West Nile Virus: Information and Guidance for Clinicians

Moderator: Loretta Jackson Brown

Presenters: Ingrid Rabe, MBChB, MMed

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Operator:
Welcome. Thank you everyone for standing by. Participants are on a listen-only mode throughout today's presentation. And if you care to ask questions during the question-and-answer session, that would be star then 1 on your touchtone phone. Today's conference is being recorded. If you have any objections, you may disconnect. I'd like to turn the meeting over to Ms. Loretta Jackson Brown. Ma'am, you may begin.

Loretta Jackson Brown:
Thank you (Fran). Good afternoon. I'm Loretta Jackson Brown and I'm representing the Clinician Outreach and Communication Activity, COCA, with their Emergency Communication System at the Centers for Disease Control & Prevention. I'm delighted to welcome you to today's COCA Webinar, West Nile virus Information and Guidance for Clinicians. We are pleased to have with us today Dr. Ingrid Rabe from the Centers for Disease Control and Prevention here with us today to review epidemiology, modes of transmission, clinical features, appropriate use of diagnostics, and treatment and prevention options for West Nile virus infections.

You may participate in today's presentation by audio only, via Webinar, or you may download the slides if you are unable to access the Webinar. The PowerPoint slide set and the Webinar link can be found on our COCA Web page at emergency.cdc.gov/coca. Click on COCA Calls. The Webinar link and slide set can be found under the call in number and call passcode.

At the end of the presentation you will have the opportunity to ask the presenter questions. On the phone, dialing star, 1 will put you into the queue for questions. You may submit questions through the Webinar system at any time during this presentation by selecting the Q&A tab at the top of the Webinar screen and typing in your question.

Today's presenter is Dr. Ingrid Rabe. She is a Medical Epidemiologist in the Arboviral Disease Branchs at the Centers for Disease Control and Prevention. She is originally from South Africa where she trained as

a medical doctor and completed a residency in Public Health Medicine. She came to the US in 2007 to commence service as an Epidemic Intelligence Service Officer with CDC. Her current work involves surveillance of arboviral diseases, and she has a special interest in transplant and transfusion associated transmission of West Nile virus.

Again, the PowerPoint slide set and the Webinar link are available from our COCA Webpage at emergency.cdc.gov/coca. At this time, please welcome our presenter, Dr. Rabe.

Ingrid Rabe:
Good afternoon. It's a pleasure to be addressing you on the subject of West Nile virus infection. After briefly covering some background information about West Nile virus and its transmission cycle, I will be discussing the pertinent aspects of disease recognition based on clinical presentation and laboratory diagnosis, followed by management and prevention. Lastly, I will present some national public health surveillance data.

West Nile virus is an RNA virus belonging to the genus Flavivirus. Other viruses in this genus include Japanese Encephalitis, St. Louis Encephalitis, and Dengue viruses. Transmission is via the mosquito-borne route. Birds are the most important vertebrate hosts responsible for amplifying the virus in the environment.

Though first isolated in Uganda in 1937, the distribution is now recognized as worldwide. The virus was first identified in the US in New York in 1999 and subsequently spread westward throughout the country. West Nile virus is now considered to be endemic in the contiguous United States.

West Nile virus is maintained in an enzootic cycle between birds and mosquitoes. Culex mosquitoes, which breed in containers or pools of standing water, become infected when they feed on infected birds. Under permissive conditions, the amplification cycle can dramatically increase the number of infected birds and mosquitoes in an area through the course of the transmission season. The most common route of transmission of West Nile virus to humans is through the bite of infected mosquitoes. Humans and other vertebrates, such as horses, are considered dead-end hosts because they do not attain levels of viremia high enough to infect mosquitoes.

Person-to-person transmission of West Nile virus can occur through blood transfusion and organ transplantation. Intrauterine transmission and probable transmission via human milk have also been

described, but appear to be uncommon. West Nile virus infection may also occur in the laboratory setting through percutaneous or aerosol exposure.

Following a mosquito bite, West Nile virus replicates in the dendritic cells at the inoculation site. From these, the virus is spread to regional lymph nodes and then into the blood stream. In some people, viremia is followed by invasion of the central nervous system resulting in neuroinvasive disease.

