PCR has detected WNV nucleic acid in equine brain and spinal cord tissues. Standardized protocols developed by reference laboratories should be disseminated, and primer design information should be included so that other laboratories can prepare primers. A proficiency testing program should be developed by the reference laboratories so that these tests can be CLIA-certified in local laboratories.
      2. Fluorogenic 5' nuclease techniques (real-time PCR) and nucleic acid sequence-based amplification (NASBA) methods have been developed and have undergone initial validation in specific diagnostic applications (Panella et al., 2001, Shieh et al., 2000, Tsai et al, 1987, Tsai et al., 1988).

D. **Training and Infrastructure**

1. **State and Local Arbovirus Laboratories**

   Greater numbers of capable state and local laboratories performing screening assays (such as ELISA) should be developed to reduce time

demands on reference laboratories. Reference laboratories should be utilized to confirm results of state and local laboratories, particularly for the initial identification of WNV in new locations and in new hosts.

2. **Training Programs**

   Laboratory training programs have been developed and implemented at the federal level. Additional regional training programs may be beneficial.

Prevention and Control

Prevention and control of arboviral diseases is accomplished most effectively through a comprehensive, integrated mosquito management program using sound integrated pest management (IPM) principles (Briese, Glass, & Lipkin, 2000). IPM is based on an understanding of the underlying biology of the transmission system and utilizes regular monitoring to determine if and when interventions are needed to keep pest numbers below levels at which intolerable levels of damage, annoyance, or disease occur. IPM-based systems employ a variety of physical, mechanical, cultural, biological, and educational measures, singly or in appropriate combination, to attain the desired pest population control.

Programs consistent with best practices and community needs should be established at the local level and, at a minimum, should be capable of performing surveillance sensitive enough to detect WNV enzootic/epizootic transmission that has been associated with increased risk of disease in humans or domestic animals. Integrated mosquito management programs designed to minimize risk of WNV transmission and prevent infections of humans and domestic animals should optimally include the following components (modified from information provided by the American Mosquito Control Association, the New Jersey Mosquito Control Association, and the Florida Coordinating Council on Mosquito Control)(Shi et al., 2001, Lanciotti & Kerst, 2001, Rose, 2001)

A. **Surveillance**

   Effective mosquito control begins with a sustained, consistent surveillance program that targets pest and vector species, identifies and maps their immature habitats by season, and documents the need for control. Records should be kept on the species composition of mosquito populations prior to enacting control of any kind and to allow programs to determine the effectiveness of control operations. All components of the integrated management program must be monitored for efficacy using best practices and standard indices of effectiveness. Refer to the original guideline document for a description of surveillance methodologies used by mosquito control agencies.

B. **Source Reduction**

   Source reduction is the alteration or elimination of mosquito larval habitat breeding. This remains the most effective and economical method of providing long-term mosquito control in many habitats. Source reduction can

include activities as simple as the proper disposal of used tires and the cleaning of rain gutters, bird baths, and unused swimming pools by individual property owners, to extensive regional water management projects conducted by mosquito control agencies on state and/or federal lands. All of these activities eliminate or substantially reduce mosquito breeding habitats and the need for repeated applications of insecticides in the affected habitat. Source reduction activities can be separated into the following two general categories:

1. **Sanitation**

   The by-products of human's activities have been a major contributor to the creation of mosquito breeding habitats. Educational information about the importance of sanitation in the form of videos, slide shows, and fact sheets distributed at press briefings, fairs, schools and other public areas are effective.

2. **Water Management**

   Water management for mosquito control is a form of source reduction that is conducted in fresh and saltwater breeding habitats. Refer to the original guideline document for detailed information on water management programs.

C. **Chemical Control**

Insecticides can be directed against either the immature or adult stage of the mosquito life cycle when source reduction and water management are not feasible or have failed because of unavoidable or unanticipated problems, or when surveillance indicates the presence of infected adult mosquitoes that pose a health risk (Newhouse et al., 1966). Chemicals used by mosquito control agencies must comply with state and federal requirements. Public health pesticide applicators and operators in most states are required to be licensed or certified by the appropriate state agencies. Refer to the original guideline document for detailed information on chemical control programs.

