REBECCA STUMPF

THE DISEASE DETECTIVE: Dr. Erin Staples and the Hunt for Hidden Viruses

How a music major turned CDC epidemiologist became one of America's leading experts on emerging vector-borne infectious diseases

BY RENÉE GEARHART LEVY

When Erin Staples MD/PhD '00 received a phone call just before Thanksgiving 2015, she could hardly have imagined it would lead her to a hospital waiting room in Brazil, staring at eight children with severe microcephaly—a devastating birth defect that is caused by abnormal brain development leading to small heads and developmental delays. What she witnessed that day would help unravel one of the most significant public health mysteries of the 21st century: the connection between Zika virus and birth defects.

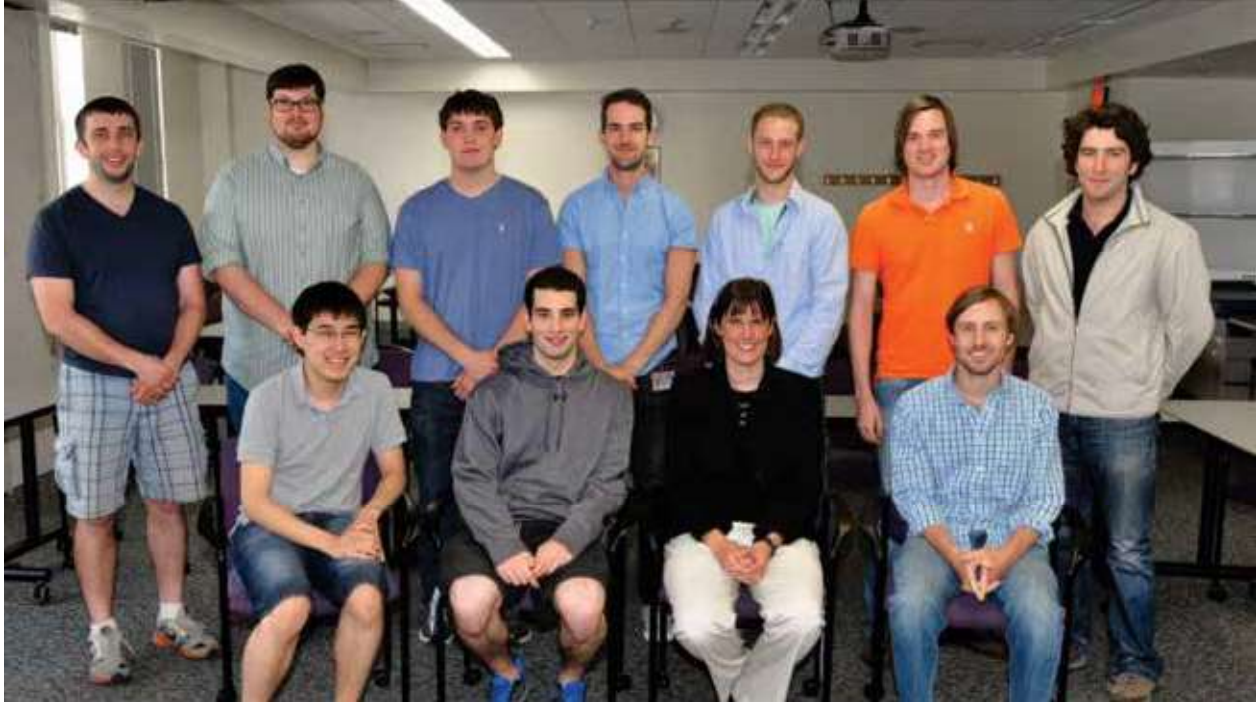
"I had seen maybe one, two cases of microcephaly in all my pediatric practice," recalls Dr. Staples, a senior medical epidemiologist at the Centers for Disease Control and Prevention (CDC). "But then I got there and I'm standing in a waiting room, and there were eight moms and their infants with microcephaly all born at the same time. That's where you start putting those blocks together. How can this be?"

