Centers for Disease Control and Prevention
Clinician Briefing
West Nile Virus
July 15, 2003

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Overview

- We are now in the fifth season of West Nile's appearance in the Western Hemisphere. It was first recognized in New York City in 1999 and has since progressed fairly relentlessly into various parts of the United States.

- During its first three years in North America the actual burden in terms of human health was quite small, with a range of 20 to 60 cases per year.

- Last year there was a tremendous change in the tone and character of West Nile viral infections. There was a phenomenal outbreak of arboviral encephalitis that was almost unprecedented in scope and scale for a disease like this in North America, certainly in the recent past. There were more than 4,000 cases and nearly 300 fatalities in the United States alone, along with an outbreak of similar magnitude in Canada. There is some recent evidence to suggest that this virus is now heading south into the Caribbean and into areas of Central America.

- Based on this history we have to prepare ourselves for the coming West Nile season, and we know that the peak period of activity in most areas of North America occurs during the months of August and September. As we are now in the middle of July, this is an opportune time to explore some of the findings from last season, particularly as they relate to the disease itself, the epidemiology of the disease, and the novel modes of transmission that occurred last year to better prepare ourselves for the next couple of months.

- While we're all certainly hopeful that we won't see a repeat of last year's experience in terms of magnitude, it is appropriate for the public health community, as well as the clinical community, to prepare for an outbreak of potentially similar magnitude.

Therefore, the purpose of this conference call session is to discuss the disease, to discuss some of the changes that have occurred in the last year, and to look towards the future, not only for this season, but also for coming seasons.

Dr. Roy Campbell
Medical Epidemiologist
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Background -- The Epidemic of 2002

- West Nile virus is a flavivirus, a family of viruses that includes many other neurotropic arthropod-borne viruses, or "arboviruses." It is closely related to St. Louis encephalitis virus, Japanese encephalitis virus, and a few other similar ones. It's endemic to the Eastern Hemisphere: Africa, Europe, and western Asia; Kunjin virus is a subtype of West Nile virus that occurs in Australia.

- West Nile virus was first recognized in the United States in 1999 in New York City. This is an example of a virus that has jumped continents. This is not unprecedented in terms of flaviviruses. Over the centuries there have been several others that moved around in a similar manner, including the yellow fever and dengue fever viruses.

- We don't know how West Nile virus entered North America and probably never will know for sure. There are a number of possibilities, including via a viremic human or bird, via a viremic imported zoo animal, or via an infected mosquito hitchhiking on an airplane from the Middle East.

- Based on genetic studies done at CDC and elsewhere, the strain of West Nile virus that entered North America probably came from the Middle East. There has been circulation of a virus of an almost identical strain in Israel in recent years.

- West Nile virus causes neurological disease in humans, and it also causes a syndrome called West Nile fever, which is a self-limited, febrile illness without neurological manifestations.

- Historically, West Nile virus infections occurred in the 1950s, 1960s, and 1970s in Israel, Egypt, and South Africa. These were mainly West Nile fever cases with very few cases of central nervous system (CNS) disease.

- In 1996, a dramatic epidemic occurred in Bucharest, Romania, signaling the emergence of epidemic West Nile encephalitis in the Northern Hemisphere. In that epidemic there were unofficially about 500 human cases and approximately 50 deaths. CDC participated in the investigation with the Romanian government. Then three years later, quite unexpectedly, West Nile virus appeared in New York City (and in Volgograd, Russia).

- Since that time the virus has marched across the North American continent from the East Coast to the West Coast in a period of only three years, which is quite remarkable. We

are almost certain that its main means of movement is via infected birds, although there may be other minor mechanisms involved. Over the past four years, most states in the United States have reported West Nile Virus activity, and most of these have reported human disease cases.

- The 2002 epidemic of West Nile virus disease was the largest epidemic of arboviral encephalitis ever described in North America. West Nile virus has now supplanted St. Louis encephalitis as the most important cause of epidemic encephalitis in North America.

- CDC received approximately 4,100 case reports of human illness due to West Nile virus in the United States last year. Of these, about 3,000 were CNS disease cases, and the others were either West Nile fever or clinically uncharacterized. Of the 3,000 cases of West Nile virus CNS disease, nearly 300 (about 10%) were fatal. In addition, many survivors have short-term or long-term sequelae. Thus, West Nile virus is now an important public health problem in North America.