An estimated 70% to 80% of human West Nile virus infections are asymptomatic. Most symptomatic people develop an acute systemic febrile illness, referred to as non-neuroinvasive disease, or West Nile Fever. Less than 1% of infected persons develop neuroinvasive disease, which typically manifests as meningitis, encephalitis, or myelitis.

In people with clinical illness, there is an incubation period of 2 to 14 days between the bite of an infected mosquito and the onset of symptoms. In addition to fever, other common symptoms include headache, weakness, fatigue, myalgia, and rash. The illness usually resolves within a week; however in some cases, symptoms may persist for weeks or months. The overall case fatality is less than 1% for cases of non-neuroinvasive disease. Most fatalities occur in people of advanced age with significant underlying medical conditions.

West Nile virus neuroinvasive disease usually presents as meningitis, encephalitis, or acute flaccid paralysis. Most cases require hospitalization. Many patients have sequelae after their acute illness, with 50% to 75% of patients needing assisted living or rehabilitation. Morbidity and mortality increase with age, and the overall case fatality rate is 10%.

Age greater than 60 years is a recognized risk factor for West Nile virus neurologic or severe disease. In addition, medical risk factors for severe disease include diabetes, hypertension, history of cancer, chronic renal disease, and chronic alcohol abuse. In 2010, one study found West Nile virus RNA in urine of 5, or 20%, of 25 patients who had acute West Nile virus disease one to seven years earlier. The virus could not be cultured. Two subsequent studies that included a total of 103 persons who were infected with West Nile virus several weeks to seven years prior found only one person, or less than 1%, with detectible West Nile virus RNA in their urine.
The one positive result came from an 83-year old woman who had West Nile virus encephalitis. Her urine was collected from a catheter bag 29 days after her illness onset. The patient died 57 days after her illness onset, so subsequent samples could not be obtained. Possible reasons for the discrepancy

between the proportions of West Nile virus infected persons with detectible West Nile virus RNA in urine between the studies include firstly, differences in test performance, then differences in the study cohorts which may result in different incidence of West Nile virus RNA in urine, or that shedding of West Nile virus RNA may be intermittent.

A recent publication reported that people with West Nile virus neuroinvasive disease may be at increased risk of developing subsequent kidney disease; however, people with preexisting renal disease, diabetes, and hypertension are all at increased risk of neuroinvasive disease and serious illness following West Nile virus infection. It is difficult to sort out whether kidney disease may sometimes occur as a result of West Nile virus infection, or whether some patients who have serious West Nile virus disease were already predisposed to develop chronic kidney disease unrelated to their infection. Further study is needed to determine what role West Nile virus infections may have in subsequent kidney disease.

Before we move on to discuss the diagnostics for West Nile virus infection, it would be helpful to consider the dynamics of the viremia and antibody responses during these infections. This chart is a schematic representation of the timing of viremia and antibody response in relation to onset of symptoms. In otherwise healthy individuals, West Nile viremia increases after initial infection, although peak levels are usually low and the viremia resolves by the first couple of days after symptom onset.

IgM antibodies become detectible within a week after symptom onset and typically last for several months, but can persist for several years. IgG antibodies are detectible within days after IgM positivity and persist for years, if not for life. Anti-West Nile virus IgM antibodies in serum or CSF are the preferred tests for diagnosis of West Nile virus infection. These tests are performed by commercial and public health laboratories and provide presumptive diagnosis of recent West Nile virus infection. IgG antibody tests in serum or CSF are also performed by commercial and public health laboratories. The finding of IgG antibodies alone is consistent with previous West Nile virus infection, or past infection or vaccination with other flaviviruses. Plaque reduction neutralization tests are performed predominantly at CDC and other public health laboratories and are used to confirm the specificity of IgM and IgG antibodies.

West Nile virus antibody testing is subject to several limitations. Serum collected within seven days of illness onset may lack detectible IgM. Because anti-West Nile virus IgM can persist in some patients for longer than a year, a positive test result occasionally may reflect past infection.
As mentioned, IgG antibody alone reflects past infection. False positives can occur due to non-specific reactivity or cross-reactivity to other closely related flaviviruses. Blood products can contain West Nile

virus antibodies and this may complicate interpretation of results. West Nile virus molecular testing for detection of RNA in serum or CSF is performed by commercial and public health laboratories. Presence of such RNA indicates recent West Nile virus infection. Unfortunately, this testing has low sensitivity as viral RNA is often absent following symptom onset.