The ability to see patterns where others might see coincidence exemplifies the work of disease detectives like Staples, who spend their careers hunting for emerging pathogens that threaten public health. Over nearly two decades at the CDC, she has investigated outbreaks of everything from influenza in Chicago to plague in Africa and novel tick-borne viruses in Missouri farmland, always asking the fundamental question: What's making people sick, and how do we stop it?

Since 2020, Staples has led the surveillance and epidemiology team for the CDC's Arboviral Diseases Branch in the Division of Vector-borne Diseases. Her team focuses on responding to outbreaks, planning and managing vaccine programs for four vaccine-preventable diseases—chikungunya, Japanese encephalitis, tick-borne encephalitis and yellow fever—and managing disease surveillance systems and public information dashboards.

Her team also assists international partners on various diseases and outbreak responses when more subject matter expertise is required than available in the affected countries, which is what landed Staples in Brazil back in 2015.

"Working together with all of the wonderful scientists at CDC, from virologists to the diagnostic laboratory personnel, and putting the information together



Dr. Staples with Upstate MD/PhD students during a campus visit in 2013

we were able to advise the Brazil Ministry of Health that this did not look like toxoplasmosis. This did not look like cytomegalovirus. This looks like a new entity, and it is likely Zika," she says.

AN UNLIKELY PATH TO MEDICINE

Staples' journey to becoming one of America's foremost experts on vector-borne diseases began in an unexpected place: a music classroom. Born south of Boston, she spent a year of her early childhood traveling the United States in a motor home with her family before they settled in Canton, New York, near the Canadian border, on a self-sustaining organic farm.

"There wasn't a lot of exposure to medicine," she says. "My grandmother had been a nurse for 70 years, starting before antibiotics were readily available and we had a lot of old-fashioned remedies from her to take care of infections and cuts."

Staples remembers often being bored in school, which is why she didn't initially consider medicine as a career option. "I thought, 'I can't spend eight additional years in school,'" she says.

She loved music and played multiple instruments. At St. Lawrence University, she majored in music, an experience that included study abroad in Vienna, Austria. "I focused on music composition," she says.

But along with her general studies requirements, she also took science courses, which provided Staples with the intellectual challenge she'd been seeking.

Through her college's alumni network, she secured a research opportunity at the NIH working with immunologist John O'Shea, MD, HS '81. "He was doing basic science research, but also took me on his rounds at the NIH, where they see all of these patients with medical conditions that didn't really have an easy answer or easy fix," she says. "He and his colleague Dan McVicar, PhD, were both approaching the same problem of understanding the immunologic response to different stimuli."

> "It was kind of a full-circle experience for me, finding and discovering something that was important for an immunologic response in bench research, identifying that as a deficiency in a person, and then being able to treat that."
>
> —ERIN STAPLES MD/PHD '00

Seeing this dual perspective—the clinician's focus on individual patients and the researcher's view of broader patterns—lit a spark for Staples, who decided she wanted to pursue an MD/PhD.

Despite having graduated magna cum laude and a member of Phi Beta Kappa, not everyone was convinced of her aptitude. "When I went to my interviews, some of the people were like, 'Wait a minute, you're an undergraduate music major, you can't be serious,'" she recalls.

THE MAKING OF A SCIENTIST

Staples arrived at SUNY Upstate Medical University in 1993 to pursue her MD/PhD, focusing her dissertation research on factors that influence T cell development. Under the mentorship of Allen Silverstone, PhD, professor of microbiology and immunology, she studied how compounds like estrogen and dioxins affect immune cell maturation, creating knockout mice to understand whether the effect was on the immune cells themselves or their supporting environment.

"With dioxin, it was pretty straightforward that it does target the developing T cells," she explains. "But with estrogen, it was complicated. We were trying to address the issue of why women potentially are more at risk for certain autoimmune diseases, why during pregnancy certain diseases get better or worse."