D. **Resistance Management**

In order to delay or prevent the development of insecticide resistance in vector populations, integrated vector management programs should include a resistance management component (modified from Florida Coordinating Council on Mosquito Control, 1998) (Lanciotti & Kerst, 2001). Refer to the original guideline document for detailed information on resistance management programs.

E. **Biological Control**

Biological control is the use of biological organisms or their by-products to control pests. Biocontrol is popular in theory, because of its potential to be host-specific and virtually without non-target effects. Refer to the original guideline document for further information.

F. Continuing Education of Mosquito Control Workers

Continuing education is directed toward operational workers to instill or refresh knowledge related to practical mosquito control. Training is primarily in safety, applied technology, and requirements for the regulated certification program mandated by most states.

G. Vector Management in Public Health Emergencies

A surveillance program adequate to monitor WNV activity levels associated with human risk must be in place. Detection of epizootic transmission of enzootic arboviruses typically precedes detection of human cases by several days to 2 weeks or longer (e.g., as found in SLE epidemics) (Reisen et al., 1985, Brogdon & McAllister, 1998). If adequate surveillance is in place, the lead time between detecting significant levels of epizootic transmission and occurrence of human cases can be increased, which will allow for more effective intervention practices (Eidson et al., "Crow deaths," 2001, Lanciotti et al., 2000, Eidson et al., "Dead bird surveillance," 2001). Early-season detection of enzootic or epizootic WNV activity appears to be correlated with increased risk of human cases later in the season. Control activity should be intensified in response to evidence of virus transmission, as deemed necessary by the local health departments.

Such programs should consist of public education emphasizing personal protection and residential source reduction; municipal larval control to prevent repopulation of the area with competent vectors; adult mosquito control to decrease the density of infected, adult mosquitoes in the area; and continued surveillance to monitor virus activity and efficacy of control measures.

As evidence of sustained or intensified virus transmission in an area increases, emergency response should be implemented. This is particularly important in areas where vector surveillance indicates that infection rates in *Culex* mosquitoes are increasing, or that potential accessory vectors (e.g., mammalophilic species) are infected with WNV. Delaying adulticide applications in such areas until human cases occur is illogical and negates the value and purpose of the surveillance system.

H. Adult Mosquito Control Recommendations

Refer to the original guideline document for detailed information.

I. Determining the Scope of Mosquito Adulticiding Operations

Refer to the original guideline document for detailed information.

J. Evaluation of Adult Mosquito Control

Refer to the original guideline document for detailed information.

K. Health Education, Public Information, and Human Behavior Change

The goals of health education, public information, and behavior change programs are to inform the public about WNV, promote the adoption of preventive behaviors that reduce disease risk, and gain public support for control measures. Health education/public information includes use of print materials (posters, brochures, fact sheets), electronic information (Web sites), presentations (health experts or peers speaking to community groups), and the media.

Information alone is seldom sufficient to encourage people to adopt new behaviors or to change old practices. Programs should include strategies to facilitate protective actions and to address barriers that hinder preventive actions. Examples of programs that go beyond information include developing a community task force, interventions to improve access to window screening materials or repellents, and social marketing to reinforce preventive behaviors.

The following section covers key prevention messages, selected best practices, and research/program development priorities for promotion of personal and community measures to decrease risk of WNV infection. Public education and risk communication activities must be ramped up to respond to the degree of WNV risk in a community, as noted in Table 1 in the original guideline document.

1. **Key WNV Prevention Messages**
    a. Address the multiple levels at which prevention can occur: personal protection (use of repellent on skin and clothing, use of protective clothing, awareness of prime mosquito-biting hours); household protection (eliminating mosquito breeding sites, repairing/installing screens); and community protection (reporting dead birds, advocating for organized mosquito abatement, participating in community mobilization).
    b. Use of DEET-based repellents on skin and clothing is the backbone of personal protection. (For current recommendations, see www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm.) Permethrin-based repellents should be promoted for use on clothing.
    c. Emphasize the feasibility of actions that can lower an individual's WNV risk through personal protection measures. Messages should acknowledge the seriousness of the disease but should not be fear-driven. Fear-driven messages may heighten the powerlessness many people express in dealing with emerging diseases.
    d. Recommendations to avoid being outdoors from dusk to dawn may conflict with neighborhood social patterns or practices of persons without air-conditioning or without other health programs seeking to increase physical activity. An alternative is to emphasize that the hours from dusk until dawn are prime mosquito-biting hours, and that protecting oneself through repellent use during these hours is important, with the option of remaining indoors.