Molecular testing is useful for screening of the blood supply and may be useful in selected situations such as fatal cases or disease in immunocompromised patients. Treatment of patients with West Nile virus disease centers around supportive care and management of complications. No antiviral or adjunctive therapies are approved or recommended for the treatment of West Nile virus. There have been case reports or trials with several therapies. There are currently no ongoing clinical trials or products available for compassionate use.

There have been a number of in vitro studies and case reports on the use of various products to treat West Nile virus infections. These products include Ribavirin, corticosteroids, polyclonal, hyperimmune, and monoclonal immunoglobulin products, and interferon. As shown on this table, several of these products have been studied in controlled clinical trials for infections due to West Nile virus or closely related flaviviruses such as Japanese encephalitis virus. None have shown benefits; however, the results of some of these clinical trials have not been published and the studies often had small sample sizes.

There is no West Nile virus vaccine licensed for use in humans. Avoiding mosquito bites is the most effective way to prevent West Nile virus infection. Community level mosquito control programs target larval and adult stage mosquitoes respectively. The larval control entails application of chemical larvicides or use of biological control measures such as larvae eating fish. Adult control using insecticides is usually undertaken through ground or aerial spraying. Household and personal protective measures to decrease mosquito exposure include using air conditioning and installing window and door screens, reducing mosquito breeding sites, wearing long-sleeved shirts and long pants, applying insect repellants, and limiting outdoor exposure during peak mosquito biting time.

For routes of transmission other than mosquito bites, additional programmatic interventions include the screening and removal of infected blood products. Transfusion associated West Nile virus infection was first documented in 2002. Routine screening of blood products for West Nile virus started in 2003, and since then more than 2500 infected products have been removed from the blood supply to prevent subsequent transmission. Although screening is extremely sensitive, transfusion events still occur, albeit

rarely, due to the failure of pooled sample testing to detect low viremic units, and because some blood products are not screened. For example, granulocytes.

Since 2002, roughly one transplant associated West Nile virus cluster has been recognized each year. Recipients infected through organ transplantation are at increased risk for severe disease. Organ donor screening practices vary. Screening of organ donors for West Nile virus is not mandatory by national policy. There is also concern for false positive tests leading to organ wasting. And, current screening techniques may fail to detect positive donors. For example, transmission has occurred from donors who test negative for West Nile virus RNA using available assays.

I'll now move on to the public health surveillance data. ArboNET is the national Arboviral surveillance system. It is a unique passive electronic reporting system that collects data on human disease cases, viremic blood donors, veterinary cases, dead birds, mosquitoes, and sentinel animals. Data collected by ArboNET are updated weekly on the CDC Web site listed here. West Nile virus is a nationally notifiable disease. Cases are reported to CDC by state health departments using standard case definitions developed by the Council of State and Territorial Epidemiologists. It is the responsibility of clinicians and laboratories to report cases to local health departments. The reporting timeline requirements vary from state to state. To find out your reporting requirements, contact your local or state health department.

This map shows the average annual incidence of West Nile virus neuroinvasive disease by county from ’99 through 2011. Cases of West Nile virus disease have been reported from 47 states and the District of Columbia. No cases have been reported from Alaska, Hawaii, or Maine.
Since 1999, the highest numbers of neuroinvasive disease cases have been reported from Texas, California, Illinois, and Colorado. This slide shows the areas of highest incidence in the mountain and plain states, and some areas along the Gulf Coast and Southwestern United States. It also demonstrates the focal nature of the disease, with almost half of all the counties in the contiguous 48 states reporting no neuroinvasive cases over the past 13 years. This slide shows the number of West Nile virus neuroinvasive disease cases reported by week of illness onset from 1999 through 2011. As expected due to mosquito activity, most cases occur from June to September, usually peaking in mid-August. This graph shows the average annual incidence of West Nile neuroinvasive disease by age group. The incidence of neuroinvasive disease increases steadily with age with the highest risk in people over 60 or 70 years of age.

