

Lessons from the West Nile Viral Encephalitis Outbreak in New York City, 1999: Implications for Bioterrorism Preparedness

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The involvement and expertise of infectious disease physicians, microbiologists, and public health practitioners are essential to the early detection and management of epidemics—both those that are naturally occurring, such as the 1999 outbreak of West Nile virus (WN virus) in New York City, and those that might follow covert acts of bioterrorism. The experience with the WN virus outbreak offers practical lessons in outbreak detection, laboratory diagnosis, investigation, and response that might usefully influence planning for future infectious disease outbreaks. Many of the strategies used to detect and respond to the WN virus outbreak resemble those that would be required to confront other serious infectious disease threats, such as pandemic influenza or bioterrorism. We provide an overview of the critical elements needed to manage a large-scale, fast-moving infectious disease outbreak, and we suggest ways that the existing public health capacity might be strengthened to ensure an effective response to both natural and intentional disease outbreaks.

On 23 August 1999, an infectious disease specialist from a community hospital in Queens, New York, called the New York City Department of Health (NYCDOH) to report 2 cases of neurological illness. Both patients had fever, altered mental status, and abnormal CSF suggesting viral illness; one patient had pronounced muscular weakness. This physician's report led to an epidemiological and laboratory investigation by the NYCDOH, including active case finding at nearby hospitals. By the end of the week, 6 additional cases had been identified; all resided within a 16-square-mile area of northern Queens. Seven of 8 had unusually severe muscular weakness, 3 with flaccid paralysis that had initially been diagnosed as Guillain-Barré syndrome; all had symptoms and signs consistent with viral encephalitis. The results of initial serological tests of serum samples and CSF done at the New York State Department of Health on 2 September and at the Centers for Disease Control and Prevention (CDC) on 3 September suggested a flavivirus

infection that was most consistent with St. Louis encephalitis (SLE) virus on the basis of the clinical, epidemiological, and laboratory data. This finding led to the decision to initiate mosquito control in the area affected by the outbreak; when continuing active surveillance identified laboratory-positive cases in other boroughs, mosquito control was expanded citywide.

Preceding the outbreak in humans by at least several weeks, a large avian die-off was occurring that primarily affected crows. Although the veterinary and wildlife community became aware of this epizootic by early-to-mid August, it was not until the outbreaks in humans had been announced in the media in early September that an intensified investigation, done by local veterinarians, of the etiology of the bird deaths found a common pathological diagnosis of encephalitis [1]. The results of reverse transcriptase-PCR (RT-PCR) testing and viral genomic sequencing of brain tissue from several dead crows and zoo birds sent to the National Veterinary Services Laboratory in Ames, Iowa, and, ultimately, to the CDC, led to the identification of West Nile virus (WN virus). Immediately after this discovery, WN virus was identified by means of RT-PCR, immunohistochemical, and serological testing, in human serum, CSF, and brain tissue specimens from the New York City outbreak [2–4]. Ultimately, through intensive case-finding efforts, 62 residents of New York City and its adjacent counties

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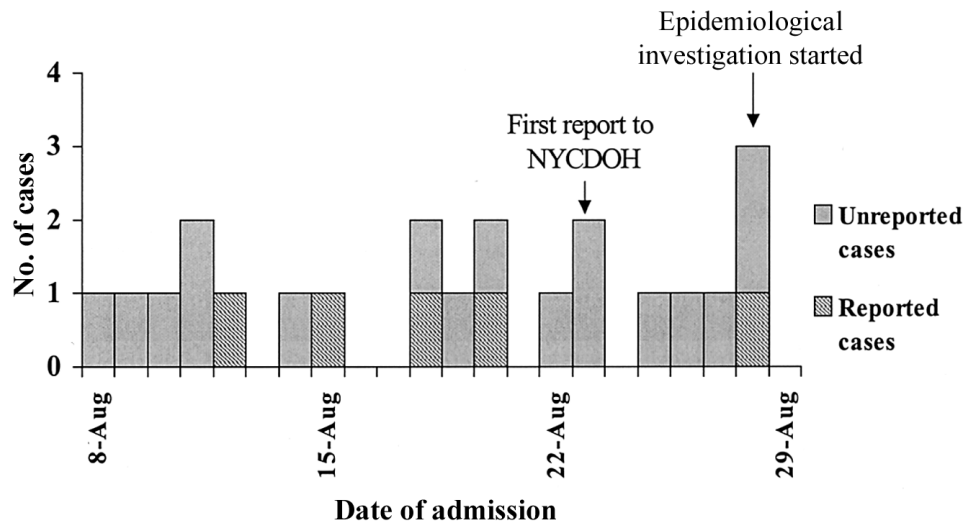


