

West Nile Virus Transmission by Solid Organ Transplantation

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Raymond Soto, an EIS officer at CDC in Fort Collins, Colorado. We'll be discussing transmission of West Nile virus through solid organ transplantation.

Welcome, Dr. Soto.

[Raymond Soto] Hi, Sarah. Thanks for having me. I'm excited to discuss our investigation.

[Sarah Gregory] So let's start with West Nile virus. It has been a term that's been around for quite a while now, but I think probably many people don't actually know where the name came from. Why the name, and when and where did it evolve?

[Raymond Soto] West Nile virus was first identified in 1937, and this was when it was detected in a febrile patient in the West Nile district of northern Uganda. Before the early 1990s, there were really sporadic human outbreaks involving febrile disease that were reported infrequently in both the Middle East and northern Africa. But beginning in about the mid-1990s, there began to be more frequent and severe West Nile virus human disease outbreaks that were caused by new viral strains, and these happened in Europe, the Middle East, and Russia.

[Sarah Gregory] And how is it spread?

[Raymond Soto] West Nile virus is most commonly spread through the bite of an infected mosquito. In nature, West Nile virus is maintained in a cycle between birds and mosquitoes, with infected birds essentially acting as reservoirs for West Nile virus and subsequently infecting mosquitoes that come and take blood meals from them. Now, humans and other mammals are generally considered incidental hosts, and by that, I mean humans and other mammals typically don't achieve high enough levels of West Nile virus in our blood (or viremia) to infect mosquitoes that subsequently come and take a blood meal.

In addition to mosquito bites, there have been other routes of transmission that have been documented and described. So these include things like exposure in a laboratory setting; transmission to an infant during pregnancy, birth, or breastfeeding; and then also through blood transfusion or organ transplantation.

[Sarah Gregory] I just want to clarify something you said a second ago. So a mosquito can have West Nile virus from, say, a bird, and bite a person and that person will get it. But if a person has it, and a mosquito that doesn't have it bites that person, then that mosquito does not get it typically.

[Raymond Soto] Yes, that's exactly right. The levels of West Nile virus that are achieved in humans, for example, they're not high enough levels to infect the mosquito that will come along and bite that person.

[Sarah Gregory] That's really interesting, that a mosquito can get it from a bird but not you.

Okay, when did it arrive in the United States and how?

[Raymond Soto] West Nile virus was first detected in the United States in 1999, and this was in New York City. And really it was identified because there was a cluster of encephalitis cases in

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humans, as well as a coincident mass die-off of birds. And so, these two events that were happening at about the same time really helped scientists to connect the dots and eventually led to the identification of West Nile virus being the causative agent. It's interesting because this initial identification in 1999 was not only the first identification in the United States, but also in the western hemisphere. And within five years after that initial detection, West Nile virus had spread across the United States and is now the leading cause of mosquito-borne disease in the contiguous United States.

[Sarah Gregory] What kinds of illness does it cause?

[Raymond Soto] There's really a spectrum of disease that West Nile virus can cause. First and foremost, most people who actually are infected with West Nile virus will actually have no symptoms at all, but about one in five people who are infected will go on to develop a febrile illness. And so, this will include symptoms such as fever, headache, weakness, muscle aches, and joint pain. And then less than 1% of people who are infected with West Nile virus will develop neuroinvasive disease, and so this could include things such as encephalitis (or swelling of the brain) or meningitis (which is swelling of the connective tissue of the brain and spinal cord). This can be a pretty severe disease, so patients who recover from neuroinvasive disease will often have long-term neurologic impairments, and approximately one in ten people who are infected and develop neuroinvasive disease will die.

[Sarah Gregory] So it can be extremely serious, rarely, but...

[Raymond Soto] Yes, in some cases.

[Sarah Gregory] Let's switch to organ transplants now. Where do most organs come from that are used for transplants?

[Raymond Soto] So in 2021, there were more than 41,000 transplants that were performed in the United States, and these organs all came from living and deceased organ donors. But the majority do come from deceased organ donors, and some of those commonly transplanted organs are kidney, liver, heart, lungs, pancreas, and intestine.