When we break down age group specific incidence of neuroinvasive disease by clinical syndrome, we see that the incidence of encephalitis increases dramatically with older age. By contrast, the incidence of meningitis increases gradually into adulthood but levels out in people over the age of 40. The incidence of acute flaccid paralysis remains low and level throughout all age groups.

The demographic and outcome data for West Nile virus disease cases by clinical syndrome for the years 1999 through 2011 are shown in this table. The majority of reported cases occured in males with a similar distribution across clinical syndrome. The median age of patients with fever and meningitis was younger than that of patients with encephalitis and acute flaccid paralysis.

Only 21% of West Nile fever cases were hospitalized compared with over 80% of neuroinvasive cases. Patients with encephalitis or acute flaccid paralysis had substantially higher mortality rates than those with fever or meningitis. Listed on this slide are the annual number of neuroinvasive domestic arboviral disease cases in the US from 1999 through 2011. West Nile virus is the leading cause of domestically acquired arboviral diseases in the US; however, several other arboviruses also cause seasonal outbreaks and sporadic cases. On average, the annual number of West Nile virus neuroinvasive cases reported to CDC is ten times the number of cases due to other arboviruses. However, La Crosse virus is the most common cause of arboviral disease among children. Furthermore, in some counties or regions, these other arboviruses are a more important cause of disease than West Nile virus.

Human West Nile virus infections and disease cases are not fully captured by the surveillance system. 31,000 West Nile virus disease cases were reported to the CDC between 1999 to 2011; however, most cases are not diagnosed and reported. Extrapolating from serosurvey and surveillance data, it is estimated that between 400,000 and 950,000 cases of West Nile virus disease may have occurred in the United States in that time period. This graph shows the average annual incidence of West Nile virus neuroinvasive disease in the US from 1999 through 2011. Incidence peaked in 2002 and 2003 then reached steady endemic levels from 2004 through 2007, before showing further declines from 2008 through 2011. However through August 28th this year, the incidence of West Nile Neuroinvasive disease is already higher than end-of-year totals for each year since 2007.

We now come to the preliminary West Nile virus surveillance data for 2012 to date. Thus far this year, 48 states have reported West Nile virus infections in people, birds, or mosquitoes. A total 1590 cases of West Nile virus disease in people, including 66 deaths, have been reported to CDC. Of these, 889, or 56%, were classified as neuroinvasive disease. And, 901, or 44%, were classified as non-neuroinvasive

disease. Approximately 70% of the cases have been reported from six states, namely Texas, South Dakota, Mississippi, Oklahoma, Louisiana, and Michigan. And, 45% of all cases have been reported from Texas. So, these 1590 cases reported thus far in 2012 is the highest number of West Nile virus disease cases reported to CDC through the last week in August since West Nile virus was first detected in the United States in 1999.

In summary, West Nile virus remains an important cause of neurological infections in the United States. Seasonal outbreaks occur annually, but are often quite focal and unpredictable in size and location. There are no proven effective treatments or vaccines; however, making a diagnosis is still important to stop unnecessary therapies, limit further diagnostic evaluation, help predict patient outcomes, and direct public health prevention measures. The following recommendations are pertinent to healthcare providers. Consider West Nile virus and other arboviral infections in the differential diagnosis of patients with aseptic meningitis or encephalitis. For patients in whom West Nile virus infection is suspected, obtain appropriate specimens for laboratory testing and promptly report laboratory confirmed cases to state or local health departments to allow for appropriate control measures. Thank you.

Loretta Jackson Brown:
Thank you Dr. Rabe for providing our COCA audience with a wealth of knowledge. Operator, at this time we will open the lines for the question-and-answer session.

Operator:
Thank you very much. Now if you would like to ask a question, please press star then 1. To withdraw that request, press star, 2. One moment please for the first question.

Loretta Jackson Brown:
And while we're waiting for the first question for the phone, I do have a question for you. And the question is coming through our Webinar system. And they want a recommendation. They want you to kind of give an overview of what you think should be done as they've found five dead doves in their neighborhood in West Texas in the last two to three weeks.

Marc Fischer:
So they should be careful in handling the carcasses and they should call their local health department to see. Some health departments will collect - either send people out to collect the dead birds, and some will

continue to test for West Nile virus in dead birds. Other jurisdictions no longer test dead birds for West Nile virus.

