

WEST NILE VIRUS: CDC's race against time

All-out effort in Louisiana: 85 cases, 7 deaths set stage for an intense scientific push to track and conquer infection.

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Slidell, La. --- On a metal shelf in a hospital lab in a small town in Louisiana, a strip of paper is slowly turning pink.

On the other side of a protective glass panel, Dr. Mike Bunning and technician Aaron Kipp of the Centers for Disease Control and Prevention are watching intently.

The paper dipstick is resting in a blood sample from an emergency room patient at Slidell Memorial Hospital. The man has been to the ER twice in two days. He has a high fever, fatigue and a headache. He may be infected with West Nile virus.

The standard tests for West Nile infection take days to complete. Bunning has a new test that could reveal the virus's presence in minutes, if it is successful. But it has not yet produced one positive.

Until, maybe, now.

A timer buzzes. Kipp leans into the lab cabinet.

"That one may be showing a little darker shadow than the rest," he says.

Bunning tilts the dipstick to catch the overhead light.

"Hey," he says. "I think you're right."

Since June, there have been 85 cases of West Nile virus encephalitis in Louisiana, including seven deaths. It is the largest single outbreak of West Nile in U.S. history, and it has called out the biggest CDC West Nile effort in three years.

For two weeks, CDC researchers have been arriving in southeastern Louisiana from agency headquarters in Atlanta and from the insect-borne disease division in Fort Collins, Colo.

By Friday, there were almost 30 scientists: epidemiologists, virologists, entomologists, a vertebrate ecologist, veterinarians, the CDC's only neurologist, several specialists in computer mapping of data and a handful of Epidemic Intelligence Officers, the rapid-response troops who serve two-year stints on the front lines of disease investigations.

The researchers make up five teams working in a triangle defined by New Orleans, Baton Rouge and the point where Interstate 10 crosses the Louisiana-Mississippi line. They are interviewing patients, reviewing medical records, trapping mosquitoes, catching birds, calling hospitals to search out undiscovered cases and running early blood tests to identify unrecognized infections.

It is grueling work. Days start at 5 a.m. and end after midnight.

"We have to stay flexible; we have to stay ahead of it," Bunning said. "It is teaching us things all the time."

Struggling to keep pace

Since West Nile virus arrived in America, researchers have struggled to keep pace with its movement across the country.

One of the biggest obstacles is basic human biology. The standard tests for West Nile measure the body's response to the virus --- not the virus itself. But the tests cannot be performed until roughly 15 days after the mosquito bite that transmitted the disease, because it takes that long for the immune response to rise to detectable levels.

Those test results help doctors, because they confirm that a patient is infected. But they are much less useful to epidemiologists pursuing the disease, because what they show is not where the virus is now, but where it was two or more weeks ago.

Knowing where the virus is, at the time infections are happening, could help focus mosquito-control measures, possibly reducing the number of cases.

There are two major hurdles: Developing a test to identify the virus in human blood, and finding victims in time for the test to be useful. The window of opportunity is narrow; in humans, West Nile reproduces for only three to five days before the immune system begins to fight it off. People do not feel sick until virus levels are at their highest --- and few people go to the doctor as soon as they start to feel sick.

Bunning's job is to clear those hurdles. To help, he has the "fever team": epidemiologists Stacie Marshall from Colorado and Judy Krueger from Atlanta; physicians Ann Buff from Tulane University and Kwame Asamoah, also from Atlanta; Ellie Click, a fourth-year medical student from Stanford University, and Kipp.

"We are looking for a needle in a haystack," said Bunning, a 47-year-old epidemiologist, veterinarian and Air Force officer who investigated the first West Nile cases in New York, the emerging Nipah virus in Malaysia and last fall's anthrax attacks. "It is purely a numbers game."

The group has set up shop in an empty building at Slidell Memorial, the Louisiana hospital that has seen the most West Nile patients so far. Dozens of rooms are furnished, wired and available, but the fever team have clustered in just one, a wide first-floor office with cafeteria tables shoved against the walls. On top of the tables are seven computers, six cradles for PDAs and more pre-paid cell phones than anyone can keep track of. Above the tables: four maps, six lists of phone numbers, charts of patients' names and test results. File cabinets hold patient records; stacks of junk food are piled on top.

Outside, the temperature is in the mid-90s and the air is steamier than usual: Tropical Storm Bertha drenched the area the previous night. Inside, the intense air conditioning labors to tame the humidity. When Click pulls a graham cracker from a box, it bends.

Thirty miles away in New Orleans, a group headed by Dr. Jose Rigau of CDC's Puerto Rico lab is phoning state hospitals to find every case of West Nile virus encephalitis, the very serious form of the disease. Bunning's group has a more subtle task: Locating any feverish patients in 11 local clinics and two hospitals and separating out the few who might be in the early stages of a milder case of West Nile.

Every afternoon, Bunning and Kipp run the new dipstick test on any blood samples the clinics have sent. Then they pack the samples in dry ice, plaster them with biohazard stickers and ship them overnight to Fort Collins for additional tests.

More than 40 feverish patients have consented to participate so far, but none of their blood samples have lit up a dipstick. When one does, the patient will be asked for five more samples over five days, to track how the virus behaves in their blood.

"I'll send a limo for them, if they'll agree to participate," Bunning said. "I'll even go get them myself. They are the ones who will give us the critical piece of the puzzle."

Mosquitoes mainstay in area

Almost all the Louisiana residents sickened by West Nile virus this summer live on the north shore of Lake Pontchartrain, in Slidell, Mandeville, Covington and Baton Rouge.