[Sarah Gregory] Are there any regulations that direct how organs are obtained?

[Raymond Soto] So in the United States, organ donation and transplantation are done by organ procurement organizations and transplant centers. And they're members of the Organ Procurement and Transplantation Network (or OPTN) which operates under the oversight of the Health Resources Services Administration (or HRSA). So a lot of oversight is involved in both organ donation and transplantation, and it's a heavily regulated system with standardized processes for both procurement and transplantation. And of course, organ procurement in the United States cannot proceed without the consent of donors or next of kin.

[Sarah Gregory] How does West Nile get into these organs?

[Raymond Soto] There are two main ways that organ donors might become infected with West Nile virus. The first is the organ donor can be infected through the bite of a mosquito prior to their hospitalization and organ procurement. The second is through blood transfusion, and when that occurs, an organ donor is infected with West Nile virus from an infected blood product that might be given during their hospitalization, say, during resuscitative efforts.

[Sarah Gregory] Is there a difference between how healthy people are affected by West Nile virus and those who get organ transplants? Do the organ recipients get sicker?

[Raymond Soto] People who receive organ transplants, they require medication to suppress their immune system. And they require this medication because this helps to prevent rejection of the organ. And so while this is, of course, very important for organ acceptance, it can make them more susceptible to certain infections, and for West Nile virus, a more severe disease. So of reported cases of West Nile virus transmission by solid organ transplant or donor direct transmission, about 70% of recipients infected with West Nile virus develop neuroinvasive disease and more than a quarter of those infected recipients die. So the rates for both neuroinvasive disease and deaths from donor-derived West Nile virus is much higher than in the general population.

[Sarah Gregory] Can different pathogens affect different organs? Or is it sort of one for all? I mean, if somebody got West Nile virus in their bloodstream, would a lung be just as affected as a kidney or a liver?

[Raymond Soto] Some pathogens that can be spread through blood, like West Nile virus, can be found in many different organs and recipients of various organs including kidney, heart, liver, and lung have been reported to be infected through donor-derived transmission.

[Sarah Gregory] Once an organ is placed in another person, how does the pathogen, let's say, activate? What causes it to make the new owner sick?

[Raymond Soto] The virus was essentially already "activated" or actively replicating in the donor's body. And then when the organ is transplanted into the organ recipient, that essentially is continuing the infection from the donor now to the recipient. And like we discussed earlier, since the recipient is immunosuppressed, their immune system can have an even harder time responding to the virus, and this will allow it to infect more parts of the body. And so, all these factors come into play and can increase a transplant recipient's risk for severe disease.

[Sarah Gregory] Does age, gender, or race play into how susceptible a recipient might be to a pathogen lurking in an organ?

[Raymond Soto] There's definitely some well documented risk factors for more severe disease from West Nile virus. So older adults, particularly males, as well as immunocompromised persons (or persons taking immunosuppressant medication) in general are at higher risk for severe West Nile virus.

[Sarah Gregory] I believe there have been other cases of this. I know that there have been some cases of organs with rabies, I've done a podcast on those. Why aren't organs checked for pathogens?

[Raymond Soto] Actually, organ procurement organizations do conduct extensive testing for infectious diseases. But there are differing policies for living donors compared to deceased donors, and currently there's no national policy requiring West Nile virus screening of deceased organ donors. But some organizations do screen their donors for West Nile virus. And the main difference when considering screening between living and deceased donors is timing. The clock starts ticking immediately for a successful organ donation once a deceased organ donor dies.

Additionally, organs are in extremely short supply and the logistics of testing and also potential false positive results could lead to organ wastage and also delays of lifesaving transplantation. So it's certainly not a simple issue. But transplant programs do inform patients and their families about the possibility of infectious diseases being transmitted by organ transplantation.

[Sarah Gregory] Your study is about two people who had organ transplants that became sick with West Nile virus. What brought these cases to your attention?