Loretta Jackson Brown:
Thank you. Operator, do we have a question from the phone?

Operator:
We have several yes. (Clyde Andera), your line is open first.

(Clyde Andera):
Yes. Hi, this is (Clyde Andera) calling. My question is if once you have contracted West Nile virus and you have the appropriate antibody response, is that going to provide lifelong immunity, or is there not enough research out there yet to say yay or nay on that?

Ingrid Rabe:
We assume that it does provide lifelong immunity, and some of that's based on data from other flavivirus research as well.

(Clyde Andera):
Okay, great. Thank you.

Loretta Jackson Brown:
I do want to let everybody know that we do have Dr. Marv Fischer also available for questions. He's the Chief Surveillance and Epidemiology - Chief of Surveillance and Epidemiology Activities at the Arboviral Disease branch. Operator, next question.

Operator:
(Carol Griswold), ma'am, your line is open now.

(Carol Griswold):
You know, my question was answered about lifelong immunity. Thank you.

Operator:
Yes, thank you. Our next request now from (Delores Barnes). Your line is open ma'am.

(Delores Barnes):

Thank you. My question is our lab director told me this morning that we have gotten two reports back that the IgM could not be run because of backordered products, so we're unable to get results. What's the recommendation on how to test in the meantime?

Marc Fischer:

Thank you. This is Dr. Fischer. We are aware that there have been some possible shortages related to the focus IgM ELISA kit, and we've been in communication with the company. They are preparing to ship an additional lot of West Nile virus IgM kits as early as tomorrow, and then have several additional lots that will be shipped in the coming months. So labs that do not have kits available should have them available soon. In the meantime, it may be possible for you to get testing done through a different commercial laboratory, the state laboratory, or here at CDC.

(Delores Barnes):

Okay. We are currently using a send-out lab for that already, but thank you very much for your answer.

Operator:

Thank you. Now if you would like to ask a question, please press star then 1 to get in queue. Our next is from (Carol Herman). Ma'am, your line is open.

(Carol Herman):

Thank you. And I missed the first part of the meeting so maybe you answered this. A patient who might have a normal IgM and an elevated IgG, what is the time course that you might expect the IgM could go back to normal if they weren't tested early on in their illness?

Ingrid Rabe:

Sorry. So are you asking if the - both IgM and - IgM...

(Carol Herman):

IgG is elevated and IgM is normal, but the diagnosis wasn't entertained until eight weeks into the illness.

Marc Fischer:
So IgM will usually persist in serum and CSF for several - a number of weeks to months. So for the patient with that specific scenario, we would typically expect them to still have IgM if their recent illness was due to West Nile virus infection. So in that scenario, typically the IgG is just representing previous flavivirus infection.

(Carol Herman):
Okay. So more than two months is - it should still be elevated.

Marc Fischer:
Well, correct. There's certainly a variation of patients, a wide range from a few weeks out to several years. So - but typically at a couple of months, most patients will still have IgM antibodies.

(Carol Herman):
Okay, thank you.

Operator:
Our next request from (We Young). Your line is open sir.

(We Young):
Thank you, and this is (We Young) speaking from the public health agency of Canada. And, I really appreciate the Dr. Rabe's presentation and it's very informative. I like to take this advantage of to quickly discuss about what we do in Canada regarding the West Nile virus surveillance. And we have the West Nile surveillance program here and run by the (PHAC), and we collected the information like the human data, and the mosquito, and horse, and also the bird data on a weekly basis. And then, disseminated the information that we had for Web site and also send by email to surveillance partners. And as August 28th, last Friday, and we have received a report about the human cases about 120 cases, but I have not finalized the number. And this the third biggest of the year in Canada, and - besides the 2003 and 2007. Is quite interesting to see our neighbors, US and report to the significant increase about the number.

And I have one question. Because of last year I was invited by the ECDC and regarding the West Nile virus surveillance, and they have the surveillance program in place. And this year we also see the human cases as the number up in the European countries like Greece and Russia. And this afternoon I got the information. They said that all the cause is by the lineage of one. Is not like we have seen in North

America lineage of two. So my question is for this year in US, typical in tendency, have you detected any lineages to ours beside the lineage of one?

