

EMORY | Medicine

WINTER 2018

**SPIN DOCTOR: The hazards
of taking care of others
at the expense of yourself** 24



WHAT'S INSIDE: HEART STORMS 16 **INSIDE A MIGRAINE 32** **LEARNING FROM LAMPREYS 36**

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THE BIG PICTURE

ON THE ROAD AGAIN

A manikin from Emory's Center for Experiential Learning appears to be enjoying an outing to Emory University Hospital Midtown on the shuttle. "Hal" breathes, blinks, has a pulse and reactive pupils, and can be defibrillated and intubated, providing a safe training environment, says his handler, Kim Fugate, associate director of the center.



Supporting Physicians



VIKAS P. SUKHATME, MD, ScD
Dean, Emory School of Medicine
Chief Academic Officer, Emory
Healthcare

As the new dean of Emory School of Medicine, I am struck by the commitment and passion of our faculty, staff, and students in keeping and making people healthy.

I am also impressed by the vigorous support of our tripartite mission of patient care, discovery, and education from alumni, board members, and Emory well-wishers.

In an academic health center, the focus is primarily on serving others—providing the highest level of patient care, developing life-saving treatments and technologies, and teaching and mentoring future doctors.

In this as in every issue of *Emory Medicine* magazine, we showcase ways our teams are helping to make others' lives better: You will hear from patients with mysterious heart maladies whose doctors diagnosed and treated them with a blend of clinical skills and creativity (p. 16), sit in on the latest Dinner with a Doctor, which focuses on migraine solutions (p. 32), and discover what researchers are learning about the human immune system by studying ancient, jawless parasites (p. 36).

But what about the level of service and care we provide to our physicians and other medical team members themselves? In "Healing the Healers," we address head-on an epidemic that medical schools and academic health centers have ignored for far too long: high rates of physician stress, distress, and burnout.

There isn't an easy fix. It will take commitment on the part of the entire medical community to change the organizational culture, implement systemic solutions, and provide appropriate resources.

Only when our healers feel strong and supported can we say we've truly fulfilled our mission of spreading wellness. Indeed, it adds another dimension to that mission: to restore the joy of working in medicine.



Download our iPad app (search under **Emory Health magazines**). Bonus features are online at emorymedicinemagazine.emory.edu.

Emory Medicine

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Emory Medicine's staff got a behind-the-scenes tour of the new Emory Sports Medicine Complex and Atlanta Hawks training facility, which had its grand opening in November. Art Director Peta Westmaas (above) compares her shoe to a Hawks player's size 20.



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“I did not feel it coming. I felt a little warmth on the top of my head, and I just ... went to sleep.”

—Nils Ericson

FEATURES

Heart Storms 16

Patients share personal stories of surviving cardiac emergencies: a tumor that caused a continual “fight or flight” response, a cardiac arrest stemming from an “electrical storm,” and a ruptured aorta at basketball practice.

Healing the Healers 24

Physician burnout is at an all-time high and, too often, preferred solutions (“Do yoga!” “Sleep more!”) are superficial at best. We go straight to the source to discover what causes physician stress and what can be done to better care for our care providers.

Dinner with a Doctor: Migraines 32

Neurologist Greg Esper, who suffers from migraines himself, sits down with a small dinner group to talk about the latest tactics and treatments to prevent migraines.

Learning from Lampreys 36

Immunology pioneer Max Cooper and researchers in his lab are hoping that an ancient immune system can provide therapeutic insights into our own.



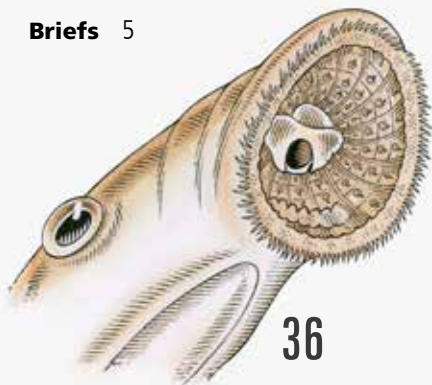
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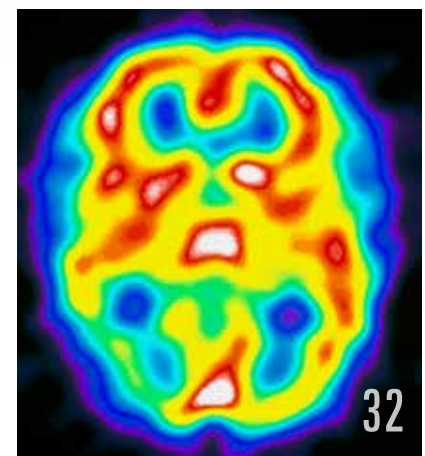
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Short pieces about what it's like to be the new doctor in the room.

Last Word: The Other End of the Stethoscope 44

A medical student learns a powerful lesson as his physician father becomes a patient in the hospital where he practices.

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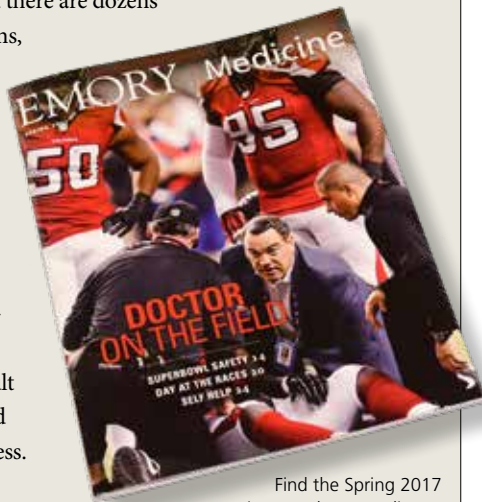


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Letters

Re: “Experts Weigh In” (Spring 2017). I am a retired pediatrician who practiced for more than 40 years. When I was in training, immunizations for children were very simple: DPT, polio, smallpox. Today, the children’s vaccine schedule runs to four fold-out pages in the *American Academy of Pediatrics* journal and there are dozens of footnotes (caveats, warnings, contraindications, etc). It changes frequently. Adults also need help getting protected from vaccine-preventable diseases, but most medical providers don’t even ask their patients about vaccines. If a patient searches the internet for information on adult vaccines and schedules he/she is quickly sent to a vaccine-denying website. Some vaccines are recommended but third-party payers may or may not pay for them. Then there is the problem that most primary care adult providers don’t have vaccines in their offices and patients are left going to a pharmacy. What a mess. It is good to be retired.

Robert Rhea Earnest 68M
Waynesville, N.C.



Find the Spring 2017 issue and more online at emorymedicinemagazine.emory.edu

Answer from Dr. Walter Orenstein: I agree that the immunization schedule has gotten very complex. I trained in pediatrics during the 1970s and one could actually memorize the schedule. My hope is that electronic medical records, with prompts, will make this easier for physicians and nurses by telling them immediately what vaccines are needed. My impression over the years is how many more diseases we can prevent. My own son had a pneumococcal bacteremia prior to the availability of vaccines. It was very scary. Thank God he recovered and is fine. But the impact of vaccines is miraculous and new vaccines are on the way. Best wishes in retirement.

A dear friend sent me the article “Dying of Embarrassment” (Spring 2017). I am 64 and was diagnosed two years ago with squamous cell carcinoma in situ of the anus after a routine colonoscopy. Because it was in situ, [meaning it had not metastasized] we kept a close watch on it. In August, I had a follow-up colonoscopy and discovered it had become Stage I. I completed six weeks of chemo and radiation last fall and was declared cancer free. Fortunately for me it was caught early, though we are still keeping a close watch. I am sharing all of this because of the stigma that is placed on this type of cancer. I found it embarrassing when trying to explain to people the type of cancer I had. Everyone assumed that I had breast cancer when my hair fell out, and when I explained, they seemed embarrassed, too. It took me weeks to be able to be comfortable with sharing that I had anal cancer. I actually had a co-worker ask me if they found it through a pap smear. Really! I then knew that I needed to educate people. I want to thank Emory for the clinical trial and wish you all the best as you continue on this journey to educate and save lives.

Pat Sebo, councilwoman
Jonesboro, Ga.

We like to hear from you. Send us your comments, questions, suggestions, and castigations. Address correspondence to *Emory Medicine* magazine, 1762 Clifton Road, Suite 1000, Atlanta, GA 30322; call 404-727-0161; or email mary.loftus@emory.edu.

Experts Weigh In

“Prior to 2004, most women and many doctors—including cardiologists—thought that heart disease was a ‘man’s disease,’ and were not even looking for heart disease in women. But now we know that particularly after menopause, which nowadays is almost half your life, there is generally a worsening of blood pressure, cholesterol, diabetes, and other cardiovascular risk factors.”

Cardiologist and Assistant Professor
Gina Lundberg, clinical director of Emory Women’s Heart Center, *Cardiology Today*.

“As we age, we lose certain aspects of our brain function—our spot-on memory for specific events and details, for one—but we gain a lot too. It’s not really a downhill process. You’re just trading different strengths and weaknesses.”

Emory Assistant Professor of Medicine
Sharon Bergquist, *SilverSneakers*.

“I can’t tell you how many providers don’t want to ask. There’s so much stigma attached to identifying women who are drinking. Alcohol is so pervasive in our culture. But no one wants to talk about it.”