[Raymond Soto] The typical way that these infections come to light is when an organ transplant recipient develops an infection that's suspected of being donor-derived, and that usually is within a month after their transplantation. The transplant center then notifies the Organ Procurement Organization and the Organ Procurement and Transplantation Network (or the OPTN, as I mentioned earlier). So once that communication occurs, that's when CDC and state and local health departments become involved to help investigate potential donor-derived infection.

[Sarah Gregory] Okay. So what alerted doctors specifically to check for West Nile virus?

[Raymond Soto] Both the recipients in this investigation developed fever and encephalitis in the fall, and that's when mosquito-borne diseases typically peak. So really it was the work of astute clinicians to recognize these risk factors and the symptoms and test them initially for West Nile virus infection.

[Sarah Gregory] Take a minute now to tell us about your study.

[Raymond Soto] So there are really two main parts to the study. In the first part, we describe an investigation of two patients that were infected with donor-derived West Nile virus. But this story in itself was not exactly unique because it was actually the 11th such cluster reported since 2002. And so that brought us to the second part of the study where we took a deeper dive into why these donor-derived cases are still occurring. And so to do that, we reviewed previously reported cases, with a focus on timing of transplantation and whether organ donor screening was performed. And then we also reviewed recent data on organ donor screening practices.

[Sarah Gregory] And after all of that, what did you find?

[Raymond Soto] For the first part of the study, we investigated this cluster. And for the organ donor in this investigation—they died in September from an apparent drug overdose—they were not screened for West Nile virus infection prior to organ procurement. And when we tested blood from the donor that had been collected prior to the donation, we found West Nile virus RNA but no antibodies specific for West Nile virus in their blood. So this is really suggestive of a very recent infection, in which someone will have West Nile virus in their blood, but their immune response will not have had enough time to develop antibodies against West Nile virus.

We also found in our investigation that there was a lot of West Nile virus circulating in the community at the time where the donor lived. And then we also found that there wasn't any evidence of infected blood donors from whom the organ donor received blood products. So kind of tying that altogether, we thought that the organ donor was most likely infected by mosquitoes shortly before they died. And then once we completed the investigation, we then reviewed all of the previously reported clusters of donor-derived West Nile virus transmission.

So when we looked at 10 previous reports of donor-derived West Nile virus, we found that only one reported screening donors for West Nile virus. Furthermore, all of the transmission events, including this one, occurred in the months of August through October, which, again, is when peak West Nile virus transmission occurs. And then taking a step back, we reviewed screening practices and looked at a recent nationwide survey of organ procurement organizations and found that only 35% that participated in that survey reported West Nile virus screening of deceased donors. And most of them that did screen deceased donors did it year-round, with only one performing seasonal screening.

[Sarah Gregory] Was there anything unexpected?

[Raymond Soto] It was really notable how many of the previous transmission events, including this one, might have been prevented through a seasonal screening approach, given that they all occurred during that peak West Nile virus transmission season and that most of the donors from reported clusters were not screened. As we have discussed, organ transplantation from a deceased donor must be done quickly, but additional screening for seasonal diseases (like West Nile virus) could potentially be included. Additionally, many of the organ donors from reported cases were found to have West Nile virus RNA in their blood on retrospective testing, and so that means that likely these donors would have been detected through screening and these infections could have been prevented.

[Sarah Gregory] Dr. Soto, how do you hope your study will be used?

[Raymond Soto] We hope that this report can be used by both advisory committees and policy makers to inform decisions about how deceased organ donors are screened for West Nile virus infection. As I mentioned before, a seasonal screening approach could potentially help prevent these donor-derived infections. Additionally, I think our study will be a good reminder for clinicians to consider West Nile virus and other arboviral diseases when patients present with febrile illness or neuroinvasive disease, especially during those months of high transmission.

[Sarah Gregory] So you just recommended more screening. Are there any further steps you recommend for these kinds of screenings in organs?

[Raymond Soto] We definitely recognize that screening is expensive and the logistics of rapid testing can be difficult, especially for deceased organ donors. So it wouldn't be helpful to screen deceased organ donors if those results couldn't be obtained very quickly. But we do think that a seasonal screening approach, such as only testing from July to October, would likely capture most cases. It would also be more cost-effective than year-round testing.