- The principal means of transmission of West Nile virus is via mosquito bite. Although there are other modes of transmission, they play a relatively minor role. The main genus of mosquitoes involved in the transmission is the genus *Culex*, which includes several peridomestic species that are common in urban and suburban areas.

- One of the most important species is *Culex pipiens*, the northern house mosquito; another is *Culex quinquefasciatus*, the southern house mosquito. These species are common in urban areas throughout the world and are directly or indirectly responsible for many human West Nile virus infections. There are other North American mosquito species that can transmit West Nile virus..

- In the 2002 epidemic, West Nile virus transmission was reported in 44 states and the District of Columbia. That compares to four states in 1999, illustrating the dramatic geographic expansion that occurred in a short period of time. The 44 states ranged from Florida to Washington with a few gaps primarily in the western United States. Of those 44 states, 39 reported human illnesses. Most of those cases were encephalitis or meningitis, while the others were mostly West Nile fever.

- In 2002 there was a broad transmission season with onset dates of clinical illness in humans ranging from May 19 through December 14. This is a longer transmission season than previously seen with other domestic arboviral diseases, for instance, St. Louis encephalitis.
- In 2002, 84% of all West Nile virus encephalitis cases were concentrated in eleven states in the central United States, primarily states in the Mississippi and Ohio River basins. The reasons for this distribution are not fully understood. It probably has to do with bird

migration routes, bird populations, mosquito populations, and climate; however, very complex epidemiological issues are clearly involved.

- The median age of patients with West Nile encephalitis last year was 64 years but ranged from one month to 99 years. Most patients with West Nile encephalitis are over the age of 55. There can be cases in pediatric age groups, some of these quite severe, but they are less common.

- For West Nile meningitis cases, the median age was 46 years. West Nile meningitis tends to be a disease of younger age groups.

- Last year CDC was invited to participate and assist the state of Louisiana in some epidemiological and mosquito-based studies, as well as other types of studies. This was because Louisiana was the first state to have a full-blown epidemic on its hands in 2002. CDC sent a team varying from 35 to 40 people including three of the speakers participating in this call today. CDC was involved in surveillance efforts, studies of West Nile fever, economic studies, clinical case series, mosquito studies, vertebrate studies, and a large serosurvey in humans.

- West Nile virus is maintained in nature in a cycle that involves primarily birds and mosquitoes. Humans are thought to be mainly incidental hosts and are thought not to typically develop high enough viremia to participate further in the transmission of the virus, although that's somewhat controversial. It is clear that birds and mosquitoes are by far the most important elements in the continued transmission of West Nile virus in nature.

- We don't know exactly how the virus survives extremes of temperature in tropical areas or in the colder areas of the Northern Hemisphere. One proven mechanism is over-wintering in adult female *Culex* mosquitoes, which in northern climates hibernate for about six months during the winter.

Dr. Tony Marfin
Medical Epidemiologist
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Clinical Aspects of the Disease

- One of the most important things to emphasize in any discussion of West Nile virus is that most persons who become infected with it develop no clinical illness or symptoms. In previous outbreaks over the past six or seven years about 80% of the people who became infected--and we know they were infected because they developed acute IgM antibody to the virus-- never developed any symptoms attributable to the viral infection.

- Of the approximately 20% of infected people who do develop symptoms, almost all develop what has been termed West Nile fever, which was the first and only clinical syndrome associated with this viral infection for about 70 years. During this time there were several large outbreaks, sometimes including tens of thousands of people who developed West Nile fever with few reports of associated encephalitis or meningitis in many of these outbreaks. However, since the outbreak in Romania and subsequent outbreaks in Russia and the Middle East, we have seen an increasing number of serious CNS infections. CNS infections reported to CDC for the most part take the form of encephalitis (with our without meningitis), and meningitis.

- Not all states report cases of West Nile fever to CDC; however, they all report essentially all cases of West Nile encephalitis and/or meningitis. Thus we have a pretty good estimate of what proportion of neuroinvasive disease manifests as encephalitis, and that is about 60% to 75%. Some of these cases have aspects of associated meningitis, but all have some aspects of encephalitis. About 25% to 35% of people with neuroinvasive West Nile virus infection have meningitis. In 2002, we described an increasing number of persons with acute flaccid paralysis as the primary neuroinvasive manisfestation of West Nile virus infection.

