Tracking insect that spreads harmful viruses

By Erin Digitale

In 2016, Stanford infectious disease expert Desiree LaBeaud, MD, sent teams of schoolchildren to hunt for mosquito larvae and pupae around their homes in coastal Kenya. In particular, they were looking for immature Aedes aegypti mosquitoes.

“The kids would say, ‘We found tons. They’re in all these piles of trash at the end of every block,’” said LaBeaud, associate professor of pediatrics at the School of Medicine.

LaBeaud remembers thinking, “Oh, God, now what are we going to do?”

The black-and-white-striped mosquitoes don’t spread malaria, the most famous mosquito-borne disease, but they spread several others, including dengue, chikungunya and Zika, which cause millions of human infections annually throughout the world.

And they adore garbage. Unfortunately, the rural Kenyan communities lacked trash collection and recycling programs. Much of the accumulated litter consisted of discarded, open plastic containers that hold water, where more than 80 percent of the mosquito breeding was taking place, the children and scientists discovered.

For the past several years, LaBeaud’s team has been studying diseases spread by Aedes aegypti and working to reduce outbreaks around the world. Dengue kills about 20,000 people every year; Zika can cause pregnancy loss and serious birth defects; and chikungunya produces debilitating, long-term arthritis in many people.

Drugs and vaccines against the viruses are lacking, so there is a pressing need to understand how mosquitoes and humans interact in order to predict and prevent outbreaks. This is what LaBeaud has set out to do.

Trained as a pediatric infectious disease specialist, LaBeaud said the work requires her to be “half ecologist, half anthropologist.” A variety of factors, such as trash collection practices, household water sources and neighborhood violence levels — can all influence local risk for the viruses in the developing world, her team is learning.

Mosquito-borne illnesses are transmitted by intimate chains of insects and humans: An infected mosquito bites a person, who gets sick and is bitten by other mosquitoes, which get infected and bite more people. Most people recover eventually, but the mosquitoes don’t. An infected insect is thought to keep spreading disease until it dies.

Viruses on the move

LaBeaud’s interest in mosquito-borne diseases began on a 2002 trip to Laos. She had recently finished medical school and was completing pediatrics training at Rainbow Babies & Children’s Hospital in Cleveland, where her residency program included an international health track with rotations in developing countries. Her two-month rotation to Southeast Asia overlapped with monsoon season and a large dengue outbreak.

“I treated a lot of children with dengue and saw a lot of children die from dengue,” LaBeaud said. Although many people make a full recovery, dengue hits hard in vulnerable populations, including babies and kids. It can cause life-threatening hemorrhagic fever — with low blood platelet.

Desiree LaBeaud leads a team that studies diseases spread by Aedes aegypti mosquitoes and that works to reduce outbreaks around the world.

Congenital heart defects vastly increase the risk of heart problems later in life

By Mandy Erickson

An infant born with a relatively simple heart defect is far more likely to develop heart problems as an adult, researchers at the School of Medicine have discovered.

The risk is so great that someone born with a heart defect who has a heart-healthy lifestyle is twice as likely to develop heart problems as someone born without a defect who has a heart-averse lifestyle.

“All of us in cardiology recognize that people with complex disease need follow-up care throughout their lives,” said James Priest, MD, assistant professor of pediatric cardiology. “But for the simple problems, we’ve been thinking that once you close the hole or fix the valve, these patients are good to go.”

The research findings suggest that the medical community should watch adults who were born with heart defects — even minor ones — more carefully. Medications and lifestyle changes may help prevent or delay major heart conditions, such as heart attacks, stroke, heart failure and atrial fibrillation.

A paper describing the research was published Feb. 28 in Circulation. Priest is the senior author; Priyanka Saha, a student at Harvard Medical School who was a research fellow at Stanford from 2017 to 2018, is the lead author.

Most common congenital condition

About 1 percent of infants are born with heart defects, the most common congenital condition. Those with less-complex defects, such as a hole in the heart or a faulty valve, nearly always survive into adulthood, sometimes unaware of the defect until later in life.

To conduct their research, Priest, Saha and their colleagues mined data from the U.K.