The research provided crucial insights into fundamental questions about immune function, but it also gave Staples something equally valuable: the methodical approach to problem-solving that would serve her throughout her career. This training proved particularly relevant when she entered pediatrics during her clinical years, drawn by the resilience and honesty of young patients.

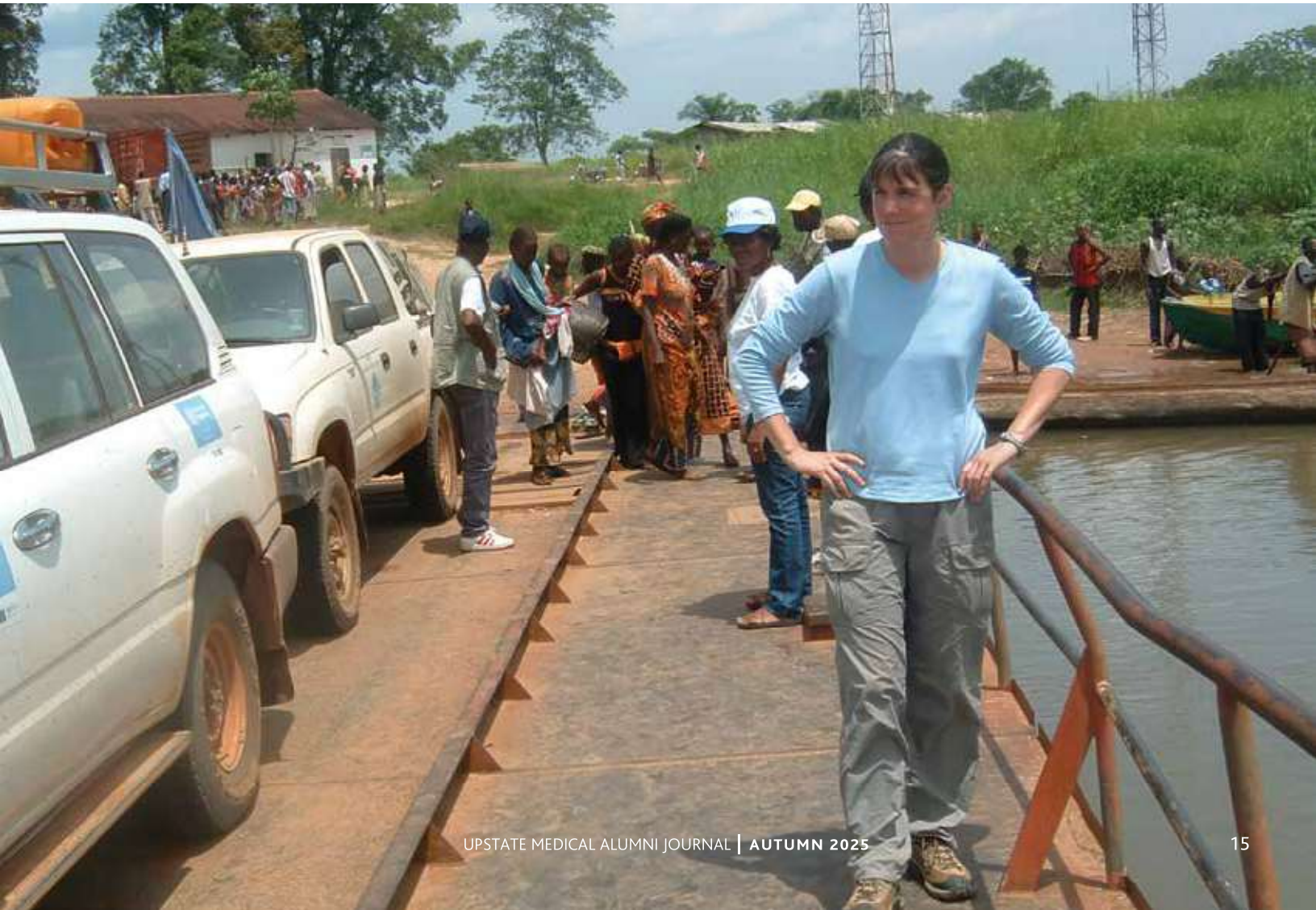
"I never met a kid who really wanted to be sick," she says. "Once we figured out that the girl who had a tonsillectomy just wanted more ice cream, and we negotiated with her mom to buy ice cream on the way home, she was out of the hospital."