Psychiatrist and Emory Assistant Professor
Julie Kable, *STAT*.

Second Sight for Ebola Survivors

There are 17,000-plus Ebola survivors in West Africa. About 20 percent have a severe inflammation inside their eye, uveitis, that can cause blindness. Even if it resolves, cataracts can follow—some in children as young as five.

Surgeons have hesitated to remove cataracts from Ebola survivors for fear that their eyes might still harbor the virus.

Making use of information gleaned from Ebola survivors treated at Emory, a team of Emory doctors is working with Ebola survivor and physician Ian Crozier on an initiative in Sierra Leone to help doctors safely perform

eye surgery on Ebola survivors.

Crozier himself experienced post-Ebola complications, including uveitis and a cataract.

By evaluating the ocular fluid in patients' eyes, the team (ophthalmologists Steven Yeh, Brent Hayek, Jessica Shantha, and infectious disease physician Colleen Kraft) can determine whether it might be possible for the virus to spread to a surgeon. All evaluations so far have been negative.

“There continues to be tremendous need—funding, resources, and education—to strengthen health systems for survivors here in the wake of the outbreak,” Yeh says.—*Emily Sullivan 18C*



Photo of young eye patient taken by Emory medical team in West Africa.

Genetic Detective Work

Two brothers from the Palestinian territories shared a strange malady. The rare disorder was characterized by significant diarrhea beginning soon after birth, low levels of fat-soluble vitamins, and evidence of liver disease.

A multinational team from Atlanta, Jerusalem, and the Palestinian territories identified what the brothers had: a previously undiscovered genetic mutation involving the transportation of bile. Researchers from Emory and Children's Healthcare of Atlanta, Makassed Hospital at Al-Quds University, and Hadassah Medical Center at Hebrew University of Jerusalem, collaborated on the cases. "Since they are the first cases of this new genetic disease ever described, we don't know how the disease will present as they get older," says Emory pediatric GI and hepatology researcher Paul Dawson. "We'll continue to closely follow them." Mutaz Sultan, a pediatric hepatologist at Makassed Hospital, treated the children and ruled out other causes, such as cystic fibrosis. Sultan and Bassam Abu-Libdeh, med-

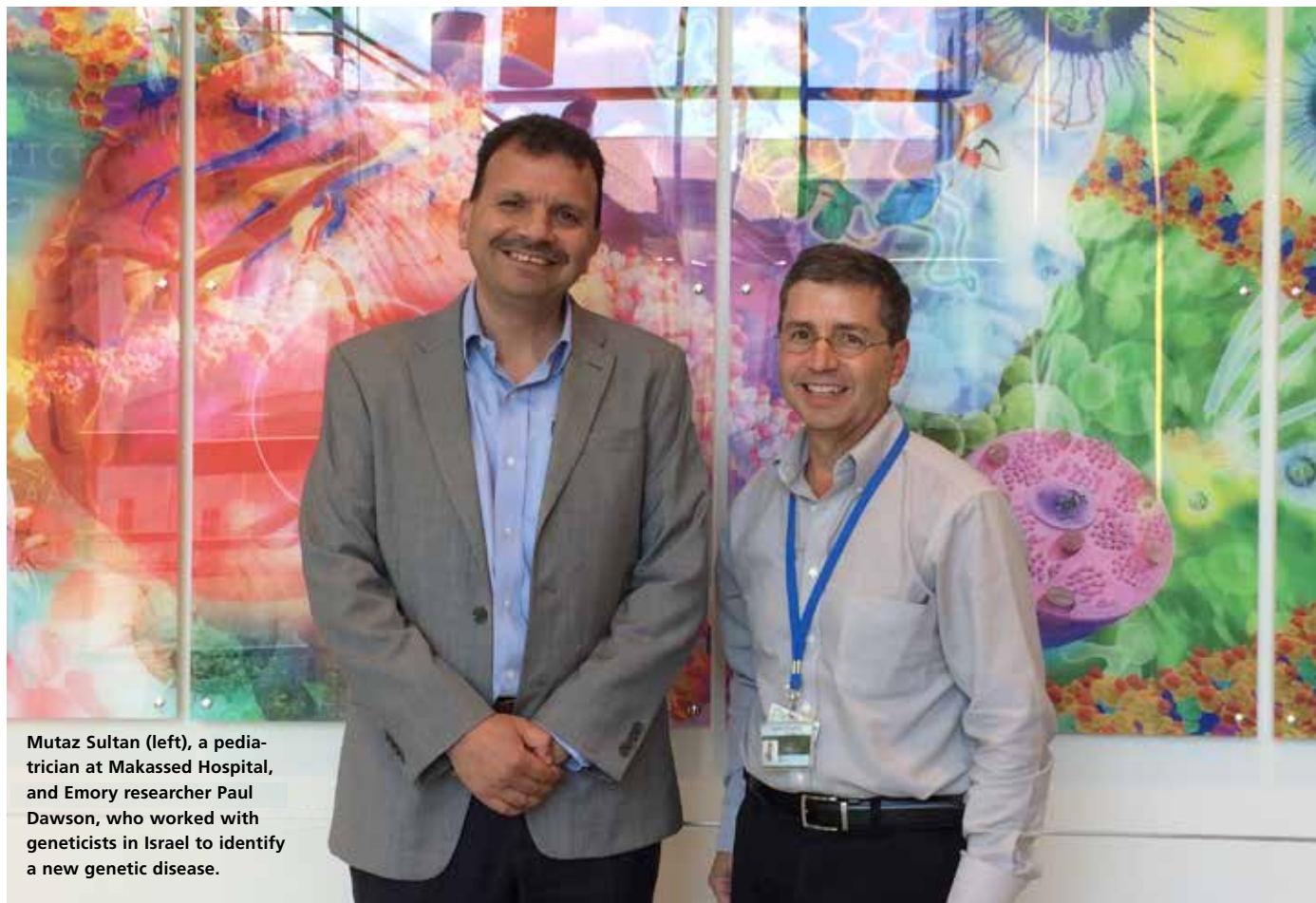
ical director at Makassed, worked with Orly Elpeleg, head of the Department of Genetics and Metabolic Diseases at Hadassah Medical Center, to perform whole exome sequencing.

Genetic testing showed that both children had inherited a mutation in a gene responsible for the transport of bile acids, which facilitates the digestion and absorption of dietary fats and fat-soluble vitamins.

Dawson and Saul Karpen, Raymond Schinazi Distinguished Professor of Pediatrics, run an Emory lab that investigates the role of bile acids in liver and GI disease. Dawson and pediatric researcher Anuradha Rao tested the effects of the mutation in cells. The discovery will help with the genetic identification of the disorder in other patients, and will help guide the boys' treatment. Medications can

help, along with fat-soluble vitamin supplements and dietary changes. "The key to discovering this new cause of childhood disease was the outstanding international team of physicians and scientists," Dawson says. ■

"The boys are doing well thanks to the efforts of their physician and parents to watch their diet and give them high doses of vitamins. I am hopeful for their future."—PAUL DAWSON