Brain response to voice of mom different in kids with autism, study finds

By Erin Digitale

For most children, the sound of their mother’s voice triggers brain activity patterns distinct from those triggered by an unfamiliar voice. But the unique brain response to mom’s voice is greatly diminished in children with autism, according to a new study from the School of Medicine.

The diminished response was seen on fMRI brain scans in face-processing regions and learning and memory centers, as well as in brain networks that process rewards and prioritize different stimuli as important.

The findings were published Feb. 26 in Elife.

“Kids with autism often tune out from the voices around them, and we haven’t known why,” said the study’s lead author, Dan Abrams, PhD, clinical assistant professor of psychiatry and behavioral sciences at Stanford. “It’s still an open question how this contributes to their overall difficulties with social communication.”

The results suggest that the brains of children with autism are not wired to easily tune into mom’s voice, Abrams said. The study also found that the degree of social communication impairment in individual children with autism was correlated with the diminished voice response.
Heart

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Biazik, which includes health data on 500,000 British residents aged 37 to 73 during the biobank’s recruitment period from 2006 to 2010. They found 2,006 people who had mild congenital heart defects.

For reasons the researchers don’t understand, the members of this group were slightly more likely to be obese, to smoke, to have high blood pressure and to have diabetes — all factors that increase the risk for cardiovascular problems.

It’s unclear why adults who were born with heart defects suffer more heart disease.

However, even after adjusting for those risk factors, they found that those born with mild heart defects were 13 times as likely to develop heart failure or atrial fibrillation, five times as likely to have a stroke, and twice as likely to suffer a heart attack than those born without heart defects.

Adult survivors of congenital heart defects with fewer risk factors for heart disease — such as smoking, having high blood pressure and being obese — fared better than those who had more risk factors. Those with a heart-healthy lifestyle were about a third less likely to develop heart conditions than those with five or more heart disease risk factors.

A mystery

It’s unclear why adults who were born with heart defects suffer more heart disease, the study said. The researchers propose several possibilities, including the timing of surgery, genetic predisposition and cellular dysfunction.

“Is it the surgery? Could it be the medications? Or is it something intrinsic to having congenital heart disease? We don’t know,” Priest said, adding, “We don’t know why infants have congenital heart disease to begin with.”

Saha said further research into why congenital heart disease leads to adult heart problems could help shape follow-up care. But physicians can begin helping these patients right away by providing more surveillance.

“This is something that can change right now,” she said. “We can start connecting them with cardiology specialists.”

Other Stanford co-authors of the study are Praneetha Abrams and Menon demonstrated.

Autism

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the degree of abnormality in their brain responses to their mother’s voice. “This study is giving us a handle on vocal stimuli that we have to make more engaging for a child with autism,” said Menon.

An important social cue

Mom’s voice is an important social cue for most children. For instance, tiny babies recognize and are soothed by their mother’s voice, while young teenagers are more comforted by words of reassurance spoken by their mothers than the same words sent by their peers via text message, prior research has shown.

The response to mom’s voice begins as a distinct brain-activation signature in children without autism, a 2016 paper co-authored by Abrams and Menon demonstrated.

Autism is a developmental disorder that affects 1 in 59 children. It is characterized by social and communication difficulties, restricted interests and repetitive behaviors. The disorder exists on a spectrum, with some children more impaired than others.

The new study included 42 children ages 7 to 12. Half had autism, and the other half didn’t. The children had their brains scanned using functional magnetic resonance imaging while listening to environmental sounds, to mom’s voice versus unfamiliar voices, and to environmental sounds, was fairly similar in children with and without autism, researchers said.

The brain response to unfamiliar voices, when compared with the response to environmental sounds, was fairly similar in children with and without autism, although those with autism had less activity in one area of the auditory association cortex.

When comparing the brain response to mom’s voice versus unfamiliar voices, children without autism had more brain areas activated: Mom’s voice preferentially lit up parts of the hippocampus, a learning and memory region, as well as face-processing regions.

Brain-connectivity patterns measured in a network that included auditory-processing regions, reward-processing regions and regions that determine the importance, or salience, of incoming information also distinguished children with autism from children without autism. The network impairments in individual children with autism were also linked to their individual level of social communication impairment.