Staples went to Duke University for her pediatrics residency, where she trained under Samuel Katz, MD, a developer of the measles vaccine and former chair of the CDC's advisory committee on immunization practices. "He was a good mentor to marry my immunologic background and experiences with pediatrics and I was thankful to match there," she says.

During her residency training, Staples cared for children with severe combined immunodeficiency (SCID)—some of whom lacked the very genes she had helped discover during her NIH research. To help one child with SCID caused by JAK3 deficiency, the team transfected cells with the missing gene. "It was kind of a full-circle experience for me, finding and discovering something that was important for an immunologic response in bench research, identifying it as a deficiency in a person, and then being able to treat it," she says.

Unfortunately, the experimental treatment failed, and the young patient died from an infection during transport to another facility. Not the outcome that the team, including Staples, had hoped for, but the experi-

Dr. Staples on a ferry traveling to a health clinic in the southwest Central African Republic as part of an investigation into the cause of an increase in yellow fever cases. Results from the investigation informed yellow fever vaccination strategy to decrease the risk of disease in the country.



ence reinforced her understanding of how basic science research could directly impact patient care and help save lives.

JOINING THE DISEASE DETECTIVES

Rather than pursuing a traditional fellowship, Staples applied for the CDC's Epidemic Intelligence Service (EIS)—a two-year program that trains physicians in applied epidemiology. The American Board of Pediatrics granted her an exception to combine this training with a pediatric infectious disease fellowship.

"Who wouldn't want to be a disease detective?" she says.

Her EIS assignment took her to the CDC's Bacterial Diseases Branch, where she investigated outbreaks of plague, tularemia, and Lyme disease. Much of her work focused on Africa, where she spent eight months studying antibiotic resistance in plague treatment and experienced the challenge of implementing clinical trials in foreign countries with different healthcare systems and regulatory frameworks.

The experience was "very, very enriching" but also "very challenging," providing Staples with crucial skills in working internationally that would prove invaluable throughout her career.

After completing her EIS training and pediatric infectious disease fellowship, Staples took advantage of an opportunity to join pharmaceutical company Sanofi Pasteur as a vaccine researcher.

"I worked on a couple of different projects, including a delivery platform—a better way to get a vaccine into a person that's easier—and also on combination vaccines in pediatrics. How many antigens or elements can you put in a vaccine and still have it be effective in terms of providing an immune response?"

Staples says the work was rewarding and provided lots of intellectual freedom and resources, yet she found herself wondering if it was the right fit. She found herself drawn back to the kind of public health work she'd done at the CDC.

"Most of what we do at the CDC is really identifying an issue that's causing an infectious disease cluster outbreak and figuring out what that cause is to figure out how to prevent people from getting sick," she says. "We do investigations relative to novel and new diseases and understanding reemerging diseases. We also do investigations to improve our recommendations for vaccines. So, it pulled in a lot of the aspects of all the different phases of the training and experiences that I'd had."

