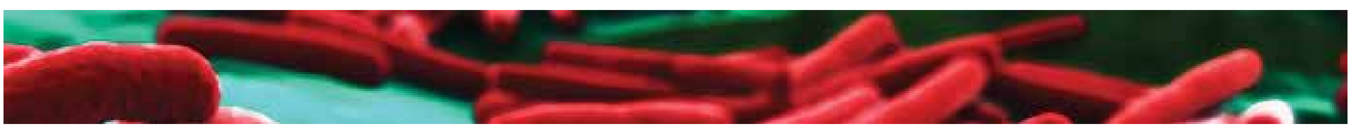
WHEN ZIKA STRIKES

OUHSC epidemiologists are ready to help when public health is threatened by anything from Ebola to E.coli



A magnified image of E. coli bacteria

By April Wilkerson

Like detectives investigating a crime, infectious disease epidemiologists must be thorough investigators and critical thinkers. They must not be easily swayed by information that seems alarming on its surface until its link is established. And they must be methodical, ever mindful that what they say affects society's health and response.

When a disease like the Zika virus enters the public consciousness, it provides a window into the domain of epidemiologists, who harness a number of complicated, meticulous approaches to establish whether and how a disease is actually affecting human health, or if something else may be the culprit.

Last fall in South America, doctors began noticing increased numbers of babies born with microcephaly, a birth defect in which the infant's head is smaller than expected when compared to babies of the same sex and age. There also was an uptick in diagnoses of Guillain-Barré Syndrome, a condition in which the immune system attacks the nerves. At the same time, officials noted an outbreak of the Zika virus. Although evidence is building that Zika can cause both conditions, saying so with certainty requires a step-by-step gathering of information.

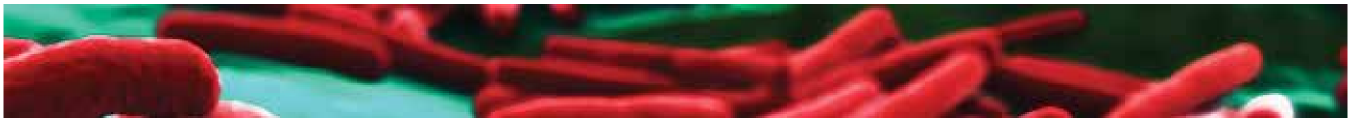
"Epidemiologists are very critical, but we have to be because our work can have drastic consequences on the population," says Hélène Carabin, DVM, Ph.D., a professor in the Department of Biostatistics and Epidemiology at the University of Oklahoma College of Public Health. "I always remind myself that the work I do is for the public because what I say publicly will impact people's chances of getting sick or not."

Carabin is not investigating the Zika virus, but the transmission dynamics models she uses in her own work are applicable to the study of Zika. So, too, is the work of her colleague Aaron Wendelboe, Ph.D., associate professor in the Department of Biostatistics and Epidemiology at the OU College of Public Health. As part of his work, Wendelboe interacts with the Southwest Preparedness and Emergency Response Learning Center, a public health training program funded by the Centers for Disease Control and Prevention and housed in the College of Public Health. During his career with infectious disease epidemiology, Wendelboe has investigated many disease outbreaks, from the more recent Ebola virus to influenza to *E.coli* outbreaks.

Among emerging infectious diseases, more than two-thirds of them are zoonotic — they can be transmitted between animals and humans, Wendelboe says. Of that segment, the majority also are viral in nature. That means many factors come into play in the emergence, or re-emergence, of a disease. "War and famine, humans going into environments we haven't gone into before, population growth, climate change — all of those things are leading to our interaction with emerging infectious diseases," he says.

In addition, the Zika virus, like SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome), is a single-stranded RNA virus, which means it is highly prone to mutation. "Because of that microbial adaptation to change, a relatively new disease could re-emerge, or we could have a brand-new virus that we've never come in contact with, either because it's been hiding in a reservoir that humankind hasn't come in contact with, or because the virus is a newly mutated type," he says.