- Age is by far the most important risk factor for developing neuroinvasive West Nile virus infections. Based on our disease surveillance data from 2002, the median age for people who developed West Nile fever following infection was about 49 years of age. For those who developed West Nile meningitis, it was 46 years. For those who developed encephalitis with or without associated meningitis, it was 64 years. We assume that the viral doses delivered by a mosquito are somewhat similar across these age groups; however, there is something associated with older age that results in more serious CNS disease.

- The median age of people who die from West Nile virus infection, and most of these are people who have encephalitis, is about 78 years.

- The symptoms of West Nile viral infection in the approximately 20% of people who are symptomatic are usually fever and headache. Sometimes it is very difficult to distinguish West Nile fever from West Nile encephalitis or meningitis on the basis of the severity of headache. In West Nile fever, we usually do see fever, headache, and some musculoskeletal pain.

- West Nile meningitis usually involves fever, headache, and stiff neck. What we usually do not see in these cases is a change in consciousness or localized neurological signs.

- West Nile encephalitis, the most severe form of neuroinvasive West Nile viral disease, involves fever and headache, but there are more global symptoms. There is usually an alteration of consciousness, which may be mild and result in lethargy but may progress to confusion or coma. Very often there are focal neurological deficits, and it is not unusual to see people with hemiparesis. Seizures are sometimes reported. Tremors and some abnormal movement disorders also have been noted.

- In 1999 and 2000, a series of 78 people were hospitalized in the New York City metropolitan area with neuroinvasive West Nile viral disease. Of these, about 90% had fever, about 50% reported weakness, 50% had altered mental status, about 50% had headache, fewer than 10% had seizures, and about 20% had stiff neck. So you can see that really it is fever that is invariably present, and in many cases diagnosis of West Nile virus disease requires a high index of suspicion.

- Interestingly, in 2000, all 19 of the hospitalized patients in the New York City area developed low serum sodium concentrations, and that is felt to be due to the syndrome of inappropriate ADH secretion.

- When we look at the cerebrospinal fluid (CSF) from lumbar puncture performed on persons who have West Nile meningitis or encephalitis, we usually see hundreds of cells, although cell counts up to 2,000 cells per cubic millimeter have been described. Normal glucose is, by far, the rule. Elevated protein is noted in the vast majority of these cases, and it's usually a level around 100 milligrams per deciliter, although levels up to 900 milligrams per deciliter have been reported.

- Sometimes during the first lumbar puncture, an increased proportion of PMNs are noted in the CSF, and in some of these series – especially the case series out of New York City in 2000– about 50% of patients had at least 50% PMNs in CSF. This can cause concern about bacterial meningitis or cerebritis. However, as the CSF cell count evolves over time in patients with West Nile meningitis or encephalitis, lymphocytic predominance is the rule.

- There have been some good studies of imaging in the hospital series from the New York City area in 1999 and 2000, and there are two points that I want to make. That is that evidence of acute disease, which most often is described as leptomeningeal enhancement, has been described only with MRI. In fact, the CT scan has not identified any signs that are consistent or unique for West Nile virus in particular, or for a flaviviral encephalitis in general. So MRI is going to be the tool for looking for acute changes, and of those people that develop serious CNS infections, an abnormal MRI will only be noted in about 25% to 35% of cases.

- One of the things that the CT scan has been valuable for in terms of discussing risk factors is that very often you will find evidence of preexisting abnormalities that must have been present prior to the infection, changes that are consistent with previous ischemia or atrophy. You will find this in about 30% to 40% of people who present with neuroinvasive West Nile virus infections.

- In terms of imaging, a clinical diagnosis of West Nile virus infection begins with the observation of fever followed by a complete neurological exam.

Dr. James Sejvar
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Louisiana Surveillance Studies

- Louisiana invited CDC to participate in a number of different studies. Several of these focused on trying to further identify some of the clinical characteristics associated with West Nile virus infection. This included a very large fever study to try to better characterize patients who develop febrile illness associated the virus. We also conducted a clinical case series in an attempt to further describe the various neurologic manifestations of the illness.