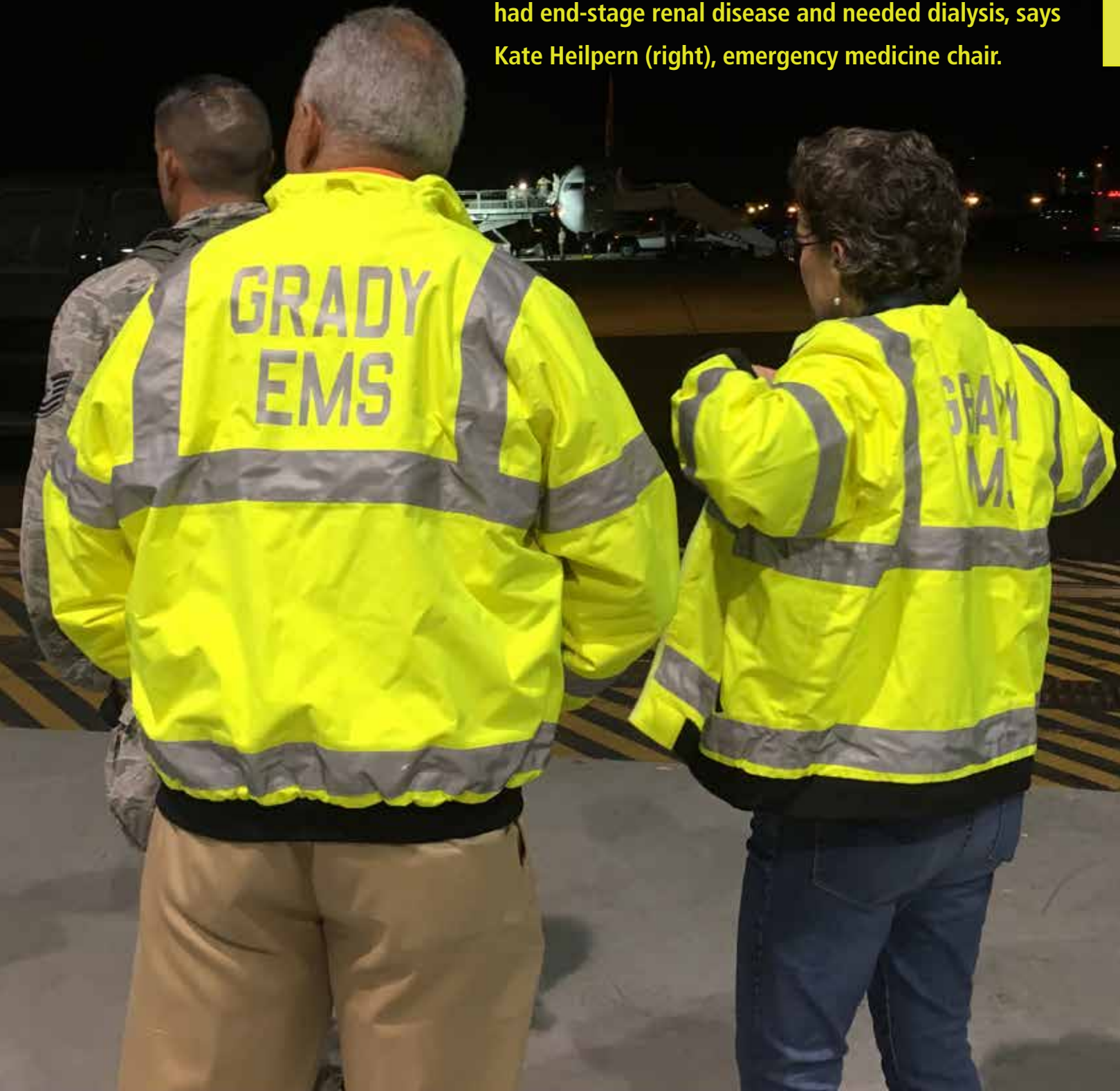


Mutaz Sultan (left), a pediatrician at Makassed Hospital, and Emory researcher Paul Dawson, who worked with geneticists in Israel to identify a new genetic disease.

PHOTO BY ANURADHA RAO

TRIAGE ON THE TARMAC

SEPT. 24: Emergency medicine physicians from Emory met nearly 70 patients flown in to Dobbins Air Reserve Base from the Caribbean after Hurricane Maria. Most had end-stage renal disease and needed dialysis, says Kate Heilpern (right), emergency medicine chair.



Extra Hours for Stroke Treatment

Current guidelines for stroke treatment recommend clot removal only within six hours of the onset of symptoms.

But a milestone study recently published in the *New England Journal of Medicine* shows that clot removal up to 24 hours after a stroke led to significantly reduced disability for some patients.

"These findings could impact countless stroke patients who often arrive at the hospital after the current six-hour treatment window has closed," says co-principal investigator Raul Nogueira, professor of neurology, neurosurgery, and radiology at Emory and director of neuroendovascular service at the Marcus Stroke & Neuroscience Center at Grady Hospital.

The international study randomly assigned 206 stroke victims who arrived at the hospital within six to 24 hours to either endovascular clot removal (thrombectomy) or standard medication therapy. Almost half of the patients who had clot removal showed a considerable decrease in disability, and had resumed independent living 90 days after treatment. Only 13 percent of the medication group had a similar decrease. There was no

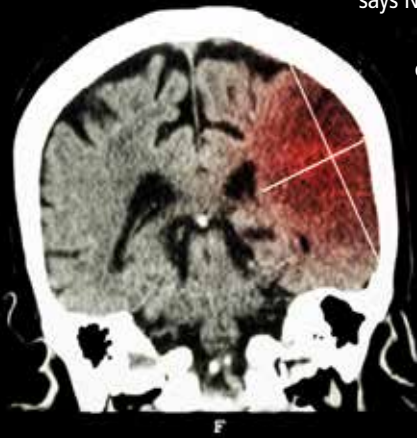
difference in mortality between the two groups.


"This does not diminish the urgency with which patients must be rushed to the ER in the event of a stroke," says co-principal investigator Tudor Jovin, director of the University of Pittsburgh Medical Center Stroke Institute. "The mantra 'time is brain' still holds true."

To select patients for the trial, the researchers used brain imaging and clinical criteria instead of time alone. "Looking at the physiological state of the brain and evaluating the extent of tissue damage and other factors seems a better way to decide if thrombectomy will benefit patients as opposed to adhering to a rigid time window," says Nogueira.

The trial was ended early after it was found that clot removal provided significant clinical benefits.

"Our teams are immensely proud of these breakthrough findings, which are so profound they will likely result in a paradigm shift that will not be seen again for many years in the field of stroke therapeutics," says Michael Frankel, professor of neurology at Emory and director of the Marcus Stroke and Neuroscience Center.—Jennifer Johnson



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THE BIG IDEA

Fighting Fire With Fire

Many of us are familiar with the quick, painful sting of the tiny red fire ant. But a recent study has shown that there might be a way to put that venom to good use.

Compounds derived from fire ant venom can reduce skin thickening and inflammation in a mouse model of psoriasis, Emory and Case Western Reserve scientists have shown.

These findings could lead to new treatments for psoriasis, a common autoimmune skin disease, by

restoring the skin's barrier function. "Emollients can soothe the skin in psoriasis, but they are not sufficient for restoration of the barrier," says lead author Jack Arbiser, professor of dermatology at Emory.

Topical steroids are frequently used for mild to moderate psoriasis, but they have side effects such as skin thinning and easy bruising. Venom-derived compounds, Arbiser says, could be used in combination with existing approaches.—*Emily Sullivan 18C*



Research Funding Tops \$628 Million

Researchers at Emory received \$628 million from external funding agencies last year, marking the eighth consecutive year that research funding has exceeded \$500 million. Growing from \$574.6 million last year, this is the largest amount of research funding in Emory's history.

Federal agencies awarded \$384 million, or more than 61 percent of the total, led by the National Institutes of Health with \$320 million. NIH funding represented more than 83 percent of total federal dollars awarded to Emory.

"Despite continued funding challenges at the federal level, our research programs have continued to attract support because of demonstrated groundbreaking results and the promise of future discoveries with the potential to change the face of science and medicine," says David Stephens, vice president for research in Emory's Woodruff Health Sciences Center (WHSC).

Researchers in the WHSC received \$584.8 million last year, more than 93 percent of the university total, with \$353.7 million in federal funding.

Emory School of Medicine received \$355.7 million, the Rollins School of Public Health received \$131.7 million, Yerkes National Primate Research Center received \$79 million, and the Nell Hodgson Woodruff School of Nursing received \$15 million.

Examples of Emory's externally funded projects included the following:

- Earning a comprehensive cancer center designation from the National Cancer Institute for Emory's Winship Cancer Institute, reflecting its research, clinical trials, and population-based science.
- Investigating improved post-transplant drug regimens for organ recipients through the Emory Transplant Center.
- Studying 3q29 deletion syndrome, a genetic mutation associated with an increased risk for schizophrenia and other neuropsychiatric conditions.
- Working to decrease HIV incidence and improve the well-being of infected individuals through continued support of the Emory Center for AIDS Research. ■



Hidden Link

Lowering blood pressure may lower Alzheimer's risk

The new threshold for high blood pressure begins at 130/80 mm Hg rather than 140/90. This adds 30 million adults to the ranks of those being treated with lifestyle changes or medicine for high blood pressure, for a total of 100 million—nearly half of all adults in the U.S.

This earlier treatment might be good news for another reason, says geriatric neuropsychologist Felicia Goldstein, a professor in Emory's Department of Neurology who believes that diseases like Alzheimer's may be linked to high blood pressure.

"Hypertension may be a modifiable risk factor for Alzheimer's disease, in contrast to other known risk factors such as advanced age, female gender, and family history," she says. "Therefore, there is the ability to make lifestyle changes."

Hypertension should be aggressively treated in young adults, given the strong evidence for a relationship between midlife hypertension and the risk for cognitive impairment and Alzheimer's disease in late life, she says. Goldstein recommends a personalized approach that addresses issues including psychosocial stressors, poor lifestyle habits, such as tobacco use, and the presence of other vascular comorbidities, such as diabetes and heart disease. ■

After Ebola Outbreak: Lessons Learned



Emory infectious disease experts train first responders on the proper donning and doffing of protective clothing.

PHOTO BY JONATHAN ROSEN

In the wake of caring for four patients with active Ebolavirus in 2014, Emory clinicians have taken stock of lessons learned in infectious disease prevention, therapeutic care, and health aftereffects and are sharing that information broadly with other health care professionals and first responders.

Alexander Isakov, emergency medicine physician and director of the Emory Office of Critical Event Preparedness and Response, was in charge of the transport of the aid workers who were infected in West Africa and flown to Atlanta, where they were cared for in Emory's Serious Communicable Diseases Unit under the direction of Bruce Ribner.

Isakov and Ribner used their experiences to improve nationwide infectious disease preparedness. "Managing infected patients requires effective education and training so workers can do their jobs safely," says Isakov, who adds that the decision to accept and treat the Ebola patients at Emory was based on confidence in the staff's preparedness, including 12 years of training in managing highly infectious diseases.

Isakov leads the Emory Ebola Biosafety and Infectious Disease Response Program, which helps to spread this knowledge and provide education and training for workers who face risk of occupational exposure. The program is part of the National Institute of Environmental Health Sciences Worker Training Program, which provides infectious disease and response training for health care providers, laboratory technicians, janitors, garbage handlers, first responders, morticians, and others.