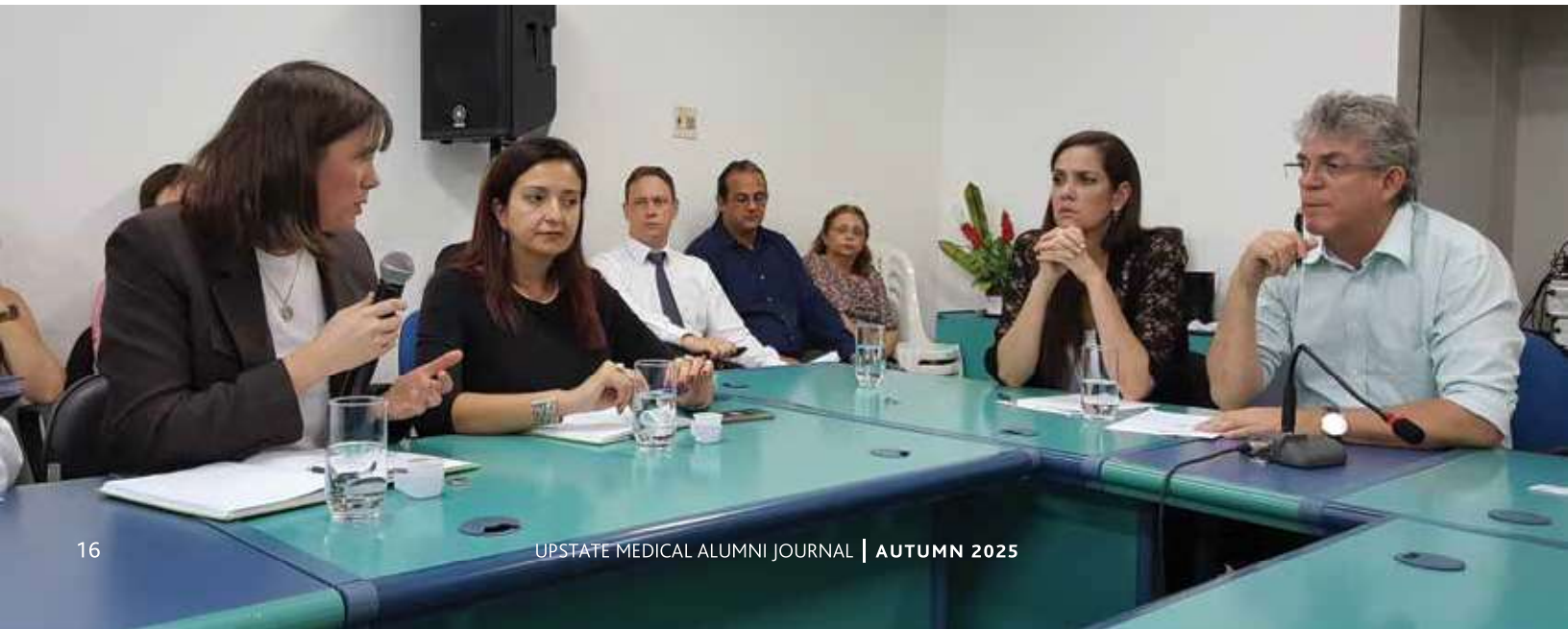
DISCOVERING THE UNKNOWN

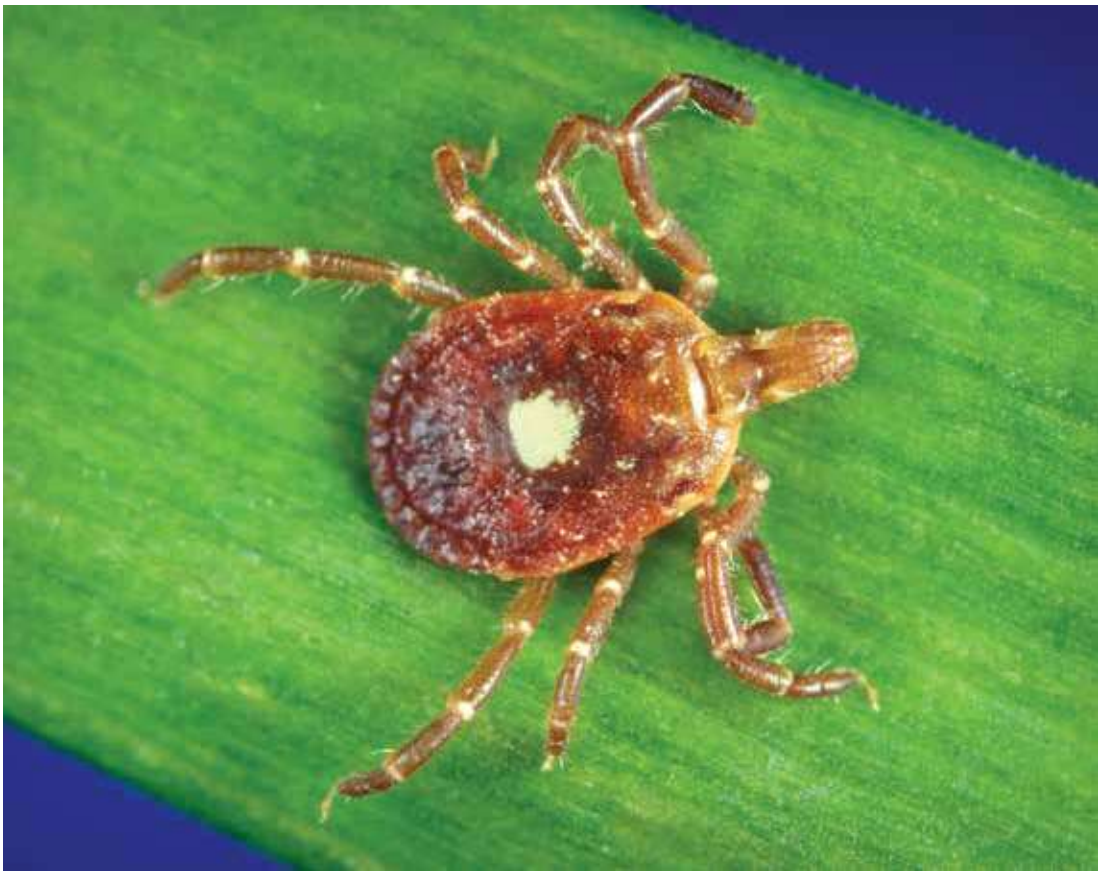
Returning to the CDC in the Arboviral Diseases Branch—focused on viruses transmitted by arthropods like mosquitoes and ticks—Staples settled into work that would define the next phase of her career. Based in the CDC's Fort Collins, Colorado, office, she found herself at the center of efforts to understand and respond to emerging vector-borne diseases.

One of her most significant early discoveries came almost by accident. In 2009, two Missouri farmers arrived at Heartland Hospital within days of each other, suffering from fever, nausea, diarrhea, and rapidly declining white blood cell counts. When their blood samples reached the CDC, laboratory analysis revealed something unexpected: both men had been infected with a previously unknown virus.

"An infectious disease doctor sent some samples to Atlanta on what he thought was patients infected with Ehrlichia," Staples explains. "Well, they cultured it and said, 'This isn't Ehrlichia,' but there was something

Dr. Staples (left) meeting with the Secretariat of Health in Paraiba, Brazil, to discuss the investigation looking at the association between Zika virus infection during pregnancy and microcephaly.





JAMES GATHANY

A female "Lone star tick," *Amblyomma americanum*, which is found in the Southeastern and Mid-Atlantic United States. This tick is a vector of several zoonotic diseases including human monocytic ehrlichiosis and Rocky Mountain spotted fever.

growing causing a problem. That led to the discovery of Heartland virus."

As a newly identified pathogen, Heartland virus presented unique challenges. Staples and colleagues had to develop surveillance systems, diagnostic tests, and prevention guidelines for a disease that had never been formally recognized. "I started with two cases, and I'm supposed to figure out what role does this human pathogen play in human disease? We just found it recently. What does it do?"