Figure 1. Unreported versus reported cases of West Nile virus encephalitis in New York City, August 1999. All cases were reported by a single infectious disease physician at a community hospital in northern Queens during the week of 23–27 August. NYCDOH, New York City Department of Health.

(Westchester and Nassau) were diagnosed with WN virus. Seven deaths, all of which occurred among people aged >65 years, were attributed to WN virus.

This event marked the first documented appearance of WN virus in the Western hemisphere and the first arboviral outbreak in New York City since the yellow fever epidemics of the 19th century. Both the outbreak itself and the city's response received prominent and prolonged attention in the local and national media. Close examination of the critical public health capacities required to respond to this relatively small outbreak should be instructive to public health, emergency management, and medical authorities preparing for biologic emergencies, whether they occur naturally (e.g., pandemic influenza) or after an act of bioterrorism.

DISCOVERY OF THE WN VIRUS OUTBREAK IN HUMANS

Encephalitis and aseptic meningitis are reportable conditions in New York City. From 1989 through 1998, the NYCDOH received a median of 9 reports of encephalitis and 172 reports of aseptic meningitis annually [5]. Because a specific viral etiology is often not identified, the diagnosis of meningoencephalitis is usually clinically based, not laboratory based. Therefore, the NYCDOH relies primarily on physician reporting to monitor trends in these diseases.

Routine surveillance data obtained during the summer of 1999 did not indicate an increase in either viral meningitis or encephalitis. The detection of the WN virus outbreak in New York City occurred because an infectious disease practitioner noticed an unusual manifestation of disease (encephalitis with

severe muscle weakness) and promptly notified the NYCDOH. The NYCDOH recommended that serum and spinal fluid specimens be sent for viral encephalitis testing, and a field epidemiologist was dispatched to the hospital to review the patients' medical records. A few days later, during a follow-up telephone call, the same infectious disease physician reported 1 additional case; while she was on the telephone, a hospital neurologist came by to report a similar case at a nearby hospital. This prompted the NYCDOH to quickly expand the epidemiological investigation, and, 2 days later, a cluster of 8 case patients was identified; all case patients were older adults from the same neighborhood in northern Queens. The clinical, epidemiological, and environmental assessment initially suggested a viral encephalitis cluster, with arboviral or enteroviral etiologies considered to be most likely.

Among the 46 New York City residents eventually determined to have WN virus infection, there were 19 (41%) hospitalized patients by the time the active epidemiological investigation was launched on 28 August; of these, 15 (79%) had not yet been reported to the NYCDOH (figure 1). Had the single infectious disease physician not reported the unusual cluster of neurological disease at her hospital ($n = 4$), it is not known when or if this outbreak would have been detected.

DISCOVERY OF THE ANIMAL OUTBREAK

Although a large number of avian deaths and a smaller outbreak of neurological disease among horses were contemporaneous and occurred over a larger geographic area than did the outbreak in humans, the initial investigations of these epizootics were conducted largely in isolation from the investigation of

human illness. The avian deaths prompted necropsy examinations of hundreds of crows at the New York State Department of Environmental Conservation in August and September; and although a common diagnosis was not reported initially, many were later found to have pathological evidence of encephalitis. Similarly, numerous crows and several exotic zoo birds died at the Bronx Zoo, and were also found to have meningoencephalitis on pathological examinations in early-to-mid September [1].