The Emory program trains first responders to do the following:

- Properly put on and remove personal protective equipment (see next page)
- Prepare an ambulance to safely transport a patient while protecting surfaces from contamination
- Recognize risks and use strategies to safely manage infected patients
- Implement standards and precautions to prevent contact with infectious bodily fluids

Emory also offers a Clinical Biosafety Awareness Course for workers who might be at risk. "Although the Ebola outbreak

was the primary impetus for our program, the training will have an impact on managing many other infectious diseases," Isakov says. "This will help our nation be better prepared for the next epidemic or pandemic."

Another effort involves the medical team that treated Ebola patients partnering with the Emory Center for Digital Scholarship to develop a virtual experience of treating critically ill patients in a place like the Serious Communicable Diseases Unit at Emory University Hospital. Ribner and colleagues plan to create a series of



Caring for patients with diseases like Ebola requires special precautions from transport to the isolation unit.

PHOTO BY JONATHAN ROSEN

360-degree videos that will simulate protocol steps such as donning and doffing personal protective equipment and being aware of points of contact to avoid cross-contamination.

A \$12 million federal grant awarded in 2015 to Emory, University of Nebraska Medical Center, and NYC Health + Hospitals/Bellevue to establish the National Ebola Training and Education Center (NETEC) has been doubled to \$24 million for additional site visits, more training courses, a special pathogens research network, and other services. ■

Suit Yourself

Personal Protective Equipment (PPE) suits are standard issue for medical team members working in Emory Hospital's Serious Communicable Diseases Unit with patients who have Ebola, Lassa, or other deadly infectious diseases.

PPEs must completely cover the clothing and skin to protect mucous membranes and broken skin.

Procedures for donning and doffing (taking on and off) PPEs are detailed and essential. A trained colleague watches to make sure a step isn't forgotten.

A powered air purifying respirator (PAPR) is used to keep the user from inhaling viral particles.

A faceguard is needed for certain viruses to keep fluids from being splashed into the user's eyes, nose, or mouth.

After being taken off, PPEs must be treated as biohazardous waste and go through a decontamination process before being safely discarded.

PPEs are made of ultra strong, waterproof synthetic material that won't easily rip or tear.

Double gloving is standard—a tiny hole would be enough to let in the virus.

Disposable booties are worn anytime a medical team member enters the special isolation unit.

YOU BE THE DOCTOR

The Case of the **Mysterious Symptoms**



The scan showed that she had some dopamine loss on the right side of her brain.

Monica Schulman, a 37-year-old teacher and mother of four, began experiencing a series of strange symptoms a few years ago.

“I noticed I was curling my left toes under when I was standing in the bathroom brushing my teeth,” says Schulman (above, with family).

Then, on a trip to New York City to visit her sister, who had been diagnosed with breast cancer, she noticed something strange when they were walking together. “My left hand was not swaying,” Schulman says.

“I thought maybe it was stiff or that I did something to it. It just didn’t want to move.” She also noticed a tremor in the same hand, which sometimes felt weak.

After Googling her symptoms she told her family she thought she might have Parkinson’s disease.

“They thought I was crazy,” she says. “No one in my family had it, I was too young . . .” She hoped they were right. But her symptoms persisted so she came to Emory to see neurologist Stewart Factor, director of the movement disorders program.

Factor says there was no question that Schulman had parkinsonism—tremor, slow movement, muscle stiffness, and other movement abnormalities.

“But at her age, there are other causes to be considered, including drug-induced parkinsonism and a rare metabolic disorder called Wilson’s disease,” he says. “We performed imaging and did some blood work.”

Schulman had a DaTSCAN, a nuclear imaging test that looks at brain chemistry—specifically dopamine cells, the loss of which can be an indicator of Parkinson’s disease.

The scan showed that she had some dopamine loss on the right side of her brain, which controls the left side of her body where her symptoms were.

What, careful reader, do you think Factor’s diagnosis was?

Young onset Parkinson’s disease.

People under 40 make up about 15 percent of all Parkinson’s cases. “We call this young onset Parkinson’s, while under the age of 20 is

juvenile onset,” Factor says. “That’s much less common. The youngest person I’ve personally seen with Parkinson’s was 18.”

Genetic causes of Parkinson’s disease are more common in younger onset cases. Schulman’s genetic tests revealed a mutated LRRK2 gene, one of the most prominent Parkinson’s-related genes. She also discovered a distant uncle who had had Parkinson’s disease late in life.

“Well over 20 genes impact Parkinson’s,” Factor says. “Five are causative—the mutation causes the disease—whereas the others just impact risk.”

Between 1 percent and 3 percent of all people with Parkinson’s in the United States have the LRRK2 mutation. It’s more common among certain ethnicities, such as Ashkenazi Jews and North African Berbers.

Schulman tried different medications: amantadine, which made her feel sick, then Sinemet (carbidopa-levodopa), which is converted into dopamine in the brain and is the cornerstone of Parkinson’s therapy.

Now 40, she quit teaching to devote more time to her health and her family. Her husband and children have been hugely supportive, she says. “My kids are 4 to 12, so we have a lot going on constantly. Fatigue is a part of the disease. But they know mommy has Parkinson’s—my oldest even did a research project about it for school.”

Shulman aims to work out at the gym, practice yoga, or do physical therapy daily. “Staying active and being surrounded by positivity has helped for sure,” she says. ■

A Change Would Do You Good

Want to reduce your risk of diabetes down the road? Don't rely on pills alone. In addition to any medications your doctor prescribes, you should also ... wait for it ... eat right and exercise. Lifestyle modifications are better at preventing diabetes among high-risk individuals than medications alone, found researchers from the Emory School of Medicine and Rollins School of Public Health. Global health researcher Karla Galaviz and endocrinologist J. Sonya Haw looked at the long-term effectiveness of several diabetes prevention strategies. The study, published online in *JAMA Internal Medicine*, found that lifestyle changes combining diet and physical activity achieved the largest risk reductions; for medications, those that regulated weight loss and insulin-sensitizing agents had the largest risk reductions. "The effect of medications was short lived, whereas the effect of lifestyle modification was sustained for several years," Haw says. ■



Biological Pacing



The adult human heart beats almost 100,000 times a day, in a rhythm dictated by a small number of pacemaker cells. "The mammalian heart beats spontaneously without conscious input from the brain," says Hee Cheol Cho (above), associate professor in the Department of Pediatrics and the Coulter Department of Biomedical Engineering at Emory and Georgia Tech. Aging and heart defects can cause the pacemaker cells to malfunction, leading to abnormal or slow heart rhythms. In these cases, doctors implant mechanical pacemakers, which are expensive and have potential complications. Cho and his team have been working to develop a device-free way to pace the heart. They discovered that an embryonic gene, TBX18, figures prominently during the formation of pacemaker cells in the embryo and can convert ordinary heart muscle cells into new pacemaker cells. Cho is testing long-term biological pacemakers in animal models. "Our technologies have matured sufficiently to draw up a roadmap toward the first-in-human clinical trial in the next few years," he says.—*Aspen Ono*

STEM CELLS IN SPACE

In a new spin on the space race, researchers at Emory School of Medicine and Children's Healthcare of Atlanta are attempting to grow cardiac cells more quickly in low-gravity conditions.

The researchers have been using space-simulation machines to enhance the ability of stem cells to turn into cardiac cells. Now they—or the cells they've carefully cultured, at least—will get the chance to transform on the International Space Station.

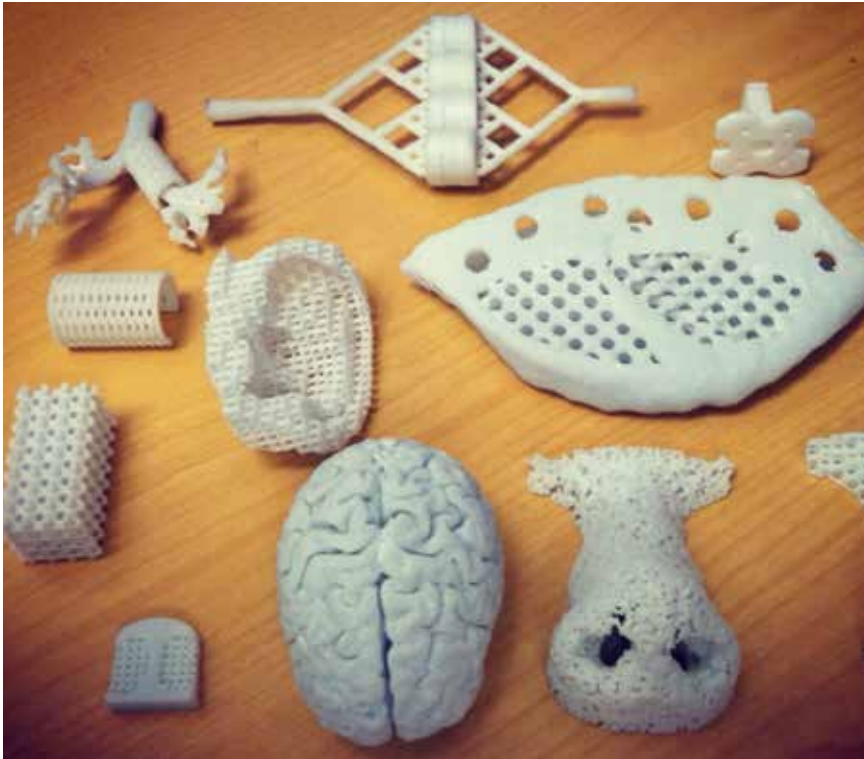
Pediatrician Chunhui Xu, pediatric cardiologist Kevin Maher, research associate Rajneesh Jha, and colleagues were awarded a two-year grant from the Center for the Advancement of Science in Space, which manages the International Space Station's U.S. National Laboratory.