e. Communication about adulticiding: Public acceptance of emergency adult mosquito control is critical to its success, especially where mosquito control is unfamiliar or unpopular. Questions about the products being used, their safety, and their effects on the environment are common. Improved communication about surveillance and how decisions to adulticide are made may help residents weigh the risks and benefits of control. When possible, provide detailed information regarding the schedule for adulticiding through newspapers, radio, the Internet, or a recorded phone message.
f. Keep messages clear and consistent with the recommendations of coordinating agencies. Use plain language whenever possible, and adapt materials for lower literacy and non-English speaking audiences.

2. **Selected Best Practices**

a. Targeted prevention

Audience members have different disease-related concerns and motivations for action. Proper message targeting permits better use of limited communication and prevention resources. The following are some audience groups that require specific targeting:

1. *Persons over age 50*: While persons of any age can be infected with WNV, U.S. surveillance data indicate that persons over age 50 are at higher risk for severe disease and death due to WNV infection.

   Collaborate with organizations that have an established relationship with mature adults, such as the American Association of Retired Persons (AARP), senior centers, or programs for adult learners. Include images of older adults in your promotional material. Identify activities in your area where older adults may be exposed to mosquito bites (e.g. jogging, golf, gardening).

2. *Persons with outdoor exposure*: While conclusive data are lacking, it is reasonable to infer that persons engaged in extensive outdoor work or recreational activities are at greater risk of being bitten by WNV-infected mosquitoes.

   Develop opportunities to inform people engaged in outdoor activities about WNV. Encourage use of repellent and protective clothing, particularly if outdoors during evening, night, or early morning hours. Local spokespersons (e.g., union officials, job-site supervisors, golf pros, gardening experts) may be useful collaborators.

3. *Homeless persons*: Extensive outdoor exposure and limited financial resources in this group present special challenges.

   Application of repellents with DEET or permethrin to clothing may be most appropriate for this population. Work with social service groups in your area to reach this population segment.

4. *Persons who live in residences lacking window screens*: The absence of intact window/door screens is a likely risk factor for exposure to mosquito bites.

   Focus attention on the need to repair screens and resources to do so. Partner with community organizations that can assist elderly persons or others with financial or physical barriers to screen installation or repair.

b. Partnerships with media and the community
   - Cultivate relationships with the media. Obtain media training for at least one member of your staff, and designate that individual as the organization's spokesperson. Develop clear press releases and an efficient system to answer press inquiries.
   - Develop partnerships with agencies/organizations that have relationships with populations at higher risk (such as persons over 50) or are otherwise recognized as community leaders (e.g., churches, service groups). Working through sources trusted by the target audience can heighten the credibility of and attention to messages. Partnerships with businesses that sell materials to fix or install window screens or that sell insect repellent may be useful in some settings.

c. Community mobilization and community outreach

   Community mobilization can further education and behavior change goals. To counter any idea that health departments/mosquito control programs are able to control WNV alone, develop community ownership for prevention activities. A community task force that includes civic, business, health, and environmental concerns can be valuable in achieving buy-in from various segments of society and in developing a common message. Community mobilization activities can include clean-up days to get rid of mosquito breeding sites.

   - Community outreach involves presenting messages in person, in addition to media and educational materials, and incorporating citizens in prevention activities.
   - Hearing the message of personal prevention from community leaders can validate the importance of the

disease. Health promotion events reinforce the importance of prevention in a community setting.

3. **Research and Program Development Priorities**

   a. Audience research

      Attitudes toward arboviral disease prevention vary considerably by region. Previous experience with nuisance mosquitoes and mosquito control will affect the acceptability of prevention efforts. Audience research can identify local attitudes, motivations, barriers to prevention, and opportunities to promote desired behaviors.