Local public health officials who were investigating the outbreak in humans first became aware of the crow die-off in early September, after the initial media reports on the SLE outbreak prompted numerous calls to the NYCDOH's emergency hotline. In response, they arranged to submit the birds to the state wildlife agency for examination. At the time, the NYCDOH officials were accurately informed by arboviral experts at the CDC and elsewhere that flaviviruses do not normally kill birds (their primary reservoir hosts) and that the avian die-offs were likely unrelated to the outbreak in humans because simultaneous avian and human arboviral encephalitis outbreaks had never been reported previously for flaviviruses such as SLE and WN virus. Bird die-offs due to various causes are not unexpected during the birds' fall migration, but the finding that the majority of these birds, especially crows, had evidence on necropsy of viral encephalitis was an important clue that these outbreaks were indeed related. This key piece of information could have been more rapidly and effectively shared with the local epidemiologists investigating the outbreak in humans, who only became aware of this finding indirectly, several weeks into their outbreak investigation and 2 days before WN virus was identified in the avian tissue specimens.

LABORATORY DIAGNOSIS

The initial identification of the epidemic as SLE primarily resulted from the high degree of serological cross-reactivity between SLE and WN virus in IgM capture ELISA testing. When arboviral disease is suspected, the CDC customarily tests for viruses that are known to occur in the geographic region where the patient resided or traveled during the incubation period. The results of initial serological tests performed on the patients from Queens who had not traveled outside the Northeast led to the presumptive diagnosis of SLE, which is enzootic in nearby areas on the Eastern seaboard. A definitive diagnosis required isolation of virus or amplification of RNA. However, unlike the avian tissues and mosquito specimens from which virus was easily cultivated in mid-September, WN virus was never cultured from human CSF and autopsy tissues. In addition, the results of initial RT-PCR assays were negative for all CSF and brain tissue specimens by use of both flaviviral consensus primers and SLE virus-specific primers. There were also clinical indications that the

outbreak was not typical of previous SLE outbreaks in the United States, because the profound muscle weakness that occurred in a substantial proportion of patients with encephalitis had not been previously observed with SLE (nor has it been reported with WN encephalitis). It should be noted that the delay in establishing the diagnosis of WN encephalitis had no impact either on decisions regarding medical or public health interventions, or on the course of the New York City outbreak itself, because appropriate measures for mosquito control had been implemented and no further cases occurred after WN virus was recognized.

During the outbreak, ongoing virological diagnosis in humans and animals was challenging for several reasons. Initially, the NYCDOH faced enormous time pressures to test suspect patients rapidly in order to guide emergency measures for mosquito control. Ensuring the timely delivery of appropriately packaged specimens to public health reference laboratories was laborious, time consuming, and costly. NYCDOH attempted to collect specimens within 24 h of the case report and send them by overnight mail to reference laboratories at both the CDC and the New York State Department of Health. Specimen transport was perilously dependent on commercial air carriers and express mail services to deliver frozen and refrigerated samples to distant reference laboratories; transport services were not readily available during weekends or 3-day holidays.

Once the etiology was found to be WN virus and not SLE, analytical laboratory capacity was even more limited, because, at the time, the CDC's Division of Vector-Borne Infectious Disease (Fort Collins, CO) was the only public health laboratory in the country that was able to diagnose WN virus. In addition to handling all human specimens, the Fort Collins laboratory was also initially the single reference laboratory for mosquito, avian, and equine samples. The sheer numbers of specimens received from throughout the New York City metropolitan area imposed a great strain on this laboratory (>2000 specimens were analyzed during a period of 3 months).