Pluripotent stem cells, or "master" cells, can be derived from human adult skin or blood cells. Stem-cell-derived cardiac muscle cells have been used to treat heart failure in animal models. They've also been used to study inherited cardiac diseases in the lab.

On Earth, Jha uses a "random positioning machine" that mimics the microgravity conditions found in space. The machine periodically shifts cells so they never get used to one direction being down, which has produced five times the previous amount of cardiac muscle cells. The results were published in *Scientific Reports* in August 2016.

For the actual microgravity experiments on the space station, the cells will be loaded into an automated incubator device approved for use in spaceflight. ■

3D Printers Move Beyond Curiosities



An array of 3D medical structures printed at Emory, including ears, brains, noses, and—in the upper left corner—a splint placed on a model of a child's airway.

As part of the DIY revolution, Emory doctors are using 3D printers to make body parts, medical tools, training models, and prototypes.

At the Emory Orthopaedics & Spine Center, sports medicine surgeons like Matthew Pombo are using 3D printers to design custom knee replacements for elite athletes during their careers and after retirement.

“In aging athletes, you can see the impact of a lifetime of sports and activity,” says Pombo, who has performed about 500 customized 3D-knee replacements at Emory Johns Creek Hospital. “The patient-specific 3D-knee implant is ideal for those with arthritic knees who are considering surgery.”

Making patients' lives easier at home is the aim of Steve Goudy, director of the Division of Pediatric Otolaryngology at Children's Healthcare of Atlanta and associate professor at Emory's School of

Medicine, who is using 3D printers to create medical devices that patients can take home with them. One of his current projects is a collaboration between Emory, Georgia Tech, and the Global Center of Medical Innovation. He is working to create a better infant nasal suction device. “As a parent, I remember nights where my kids could not breathe or eat,” says Goudy. “All parents want to give their kids the best medical attention possible. This device would allow them to be more self-sufficient at home.”

Tissues and cells are the inks that Michael Davis, associate professor of cardiology and biomedical engineering and director of the Children's Heart Research and Outcomes (HeRO) Center, is using in his lab.

“We are printing patient-specific heart valves and heart patches for pediatric patients,” he says. “Children are often treated using repurposed adult medi-

cines or other, less effective treatment methods.”

Transplanted donor valves have drawbacks, sometimes requiring antirejection medications and subsequent surgeries to replace the initial valve since it does not grow as the child ages. Davis and his team are developing child-sized valves using the patient's own cells through Induced Pluripotent Stem Cells technology. “We want to fix the patient, using the patient, within the patient,” says Davis.

Stitches and staples are effective at closing wounds, but they can also be invasive and painful and leave visible scars. Felmont Eaves, professor of plastic and reconstructive surgery at Emory and director of the Emory Aesthetic Center, has spent six years using 3D printing to transform the way surface lesions and wounds are treated.

“We created a very dynamic and flexible device that will pull a wound together and relieve its tension,” he says. “3D printing allowed us to cost-effectively make hundreds of models and prototypes to perfect the dimensions, shape, and thickness of our device design.”

Doctors were at a loss for ways to treat a baby with a windpipe so weak it often collapsed, so they approached biomedical engineer Scott Hollister, who used 3D printing to craft a custom, infant-sized tracheal splint to open the baby's windpipe. Hollister, the Patsy and Alan Dorris Chair in Pediatric Technology at the Coulter Department of Biomedical Engineering at Emory and Georgia Tech, is now setting up the Center for 3D Medical Fabrication. “We want to support clinicians' ideas by providing them with the capability to design and 3D-print patient-specific devices,” he says. “This new center makes it clear that the development of groundbreaking 3D-printed creations by Emory innovators will continue to grow, evolve, and proliferate.”—*Aspen Ono*



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REGULATING A RACING HEART

In a pinch, epinephrine is a good thing. It prepares the body to respond to a threat. When sustained over time, however, the effects of epinephrine—also known as adrenaline—can be threatening to the heart.

Brittany Martin, a children's dance coach, experienced troubling cardiac symptoms over the course of a year, culminating in a visit to Emory University Hospital. "My body was in fight or flight all the time," she says.

In 2015, Martin began seeing a doctor in McDonough for an elevated heart rate and was prescribed beta-blockers. She had been concerned about thyroid problems because of her family history. She attributed her heart's racing to stress: Her dance team at the Platinum Peaches studio in Decatur was getting ready for a competition.

Then, one Monday last summer, she felt much worse. After putting her daughter on the bus to school, she grew concerned about an increasingly bad headache, chest pain, and heart palpitations.

Her husband drove her to the emergency room, where doctors ran tests to determine if she was having a heart attack. They performed an electrocardiogram and looked for troponin in her blood, a sign of damage to the heart muscle. Everything looked fine, which was puzzling.

She was sent for a head CT. The severity of her headache by that point made her kick and scream, she recalls. After an extra troponin test was in the suspicious range, Martin was sent to the cardiac catheterization lab. She remembers thinking: "I'm 30 years old—why am I having a heart cath?"

Doctors didn't see any blockages that would cause her problems. But an ultrasound examination of her heart showed that the walls of the base were not moving, although the apex or lower conical tip was still contracting. And she had an ejection fraction (a measure of the heart's pumping efficiency) of 30 percent, similar to someone with heart failure.

To supervising cardiologist Stam Lerakis, this pattern indicated a rare condition called reverse Takotsubo cardiomyopathy. The standard form of Takotsubo cardiomyopathy is known as stress-induced cardiomyopathy or "broken heart syndrome," and occurs mainly in post-menopausal women.

"We do see [standard Takotsubo] regularly," says Lerakis, recalling a case in which a man had a stroke and his wife, because of her distress, developed the syndrome.

In the reverse form, which Martin appeared to have, the apex still contracts. It is more common among younger women, possibly because of age-related changes in how the heart responds to epinephrine. Lerakis and his team sent Martin for a cardiac MRI to solidify the diagnosis.

"The catheterization results did not explain the weakness of the heart," he says. "We needed to determine if there was a problem with the heart walls and see if the muscle was still alive. That's how we found the tumor."



Brittany Martin with her husband, Christopher, and daughters, Makayla (front) and Madison, experienced troubling heart racing.

A mass about the size of a quarter was discovered close to Martin's spine. Based on her symptoms, the doctors suspected it was a paraganglioma, a tumor that produces epinephrine and its chemical relative, norepinephrine. Adding to doctors' suspicions, her blood and urine showed high levels of normetanephrines, metabolic products of epinephrine and norepinephrine also known as catecholamines. "In Takotsubo, the heart is essentially stunned, but we expect that it will be able to recover," Lerakis says. "Her heart was being bombarded by catecholamines."

To learn more, Lerakis turned to endocrinologist Sol Jacobs, who called for an octreotide scan—a diagnostic technique used to find catecholamine-producing tumors. "Given her clinical presentation and biochemical data, we still suspected this was a paraganglioma," Jacobs says.


Martin was prepared for surgery. To counteract the effects of the catecholamines, she was given alpha- and beta-blocker drugs, which restored her heart to normal pumping efficiency. But she wasn't out of danger. "Any manipulation of the tumor could cause a sudden release of catecholamine, leading to severe increases in heart rate and blood pressure," says thoracic surgeon Seth Force, who removed the tumor. "That's why the blood pressure and heart rate have to be controlled by medicines prior to surgery, to avoid any cardiac issues."

Genetic tests revealed that Martin has a mutation that increases the risk of developing a paraganglioma. One of her daughters has the genetic mutation as well, so they both will need to get periodic scans. As for now, she is planning more dance competitions. "I'm doing great," she says. "My relatives can't believe that I was in the hospital last year."



“I’m 30 years old—why am I having a heart cath?”



A man with short brown hair and black-rimmed glasses is seated in a wooden church pew. He is wearing a light blue button-down shirt and has his hands clasped in front of him, resting his chin on them. He is looking off to the side with a thoughtful expression. The background is filled with the warm, colorful light of stained glass windows, creating a bokeh effect. A semi-transparent dark grey rounded rectangle is overlaid on the lower left side of the image, containing white text.

**"I did not feel it coming.
I felt a little warmth
on the top of my head, and
I just ... went to sleep."**

CALMING A HEART STORM

The first time Nils Ericson's heart slipped out of its normal rhythm was on a Sunday. He was in church with his family when he suddenly slid out of his seat and started shaking, leading his wife to think he was having a seizure.

"I did not feel it coming," says Ericson, a vice president at Olympus. "I felt a little warmth on the top of my head, and I just ... went to sleep."