‘Really striking relationship’

“There is this really striking relationship between the strength of activity and connectivity in reward and salience regions during voice processing and children’s social communication activity,” Abrams said. This suggests that brain responses to mom’s voice are a key element for building social communication ability, he added.

The findings support the social motivation theory of autism, which suggests that social interaction is intrinsically less engaging for children with the disorder than those without it.

Many current autism therapies involve motivating children to engage in specific types of social interaction, and it could be interesting to conduct future studies to see whether these therapies change the brain characteristics uncovered in this study, the researchers said.

“Mom’s voice is the primary cue for social and language communication and learning,” Menon said. “There is an underlying biological difference in the brain circuitry in autism, and this is a precision-learning signal we can target.”

Other Stanford authors of the paper are Aarthi Padmanabhan, PhD, scientific research director in the Menon lab; former postdoctoral scholar Tianwen Chen, PhD; former research assistants Paola Odrizola and Amanda Baker; graduate students Linda Chen and Jacques Penney, PhD, and clinical associate professor of psychiatry and behavioral sciences.

Menon is a member of Stanford Bio-X, the Stanford Mater- nal & Child Health Research Institute and the Wu Tsai Neurosciences Institute at Stanford.

The research was supported by the National Institutes of Health and the Sarnoff Cardiovascular Research Foundation. Stanford’s departments of Pediatrics and of Cardiothoracic Surgery also supported the work.

Autism

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For most children, their mother’s voice is an important social cue.

The disorder ex-
levels and breeding — as well as dangerous drops in blood pressure. "It's terrible to have to say, I'm sorry, we can't save them," LaBeaud said.

The suffering of her young Laotian patients motivated LaBeaud to study outbreaks of neglected tropical diseases. After her residency, her pediatric infectious diseases fellowship had taken her to Kenya, where she fell in love with the complexity of figuring out how mosquitoes and their insect-borne viruses interact. "These viruses have both sneaky, insidious transmission and large, overwhelming outbreaks," she said.

LaBeaud said she learned that insect-borne viruses were on the rise globally. "I watched 70, 80, 100, documents have been documented in nine countries. Today it's in more than 100 countries, putting more than 40 percent of the world's population at risk," she said. "Chikungunya has been found only in Africa, Asia and India, but it is now being reported in Europe and throughout the Americas. Zika has also continued from page 1

"We pivoted our study; the message really became 'Dump out your buckets.'" Forsyth said. The researchers worked with local residents on taking actions that could reduce mosquito breeding, such as storing unused containers upside down. And they challenged 250 children involved in the study to see who could collect the most no-purpose containers. The kids collected 1,000 kilograms of plastic waste, consisting of more than 17,000 containers. They used 4,000 of the containers to sprout native tree seedlings, which were planted around their communities.

"We pivoted our study; the message really became about reducing and reusing plastics," Forsyth said. The researchers worked with local residents on taking actions that could reduce mosquito breeding, such as storing unused containers upside down. And they challenged 250 children involved in the study to see who could collect the most no-purpose containers. The kids collected 1,000 kilograms of plastic waste, consisting of more than 17,000 containers. They used 4,000 of the containers to sprout native tree seedlings, which were planted around their communities.

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Stanford Medicine magazine details efforts to improve health worldwide

By Patricia Hannon

Whether enlisting children in Kenya to scour neighborhoods for mosquito larvae or helping Zimbabwean children get treatment for chronic conditions, Stanford Medicine doctors and physicians are taking on some of the world’s most pressing health issues know they can’t do it alone.

“We share this planet with billions of people, a rich panoply of cultures, languages, beliefs and interests. Yet amid this diversity, we also share a universal yearning: to enjoy healthy lives,” Lloyd Minor, MD, dean of the School of Medicine, wrote in his letter introducing the new issue of Stanford Medicine magazine.

The issue explores Stanford’s Medicine’s collaborative efforts at home and abroad to battle conditions that are central to some of the world’s overarching health concerns — poverty, pollution, mosquito-borne disease, a dearth of trained clinicians and limited access to care.