EPIDEMIOLOGICAL INVESTIGATION

Once it was established that the encephalitis outbreak was due to transmission of an arbovirus within New York City, the essential next steps included defining the geographic extent of human transmission and obtaining appropriate laboratory specimens to determine whether the patient was infected with WN virus. After the recognition of the initial cluster of encephalitis in northern Queens, intense efforts were made to identify potential cases in other parts of the city. Health alerts and frequent updates were sent by a broadcast facsimile system to all 72 hospitals in New York City. Facsimiles were sent to infectious disease departments, infection control nurses, emergency departments, and laboratory directors, with instructions

to share the alerts widely among other clinical departments. NYCDOH staff made weekly telephone calls to up to 9 different medical specialists at each hospital (including specialists in infection control; general pediatrics and internal medicine; and adult and pediatric infectious disease, neurology, and intensive care), and asked for reports of any cases of encephalitis or aseptic meningitis. More than 650 suspected cases of WN virus infection were identified through these efforts. Each suspect case was evaluated and prioritized for laboratory testing of serum and CSF samples. When the results of tests of acute-phase specimens (obtained <8 days after onset of illness) were negative, outpatient phlebotomy teams collected convalescent-phase serum samples from patients who had been discharged from the hospital. When suspect patients tested positive for WN virus, the patients or their families were interviewed immediately to determine travel history and potential sites of exposure, and medical records were reviewed.

Tracking suspect patients and outstanding laboratory specimens and results was another formidable challenge, made more complicated by the multijurisdictional nature of the outbreak. Agreements did not exist for the sharing of confidential patient information among the states and local jurisdictions involved. Interim arrangements for sharing data, especially regarding patients who were hospitalized outside their jurisdiction of residence, were uncoordinated and haphazard. The importance and complexity of tracking suspect patients, including their laboratory testing status, ultimately required the rapid establishment of a sophisticated, relational data management system in New York City. This database was needed to track patient, specimen, and laboratory result findings to facilitate the classification of suspect patients and to ensure that appropriate specimens were collected, especially convalescent serum samples when required for diagnosis.

These surveillance activities were extremely labor intensive and were maintained from early September through the end of November. In addition to mounting this unprecedented effort, the NYCDOH needed to maintain its normal public health functions. Staff worked overtime, and many were temporarily reassigned from other offices to the Communicable Disease Program. In addition, several CDC staff members, including Epidemic Intelligence Service officers, were sent to assist the NYCDOH investigation. This outbreak, though considered to be modest in overall size, severely stressed the limited human resources of the public health system. Although the NYCDOH Communicable Disease Program had only 13 surveillance staff members (including field epidemiologists and public health nurses) and 3 medical staff members at the time this outbreak was detected, this program is larger than most local health departments in the country.

Clearly, the many challenges associated with managing this outbreak would also be confronted during even a small bio-

terrorist event. During a bioterrorist attack, the pressure to determine the site and time of the exposure through epidemiological investigations would be extremely intense, and the level of public panic much higher. Public health agencies would likely need a substantial infusion of human and technical resources (e.g., from other local, state, or federal institutions) to support these efforts.

RESPONSE AND CONTROL MEASURES

The public health response required rapid reduction of the adult mosquito population in areas where transmission had been documented. Human, avian, and mosquito surveillance was used to evaluate the effectiveness of mosquito-control measures, because positive findings would indicate ongoing transmission and the need for additional spraying of pesticides. The implementation of emergency mosquito-control measures required the rapid mobilization of equipment and supplies, establishment of emergency contracts, and tremendous logistical support. Mosquito and avian fatality surveillance programs were rapidly initiated citywide. Other city agencies were recruited to clean up the environment to reduce mosquito breeding sites and to rapidly identify stagnant water and other sites for larvicide application. A program for mass distribution of mosquito repellent was established as a result of concerns that supplies in local pharmacies would rapidly be depleted; >400,000 cans of *N, N*-diethyl-meta-toluamide (DEET) were purchased by the city and distributed free of charge at neighborhood firehouses and police precincts.

