Bird Migration and West Nile Virus in the U.S.

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

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Alan Barrett. Dr. Barrett's a professor of pathology at the University of Texas, Medical Branch, in Galveston. Today we'll be talking about his article on the migration of birds and what drives West Nile virus circulation in the U.S. Welcome, Dr. Barrett.

[Alan Barrett] Good afternoon, Sarah. It's delightful to talk to you.

[Sarah Gregory] Okay, so to begin with, give us a brief history of West Nile virus. When did it reach the U.S. and how prevalent is it now?

[Alan Barrett] So, West Nile virus was originally discovered in the 1940s in the West Nile District of Uganda. It was associated with febrile illnesses and no one took it really seriously. And then, in the early 1990s, we found outbreaks of neurological disease taking place in Europe. And this was the first evidence that West Nile had emerged out of Africa into Europe, and then subsequently, United States.

The virus came to New York in 1999, and as we all know, we had an outbreak of West Nile encephalitis in New York City and surrounding areas. And this was the introduction of West Nile virus in United States. And the virus has been in the U.S. since 1999, and for the last nearly 20 years, the virus has been moving across America, causing outbreaks every year, of varying amounts. And we have peaks of activity, with about 2,000 actual cases every eight to 10 years. The last one was in 2012, and so we can anticipate in the early 2020s we'll see another large outbreak of West Nile. So, it's a virus that's emerged into the New World and it's here to stay, and causes these periodic outbreaks.

[Sarah Gregory] West Nile virus often infects birds and mosquitos, as well as humans. Would you explain what this transmission cycle looks like?

[Alan Barrett] West Nile is a mosquitoborne virus, what we call an arthropod-borne virus or arbovirus. And these viruses are characteristic of being what we call "zoonotic," that is to say they exist in an animal species. They get bitten by a mosquito, the virus gets transmitted from the mosquito into the animal, and then we have an amplification in the animal, then a mosquito bites it again, and that causes a transmission cycle between, in the case of West Nile, birds and mosquitos. Now, this transmission cycle takes place continually and that's how the virus maintains. And another good example would be Zika, with nonhuman primates and humans, or dengue, between humans and mosquitos. So there's quite a lot of these different viruses around.

However, one of the strange things about the transmission cycle that we don't really understand is how you get these outbreaks of disease in humans. Now, for West Nile, birds are the vertebrate hosts, but the virus can infect other species besides birds. So, it's well known for causing disease in humans and horses, where it causes neurological disease. But we call these "dead end" hosts, because the amount of virus multiplying in the blood of humans and horses is not enough for a mosquito to come along and pick the virus up from the blood and transmit it to another species. But, although we're dead end hosts, we get these periodic outbreaks of West Nile encephalitis. They occur because of ecological reasons. We don't really understand why it peaks in one year

and not another year. The last peak was in 2012 and the one before that was 2002 and 2003. So, as I said, we can expect something in the early 2020s. But, we don't understand why it takes place, and we think it's ecological reasons. And that's why we got into doing these studies—to try and be able to start to predict when outbreaks are going to take place. This is very complicated, but the more evidence we can get to understand how a virus moves and where it appears, will give us an insight into how we can help control the disease.

[Sarah Gregory] What role do birds and their migrations play in this spreading of the disease?

[Alan Barrett] So, in the case of the birds and West Nile, they're what we call amplifying hosts. That means, if we…a mosquito is infected with West Nile virus, the mosquito then feeds on the bird to get its blood meal and feed. The virus goes from the saliva in the mosquitos into the bird, and then the virus multiplies inside the bird. In bird species, West Nile multiplies to very, very high titers, maybe as high as 10 to the power of 12. That's somewhere in the region of 1,000,000 times 1,000,000 amounts of virus infectious units transmitting through their blood against a very high titers. And so, these are great hosts for transmitting the virus between mosquitos.

Now, as we all know, birds tend to move around. Some bird species tend to stay in areas, but a number of birds are migratory, and they move around across different countries and sometimes continents, and they can take the viruses with them. And probably the best example of this is influenza, where influenza moves in birds, water fowl, across the world. And that's how the virus gets transmitted across different seasons, and why we need to have a vaccine each year. So, with West Nile virus, it's not transmitted by waterfowl. The bird species are passerine, so may tend to be what we call terrestrial birds. And these are birds that migrate across different countries in a northward and southward directions, according to seasons. And so, for West Nile, so…excuse me, for the terrestrial birds, they tend to move southwards in the winter, and then in the spring, they move northwards. And so, because of this migration of the birds, they're carrying West Nile virus, and so they can carry it over large distances while the virus is multiplying in the birds. And, so, when the birds stop to have a rest in a certain area, then if mosquitos are in that area, they can feed on the birds and then the mosquitos will then feed on other species of birds and, potentially, humans, and that's how the virus is spread and how it can cause disease in different parts of the country.

[Sarah Gregory] So your study used genetic sequencing to map out a family tree of the virus. Tell us about that.

[Alan Barrett] Yes. So, I always think of science as being a jigsaw. And what we want to try and do in science is work out all the pieces of the jigsaw and put them together. And if you want to look at the fine detail of a virus, the best way to do it is look at the genetic material. In the case of West Nile virus, it's an RNA virus; it has 11,000 nucleotides in the genome. And so, if we sequence the genomes of the West Nile virus, we can find the changes in the viruses, and then we can start to map those, being a detective, over time and space.