      Audience research should ideally combine qualitative and quantitative efforts. Surveys assessing knowledge, attitude, and practice levels in the target population can be very helpful, especially in evaluation, though they are a substantial undertaking. Qualitative research techniques, such as interviews and focus groups, can yield valuable data, and are more adaptable to resource levels. Expertise to undertake such efforts may be available from other divisions within a health department (e.g., chronic disease programs, maternal and child health).

      Pretesting of educational materials is an important step to ensure the usability of materials by the intended audience. Pretesting does not always have to involve considerable time or expense; simply having representatives of the intended audience review materials before printing will be useful.

   b. Evaluation

      Outcome evaluation should be conducted whenever possible to measure the efficacy of the intervention in achieving protective behaviors (e.g., frequency of repellent use, presence of household mosquito breeding sites). Outcome measurement requires extensive effort and must be planned from the outset of a program.

   c. Social marketing and risk communication

      The goal of social marketing is to achieve specific behaviors, using the concepts of product, price, place, and promotion. Use of social marketing approaches can help programs plan to achieve specific behavior change goals.

      Risk communication is already used by many health departments, and can be useful in refining communication messages for WNV, especially as the disease becomes endemic in new areas, and in discussing community control. Risk communication can help people analyze the choices that are available to them and to their community.

4. **Resources**

The CDC Web site (www.cdc.gov/westnile) is updated frequently to reflect new findings and recommendations. Materials on the CDC Web site are generally in the public domain and serve as a resource for state and local health departments and other organizations.

CDC staff can provide technical assistance in the development of audience research and strategies for public education and community outreach. Contact CDC/Division of Vector-Borne Infectious Diseases´ health communication staff at 970-221-6400. CDC can provide other communication planning resources, including CDCynergy (http://www.cdc.gov/communication/cdcynergy.htm), an interactive CD-ROM designed to help systematically plan health communication programs.

Other organizations that can provide useful information are the American Mosquito Control Association (www.mosquito.org/) and the National Pesticide Information Center (NPIC) (www.npic.orst.edu), a program of Environmental Protection Agency (EPA) and Oregon State University concerning pesticides and repellents. They can be contacted at 1-800-858-7378.

L. **Legislation**

In addition to statutes permitting legal action to abate mosquito-related public health nuisances, legislation must be in place to allow creation of and provide funding for municipally-based integrated mosquito management programs. Local jurisdictions can contact state mosquito control associations to provide examples of enabling legislation.

M. **Guidelines for a Phased Response to WNV Surveillance Data**

The principal goal is to minimize the health impact of the WNV in humans, as well as in domestic and zoo animals. Given the limited understanding of the ecology and epidemiology of WNV in the U.S., the low incidence of arboviral encephalitis, and the limitations of prevention methods, prevention and control measures, regardless of intensity, may not prevent all WNV infections in humans.

The recommended response levels for the prevention and control of WNV should augment, but not replace, long-standing mosquito control efforts by established programs. These programs have established thresholds for response based on historical data. Longstanding experience with WNV does not exist in the U.S.

Health Department Infrastructure

State and Local Health Departments

In the 48 contiguous United States, state and local health departments should have a functional arbovirus surveillance and response unit, staffed by well-trained personnel who have adequate data-processing resources, appropriate laboratory facilities, and an adequate operating budget. The size and complexity of these units will vary by jurisdiction, depending on both the risk of arboviral transmission in the area and available resources. A functional arbovirus surveillance unit at the state level should be considered an essential component of any emerging infectious diseases program. Local health department expertise and capabilities should be supported in a manner that complements statewide programmatic goals.

Refer to the original guideline document for detailed information on staffing and personnel, training and consultation, laboratory capacity, and developing local public health agency infrastructure.

Interjurisdictional Data Sharing and National Reporting of Human Cases

The public and animal health response to West Nile virus (WNV) epidemics/epizootics involves all levels of government, including the federal governments of the U.S. and neighboring countries, and the Pan American Health Organization. In addition, multiple government agencies at each level are often involved. Rapid, efficient, secure, and coordinated systems are needed to allow the sharing of human and ecologic data between these multiple agencies to support long-term surveillance activities, and to support activities that are part of the rapid outbreak response.