A massive public education effort was conducted to provide information on the outbreak, the pesticides used, and the personal protective measures recommended to avoid mosquito bites. The effort was conducted through media releases, a public hotline, the NYCDOH Web site, and printed brochures and fliers that were translated into 8 different languages. The hotline was staffed 24 h per day to answer questions from the public; ultimately, >150,000 calls were answered by the 25–75 staff members required per shift during the 2 months the hotline was operational. Education was also targeted to medical providers; a provider hotline staffed by physicians was established, and weekly broadcast facsimiles which were sent to all 72 New York City hospitals, provided current updates on the outbreak and detailed the reporting requirements, laboratory testing procedures, and medical management. The political and media demand for up-to-date information on suspect and confirmed cases in humans required significant epidemiological staff time each morning to prepare accurate daily updates. Daily press conferences were held by the Mayor and Commissioners of Health and Emergency Management to offer consistent and timely information.

All these efforts required intensive coordination and com-

munication among a number of city agencies, including the following offices and departments: Emergency Management, Public Health, Fire, Environmental Protection, Parks, and Sanitation. The NYCDOH's preexisting relationship with the Mayor's Office of Emergency Management, developed during >4 years of bioterrorism preparedness efforts, greatly facilitated the city's public health response.

After cases were identified in humans in the counties adjoining New York City, and after WN virus-infected birds and mosquitoes were found throughout the tristate area (New York, New Jersey, and Connecticut), there was a need to coordinate surveillance and control efforts among jurisdictions. This required daily conference calls among officials from as many as 18 different local, state, and federal agencies to review current data and to share protocols, questionnaires, reporting forms, and educational materials. The concurrent epizootic required involving nontraditional public health partners, such as wildlife biologists and veterinarians. Given the multidisciplinary and multijurisdictional response, there was a need for central coordination of these efforts; unfortunately, it was often unclear which agency was in charge.

RECOMMENDATIONS FOR IMPROVING PUBLIC HEALTH CAPACITY TO RESPOND TO BIOTERRORISM

The successful strategies used to detect and control the WN virus outbreak, along with the critical gaps that were recognized in the multijurisdictional response, suggest ways the existing public health capacity might be strengthened to improve the nation's preparedness for a bioterrorist attack or any other large-scale infectious disease outbreak.

Enhance Awareness and Training of Clinicians

As happened with WN virus, the initial detection of an unannounced bioterrorist incident will likely occur when practicing physicians notice an unusual case or cluster and report their concerns to local public health authorities. For this reason, physicians and other medical professionals should be trained to recognize characteristic features of the diseases that could represent either naturally occurring, novel infectious disease outbreaks or acts of bioterrorism, and to remain vigilant for unusual cases or clusters of infectious disease. The reporting of suspicious cases or clusters to a centralized local public health authority is critical, because a single physician practicing at one institution may see only one or just a few cases during a communitywide outbreak and may thus be less able to recognize common features or to evaluate the cluster in the context of data coming from the entire jurisdiction. Patients infected with bioterrorist agents, such as smallpox or anthrax, may first come to the attention of subspecialists such as dermatologists, ra-

diologists, or intensivists. Because these specialists are less likely to report to public health authorities on a routine basis, public health agencies should target these groups for educational outreach regarding disease reporting. Education and training of medical professionals to raise awareness of the importance of reporting might be accomplished through improved collaboration between public health, specialty societies, medical journals, and academic medicine.

Build Public Health Resources and Expertise

Health departments should ensure that medical providers know whom to call with suspicious cases and clusters, and they should work to build a good relationship with their local medical community. To achieve this, public health agencies will need to make reporting diseases less burdensome and more relevant to physicians, with concomitant enhanced educational outreach and frequent feedback on local surveillance data. When physicians do call to report possible outbreaks, public health authorities should have sufficient staff resources to respond rapidly and effectively. This will require that health departments have both infectious disease and epidemiological expertise and possess sufficient resources to be able to respond 24 h per day, 7 days per week.