- Regarding acute flaccid paralysis syndrome, flaccid paralysis has, in the past, been associated with West Nile virus, but it became much more prominently noted during the 2002 season. Early in the Louisiana outbreak we identified several patients in Louisiana and Mississippi who had developed acute flaccid limb paralysis in the setting of acute West Nile virus infection. We had the opportunity to assess these patients very closely and perform detailed neurodiagnostic testing.

- Patients developing flaccid paralysis presented with a very distinctive picture. They developed flaccid paralysis generally within 48 hours or so of the first onset of symptoms, and often the paralysis reached maximal weakness within 24 to 48 hours. The paralysis was asymmetric. In other words, it affected one side of the body or even one

limb more than others. The weakness was generally painless, and it was unaccompanied by any numbness, tingling, paresthesia, or other sensory symptoms.

- When the CSF from patients with acute flaccid paralysis was characterized, there was an elevation of both white cells and protein.

- Some of these patients tended to be a bit younger than the patients who developed encephalitis. Also, they seemed to have fewer underlying medical problems or other risk factors. In other words, people developing West Nile-associated acute flaccid paralysis were, in general, otherwise healthy younger people.

- Some of the people developing flaccid paralysis did so in the absence of other symptoms generally associated with West Nile infection, including headache, neck stiffness, or alteration of consciousness. This could make diagnosis fairly confusing.

- The combination of signs and symptoms just described are particularly unique. In fact, when these patients underwent detailed electrodiagnostic testing, we found that the acute flaccid paralysis syndrome actually seemed to be localizing to the so-called anterior horn cells of the spinal cord, essentially resulting in poliomyelitis.

- Poliomyelitis, in general, is an anatomical term. It refers to diseases of the gray matter of the spinal cord. The most common etiology for this particular syndrome is infection with poliovirus, but there are other viruses that can cause this syndrome, and certainly it appears that West Nile virus is one of them.

- In the short term, these patients developed fairly persistent weakness.

- One of the offshoots of our clinical studies in Louisiana was an assessment of the long-term outcome of patients with acute West Nile infection. Essentially we tried to characterize patients with West Nile encephalitis, meningitis, and flaccid paralysis during the acute course of their disease, and then eight months later we went back to Louisiana to reassess these patients.

- For the most part, we found that among patients with meningitis and encephalitis there did seem to be continuing problems, particularly in the areas of continued headache, continued fatigue, and subjective problems with memory. On the other hand, we found that some patients who initially had even very severe encephalitis that rendered them comatose did, in fact, go on to have a good outcome, basically regaining nearly baseline levels of functioning.
- For patients who had developed flaccid paralysis, the longer-term prognosis does not appear to be good. These patients continued to be weak and had no improvement in their

strength at eight months. We are going to continue to characterize the various manifestations of West Nile infection and continue long-term follow-up.

Dr. Marfin

Alternative Modes Of Transmission

- The most important point to make about transmission of West Nile virus is that most of the infections that occurred in the United States in 2002 were the result of mosquito bites.

- Some of the alternative modes of transmission are very interesting as they help us identify and discuss new aspects of the virus, but, in fact, only about 1% of the reported cases in 2002 were due to alternative modes of transmission.

- Except for occupational transmission, none of these new modes of transmission had been associated with West Nile virus or the transmission of any closely related flaviviruses prior to 2002.

- Last year, because of the magnitude of the epidemic and because of the development of new molecular laboratory tools, we were able to identify extremely low concentrations of virus during investigations and thus were able to document some of these transmissions. In addition, we had ArboNet, which is a cooperative group of 54 local and state health departments that were trying to identify new modes of transmissions. So we had a unique situation last year.

- As a result of that unique situation, we were able in 2002 to identify 23 cases of West Nile infections that resulted from transmission through transfused blood products, four through transplanted solid organs, and one through a stem cell transplant. There was one case that probably resulted from breast milk transmission, and there were two cases of occupationally acquired infections. This is a total of 30 cases through alternative modes of transmission out of a total of more than 4,100 total cases reported.

- This discussion will concentrate on blood products because they are the ones with which our listeners or participants may have more interaction than some of the others. West Nile virus is transmitted in all the components of blood products. We've made isolates from red blood cells, from platelet packs, and from bags of plasma that had been stored, as well as those that had been shipped. We were able to recover virus in all of these settings.

