Centers for Disease Control and Prevention Clinician Outreach and Communication Activity Clinician Briefing (July 12, 2005)

2005 West Nile Virus Update

Theresa Smith, MD
Emily Zielinski-Gutierrez, DrPH
Division of Vector Borne Infectious Diseases (DVBID)
National Center for Infectious Diseases (NCID)
Centers for Disease Control and Prevention (CDC)
Fort Collins, CO

Please note: *Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases; therefore updates may be forthcoming elsewhere on this website, through publications such as CDC's Morbidity and Mortality Weekly Report or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations.*

Overview (Dr. Smith)

West Nile virus is:

- An arthropod-borne virus
- First discovered in 1937 in the West Nile district of Uganda
- Now found in Asia, Southern Europe, and Africa

In 1999, it was found in the United States, although it could possibly have had some activity in the United States before then. It is a flavivirus in the Japanese encephalitis antigenic complex, which includes Yellow Fever virus.

West Nile Virus Transmission

West Nile virus (WNV) is transmitted by mosquitoes. The most important cycle goes from mosquito to bird to mosquito. This is how WNV is maintained in the environment, with birds mounting a rather weak response initially to the virus that allows the virus to gain large numbers within their blood stream allowing the next mosquito feeding on that bird to pick up the virus.

Because mosquitoes do not feed on any single animal, they can spread the virus. Animals we know of that regularly can get sick from the virus are humans and horses. Humans and horses do not have large numbers of viral particles in their blood, and so are not thought to play a role in further transmission – e.g. they are considered to be incidental to the basic transmission cycle.

Regarding humans, we find there are other methods of transmission that occur, but they are not nearly as common as the mosquito. It's worthwhile looking at the methods of prevention that can be used regarding the transmission through a mosquito.

Prevention

People have personal aspects of their own activities that they can control and needs to be emphasized at times of high mosquito activity, usually at dawn or dusk.

Personal Protection:

- Choose to stay indoors if you are at high risk
- Use mosquito repellent (now there are more choices that people might find acceptable)
- Wear longer sleeves and pants, decreasing the amount of skin available for mosquitoes to bite.

Household Tips:

- Fix and use screens on doors and windows to keep mosquitoes out
- Use air-conditioning if available, because doors and windows tend to be shut during when air-conditioning is on; and air-conditioning has a dehumidifying effect that can decrease the length of life of a mosquito
- Empty standing water, which is also a choice that communities and environmental projects can use: being careful with standing water and filling in low areas around your home or nearby

Additional Guidance Notes (Dr. Zielinski-Gutierrez)

We were pretty pleased to be able to get a bit of information about repellents out into the media, so you may find that patients are asking you questions about what they should use and we wanted to make sure you have that information.

For a long time, CDC just talked about DEET, which can be used on exposed skin as well as sprayed on clothing; and permethrin, which is registered with the EPA for use on clothing or on a camping equipment (e.g., for tents), though not on skin.

In addition to DEET, there is sufficient evidence and additional products have gained registration through EPA. Picaridin and oil of lemon eucalyptus are included with DEET in our repellent guidance. Picaridin is a 7% formulation (the only one that's available in the U.S. at this time). That's similar to low concentration DEET products. This is not going to be the choice for your patients if they're out canoeing all day, but if there are a couple of hours in the backyard, it's a good option. For persons who are really looking for a plant-based repellent, oil of lemon eucalyptus shows efficacy similar to low concentration DEET. There are a lot of different products out there, most of which have very little efficacy (for example citronella oil, and some of the other things that are sold in health food stores). They're not efficacious and often—their safety is really unproven. For additional information please see: http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm

WNV Transmission Methods (Dr. Smith)

There are some other methods of transmission of this virus for humans, although the most common mode of infection remains the bite of an infectious mosquito. In 2002, it was revealed that there seemed to be other modes:

- Blood transfusion
- Organ transplantation
- Intrauterine transmission
- Cutaneous exposure (e.g., occupational exposure in laboratories)
- Breast milk (probable)

Blood transfusion:

- The response of the Department of Health and Human Services predominantly through the FDA and CDC began screening the blood supply
- As of July 2003, all blood donated in the U.S. is screened for WNV using a nucleic acid-amplification test (NAT). The FDA has been so very closely associated with this work, and the use of the NAT test continues to be refined. The transfusion-associated risk is very, very low and blood, of course, remains a lifesaving intervention when needed.
- In 2004, we found 224 presumptive viremic blood donors and those blood donations were all removed from use in blood products and packed red blood cells. There was one transfusion-associated transmission that was associated with the change in the use of the nucleic acid test. The transfusion risk is decreasing. Part of that is because we've been refining the use of this NAT and this last transfusion-associated transmission occurred just before a change in how they are administered.

To see the 2005 viremic blood donor map:
http://www.cdc.gov/ncidod/dvbid/westnile/surv&control05Maps_Viremic.htm

Intrauterine evidence of transmission

- There was one confirmed intrauterine WNV infection in 2002
- A registry of women who are pregnant and have been infected with WNV has been kept since then and there have been zero cases of WNV intrauterine transmission detected in the 79 pregnancies that were found between 2003 and 2004 associated with WNV
- There were three cases of very early postnatal WNV infection that may have had a transplacental or possibly a delivery-associated transmission
- There were nine major birth defects detected (approximately 12% of live births)

This is a registry, which means that it has the problem of having people who might be at a higher risk for other problems being more likely to enter the registry; or people who already know that they have a problem being more likely to enter the registry. The birth defects were felt overall to be chance occurrences that simply do not have an adequate denominator. This was based on the phenotypic inconsistencies between what we were seeing; there wasn't a lot of pattern. There is some evidence of possible microcephaly being a pattern, but again, with the small numbers, that may not hold out in the long run.

The maternal WNV infection often *followed* rather than preceded the expected timing of the defect that was seen adverse, but the registry for pregnant women with WNV continues.

WNV Human Infection

For every case of illness involving the brain or spinal chord we're going to see about 150 total WNV infections. There's less than a one percent chance of there being CNS disease

- Eighty percent of the infections with WNV are asymptomatic
- Approximately, 20% developed what we call West Nile fever, which is a self-limited, relatively benign disease.
- Of the less than one percent of people who will develop neurologic disease the risk of death in that group is higher and it is at approximately 10%, still making it well below *a tenth of a percent* of the total infections

West Nile Fever

West Nile Fever is seen in the majority of people who actually get sick from WNV. The time from the mosquito bite to an illness on average is three to five days.

- Fever, chills, headaches and fatigue can be seen and can be rather severe
- Nausea and vomiting can also be seen
- A rash can be helpful in the diagnosis; usually not itchy, and lasts a few days (It's mainly seen on the chest, back, abdomen and upper arms or central rash)

Most people are better within a week, although persistent headaches and fatigue can be common and we're currently looking into repeated reports of people who have fatigue and headache for much longer.

WNV meningitis

- Usually starts with a fever, headache, meningismus and photosensitivity
- White blood cells consistent with viral meningitis are seen in CSF
- Headache can be quite severe
- Most people improve, although persistent headache and fatigue are common

WNV encephalitis

WNV encephalitis has a severity ranging from:

- rather mild confusion
- coma
- death

There is some evidence of deep nuclear involvement in encephalitis with other symptoms being seen such as tremor, myoclonus, and dizziness. Some have felt that the deep nuclear involvement is a useful way of looking at the MRIs and that kind of sign.

WNV-associated flaccid paralysis

WNV associated flaccid paralysis (or a poliomyelitis in its strictest term) has been recognized more frequently in the last two years.

- It affects relatively healthy young people as opposed to the encephalitis and meningitis that tend to affect older people
- There may not be any symptoms before the onset of the paralysis
- Usually, one of the first signs, weakness can be in one limb
- As you might imagine, being poliomyelitis, there's an absence of numbness although pain, again similar to other poliomyelitis, can be present.