Marc Fischer:
Yes. All of the virus that so far has been evaluated in the United States has shown to be the same strain that has been circulating in the United States essentially since 2002. There will be some additional evaluations that are done ongoing, but so far we have not detected any difference or changes in the genetic information or new strains.

(We Young):
Oh, thank you.

Operator:
Thank you. Our next now is from (Cathy Horn). Ma'am, your line is open.

(Cathy Horn):
Thank you. In the Culex mosquito that carries this virus, does it typically bite only at dawn and dusk, or do we need to advise people to avoid mosquito bites all the time?

Marc Fischer:
Yes. For most - obviously, the specific biting habits and habitats would be different for different Culex species. But in general for Culex species, there are sort of peak biting times that are late evening, at dusk, and then at dawn. There is probably biting throughout the night. It's not like there's no biting during the day or no biting at night. That will vary again on location, on temperature, on the habitat. But in general, those are the highest risk biting times for Culex mosquitoes.

(Cathy Horn):
Thank you.

Operator:
Our next request now is from (Umo Mammal). I believe your line is open now, ma'am.

(Umo Mammal):

Thank you. I have a quick question on - we have some cases that are presenting clinically with neuroinvasive disease. They're having CSF and serum tested. Serum has come up as IgM positive and IgG negative, but CSF has come up both IgM and IgG negative. Could there be a delay in CSF - the IgM in CSF presenting?

Marc Fischer:

I'm not sure. That's sort of an unusual scenario. In general, we expect IgG antibodies to move fairly freely across the blood/brain barrier. So if they're in one location, we expect them to be in the other. In general, for reasons that I don't know why, IgM antibodies when there is neuroinvasive disease, tend to come up a little faster in the CSF than they do in the serum, even though the patient presumably had viremia first before invasion. But, I'm not aware of a scenario as you're describing where the IgG antibodies are only being found in CSF and not serum.

(Umo Mammal):

Thank you.

Operator:

So thank you. Our next now is from (Connie Austin). Ma'am, your line is open.

(Connie Austin):

Yes, this is (Connie) from Illinois. I was wondering if this year the commercial labs are performing well compared to public health testing?

Marc Fischer:

(Connie), I'm not sure what you mean by performing well. We don't typically receive specific information regarding how cases were confirmed. That is information that we've recently started to request as part of ArboNET. But in general, the reports that come to us, as you know, go to the state health departments, and then those reports come to us, and we don't have further really evidence or evaluations that would compare public health departments to commercial labs. But I apologize if I didn't answer your question if you want to follow-up.

(Connie Austin):
Yes. I was just wondering if you'd had any complaints from any states saying that they're getting in commercial lab results that are positive but they don't confirm at the state lab.

Marc Fischer:
Oh, I see. I'm not aware overall. There are always scenarios where there are cases that do not confirm at a second laboratory, including specimens that are received at CDC and were tested previously at commercial or state health labs. But I'm not aware of any patterns of problems in specific areas or large numbers of cases.

Operator:
Thank you. Our next request then is from (Mandiego Soongove), and your line is open.

(Mandiego Soongove):
Thank you. Looking at the risk factors, you know like cancer, diabetes, kidney disease, solid organ transplant, it's clear why these risk factors will lead to or will facilitate the evolution of West Nile virus. But what I don't understand is hypertension alone is in that list as well. I don't really see how the mechanism through which hypertension alone without kidney disease and so on will actually be a risk factor for West Nile virus.

Marc Fischer:
Yes, that's a fair question. These are based on epidemiologic studies. There have been a number that have identified these factors, and they have been identified as independent risk factors. But obviously, it's very difficult in those type of studies to fully account for all confounding and many patients who have one or more of these risk factors have other conditions, either medications or illnesses, underlying medical conditions that they have. And so, we don't have specific data regarding the pathogenesis or specific reasons why hypertension in and of itself might be a risk factor for severe West Nile virus disease or neuroinvasive disease.

(Mandiego Soongove):
Thank you.

Operator:
If you do have a request, please press star then 1 at this time. My last at this time is from (David Zane), and your line is open.

(David Zane):
Are you aware of any community surveys that have been conducted in a West Nile virus outbreak that tried to assess the community's knowledge, attitudes, and behaviors about West Nile and their personal protection behaviors as well as how they're getting communication messages?