If seasonal screening weren't an option, there are also alternatives that could be considered, such as triggering strategy using local blood donation screening results, so blood donations are required to be screened for West Nile virus. Or alternatively, working with local or state health departments to determine times of increased West Nile virus circulation.

[Sarah Gregory] How can public health help promote better vetting of organs?

[Raymond Soto] One of the main issues with transplantation is that there's not enough organs available to everyone who needs them. The overall goal of public health and transplantation is to ensure that every usable organ is used safely. And I also want to make a point that donor-derived infections are very rare. So they're suspected in about 1% of transplants and confirmed in far fewer, so the policies that are in place to test organs for infectious diseases have done a good job of preventing many donor-derived infections. But public health can help with prevention of donor-derived infections when suspected donor-derived transmission events are reported by organ procurement organizations or transplant centers to the OPTN for investigation. And when these specific infectious disease-related risks are identified, public health authorities can work with the OPTN to identify prevention and control strategies to help prevent infections.

[Sarah Gregory] What about policy? Are there any policy changes that could help?

[Raymond Soto] There are policies in place to test for infectious diseases in organ donors, but there's no national policy in place for West Nile virus screening of deceased organ donors. You

know, I think our findings from the study support consideration of a seasonal or trigger-based screening approach to prevent donor-derived West Nile virus infections.

[Sarah Gregory] You're an EIS officer. Tell us what that is and how it relates to your job at CDC and how you are involved in the study of organ transplantation.

[Raymond Soto] So EIS is a two-year training program with the CDC. So during EIS, you're assigned to a branch or a team or potentially a state health department, but I've been assigned to the Arboviral Diseases Branch in Fort Collins, Colorado where I've been receiving training in applied epidemiology.

During EIS, I've had the opportunity to work on a lot of interesting investigations, and this includes suspected infections with arboviral diseases following organ transplantation. While it's not the only thing I work on, they have been really valuable investigations to work on, especially because I've had the opportunity to work with a lot of different partners with these investigations. So that includes the Blood, Organ, and Other Tissue Safety Office at CDC, and then many local and state public health partners and agencies, as well as academic medical centers. And it's these partnerships that really make it possible to have a successful investigation because they can become very complex very quickly. So it has been a great learning experience, for sure.

[Sarah Gregory] So I know EIS officers can be anything from PhDs in data to epidemiologists to medical doctors to vets. Which are you?

[Raymond Soto] Yeah, so I have a PhD in microbiology and immunology. So I was a bench scientist for my training, and then I had a bit of a switch where I then went on to do a fellowship in primary care research where I also did a Masters of Science in Public Health. So that really led to my career switch to move into public health, and it's been really valuable, and I definitely really, really enjoy it.

[Sarah Gregory] With COVID still causing mayhem in the United States, what do you like to do for fun?

[Raymond Soto] I really enjoy getting out and enjoying the outdoors. I do a lot of rock climbing, so whenever I have the opportunity to get outside and go rock climbing, I definitely do that. Then I also do a fair amount of snowboarding and fishing. So there are a lot of opportunities for outdoor recreation here in northern Colorado. It's a great place to be. But if I'm not outside, I also enjoy watching football, especially for my alma mater, the University of Wyoming. So I have to throw out a "Go Pokes!" for them.

[Sarah Gregory] Okay. So you're actually from that area, anyway. You're familiar...

[Raymond Soto] Yeah, yeah. I was born in northwest Wyoming, kind of close to Yellowstone. So definitely love the Mountain West area.

[Sarah Gregory] It's a beautiful area.

Well, thank you so much for taking the time to talk with me today, Dr. Soto.

[Raymond Soto] Thank you very much.

[Sarah Gregory] And thanks for joining me out there. You can read the February 2022 article, West Nile Virus Transmission by Solid Organ Transplantation and Considerations for Organ Donor Screening Practices, United States, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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