The highest risk for severe disease, meaning, that which puts you at risk of death is in:

- Persons over 50
- Persons who have received solid organ transplants

The diagnosis needs to, of course, begin with the suspicion and meningitis, encephalitis or flaccid paralysis from summer through fall (even into December in the South) should make one think of the possibility of WNV infection. And throughout the U.S., consider other arboviral diseases, such as St. Louis encephalitis.

Knowing what the local enzootic activity, whether WNV or other arbovirus is going on, can help make a decision about what the most likely concerns are. Other human cases in the area can also raise suspicion. It's worthwhile noting what travel history has occurred; in case people have gone to areas where there is more WNV activity. State labs can help with diagnostic testing of serum or CSF, for WNV, IGM and IGG; they can also help with testing of the most likely organisms that might be in your area, for instance St. Louis encephalitis.

Reporting of these diseases varies in terms of procedure by state, although these are all reportable in all states. If you check with your state WNV coordinators and state websites, they can tell you what their reporting procedures are. Usually, the laboratory will also know

reporting procedures and may well be willing to report for you. **All human WNV illness is reportable as of last year.** In the past, only neurologic disease was reportable.
There is no specific treatment for WNV disease, but we do have three IRB-approved randomized, double-blinded, placebo-controlled clinical trials available with information through our website. As more people tell us about trials, and if they have met these criteria, we will continue to add them.

WNV Outcomes

- The outcomes for WNV disease vary by clinical syndrome presentation. Most people with West Nile fever have a self-limited disease, it may take sometime to get over the fatigue, but overall they do well.
- Neuro-invasive disease has approximately 10% mortality. There are groups that have some higher mortality and specifically those would be the elderly and the immunosuppressed.
- Flaccid paralysis associated with WNV has, again, a variety of outcomes, but they do tend to be associated with the initial presentation. While some people have almost complete recovery and others have continued weakness, this tends to be commensurate with how they presented. Those with less severe initial weakness having a better prognosis. There is a problem associated with those people who do have respiratory difficulty with the paralysis with their outcomes being, as you might imagine, often a little worse.

- **For WNV Statistics, Surveillance, and Control of WNV in the U.S. (2004)**: http://www.cdc.gov/ncidod/dvbid/westnile/surv&control04Maps.htm

- **For WNV Information and Guidance for Clinicians**: http://www.cdc.gov/ncidod/dvbid/westnile/clinicians/

- **For Information on WNV Clinical Trials**: http://www.cdc.gov/ncidod/dvbid/westnile/clinicaltrials.htm

- **For WNV Diagnosis Fact Sheet:** http://www.cdc.gov/ncidod/dvbid/westnile/resources/fact_sheet_clinician.htm

- **For the Registry for Women Infected with WNV while pregnant:** http://www.cdc.gov/ncidod/dvbid/westnile/DuringPregnancy/WNV_duringPregnancy.htm

This week's report for WNV shows 25 human case patients from Arizona, California, Colorado, Georgia, Indiana, Kansas, Missouri, New Mexico, Ohio, South Dakota and Texas. Fifteen of those were West Nile fever. Nine of those were neuro-invasive disease. One of those is not a complete report and I'll probably get more information later.

There have been, again, presumptive viremic donors, as I mentioned in the one slide, five in Texas and two in Arizona. There have been 26 States in total that have reported any type of West Nile disease in humans or in animals. Animals including birds, horses and there have been mosquito pools reported from 13 states and 40 sentinel chickens have been reported from four states. That gives you the most recent numbers for WNV for this date. Are there any questions?

Q&A

Question: When we were talking about the data with the pregnancy, what are your thoughts on any kind of screening for pregnant women in — I can't even say highly endemic states because it's pretty much nationwide — but I wondered if that has come up in discussion and into recommendations?

Answer: *(Dr. Smith)* As I'm sure you're aware, screening would, of course, require that we had something that we could do about what we found out. At this point, the registry is helping us understand what risks are present and whether or not the outcomes of pregnancy included in illness with WNV have definable, discernible, known outcomes. As we mentioned, there was definitely an intrauterine transmission. Whether or not this is actually an organism that causes problems, it's still not known. Even though we can tell you that of the 79 women who had both a pregnancy and an infection at the same time, it's not clear that any of the outcomes of those pregnancies were associated with WNV infection.