Marc Fischer:
Yes. There have been some that were done. I believe one was done in Connecticut, although that was a number of years ago, I believe in 2003 - 2002 I'm told. We are actually working with Maryland to currently work on a knowledge, attitudes, practice survey there to look at attitudes and knowledge, mostly in elderly populations there.

Loretta Jackson Brown:
Thank you. We have several questions from the Webinar system, and one is when do you recommend ordering PCR for diagnostic purposes? And should ordering diagnostic studies be limited to patients with severe disease or signs consistent with neuroinvasive disease?

Ingrid Rabe:
So I think first to address the PCR testing. The molecular testing is usually of limited value because of that transient and relatively low level of viremia. So by the time onset of symptoms takes place, a lot of the time the viremia has waned below detectible levels. But, there are exceptions to that. In situations where it might be more useful, and that would be for example, in suspected West Nile virus disease in immune compromised patients. And then of course, the molecular testing is used for a blood product screening as well, but that's obviously not in a diagnostic setting. And then the last scenario in which the testing is used would be for example in post-mortem tissue testing where there've been fatalities suspected to be caused by West Nile virus. And then in terms of conducting testing as to which patient profiles or what kinds of clinical presentation patients should be tested for West Nile? Again, I think there would be an individual clinical decision that would span across the clinical spectrums that had discussed.

Loretta Jackson Brown:
Thank you. I have an additional question for you, and that is, are there any commercially available rapid West Nile virus tests? And if so, how reliable are those?

Marc Fischer:
So in terms of rapid, the molecular tests obviously are - still would have turnaround time. Are not a bedside test. They would mostly be sent out. But, there are molecular tests that are available commercially. But again, there are very few scenarios where we would recommend that for patient testing. The serologic assays. There are commercially available kits, but still would need to be sent to a commercial lab or some hospital labs will perform those, and then they could be performed at CDC. There are no essentially bedside or rapid tests, such as a you know Group A Strep kind of rapid test or pregnancy test in that manner.

Loretta Jackson Brown:
Thank you. And our clinician states that they know that the West Nile virus can be transmitted from blood transfusions, but can it also be transmitted from blood-borne pathogens?

Marc Fischer:
Sorry, we don't quite understand the question. Maybe they could clarify it.

Loretta Jackson Brown:
It's transmitted through regular exposure to blood-borne pathogens, so I'm just going to toss it out there. So if they - I don't - hepatitis. Could it - I don't know if they - does it tie onto another pathogen? And if (Scott), who send the question through the Webinar system is still listening, if you want to dial in and clarify that?

Marc Fischer:
I think we could try to answer that. There's no known association between sort of co-infections with other blood-borne pathogens and West Nile virus, if that was the answer. And, we're not aware of really any other blood-borne mechanisms of transmission if that was the question, other than through blood transfusions themselves.

Loretta Jackson Brown:
Thank you. Operator, do we have any more questions from the phone?

Operator:
We do. (Kelly Beard), your line is open now.

(Kelly Beard):
Hi. I had a question about the case definition requiring a temp of 100.4 degrees. And even if they have other symptoms, including neuroinvasive systems and IgM positives, then I'm told that it's not counted as a case of West Nile if they don't have a fever of 100.4 or higher.

Marc Fischer:
Yes, that's correct. That's the way the case definition for the clinically compatible illness is listed and was decided. And it's recognized that there certainly are patients who have clinical illness that may not include fever. That has been published.

But from a surveillance case definition, because many of the other symptoms are relatively non-specific and very common, that was used as sort of a separating mark for especially non neuroinvasive disease illness. You're right that, you know, in a scenario where you have evidence of neuroinvasive disease, specifically with IgM antibodies or certainly RNA and CSF, that really provides evidence of a recent infection. And, those cases rarely can occur without fever. And so unfortunately, the case definition from a surveillance standpoint can't really account for every scenario. It's still really up to a local or state health department whether or not to report a case. And so, they could report a case like that even if the patient did not have a documented fever.

Operator:
Thank you. I have no further questions over the phone lines.

Loretta Jackson Brown:
Here's our final question and it's coming through the Webinar system. And the question centers around whether or not there were early signals of increased virus circulation in mosquitoes or birds that suggested the timing and/or intensity of the current outbreak would be different than from previous years?