It is not the Louisiana that out-of-state tourists would recognize. Cajun country's spicy food and fast fiddle music lie miles to the west; New Orleans' delicate architecture and raucous partying are a long causeway to the south. The heritage is English and Italian, not French. Until New Orleans commuters began to colonize it, this was an area of small farms and mineral springs where city residents came for vacation.

But it is a great place to be a mosquito: warm, flat and very wet. Slidell is ringed by state swamps and federal wildlife areas. Rural houses use individual sewage plants that spit out copious amounts of water. When it rains, as it did for five straight days last week, the deep ditches along roads and highways spill over and soak gardens and lawns.

Louisiana is accustomed to living with mosquitoes, even to dying because of them. Persistent yellow fever epidemics were one reason Napoleon gave up the territory in 1803. New Orleans was so plagued by malaria, dengue and yellow fever that it founded the country's first city health department in 1817.

Bug-borne diseases are a problem still. In most years, there are sporadic cases of St. Louis encephalitis, a virus in the same family as West Nile. Last year, an outbreak in northern Louisiana sicked 62 residents and killed three.

But the casual relationship between Louisianans and the bug they jokingly call the state bird may have been changed forever by the arrival of West Nile.

"St. Louis (encephalitis) was always considered a poor man's disease," said Madeline McAndrew, assistant secretary of the Louisiana Department of Health and Hospitals. "The difference with West Nile is, it doesn't care who you are. This has been a yuppie issue, more than a poor man's one."

Until this summer, mosquito control was considered local business. The West Nile threat has changed that. State officials plan to spend \$3.4 million in federal emergency money to start mosquito-control programs in areas that had voted them down.

But controlling mosquitoes is complicated and labor-intensive. It requires picking the right chemicals for the landscape, and finding workers willing to visit every pond and ditch.

There has not yet been enough time, as CDC researchers found while they trapped mosquitoes on the north shore last week. After a week in Slidell, which just beefed up

an existing mosquito-control program, Dr. Roger Nashe of the Fort Collins lab was preparing to move his team to the next parish over.

"We have had several different kind of traps out, and we barely found one mosquito pupa, so it seems Slidell's control measures are working," he said. "Then we moved next door, and we immediately pulled in buckets of mosquitoes."

Protection key to prevention

"The key thing is to get their heads covered," Bunning said. "That way, they can't see to kick you."

The potential West Nile patients he is talking about are eyeing him uneasily through a chain-link fence. They are emus: Three shaggy pets that share a big backyard with a herd of goats and several barnyard cats. They all belong to Chuck and Rita Walling, retirees who have lived on the east side of Slidell since 1968.

"My grandson found three dead blue jays in the lawn last week," Rita said. "A horse died, several blocks away. And our neighbor over there, she was terribly sick a week ago. They didn't know it was West Nile virus at first."

The Wallings' emus were spotted from the street by a separate CDC team taking blood samples from wild birds in the neighborhood. That team is headed by Nicholas Komar, a vertebrate ecologist from Fort Collins who led last year's West Nile investigation in south Georgia.

Birds, unlike humans, are "amplifiers" of West Nile: They not only acquire the infection from infected mosquitoes, but pass it back to uninfected mosquitoes after the virus reproduces in their systems. But the virus doesn't behave the same way in all species of birds, so figuring out the role of different species is important for predicting the spread of the epidemic.

Komar asked Bunning's team for help because his people are used to bleeding house sparrows and woodpeckers --- birds that can be held in one hand. The emus come up to the brim of Walling's cap.

Members of both teams arrange themselves in a line across the back yard, closing off the emu's escape route while Walling leads the way with a coffee can of emu chow. Two of the birds retreat; the greediest --- or bravest --- one sticks his beak into the kibble.

Four scientists tackle the bird. One researcher wraps an old T-shirt over its face; three others pull it to the ground, trapping its powerful legs under its body and lying on it. It takes all four of them to hold the bird down while it bucks to throw them off. Bunning edges between them with a syringe, fishing for an artery under the bird's wing.

Within 20 minutes, all three emus are caught, bled and released, hissing and kicking. Bunning peels scraggly feathers from his shirt cuff. The bird team staggers out of the mud, filthy and drenched with sweat, as Komar appears from behind their van with a panicky cardinal in one hand.

"Oh," he says. "Are you done already?"

Early detection a plus

The dipstick was positive for West Nile virus. But the patient, it turned out, did not have the disease.

Late Wednesday evening, lab results from Fort Collins rolled out of the fax in Bunning's makeshift command center. All six patients on it were clean of West Nile virus antibodies, including the patient whose blood made the dipstick test react.

The CDC researchers don't have enough data to explain the result. The man may have a related disease: St. Louis encephalitis also might light up the dipstick. He might have been in the very early or very late stages of West Nile when his blood was drawn. He almost certainly has something; he has been admitted to Slidell Memorial and is seriously ill.

Bunning summons the discouraged team for an emergency meeting.

"I don't often give a lot of accolades," he says. "But you are doing very good work. Hopefully, we will still strike it rich with a sample. In a few years, you will be able to look in the scientific literature and see references to the 'Slidell isolate,' and you'll know you were there at the start."

Meanwhile, time is running short. Bunning must return to Fort Collins: He has not been home for five weeks, he has missed his youngest son's birthday for the second year in a row, and he is needed at a West Nile strategy meeting.

Before he goes, he must decide whether to split his team in half, sending some of them to another hot spot in hopes of catching West Nile virus there.

"I don't have enough people or resources to move more than once," he said. "So I only get one shot at deciding. It has to be the right decision, and it has to be at the right time."