Question: As the registry progresses, we may get a better idea. Like you said, is this even a significant kind of event for surveillance.

Answer: *(Dr. Smith)* Exactly. *(Dr. Zielinski-Gutierrez)* And we'd certainly be glad if — through your organizations — you can encourage anyone who does have a patient that has a West Nile infection [during pregnancy], we would very much like to get them in the registry in order to be able to have the largest database as possible to make further associations.

Question: I wondered if you can give us a small update on any data you might have about a vaccine. Clinicians I work with want to know when we're going to have a vaccine against WNV. Any information you can give us on that?

Answer: *(Dr. Zielinski-Gutierrez)* We know that nothing is going to happen this year, or probably next. It's still several years off in the future though there are a number of different companies that are working on this. You may have heard that there is a very small clinical trial currently occurring, sponsored through the NIH through their vaccine research center, and that is with the West Nile DNA vaccine. We'll have a news release probably later today or tomorrow that CDC was integral in developing a new WNV horse vaccine that just gained licensure through USDA. It's actually the same technology that provides the backbone for the West Nile DNA vaccine that's in trial for humans. It's a whole new category of vaccine technology. We're really quite excited about that, but it's several years off before there would really be anything for humans. In the meantime, people really just need to take that personal responsibility and prevent mosquito bites.

Question: I was interested a little bit in the epidemiology of West Nile this year as compared to last. Are you seeing it increase in encephalitis or acute flaccid paralysis that you could discuss?

Answer: *(Dr. Smith)*
None so far. It's really very much the beginning of the season; cases continue from here. *(Dr. Zielinski-Gutierrez)* The numbers are too small to be able to compare.

Question: I have a second question if that's okay to ask. What is the pediatric case count this year compared to last?

Answer: (*Dr. T. Smith)* I don't have all the ages right now. We have 25 cases.

Question: Then you have some interim guidelines available for evaluating infants born to mothers with WNV infection. Are final guidelines available expected shortly or when do you anticipate those to be out?

Answer: *(Dr. T. Smith)* I would not expect this very soon. With the small numbers that we have currently, those were our main interim guidelines until we have [additional] information.

Question: Based on the decline in cases in some of the states where West Nile initially appeared in this country, what do you expect to happen with disease incidence over the next few years, particularly in some of the states that had such high incidence last year?

Answer: *(Dr. T. Smith)* Well, I think, if you take a look at some of the Midwestern states, you'll see that they seemed to be maintaining (in the last few years), a relatively high incidence. I think what we'll see over the United States is . . . where this organism likes to live most and we won't know what that's going to look like for a while.

Question: As a follow up to excellent question, I wondered if you might want to comment [on] the concept of a cyclical occurrence, as well as the numbers being affected by the fact that it's now a reportable illness; those are both factors. I wondered if you wanted to comment at all about the proposed or a suspected cyclical nature of West Nile, as well as many other agents?

Answer: *(Dr. T. Smith)* I don't think that we can speak to that entirely. If we look at where it has been in the past, it doesn't entirely have a cyclical nature other than the fact you aren't going to see it probably a lot in January and February. It has a seasonal nature, but not truly cyclical in nature; at least in places where it has been in the past, Africa, Asia, and Europe.

Answer: *(Dr. Zielinski-Gutierrez)* There's really been a lot of effort from various sectors inside and outside the medical field to look at whether or not any projections are available if you examine the data and trying to make a forecast. But I think what we have to emphasize to people is that, it's such a relatively short period of time that we have experience with the virus in this ecology. A lot of the efforts to [reach] conclusions are not misplaced, but not made with the full balance of information that would be necessary to draw some conclusions.

Question: That is true also and I think we forget that as clinicians—West Nile, I mean prior to when '99, we hadn't even heard of it or even mentioning…

Answer: *(Dr. T. Smith)* Yes, '99 was the first time it was identified in America, in the U.S.

###