The principles for investigating a virus like Zika involve several types of surveillance. Syndromic surveillance leverages large medical electronic



databases to look for clusters of symptoms. Wendelboe is now working with the Department of Veterans Affairs database for his own work. Each day, he runs an algorithm based on codes for various symptoms; when there's a spike in a cluster of symptoms, that signals the need for further investigation.

Another type of surveillance is sentinel surveillance, which aims to determine where a virus will attack. Because Zika is caused by mosquito bites, sentinel surveillance involves going where mosquitoes tend to breed — near water. This type of surveillance was important during the last outbreak of West Nile Virus, and a similar approach would be appropriate for Zika, Wendelboe says. To monitor whether the Zika mosquito vector is in an area, caged chickens can be placed near lakes and ponds, where they will be bitten by mosquitoes. Blood samples are collected from the chickens to see if they've made antibodies for the Zika virus. If they have the antibodies, it's likely that Zika has moved into the area.

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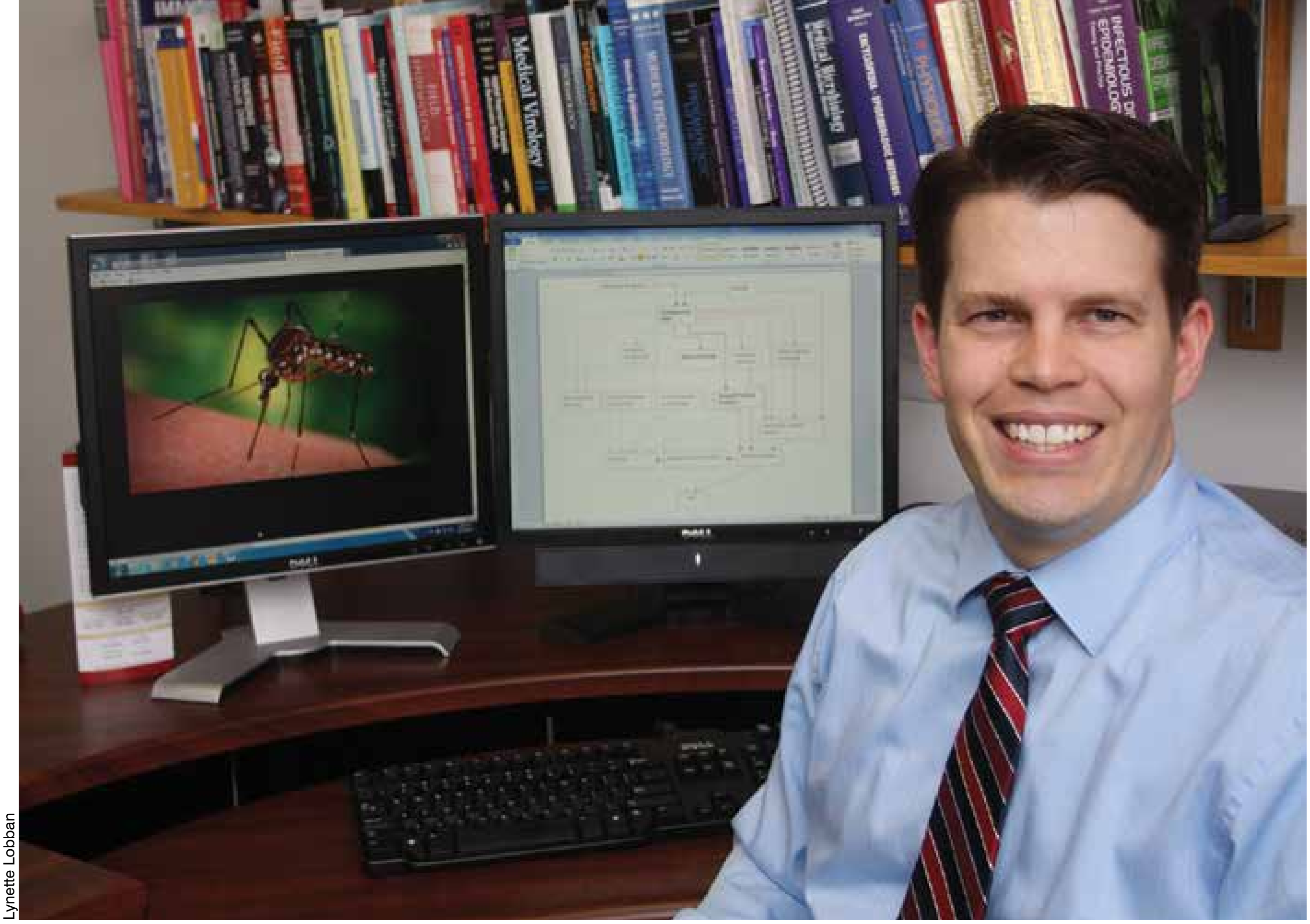
Professor Hélène Carabin and colleagues at the OU College of Public Health are on the front line of research on the transmission of infectious diseases like the Zika virus.