The work required collaboration with state health departments to identify additional cases and develop a registry that has now documented more than 60 infections. While searching for Heartland cases, the team made another discovery: Bourbon virus, which causes similar symptoms and is also transmitted by ticks.

"Once we start looking and understanding what we're seeing, we find more things that have probably been present and causing disease for longer than we even knew about," Staples says.

THE ZIKA INVESTIGATION

Staples' experience with novel pathogen discovery proved invaluable when she received that Thanksgiving phone call in 2015. Brazilian health officials were reporting unusual clusters of microcephaly cases, and they needed experts to investigate. The Pan American Health Organization invited her to join an international team assessing the situation.

While the team was investigating, laboratory testing suggested that Zika virus—previously considered a relatively mild tropical disease—might be responsible for the birth defects. The implications were staggering. Zika had been causing occasional outbreaks in Africa and Asia for decades without any reported association with birth defects.

"We had to go back and put those pieces together to prove that it was associated," Staples explains.

The investigation required coordinating multiple scientific disciplines: epidemiologists to track cases, laboratory scientists to confirm diagnoses, and clinicians to document symptoms. In addition to proving causation, the work involved understanding why Zika suddenly seemed more dangerous than before.

The answer lay partly in human susceptibility. "When it came into the Americas, Zika caused large outbreaks because no one had any immunity and

you can see rare complications when more people are infected," Staples explains. As to why we are not seeing the risk from Zika virus as much now, Staples says, "We call it a reservoir in our terminology. After a lot of people were infected, that element was removed. As more people became immune, fewer people could amplify it."

A similar threat Staples is currently investigating is Oropouche virus, another previously obscure pathogen that has recently expanded its geographic range and developed new, more serious symptoms.

"Oropouche virus had been causing periodic outbreaks in the Amazon Basin in South America, particularly in the 70s and 80s," she explains. "But more recently, it kind of pushed its boundaries."

Like Zika before it, Oropouche has begun causing deaths and birth defects—outcomes never previously associated with the virus. "Starting around August 2024, the first deaths due to this virus were recognized. And then the association between children that were born with microcephaly and mothers who had been exposed to Oropouche during pregnancy," she says.

There are many factors that contribute to the emergence of these new threats, including global travel, changes in temperature and weather, deforestation, and urbanization, all of which contribute to bringing humans into contact with previously isolated pathogens. Meanwhile, advances in genetic sequencing allow scientists to identify new viruses faster than ever before.

"There are hundreds of arboviruses or viruses that are transmitted by arthropods—ticks, mosquitoes, and biting midges—that we know about in this world," Staples says. "They've been discovered for decades in several cases, but it's more thinking about 'how do these viruses spread?'"

THE DETECTIVE'S TOOLKIT

Modern disease investigation requires a sophisticated toolkit that has evolved dramatically since Staples began her career. "In the 1990s, PCR (polymerase chain reaction) was brand new. Now we can do sequencing of a whole genome to look for the presence of something that we don't expect there," she says.