- Of the people who received infected blood products, about 89% of them developed illness, and the vast majority of them developed meningitis or encephalitis, although some developed West Nile fever. For the remaining ones, it was very difficult to

distinguish their underlying illness for which they were receiving transfused products from a clinical presentation that may have been consistent with West Nile virus infection.

- We never identified a person who was given an infectious unit who did not have laboratory evidence of a recent infection. We were able to chase down essentially all recipients of products that were derived from the 16 donations that we identified last year, and in all of those people there was laboratory evidence of a recent infection.

- Although we were able to isolate virus or demonstrate the presence of West Nile virus nucleic acid in all of the blood products from these 16 donations, there was an extremely low titer of virus in all of these products, as low as one plaque-forming unit per mL, which is extremely low when we are talking about viruses in blood.

- One of the other problems that arose last year was that most donors were asymptomatic or had symptoms that occurred so remotely before donation that we were unable to associate them with the donation. The low virus titer and the lack of symptoms in donors have created a unique situation in terms of ways to prevent further transfusion-associated transmission in 2003.

- As of yesterday, all blood banks in the continental United States and Alaska are doing nucleic acid amplification testing for West Nile virus. Roche and Chiron have INDs with the FDA in which they're using experimental techniques to identify viremic donors.

- In 2003, one viremic asymptomatic donor has been identified in the Houston metro area where, in fact, we have been able to identify three other confirmed cases of West Nile meningoencephalitis. That is epidemiologically consistent. Therefore we have a great deal of hope that this method is going to be able to ensure the safety of our blood supply.

Dr. Campbell

Specimen Collection and Submission

- Serology continues to have a dominant role in the laboratory diagnosis of West Nile viral infections and most other arboviral infections in humans. This is because the viremia in human West Nile virus infections is usually transient and of low titer, so that when patients present with West Nile meningoencephalitis, they're almost never viremic at that point. So you generally have to make the diagnosis serologically.

- The screening test that is most used is the IgM ELISA test for detecting acute antibody, and it's usually done by ELISA, although there are a few techniques using the IFA approach as well.

- That screening result should generally be backed-up with neutralizing antibody tests, and the ideal samples for confirming a case would be acute and convalescent serum as well as acute-phase CSF. The acute and convalescent serum would be separated by two to three weeks ideally, although we have seen that virtually all patients presenting with West Nile meningoencephalitis have IgM antibody to West Nile virus by the end of the first week to ten days of illness.

- One caveat is that with flaviviruses there is serological cross-reactivity, so that you have to use a laboratory that can test for antibodies to other closely related flaviviruses. Just to give a simple brief example, let's take someone who has returned from travel to a tropical country who develops a febrile illness that might be West Nile fever. If you test only for West Nile virus IgM, you may get a positive test when that patient may actually have a dengue infection. The viruses that cause dengue and West Nile fever are both flaviviruses, and they can cross-react serologically. So you have to tailor your testing battery to be geographically appropriate for the situation.

- There are cross-reactivity issues with the neutralizing antibody test as well, but generally you can sort these infections out if you have a good laboratory. Many state health department laboratories do the IgM testing. A few of them – perhaps a half-dozen -- do the neutralizing antibody testing. CDC is able to do all of these tests.

- There are a number of commercial laboratories that now offer the IgM testing but none that we know of that offer the neutralizing antibody testing. The latter generally has to be done at a government reference laboratory at the state or federal level.

- PCR is used in the diagnosis of West Nile virus infections in humans, although it has limited usefulness because of the transient and low viremias. With PCR, you can detect West Nile virus genetic material in CSF in up to 50% of patients who present with acute West Nile meningoencephalitis. This is not a very good sensitivity, so a negative test does not mean much. You will have to use serology in these patients for the most part.

- Virus culture is the gold standard, but it's rarely positive except in autopsy material, generally from brain and other solid organs.

- If you're submitting samples to a reference laboratory, the serum or the CSF can be refrigerated or frozen. If you are submitting autopsy specimens to a reference laboratory for testing for West Nile virus, there are several things that can be done with those materials: PCR tests on fresh-frozen material, virus culture on fresh-frozen material, and histology and immunohistochemistry on formalin-fixed tissue. At CDC we can use all of these techniques, but we need some samples that are fresh-frozen and other samples that are formalin-fixed to do the whole gamut of available tests.