This was the start of a medical mystery that took several unexpected twists and turns. In fact, Ericson's diagnosis, treatment, and recovery were the basis of a lecture given to Emory first-year medical students this spring, which Ericson himself was able to attend.

Cardiac electrophysiologist Michael Lloyd used Ericson's case as an example of a common heart disorder: ventricular tachycardia (fast heartbeats) that turned into cardiac arrest.

Later, at the hospital, Ericson experienced a type of arrhythmia called "refractory electrical storm," which is rare and carries a high mortality rate.

He survived because, in the middle of the night, Lloyd thought to ask anesthesiologists to perform a procedure he had only read about—a stellate ganglion block, an injection of local anesthetic into the neck that can have a heart-calming effect.

Emory doctors have used the procedure to stabilize the heart of other patients with stubborn arrhythmias. For Ericson, it worked well enough that it gave doctors time to discover the source of his trouble and provided a clue as to how he should be treated long-term.

Still, two frightening days passed before that moment of inspiration.

After Ericson regained consciousness at church and sat up, he passed out again. Members of the congregation tried to revive him and were preparing to use an automated external defibrillator, but he was able to walk to an ambulance that took him to Emory Johns Creek Hospital.

There, doctors looked for a blockage of Ericson's coronary arteries. When they found none, they decided to send him to Emory University Hospital. Kathryn Ericson remembers hearing staff shout "Code blue" when her husband needed to be resuscitated another time.

A nurse urged her to repeat words of encouragement to her husband during the ambulance ride in the rain. "I consider it a miracle he didn't code on the way there," she says.

At Emory University Hospital, doctors stabilized Ericson and told his wife to go home and rest. She returned the next



Cardiologists Michael Lloyd and Stam Lerakis use creative problem solving to diagnose and treat their patients' perplexing heart issues.

day optimistic. But on Monday night, the electrical storm began.

On multiple occasions, Ericson's heart began beating quickly and then stopped altogether, requiring an electrical shock to bring it back. This kept occurring, despite doctors' interventions—administering anti-arrhythmic drugs, calming beta-blockers, and, eventually, propofol sedation.

"We were escalating with several kinds of drugs," says cardiology fellow Matthew Crim, who was on duty along with attending cardiologist Maan Jokhadar. "But all those shocks send the heart into a spiral. He was deep in the spiral."

By this time, Ericson's sons had arrived at the hospital. His oldest, then a first-year student at Medical College of Georgia, knew enough about what was happening that every time he heard the "buzz—boom" of the defibrillator, he became upset.

"Dr. J cautioned us not to Google 'electrical storm,'" says Kathryn Ericson. "But we did anyway. We must have had a dozen people in there praying."

Around 2 a.m. Tuesday, Lloyd called anesthesiologist Boris Spektor, who was on acute pain service, and asked him to try the stellate ganglion block.

The block involves injecting anesthetic into a star-like cluster of nerves in the neck, guided by ultrasound. Spektor says he performs the procedure around once per month but mostly to alleviate escalating chronic pain. The delicate procedure is relatively convenient because it can be performed at the bedside, he says.

Lloyd and Spektor's aim was to temporarily disconnect Ericson's heart from the stimulation it was getting from the sympathetic nervous system. The intended effect was similar to that of the beta-blockers doctors already had tried: to shield the heart from adrenaline.

"It was one of those situations when all other options had been exhausted," Lloyd says. "It gave us a window of time to

do imaging on his heart, which we couldn't do before."

To extend the duration of the anesthetic block, Spektor added dexamethasone, an anti-inflammatory steroid.

When Ericson's heart calmed down in response to the stellate ganglion block, it was a clue that inflammation was part of what was causing his arrhythmia.

MRI and PET imaging showed a hot spot in the left ventricle, which doctors suspected was cardiac sarcoidosis. Usually found in the lungs, sarcoidosis is the body's response to an unknown irritant.

"Nobody knows where sarcoid comes from," Lloyd says. "It's known as a great mimic of other disorders."

Under the microscope, sarcoidosis looks like the lumps of immune cells, called granulomas, that surround tuberculosis bacteria. In Ericson's heart, those lumps were interfering with the signals carried from the pacemaker region to the rest of the muscle, and triggering spikes of their own.

Ericson's long-term treatment would need to include shrinking the sarcoidosis, so he started anti-inflammatory treatment with corticosteroids.

Since then, he has transitioned to a milder anti-inflammatory drug, methotrexate. For preventive purposes, he also has an ICD (implantable cardioverter-defibrillator), but it has not been triggered.

When questioned by medical students about his recovery during the lecture, Ericson explained that a revamp of his diet came out of discussions with Jokhadar about side effects of the corticosteroid treatment. He learned that the drugs often induce hunger and weight gain. Encouraged by his vegan mother-in-law, he resolved to eliminate meat as well as alcohol from his diet.

"I would eat cardboard if it meant staying alive," Ericson says. "I don't crave meat, but I did recently start eating fish because I found my legs were feeling weak."

Before the electrical storm, Ericson was doing yoga and "P90X" workouts, but upon first coming home, he had difficulty just walking down the driveway. A complication of his long hospital stay was irritation of the sciatic nerve, which made walking or even sitting painful.

Ericson recalls that his father, after quadruple bypass surgery, was not able to return to normal activities.

He is working hard to recover and is now running a minute at a time with walking breaks. He has also returned to traveling for his job.

"I refuse to let this thing beat me," he says.

Windows of Opportunity

Individual donors and organizations help Emory researchers' efforts to develop therapies to improve blood flow, prevent inflammation, and encourage healing from cardiovascular disease.

To find out more, contact **Gabrielle Stearns**, director of development, at **404.727.2512** or **gabrielle.stearns@emory.edu**



“Before he went to surgery, he told me, ‘I am coming back mommy. Don’t cry. Don’t cry.’” —Bah’s mother, Kumba Cham



Clockwise from top: Cardiothoracic surgeon Bradley Leshnower, assistant professor of surgery, (far left) shows Ebrima Bah a stent similar to the one that saved his life; Bah, pictured here after his surgery, was able to go home on Christmas Day; a post-operative CT scan shows the stent graft in the descending thoracic aorta with aortic remodeling.

IMAGES COURTESY OF WAGA-TV FOX 5 ATLANTA

REPAIRING A RUPTURED AORTA

Marietta high school student Ebrima Bah, 16 and already 6-foot-4, came home from school one winter afternoon a year ago and, as he often did, headed to a nearby gym to play basketball.

Not long after, his sister received a panicked call from Ebrima, saying that he was having stomach cramps and difficulty breathing. When Fatima Bah arrived, she found her brother surrounded by other players, grabbing at his chest.

She called 911, and an ambulance rushed him to a local hospital, where doctors initially thought Ebrima had pneumonia. After further imaging, however, they discovered that he actually had a ruptured type B aortic dissection, a rare, life-threatening condition that usually occurs in older men in their 60s and 70s. The large blood vessel branching off from his heart, his aorta, had torn and temporarily resealed, leaking two liters of blood into his chest.

The hospital called to have him transferred to Emory for emergency surgery. Cardiothoracic surgeon Brad Leshnower and vascular surgeon Yazan Duwayri performed a one-hour thoracic aortic stent graft repair.

“We were able to mobilize our aortic team immediately after receiving the phone call,” says Duwayri, associate

professor of surgery. “We brought Ebrima directly into the preoperative area and rapidly to the OR after we confirmed the diagnosis. The short time from arrival to repair allowed us to save his life.”

Emory Aortic Center, which combines expertise in cardiothoracic and vascular surgery, pediatric cardiology, radiology, and genetics, is uniquely qualified to treat patients like Ebrima, adds Leshnower, assistant professor of surgery.

They threaded a long stent up into his aorta to cover the tear. “We were able to do this totally percutaneously,” says Leshnower. “So, no incision. Just with needles and wires.”

Ebrima was released from the hospital on Christmas Day. “I’m really happy,” he told reporters. “Because, you know, they did save my life. I’m really blessed to be alive right now.”

While Ebrima was in the hospital, doctors ordered testing to see if he had any genetic diseases that might have led to the dissection. The testing did not confirm any, which is frequently the case.

“We have seen Ebrima multiple times in follow-up,” Leshnower says. “His thoracic aorta has been completely remodeled by the stent grafts, and he is doing well. We will continue to follow him with life-long aortic imaging surveillance.” ■

SPIN DOCTOR: The hazards of taking care of others at the expense of yourself

BY Patrick Adams AND Mary Loftus ■ ILLUSTRATIONS BY Andrew Baker



“You okay, doc?”

“Who me?” I pointed at my chest.

“Yeah, you.”

I turned my head away from the television and back toward him. I poked out my lip and furrowed my brow.

“Look like you got something heavy on your soul.”

Heavy on my soul. I didn’t say anything. Instead I just stared at him, surprised at how warm my face was becoming and how my eyes were stinging with tears.

“I’m okay,” I finally said, speaking quietly. “But yes. That’s a good way to put it.”

I wanted to tell him. I wanted to tell my patient all about what was weighing me down.

But I was his doctor. So when he asked, I just stayed silent.

As soon as I got out of there, I turned my forehead into the nearest wall and let myself cry.