Marc Fischer:
There was some evidence kind of earlier of some areas having mosquito activity or West Nile virus positive mosquitoes earlier than is typically seen in most years or in recent years. And then some of those

building to more intense levels. However, there are years where you get high activity early on and then you get sort of a normal peak, but then it wanes.

And so this year what's been most surprising so far is not only that there was early activity, again mostly in some limited areas, and then other areas it spread later in a more typical timeframe. But that in those areas, the activity has been sustained and so the season has continued to remain fairly active and high even through the typical peak season of mid-August and into early September. And, I think it really remains to be seen whether these interim or preliminary numbers will hold up and exactly how high the final case numbers will be by the end of the year.

Loretta Jackson Brown:
Thank you. We actually got two more questions that came through the Webinar system, and it has to do with the slide that said 56% of 2012 cases are neuroinvasive. And, they want to say isn't that disproportionately high considering 80% of West Nile virus infections are thought to be asymptomatic?

Ingrid Rabe:
So again, that's - it's probably more a reflection that more neuroinvasive cases may be likely to be reported, so there may be underreporting of non-neuroinvasive cases, and obviously we wouldn't be capturing asymptomatic cases in our surveillance.

Marc Fischer:
Yes. And just to reiterate that, that you know the reflection of the proportion of cases reported to national surveillance is totally a reflection of people who are being tested. And so, most people with non-neuroinvasive disease are never tested, maybe never even present to a healthcare provider, and so those cases aren't captured. For neuroinvasive disease, although not all patients certainly are tested, there's a higher proportion and a higher capture of those type of cases.

Loretta Jackson Brown:
And this will be our final question. So would areas that have both West Nile virus and EEE clinical diagnostic or imaging clues to distinguish between the two, are those available? And, how does a clinician address that?

Marc Fischer:

Well, it's difficult to distinguish them clinically. Certainly, Eastern Equine Encephalitis virus is the most severe of the arboviral diseases, has a case fatality rate, at least among reported cases, of almost 40%. But, there certainly are more mild cases of EEE and there are severe cases of West Nile virus. As far as I'm aware, there's not really clinically distinctive pictures that would help the clinician distinguish those. And so, it's most important that the clinician obtain testing for both of those arboviruses, and that would apply in other areas where more than one arbovirus circulates. For example, areas that have La Crosse virus. So in those cases, they have really several options available to them. There are the commercially available assays, IgM assays to test for West Nile virus. There's also a commercially available kit - a separate kit that tests for other arboviruses that would include Eastern Equine Encephalitis virus as well as St. Louis Encephalitis virus and La Crosse virus. So, they can send testing for both of those. They could also send specimens to their state health department or here to CDC. And in most state health departments, and certainly here at CDC, when we receive specimens from patients from a certain area during the arboviral season with symptoms consistent with a possible arboviral encephalitis or meningitis, we will test for all of the viruses that may circulate in that area. And so I think really, that's the most prudent thing to do is if there's virus that could circulate or you're aware of circulating in that area, would be to do testing for all of those rather than try and distinguish it clinically.

Loretta Jackson Brown:

Thank you. On behalf of COCA, we would like to thank everyone for joining us today, with a special thank you to our presenter, Dr. Rabe. If you have additional questions for today's presenter, please email us at coca@cdc.gov. Put August 31st COCA Call in the subject line of your email and we will ensure that your question is forwarded to the presenter for a response. Again, that email address is coca@cdc.gov. The recording of this call and the transcript will be posted to the COCA Web site at emergency.cdc.gov/coca within the next few days. There are no continuing education credits for this call. West Nile virus resources for clinicians are available on the COCA Web page for this particular call. Go to emergency.cdc.gov/coca, click COCA Calls, and then follow the link for the West Nile virus call. To receive information on upcoming COCA calls, subscribe to COCA by sending an email to coca@cdc.gov and write subscribe in the subject line. CDC launched a Facebook page for health partners. Like our page at Facebook.com/cdchealthpartnersoutreach to receive COCA updates. Thank you again for being a part of today's COCA Webinar. Have a great day.

Operator:

The conference is concluded. The lines may please disconnect. Thank you very much.

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