Dr. Emily Zielinski-Gutierrez
Behavioral Scientist
Division of Vector-Borne Infectious Diseases
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Prevention

- The prevention point to stress for this clinician audience is that if you're seeing patients who are over the age of 50 for any reason, this is an opportunity to advise them that they're in the high-risk group for West Nile virus infection and to educate them about reducing their risk of infection. Many people who are otherwise healthy don't realize that they fall into a high-risk group. People tend to think of children and they tend to think of people who have other underlying health conditions. But it really is healthy people who are active, who are outdoors, who might be exposed to mosquito bites who need to consider that they're at risk and to take some prevention steps.

- The primary prevention step that we recommend when people are outdoors is using repellant, especially repellant that contains DEET. These repellents are the most effective and really the most studied. We have a significant amount of information on the CDC Web site concerning repellants as well as safety information about the use of DEET products.

- Other options include protective clothing: long sleeves, socks, and long pants when people are outdoors. Certainly there's some consideration of temperature in the summer with that, but it's an option that may be useful in the evening, noting that the primary mosquito biting hours for many of the species that are important as vectors of West Nile virus are from dusk to dawn. You can either suggest to people that they may want to consider staying indoors during those hours or that they use protective clothing and repellant during those hours.

- Household source reduction is also important, recommending that people check around their houses to see if they're breeding mosquitoes. All of these are steps that people can take to reduce their risk of infection.

Questions and Answers

Question 1
Dr. Anthony Suruda
University of Utah
Association of Occupational and Environmental Clinics

Two questions: Does infection confer immunity to future infection from the virus, and would you briefly discuss the two occupationally transmitted cases?

Dr. Campbell

With West Nile virus and all other flaviviruses that have been studied, if you get infected and survive, you're felt to have long-term immunity. So you probably can get infected with these viruses only once. Generally you develop neutralizing antibody within about 10 to 14 days to three weeks after illness onset, so by then you're probably immune for life.

On the issue of occupationally acquired West Nile virus infections, there were 18 cases of West Nile virus infection described in laboratory workers prior to 2001, and these were mainly in the old literature from the 50s and 60s. These were laboratory workers with either percutaneous or aerosolized exposure. Then in 2001, there was a case in a laboratory worker in New York State, which has not been published. That patient developed West Nile meningitis. It's unclear how that person was actually exposed and it is possible that exposure occurred via mosquito bites in his periresidential environment rather than through occupational exposure.

The two occupationally acquired cases in 2002 that we described in the *MMWR* were both in reference laboratory workers, i.e., microbiologists. One was an adult female who suffered a scalpel wound to the finger while she was dissecting an infected dead bird that had been submitted for testing through the state system. The second was a laboratory worker who was dealing with infected mice and suffered a needle stick injury to a finger.

In the first case that I mentioned, the woman developed a classic case of West Nile fever, did very well, recovered completely, and developed neutralizing antibody. In the second case it's unclear whether the worker developed any illness. She developed what appeared to be a sinusitis concurrently with this, and she may have had a mild fever for about a day, at most a mild illness. Fortunately, both of these people did very well.

I am not aware of any fatalities among the 21 cases in laboratory workers.

Question 2(submitted in advance)
Should the application of DEET be recommended only where there is evidence that West Nile virus is active in the area?

Dr.. Zielinski

The use of repellants with DEET is recommended any time there may be mosquitoes biting. Many people use it simply to avoid the nuisance of mosquito bites. People should pay particular attention to avoiding mosquito bites once transmission of West Nile virus has been identified in an area, but often people do not check day to day to find out whether an infected bird has been discovered in their local area. Certainly just because an infected bird has been discovered in the next county doesn't mean that there's no risk in your county.

There have been billions of applications of repellants containing DEET, and it is overall a very safe product when used according to directions. Repellants with DEET are not something that people should save just for when they know that there's been West Nile virus activity in their area.

Dr. Campbell

There are other arboviral diseases in the United States that are of public health importance besides West Nile virus, including St. Louis encephalitis, eastern equine encephalitis, western equine encephalitis, La Crosse encephalitis, and a few others. Surveillance is not necessarily as intense for the viruses that cause these other diseases. You may live, for example, in the north central United States where La Crosse virus is an issue, and that would be another argument for using DEET when you're in mosquito-infested areas.