I could feel the people looking at me as they walked by, their feet slowing down and wondering what could be going on with this doctor and the muffled, guttural sounds she was making. No one said anything.

Maybe my actions spoke enough. I mean, whatever it was had to be awful. A doctor facing a wall with shoulders shaking and body heaving in a stiff white coat said plenty.—*Dr. Kimberly Manning’s blog, “Reflections of a Grady Doctor”*

Kimberly Manning is a hospitalist at Grady Memorial Hospital in Atlanta, an associate professor of medicine at Emory, and an adviser in the Semmelweis Society—one of 16 faculty who work with the same small group of students throughout their time in medical school.

Her interests include humanism in medicine and the use of reflective writing. She practices what she preaches by writing a blog about her

experiences at Grady. “I write to share the human aspects of medicine and teaching and work-life balance,” Manning says, “and to honor the public hospital and her patients, but never at the expense of patient privacy or dignity.”

She also writes about her frustrations and ways that she stays energized and optimistic in the face of daunting amounts of human tragedy.

Usually, she copes very well, find-



Drs. Kimberly Manning and Alanna Stone

ing joy in the job on most days. This is not a story about one of those days.

Manning first came to know Alanna Stone when Stone was a medical student in her small group of advisees, and was delighted when they ended up working together at Grady. Like many of Stone’s friends and colleagues, Manning rallied around the young doctor when, having overcome breast cancer, Stone developed acute leukemia.

After months of staying hopeful, Manning got the news that Stone had taken a turn for the worse and wasn't going to make it. Unable to hide her preoccupation from one of her patients, Manning shared the basics of what was happening and left the room before bursting into tears. Crying in the hallway, she admits, "is not in the physician playbook."

"I was crying because I would miss seeing the life of this beautiful woman continuing to unfold," Manning wrote in her blog. "I was crying because 34 is too young to die. Crying because a little boy had lost his mother and a husband had lost his wife. Crying because one of the most epic students-turned-doctors that I have ever witnessed has had her career cut short, and because patients like the one I'd just left would never get to meet her. But, also, I was crying because of that moment with that patient, and how Alanna herself understood more than anyone that patients take care of doctors, too. That patients save their doctors' lives every single day."

TAKE ACTION

Physicians are, of course, human. They experience sadness and fear, illness and loss, anxiety and depression. They get overwhelmed, overloaded, and overextended.

But something has changed. Physician burnout is at an all-time high, with more than half of physicians saying they experience symptoms: emotional exhaustion, a loss of meaning in work, a sense of ineffectiveness, or a lack of engagement with patients. This represents a 25 percent increase over the past four years and cuts across physician gender, age, and ethnicity.

On any given day, 30 percent of physicians say they feel stressed out, and 39 percent feel depressed. Such feelings can be fatal. Every year, about 400 physicians die by suicide. Many of them had not sought treatment or professional help beforehand, telling friends and family they feared it could

have a negative impact on their careers.

"The day they start school, medical students actually are happier and better adjusted than their education-comparable peers," says Philip Shayne, professor of emergency medicine and assistant dean for Graduate Medical Education (GME) at Emory School of Medicine. "Then there's this big rise in



burnout and depression that continues into their 50s."

The American Medical Association calls physician burnout a "matter of absolute urgency," and has issued a call to action. What accounts for this epidemic, and what can be done to combat it? Quite a lot, it turns out.

How physicians and the institutions that train and employ them deal with these stressors—in community or isolation, with support or silence—is

proving to be a powerful predictor.

Physicians say their top stressors are bureaucratic tasks, heavy workload, computerization, and feeling like "a cog in the wheel."

Privately, they share stories of patients lost, violence witnessed, childhoods shattered, and families reeling.

Not to mention the fear of making a mistake. "The system depends on individual infallibility," says Emory hospitalist Anna Austin Von. "How we as physicians deal with that expectation is very much in the closet."

Tait Shanafelt, chief wellness officer at Stanford Medicine who spoke at Emory's annual medical education day in March, says a "blame the victim" mentality is pervasive in the field. "We tell physicians to get more sleep, eat granola, do yoga, and take better care of yourself. These efforts are well intentioned. The message to physicians, however, is that you are the problem and you need to toughen up."

Instead, he says, academic health centers, hospitals, medical schools, clinical practices, and other institutions that train, hire, and rely on physicians must take the lead by focusing on change within the organization, culture, and system from the top down.

Proven antidotes to burnout include promoting autonomy, creating a sense of collegiality and community, and allowing time for meaningful work. "An individual organization that is committed to this at the highest level of leadership, and that invests in well-designed interventions, can move the needle and run counter to the national trend," Shanafelt says.

TEACH SELF-CARE

Emory's GME program, under the leadership of Shayne and Associate Dean Maria Aaron, has 104 specialties with 1,292 residents, making it the seventh-largest GME program in the country.

Shayne remembers his own experiences, first at Chicago's Cook County Hospital, where he trained in one of the

country's busiest trauma units, and later at Emory, that led him to become an advocate for physician wellness.

"In the beginning of my career, I didn't know how to process things," he says. "You think you're just supposed to be tough and that it's not supposed to affect you. But those images—there was this one little boy I remember with a bullet wound to the head—they stay with you. To this day, those are the things that haunt me."

During his 17-year tenure as program director for emergency medicine, Shayne took pains to engage in personal interactions with his 60-some residents. "One of the great things about training at Emory is that you get these incredibly diverse sites, which means you see a lot of very sick patients," he says. "But it also means you're being exposed to the things that we think cause burnout. Emory's medical students and residents see a lot of really bad stuff"

Wherever possible, Shayne tries to intervene. "I found that if you take a moment to pull residents aside and talk to them, they start processing in a way they hadn't realized they need to. They learn to reflect and grieve."

Physician training programs nationally are now required to provide residents access to confidential, affordable health care, including counseling and urgent care, 24/7. The new guidelines also urge improved interactions between residents and faculty, and providing residents with time and techniques for self-care.

All Emory residents were asked in late June to participate in the first-ever "burnout survey" conducted on campus. "We know what the numbers are nationally, but we don't know what they are here, so we're collecting data that will give us a baseline for future comparison," Shayne says.

Residents need to know that help is available and confidential. "We're lucky here," he says. "We have a really supportive administration and faculty, and with the faculty staff assistance program (FSAP), we have the Rolls Royce of support services." FSAP offers one-on-one counseling, group workshops, and other wellness services for Emory faculty and staff. "It's free, it's anonymous, and it's offsite, so nobody sees you going in or out. They'll even make accommodations for extra hours."

Still, telling residents about available resources is one thing; making sure they hear that message is another. Medical students and residents tend to be high performers driven to perfection, Shayne says. "They didn't get where they are by accident. You have to show them that this is not punitive and that the resources really can help."

Von, a hospitalist at the Atlanta VA Medical Center, remembers vividly the anxiety she felt throughout medical school at Emory. "The weight of the responsibility of caring for other people became paralyzing," she says. "During my sub-internship, I would call my husband crying every time I walked out of the hospital."

Then came the morning that she had rounds at Hughes Spalding and was put in charge of an infant's care. A nurse reminded her to put up the siderail on the baby's crib when she left. "After I returned nine times to make sure I had put the siderail up, I realized I needed help," Von says. She went to see a psychiatrist through FSAP who was able to help her address her anxiety. "The same themes always cropped up—fear of not doing something that needed to be done or of making a mistake."

PAY ATTENTION

Even when physicians think they are managing just fine, stress may be taking a silent toll. Six years ago, Lucky Jain was at the peak of his career. A tenured professor of pediatrics with a well-funded lab and prestigious academic appoint-



DR. KIMBERLY MANNING: "Patients save their doctors' lives every single day."



DR. LUCKY JAIN: "I have a better appreciation of life and its vulnerabilities, but also its gifts."



DR. SHERYL HERON: "We become so acculturated over time, we strip ourselves of essential human needs that make us want to return to work with joy and empathy."



DR. NADINE KASLOW: “Every time I give a talk on this, people follow me out of the room to tell me about something they haven’t dealt with.”



DR. GEORGE GRANT: “Most clinicians, to devote the fullest attention to patient and problem, are taught to suppress their own concerns and feelings.”



DR. WENDY BAER: “Apply that ‘can do’ fighting spirit and desire to heal to your own life.”

ments, Jain also continued to care for the sickest patients in the neonatal intensive care unit. He worked long hours with little down time. But at age 54, he had never suffered a major health event, and at 140 pounds, he weighed the same as he had as a medical student in India.

Then one morning, at a national medical meeting in Orlando, he collapsed as he was walking to the podium to speak, felled by a major heart attack.

Colleagues resuscitated Jain on the spot, performing chest compressions until an ambulance arrived. Minutes later, he was rushed to a local hospital where an Emory-trained cardiologist removed a clot from his left anterior descending artery and inserted a stent to keep it open. He returned to Atlanta to recuperate. “The weeks and months that passed after the episode felt like eternity,” he says. “Would I be able to go back to work? Would I be around to celebrate the weddings of our two daughters? Had the arrest left any residual damage? My attention became increasingly inwardly focused as I tried to get my arms around what went wrong.”