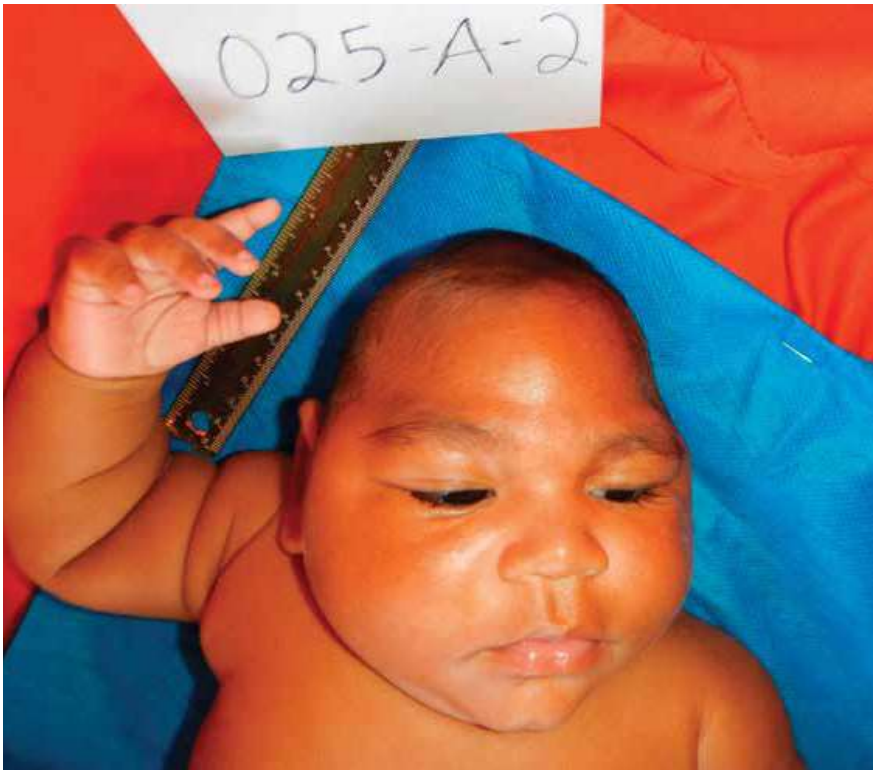
These technological advances have revolutionized pathogen discovery, but they've also highlighted how much remains unknown. Among patients with encephalitis of unknown cause, doctors can identify the culprit in only 20–30% of cases. "It's that 70% of the unknown cases that we're still challenged by," Staples says.

The work requires technical expertise as well as the intellectual curiosity to question assumptions and recognize patterns. "Sometimes we don't think enough, but it's really astute clinicians that are the ones that often bring something to us that lead us to understand in a new way," she says.

This collaboration between frontline clinicians and public health investigators has led to several important discoveries, including the identification of yellow fever vaccine virus transmission through organ transplantation—a previously unknown risk that led to updated prevention guidelines. She's learned through decades of investigation that the next pandemic is just a phone call away.

"Unfortunately, I don't think we're done," says Staples, who has received numerous honors for her work, most recently the CDC's Schuchat Berger Excellence in Leadership in Public Health Service Award for exceptional and unequalled leadership in prevention and control of emergent and domestic arboviral diseases. "There are just a lot of different viruses out there that are able to cause people to get sick that are transmitted by arthropods."

Staples remains committed to the work, driven by the same motivation that led her from music composition to medical research to public health. "It's the ability that I have really to mirror what I love to do



One of the initial infants with Zika virus congenital syndrome from the CDC's investigation in Brazil, which studied the association between Zika virus infection during pregnancy and microcephaly.

Dr. Staples being interviewed for the BBC in Pariaba, Brazil, about Zika virus.

and still feel like I'm making that difference that drew me into medicine in the first place," she says.

Her advice to aspiring physicians and scientists: "Pursue your passions," says Staples, who continues to enjoy playing music in her spare time, particularly when she's joined by her teenage son.

"You don't have to necessarily end up in clinical practice and do the same thing every day if you don't like it. Find where you can pull all of what interests you together and pursue a career that you find incredibly rewarding." ■

AN OUNCE OF PREVENTION

Despite the sophisticated tools available for pathogen discovery and investigation, prevention often remains frustratingly simple—and ignored. "Use your insect repellent," Staples says emphatically. "I've got a can at my front door and my back door, and I don't go outside without it." Other preventive measures include wearing protective clothing (long-sleeved shirts and pants), and being aware of disease risks in different geographic areas. The CDC provides updated surveillance data through online dashboards that track disease activity across the United States. For healthcare providers, Staples emphasizes the importance of maintaining diagnostic curiosity. "Be curious," she says. "Think about what you're seeing and whether it makes sense. Don't just use your UpToDate. Put your minds together and ask, 'Is this normal? Is this really what I think this is?' And if it's not normal, talk it through."