Active surveillance is another part of the response to the Zika virus. It involves asking people who have traveled to endemic areas, particularly pregnant women, to be tested to determine if they've been bitten by a mosquito carrying Zika. There have been 153 travel-associated Zika disease cases reported in the U.S. and an additional 108 in U.S. territories. Thus far, the Oklahoma State Department of Health reports that four people in Oklahoma have tested positive for the Zika virus after returning from international travel.

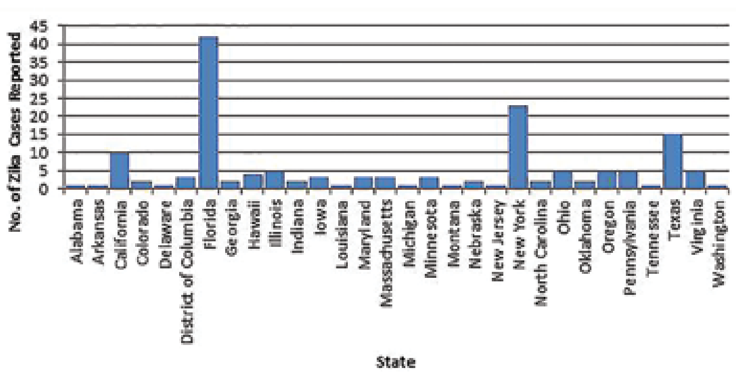
Transmission dynamics models are a tool that epidemiologists use in an effort to predict the spread of viruses like Zika; their findings are used by public officials and policymakers to determine a response and how to allocate resources and



Lynette Lobban

OU Associate Professor Aaron Wendelboe daily runs an algorithm looking for clusters of smptoms that might signal a disease outbreak.

funding. For a transmission dynamics model of Zika, epidemiologists would seek information about the bite rates of mosquitoes, the population size of the mosquitos and their density, as well as the density of the human population. They also need information about the probability of the virus being transmitted when a mosquito bites a human, as well as the probability of a mosquito acquiring the virus when it bites an infected human.



Distribution of reported cases of Zika disease, updated March 3, 2016.

"By gathering information on the human population and their chance of giving the virus to the mosquito, and information on the mosquito and its chance of giving the virus to humans, you can try to predict how many cases you would get if you drop one case in the population," Carabin says.

But there are many other variables to consider for such models. Once a pregnant woman is infected with Zika, what is the probability that the infection will be transmitted to her fetus? And then what is the probability of that fetus developing microcephaly? Epidemiologists also must consider whether babies classified with microcephaly might be considered part of the normal distribution in their own population area, but not part of the normal distribution by international standards. In addition, they must consider whether something else might be causing the rise of babies born with microcephaly; in the case of Zika, some have suggested larvicide as a potential cause.

Temporal associations may or may not end up being causal associations, and it is the epidemiologist's role to gather the evidence for that determination.

"A lot of people jump to conclusions with temporal associations that are not necessarily causal," Carabin says. "We need to study at the individual level to make sure the association is causal. That's our role in public health."

April Wilkerson is editor of OU Medicine, *the official publication of the OU College of Medicine at the OU Health Sciences Center in Oklahoma City.*