Many of the stories in the issue examine partnerships between clinicians, universities, businesses and government agencies to improve health internationally:

• While serving as an adviser in establishing the first pediatric ear, nose and throat clinic in Zimbabwe, a pediatric otolaryngologist witnesses the incredible demands that clinicians there face in treating children with conditions that have historically been neglected. Also, longtime partnerships are helping clinicians and educators at Stanford and in Zimbabwe learn from each other and improve health care in the process.

• An epidemiologist who has spent eight years in Bangladesh describes the challenge of reducing air pollution in the country by convincing brick kiln operators to convert to cleaner brick-making technology.

• Working in the United States, an infectious disease expert and her colleagues aim to predict and prevent deadly outbreaks of diseases that insects spread by better understanding how mosquitoes and humans interact.

• A call to cultivate more women in leadership positions at medical institutions has led to a global movement among women in health care to take charge of improving health outcomes around the world.

• The first physician to lead the World Bank — Jim Yong Kim, MD — talks about initiatives to end poverty that call for investing in better education and health care for the poorest people.

• A program for medical residents who are interested in global health is designed to give them the skills and understanding they need to help develop solutions.

• A doctor and an engineer participating in a Stanford-India Bodesign Fellowship team up to invent a resuscitation device that improves on the cumbersome technique used to help newborns breathe on their own.

Also in this issue, read about researchers who are on a quest to learn why some pain becomes frustratingly chronic and agonizing, and how research they’re doing on mice might provide answers that help patients.

And read about how the chemical interactions that lead to cell death could inspire therapies for such diseases as cancer, rheumatoid arthritis and multiple sclerosis.

Print copies of the magazine are being sent to subscribers. Others can request a copy at (650) 723-6911 or by sending an email to medmag@stanford.edu.

IS M

LEAH BACHKUS, MD, MPH, associate professor of cardiothoracic surgery, was awarded $55,000 for the Levis, Innova-tion and Leadership Development Scholarship from The Thoracic Surgery Foundation. She also won the Thoracic Scholarship from The Thoracic Surgery Foundation. She also won the Thoracic Scholarship from The Thoracic Surgery Foundation.

MITCHELL LUNN, MD, MPH, associate professor of pediatrics, was appointed to the Committee on Assessing Health Outcomes by Birth Settings, a project within the National Academies of Sciences, Engineering and Medicine. The project aims to provide an evidence-based analysis of research findings about improving birth environments, such as hospital versus home, focusing on the health outcomes of sub-populations of women. His term ends on March 31, 2020.

NOLAN WILLIAMS, MD, was appointed assistant professor of psychiatry and behavioral sciences, effective Feb. 1. His research focuses on understanding the factors of influence the health of sexual and gender minority people, including health disparities, societal experiences, provider education and institutional and structural inequity. He co-directs the PRIDE Study, a longitudinal study of sexual and gender minority adults.

RUTH O’HARA, PhD, was promoted to professor of psychiatry and behavioral sciences, effective Dec. 1. Her research investigates the relationship between neurocognitive and neuropsychiatric symptoms across the lifespan, with emphasis on the identification of biological and sleep biomarkers of neurodevelopmental and neurodegenerative disorders.

ZARA PATEL, MD, was promoted to associate professor of otolaryngology-head and neck surgery, effective Jan. 1. She specializes in advanced endoscopic sinus and skull base surgery, and her research interests include studying ways to avoid complications in sinus surgery, developing new devices and techniques for sinus and skull base surgery, and improving treatment for olfactory loss.

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MELINDA TELLI, MD, was promoted to associate professor of medicine, effective Jan. 1. She leads the breast oncology clinical research group at the Stanford Cancer Institute, and her research focuses on developing new therapies to treat triple-negative and hereditary breast cancers, including targeting tumors with DNA-repair defects.

NOLAN WILLIAMS, MD, was appointed assistant professor of psychiatry and behavioral sciences, effective Feb. 1. His research focuses on developing new therapies to treat triple-negative and hereditary breast cancers, including targeting tumors with DNA-repair defects.

OF NOTE

Leah Backhus
Robert Castro
Dylan Griswold
Eleni Linos
Mitchell Lunn
Ruth O’Hara
Zara Patel
Jochen Profit
Melinda Telli
Nolan Williams

Reports on significant honors and awards for faculty, staff and students.

ZARA PATEL

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