Dr. Marfin

There are other vector-borne infectious diseases that are of importance as well. DEET is not just a mosquito repellant; it's an arthropod repellant. In many parts of the country people use it to reduce their risk for Lyme disease and other tick-associated diseases.

Another product that's useful is permethrin, which is a product that's approved for use on clothing. It impregnates the fibers of clothing and has a long residual life and can survive through several hot-water washings. The Army uses it for their troops that are training in tick-infested areas, but it also has good mosquito repellency.

Question 3
Dr. Anthony Suruda

One of our member clinics inquired as to whether there was any data or studies on the health risks of aerial applications of malathion for control of West Nile virus.

Dr. Zielinski

This has been a topic of study at CDC, and actually in last week's *MMWR* from July 11th there's an article discussing surveillance for acute insecticide-related illness associated with mosquito control efforts. The article looks at, I think, nine different states and the US overall. Investigators found that there's very low risk for acute temporary health effects amongst persons in areas that were sprayed. The article also discusses risk among workers handling and applying insecticides.

Dr. Campbell

The New York City Health Department did a study about two or three years old ago. This was a quite detailed, million-dollar environmental impact study after the 1999 epidemic in New York City during which multiple aerial applications of pesticides were made under Mayor Giuliani's order. That study also found minimal acute health risks associated with the aerial spraying. I don't remember exactly which chemicals had been used.

Malathion is not necessarily the most commonly used chemical these days for mosquito control. Synthetic pyrethroids are mainly used, resmethrin and other chemicals that are related to permethrin. These chemicals are fairly short-lived in the environment. They break down with ultraviolet light and so forth, and they have a very low toxicity profile in humans.

Dr. Zielinski

A study conducted by CDC's National Center for Environmental Health in collaboration with Mississippi health authorities examined human exposure to pesticides. It looked at four Mississippi cities, two of which conducted fogging for mosquitoes. Upon consulting with one of the study authors, I learned that this work is currently in submission for publication. When released, we will note the citation on the CDC West Nile virus Web site.

Dr. Campbell

Once again, these studies that Dr. Zielinski mentions look mainly at acute toxic effects of these low concentrations, what are called ultra-low-volume applications of aerial pesticides. The issue of long-term effects is much more complicated, much more difficult to sort out

epidemiologically. I don't think any of us here pretend to be experts in that area, and there are many questions.

The decision to use aerial spraying for mosquito control is a public health decision that health officials in a given area need to make. For instance, in Chicago where we have seen multiple elderly individuals develop potentially fatal encephalitis, we have to balance that reality against a very small risk of acute toxicity from aerial applications. These decisions are made by courageous people, but generally these chemicals seem to be, at least in the short term, very safe.

Question 4
Dr. Daniel Cobaugh
American Health System

This goes back to the DEET issue. Does CDC have a recommended maximum concentration for DEET-containing products to be effective but still minimize the risk of toxicity? This is especially an issue in young children with small body surface areas, who may be at risk when a parent applies a large amount.

Dr. Zielinski

The efficacy of DEET products plateaus at 50%. People occasionally want to use the 100% DEET products, and there's really no evidence that those provide additional protection. Overall, the recommendation is to choose a repellant that is in proportion to the time that's going to be spent outdoors. Products that contain around 30% DEET, which are more typically what you see with the sort of Deep Woods products, provide approximately five hours of protection. If somebody is going to be outside for an hour and a half, the products that contain less than 10% DEET are adequate.

The American Academy of Pediatrics Committee on Environmental Health had been recommending that repellants containing less than 10% DEET be used on children. They recently altered their recommendation to say that products with a concentration of 10% appear to be as effective as products with a concentration of 30% when used according to the instructions on the product labels. So that really did mark a shift, and we're certainly trying to make sure that we keep CDC recommendations in line with the other recommendations from organizations such as AAP.

That does provide a little bit more cushion for parents who are saying, "Well, we're going on a camping trip. What do we do with the kids?" So again, efficacy tends to plateau after 50%, but you can use products containing only 30%. As long as these are used according to instructions, the data for safety, at this point, tends to be pretty encouraging.