Even though the 1999 WN virus outbreak was relatively small in terms of human morbidity and mortality, it required the full-time attention of hundreds of officials from numerous local, state, and federal agencies for weeks and greatly strained available resources. A large-scale outbreak of disease caused by bioterrorism would require a rapid, prolonged, and substantial augmentation of the public health and medical workforce. To establish an adequate surge capacity to initiate a rapid investigation of the outbreak, educate the public, begin mass distribution of antibiotics and vaccines, and ensure mass medical care, local plans need to be put in place and coordinated with emergency management agencies, the local medical community, and state and federal public health agencies. Contingency plans are needed to ensure a rapid and smooth integration of outside emergency assistance staff into the existing workforce for the duration of the outbreak response. Lines of authority for coordinating the response to a bioterrorist event must be clearly defined ahead of time. Prepreparation of integrated epidemiological and laboratory databases and other tools for the tracking, analysis, and mapping of suspect and confirmed cases would better prepare health departments to respond to any infectious disease outbreak and would be an indispensable tool in the event of a bioterrorist attack.

Improve Communication between Human and Animal Health Authorities

Closer communication links between animal health authorities (e.g., practicing veterinarians, wildlife specialists, biologists,

and agriculture agencies) and human health authorities should be fostered on local, state, and federal levels. Infectious disease reporting systems for animal diseases should be augmented, because many potential bioterrorist agents are zoonotic diseases, and veterinarians need to recognize the importance of rapidly reporting unusual animal illnesses or clusters to public health agencies. Laboratory capacity for diagnosing rare veterinary diseases needs to be enhanced at the federal and state veterinary reference laboratories, and veterinarians should be included in local, state, and federal planning processes for bioterrorism.

Strengthen Laboratory Capacity

Improved local and state public health laboratory capacity is needed for diagnosing unusual microbial pathogens, especially the most serious bioterrorist agents (e.g., anthrax and plague), so that public health agencies are not dependent on a single reference laboratory for diagnostic support. The CDC and Association of Public Health Laboratories' National Laboratory Response Network has begun to address this need by enhancing the diagnostic capabilities for potential bioterrorist agents at state public health laboratories and by increasing the number of Biosafety Level 3 facilities nationwide.

Prepare Comprehensive Public Education and Media Outreach Programs

Unified, consistent public health messages will need to be given to the public in the event of an act of bioterrorism. Advance preparation of multilingual materials to educate health care providers, the media, and the public about potential bioterrorist agents will facilitate a fast, effective response. Recognized and trusted health officials and experts on the subject matter in question should be identified and consulted ahead of time regarding delivery of public health information to the mass media.

In the event of an epidemic with catastrophic numbers of critically ill patients who require rapid medical attention, medical professionals and health care facilities would be called upon to provide mass medical care. Such a response was not required during the WN virus outbreak, but if needed in future epidemics, it would demand that substantial medical expertise and resources be urgently redirected to cope with the crisis. Hospitals will need to have comprehensive contingency plans in place to respond to such an event, and these plans should be integrated into the planning processes of the local, state, and federal government.

Within the past year, federal funding has been made available through the CDC to improve local and state public health capacity for responding to a large-scale bioterrorist event. These

funds are targeted toward the development of bioterrorism response plans, improvement of surveillance and epidemiology for potential bioterrorist events, enhancement of laboratory capacity to identify unusual agents, and establishment of communication networks between federal, state, and local public health authorities, other government agencies, and medical institutions. All of these efforts will also have the dual benefit of improving our country's response to natural infectious disease outbreaks, such as pandemic influenza, or new, unexpected emerging infectious diseases, such as WN virus. In the past, such funding for public health infrastructure has often been crisis driven, and it has not been maintained in the absence of an ongoing disease threat. A commitment for enhancing and continuing this federal funding to ensure an improved public health epidemiological and laboratory capacity is essential in preparing to cope with the continuing threats of both natural and deliberate epidemics of infectious diseases.

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