And so, what we did was, we took genetic sequences of West Nile isolates found in Texas, New York, Virginia, Colorado, North and South Dakota, and Illinois, and we did this across seven different years, between 2001 and 2009. We did this because we had isolates available from all these areas in all the years. And so we could get a jigsaw by analyzing the genetic sequences of these viruses, to look at the relationships between viruses in each of these different geographic

locations across different years. And so, if you like, it's a way of looking at viruses over time and space. We knew where these viruses were isolated; we knew what species they came from, be it birds or mosquitos; we know the exact dates they were isolated. And so, we can be detectives and put the genetic information together with all the geographic information, and the times, to work out…information, to work the relationships out between the movement of the virus over time and space. And so, that enabled us to be detectives and look at the relationships between the viruses in the different parts of the country.

[Sarah Gregory] So then you compared the possible trees to known avian migration routes—and how did you do this?

[Alan Barrett] Yeah, so that was fortuitous. In the lab, Daniele Swetnam is a…was a very talented graduate student, and she came up with the idea of looking at the migratory pathways of birds. And this was her PhD studies. And she investigated the migratory pathways, what was known in the literature about these pathways, across the country, and the difference between waterfowl migratory pathways and terrestrial bird pathways. And it came clear that there were different pathways in the U.S. There was one on the West Coast, and then there was one on the East Coast, called the Atlantic pathway, and then there was…pathways going across the middle of the country.

Now, because the Rocky Mountains are very high—they go up to about 15,000 feet—the birds can't really fly over the Rocky Mountains. And so, California's a very different part of the country, compared to the rest of the country. And if you look at genetic sequences of West Nile, the West Coast, California, is very different than the rest of the country. And so, we ignored California in our studies.

And so, we looked at the Midwest part of the country, the so-called middle path flyway in the country, and compared it to the eastern flyway, looked at the geographic areas, and compared the sequences that were found in the Atlantic pathway to that found in the middle of the country. And we identified that the genetic sequences of the viruses found on the East Coast demonstrated that the virus was moving southwards down the Atlantic migratory route for the birds, and then it was going northwards through the central flyway in the middle of the country in the spring. And so this told us the virus, as I said, was moving north with the migratory birds in the spring and then it was coming southwards along the East Coast in the fall. And so, that enabled us to actually look at the origins and spread and movement of the viruses.

[Sarah Gregory] And what did you ultimately find?

[Alan Barrett] So, we ultimately found that the…Illinois is a very interesting area, where West Nile comes in, goes out, 'cause it's that mixture of the flyways in the middle of the country. And this led to dispersal of the virus to different parts of the country. We found that Texas was an important part for dispersal of the viruses moving into the Midwest, particularly the Dakotas and Colorado. And just to go sideways, Texas is a very important part of migratory pathways of birds because over 90 percent of migratory birds in United States go through the gulf areas of Texas. So, it made sense looking at Texas, because this is really a very important part of the country for migratory pathways. And the data we had from the East Coast also made sense, because West Nile virus was introduced into New York in 1999, and then historically we knew it spread

southwards down the eastern seaboard in 2000–2001, and then spread westwards across the country in 2002. And that made sense with the migratory pathways of the birds.

[Sarah Gregory] So, what could these results mean for future disease surveillance efforts?

[Alan Barrett] Well, for West Nile, I think this is the start of moving forward. One of the problems of studying West Nile is it comes and goes, as I said, with big outbreaks every 10 years or so. There's not a lot of active research programs. And so, isolates are only sequenced every year in California, New York, and Texas. And we need more areas in the country. And what this study showed was how important it is to continue surveillance activity in various parts of the country, because by nucleotide sequencing, we can predict what viruses are going to go where, when. Of course, this is somewhat limited by the amount of virus that moves every year, of course, as it varies. But it does give us the opportunity to try and predict when West Nile will actually appear, over time. Now of course, that's very hard. This should start; we need more sequence data to make predictions for the future. It's obviously very hard. You can always go backwards and study what happened, but trying to predict the future's really very hard. But I think as we get more and more sequence data, I think this study shows very nicely how different techniques can be put together as a multidisciplinary project to actually understand how viruses migrate and move over time and space.

[Sarah Gregory] Can you get West Nile virus more than once?

[Alan Barrett] The quick answer is no. Serologically, there's only one type of West Nile virus, so once you've been infected, be it a bird, be it a human, or a horse, with the normal virus infection, you are protected for life.

[Sarah Gregory] Would you like to tell us about your job and how it relates to West Nile virus?

[Alan Barrett] So, I've been interested in arthropod-borne viruses throughout my career. I started work on arthropod-borne viruses when I did my PhD. I worked on a virus called Semliki Forest, which you've probably haven't heard of. It turns out Semliki Forest is actually was where this virus was discovered, and the man who was collecting mosquitos said, "Where are we?" and the guide said, "Semliki." And Semliki means "I don't know." So I worked on I-don't-know virus for my PhD; it was a great virus to work on as a model, but it doesn't really cause much in the way of human disease.

Then I moved to work on yellow fever virus, and that's one of my big loves. It's a nasty virus, very pathogenic, but it's really great to understand how the virus causes disease. So, I spent my entire career as a researcher working on arthropod-borne viruses—West Nile, yellow fever, Japanese encephalitis, dengue, and tickborne encephalitis.

In my current position, I am director of the Sealy Institute for Vaccine Sciences at University of Texas, Medical Branch, and so, I'm always interested in vaccine development. And we have an active…program working on development vaccines for arthropod-borne viruses. But if you're going to do vaccine development, you have to have a whole…a holistic view of understanding the pathogen to understand where you're going to vaccinate. And so, why do we do these studies? Because you want to try and predict where the virus is going to be and where you want to implement the vaccine in the future.

[Sarah Gregory] Thanks so much for taking the time to talk with me today, Dr. Barrett.

[Alan Barrett] It's a pleasure.

[Sarah Gregory] Listeners can read the December 2018 article, Terrestrial Bird Migration and West Nile Virus Circulation, United States, online at cdc.gov/eid.

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

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.