Refer to original guideline document for more information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate national, state, and local public health management of the West Nile virus through surveillance, prevention, and control measures may decrease rates of confirmed or suspected West Nile virus infection in individual mosquito pools,

sentinel species, birds, humans, horses, or other species in the United States, and thus decrease rates of morbidity and mortality from this disease.

Subgroups Most Likely to Benefit

- Persons over age 50
- Persons engaged in extensive outdoor work or recreational activities
- Homeless persons
- Persons who live in residences lacking window screens

POTENTIAL HARMS

- Collectors involved in mosquito surveillance programs may be at risk from mosquito bites, especially if day biting species are important bridge vectors.
- Recommendations to avoid being outdoors from dusk to dawn may conflict with neighborhood social patterns or practices of persons without air-conditioning or without other health programs seeking to increase physical activity.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines for the prevention and control of West Nile virus (WNV) should be interpreted according to the following considerations:

- All states should prepare for WNV activity. Given the extensive geographic spread of WNV since 1999, its occurrence in many different habitats and ecosystems in the Old World, its expansion into numerous habitat types in the Western Hemisphere, and the fact that St. Louis encephalitis (SLE) virus, a related flavivirus, is widespread in the U.S., there appear to be no barriers to the spread of WNV throughout the U.S. At a minimum, a plan for the surveillance, prevention, and control of WNV should be developed at the state and local levels.
- Measures of the intensity of WNV epizootic in an area should be considered when determining the level of the public health response. Accumulating data analyses indicate that intensity of epizootic WNV activity as measured by avian mortality and mosquito infection rates are good indicators of subsequently increased human infection risk. Also, analysis of 2001 and 2002 surveillance data indicate that counties reporting WNV-infected dead birds early in the transmission season are more likely to report subsequent WNV disease cases in humans than are counties that do not report early WNV-infected dead birds. These observations should be interpreted as a guide rather than an absolute. Levels of epizootic activity that correlate with increased human risk will vary by region.
- Flexibility is required when implementing the guidelines. Knowledge gained from ongoing surveillance and research could change the phased response recommendations. Specific and detailed recommendations that will fit all possible scenarios are not possible, particularly at a local level. Therefore, public health action should depend on interpreting the best available surveillance data in an area, in light of these general guidelines. In addition,

the following factors should be considered when translating these guidelines into a plan of action:

- Current weather and predicted climate anomalies
- Quality, availability, and timeliness of surveillance data
- Feasibility of the planned prevention and control activities, given existing budgets and infrastructure
- Public acceptance of the planned prevention and control strategies
- Expected future duration of WNV transmission (surveillance events earlier in the transmission season will generally have greater significance)
- Other ongoing mosquito control activities, such as nuisance mosquito control or vector mosquito control for the established arboviral encephalitis viruses

The recommended phased response to WNV surveillance data is shown in Table 1 in the original guideline document. Local and regional characteristics may alter the risk level at which specific actions must be taken.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

To assist guideline implementation in 2000, the Centers for Disease Control and Prevention (CDC) developed an electronic-based surveillance and reporting system (ArboNet) to track West Nile virus (WNV) activity in humans, horses, other mammals, birds and mosquitoes. In 2003, the ArboNet surveillance system has been updated to streamline reporting to CDC of WNV activity by the state public health departments.

Today's rapid transport of people, animals, and commodities increases the likelihood that other introductions of exotic pathogens will occur. CDC continues to implement its plan titled "Preventing Emerging Infectious Diseases, a Plan for the 21st Century."

Appendix A in the original guideline document details the national West Nile virus surveillance system.

Table 5 of Appendix A in the original guideline document provides instructions for submitting laboratory specimens to the CDC for West Nile virus testing.

Table 1 in the original guideline document lists the recommended phased response to West Nile virus surveillance data based on probability of human outbreak.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Epidemic/epizootic West Nile Virus in the United States: guidelines for surveillance, prevention, and control. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2003. 75 p. [77 references]

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Not applicable: The guideline was not adapted from another source.

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Not stated

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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