In six months, Jain was back at work—but he had changed. The experience opened his eyes to the insidiousness of chronic stress. “It may not manifest until much later and in different ways,” he says. “But that doesn’t mean the wear and tear is not happening.”

Since, Jain has turned his attention to improving physician wellness at his worksites at Emory and Children’s Healthcare of Atlanta. He’s helped start wellness programs for physicians, corporate athlete training for physician leaders, “second victim” programs, junior faculty mentoring, and “Wellness Wednesdays” on topics such as nutrition, yoga, walking, and mindfulness. “We are creating a culture of wellness and caring,” he says, “and people are beginning to pay attention.”

Jain himself began a strict exercise regimen and enrolled in mindfulness and meditation programs. “The world has suddenly slowed down around me,

and I feel much more able to handle situations that in the past would have been disruptive,” he says. “I have a better appreciation of life and its vulnerabilities but also its gifts.”

FILL THE TANK

Stress is cumulative, so it must be managed early and continually, says Sheryl Heron, who is a physician at Grady Hospital, a professor and vice chair of Emory’s Department of Emergency Medicine, and chair of the school’s wellness and well-being committee.

Factors include sleep deprivation, exposure to infectious disease, and no time for self-care.

“In the emergency department,” she says, “we drink pain and suffering every day.”

After all, patients don’t make appointments to come to the emergency department. “They don’t want to be there. They’re there due to violence, car crashes, horrible injuries,” Heron says. “What happens to doctors in our attempts to cope, keep it moving, jump on the train?”

She remembers a family she encountered early in her career—three children and an adult with multiple gunshot wounds from family violence. “One had been shot in the temple and was blinded, another in the neck and was paralyzed, another in the arm with an open fracture,” she says. “Two of the children reminded me of my nieces. I had a visceral reaction that upended me.” Fortunately, it was during a change of shift and there were other physicians there to take over. She went home, distraught, and later talked to a colleague who encouraged her to write about the experience as catharsis, which she did.

“I suspect everyone was impacted, not just me,” she says. “Now at Grady we have a debriefing team and the ability to stop for a moment, reflect on the tragedy that just occurred, and feel the pain. And we routinely honor the lives of patients who die in the ER by pausing to reflect on the somberness of the moment. We then go and tell their

family members with compassion and respect.”

To cope with stressors like these, you have to “fill the tank,” says Heron. “In my younger days, I didn’t take a break to eat,” she says. “Now I do. We have to create a culture where we believe going to eat when one is hungry is normal. We become so acculturated over time, we strip ourselves of essential human needs that make us want to return to work with joy and empathy.”

Emergency medicine is simultaneously the specialty with the highest rates of burnout and the top-rated for physicians who say they love their job, which is “a bit of an enigma,” admits Heron.

Personally, she makes it a priority to go on vacations, carve out family time, exercise and eat properly, go to bed at 10, wake up early, practice meditation, and read devotionals. “I also step outside the grind and explore, reinvent myself, tap into things that intrigue me,” she says. “This is what I need to do for me and what I need to model for my residents, students, and faculty colleagues. Your life and career should go forth in tandem.”

BOOST EMPATHY

When psychologist Nadine Kaslow hears of a mass casualty event near downtown Atlanta—the Centennial Olympic Park bombing, a multiple shooting, a plane crash—she will often head to Grady Hospital, no matter the hour. “It’s not that they need me to take care of patients, but I know the doctors and nurses need support,” Kaslow says. “So I let them tell me about what they’ve seen.”

As chief psychologist at Grady and professor and vice chair of psychiatry and behavioral sciences at Emory, Kaslow serves as a kind of unofficial wellness counselor to a hospital staff charged with treating critically injured patients on a daily basis.

“Whenever there’s something really bad, people know to call Nadine,” says Shayne. He recalls an episode earlier this year when a nurse in Grady’s burn unit died of a heart attack on the job: “Right then, Nadine came down to debrief everyone—to help them process what had happened.”

“It’s talking about what happened, but it’s also talking about the person’s experience of what happened,” says Kaslow, who over the years has recruited other colleagues to share the load, assembling an informal debriefing team.

While the team doesn’t have an official title or role, it’s clear that there exists a significant unmet need for what they do. “Every time I give a talk on this, people follow me out of the room to tell me about something they haven’t dealt with,” she says. “Every single time.”

Out of 100,000 consults by Spiritual Health at Emory Healthcare this past year, more than half have been for professional and support staff, says executive director George Grant, and one-third of those were physicians.

“A major cause of physician stress and burnout is empathic imbalance,” says Grant, a psychologist and theologian. “Most clinicians, to devote the fullest attention to patient and problem, are taught to suppress their own concerns and feelings.”

While well-intentioned, this approach can overwhelm the physician with collateral emotions and lessen the trust of the patient, who senses the doctor’s guard is up. “Staying engaged with one’s story

Doctors as ‘Second Victims’

On a recent evening at the Sibley Heart Center, Kurt Heiss, professor of surgery and pediatrics at Emory School of Medicine and a pediatric surgeon at Children’s Healthcare of Atlanta, asked a roomful of cardiologists to consider for just a moment the Summer Olympic Games in Beijing.

“Do you remember what happened?” he said. “The U.S. men’s 4x100 relay team had always won gold. But in 2008 in Beijing, they dropped the baton in the qualifying round. And 30 minutes later, the women did the same thing. They didn’t even get to compete.”

On the wall was a slide with images of the catastrophe as it unfolded: outstretched hands, anguished expressions, a baton just out of reach.

“So what does this have to do with any of us?” he said. “Well, like you, these people trained their whole lives for this. They’re spectacular at what they do. Yet they made a mistake—and they don’t get that back.”

Heiss was using the analogy to kick off a presentation he has made dozens of times to doctors across the spectrum of specialties. His aim: to foster openness and honesty around medical errors and to advocate for the compassionate support of “second victims”—physicians who, having made a mistake, struggle to cope with the outcome.

If patients are the first victims of medical mistakes, then providers are the second, argues Albert Wu, professor of health policy at Johns Hopkins Bloomberg School of Public Health, who coined the term in 2000.

Yet, historically, institutions have done little to support these physicians. Anxious, depressed, and demoralized, they often suffer alone, tormented by guilt for months or even years. “It’s not only the emotional anguish,” says Heiss, who has researched the topic extensively. Plagued by repetitive replays of the event, second victims begin to think differently—they lose confidence in their skills, second-guess their decisions. In some cases, second victims switch jobs or locations, or abandon medicine altogether.

Heiss speaks from experience. A few years ago, he led a team tasked with operating on a boy who had been badly injured in an accident. The



DR. ANNA VON: “I can never reach the elusive goal of work-life balance. My life more often feels like a job share between work guilt and home guilt.”

and emotions, our inner conversation, allows the clinician to model self-compassion, which is vital to a healing collaboration and builds instant rapport,” says Grant, who gives his own staff the same advice. “By practicing with our personhood intact, we are saving time and saving ourselves.”

CHAMPION WELLNESS

During medical training in Philadelphia, Wendy Baer remembers her own attending encouraging her to take a break from studying for her boards to go to an art museum. He told her, “You’ll be a better doctor if you have something interesting to talk with your patients about.”

Baer sees both patients and staff in her role as on-staff psychiatrist at Winship Cancer Institute. It’s particularly hard on doctors when they become ill and take on a patient role.

“The ‘should’ issue comes up a lot—‘I should be handling this better, I should be stronger, I shouldn’t cry or be upset.’ They have to understand they are going to experience a broad range of emotions, just like other patients do,” she says.

Physicians are quick to tell patients to eat better, exercise, quit smoking, and find healthy ways to relax. But the

very practitioners that should embrace and embody healthy living and self-care have too often chosen for themselves long hours, late nights, perfectionism, and pushing past emotions.

Add to that the fact that physicians carry an average load of 2,300 patients annually. “Doctors who are super busy with their clinical practices have an awfully hard time balancing their own healthy lifestyle choices,” Baer says. “If you’re going to avoid burnout, you have to pay attention to this.

“We all need to be wellness champions in our own workplace: hold medical classes outside sitting on that beautiful lawn, spend time in nature or doing something creative,” she adds. “Apply that ‘can do’ fighting spirit and desire to heal to your own life.”

But individual resilience and healthy habits can only go so far.

As a wife and doctor, says Von, “It seems like I can never reach the elusive goal of work-life balance. My life more often feels like a job share between work guilt and home guilt.” She believes a broader culture shift must occur: supportive and exemplary leadership, caring and encouraging peers, and a corporate commitment to humanity.

To start the dialogue, she and colleague Julie Jackson-Murphy started a newsletter for Emory’s Division of Hospital Medicine called “Not Enough Said: Candid Conversations about Life and Medicine.” “I’d love to see our community’s commitment to clinician well-being intensify, expand, and be encoded into our professional structures,” Von says. “That’s when you start to come up with some real solutions.”

STRENGTHEN COMPASSION

Despite the emergence of ethics training as a core component, doctors and researchers say medical school’s so-called “hidden curriculum”—the socialization process by which norms and values are transmitted to future physicians—instructs students to be detached, objective, and self-interested.

One way to instill compassion

during medical school is to teach it. While conventional wisdom might view compassion as an inborn trait, research has proven the opposite—much like other skills, compassion can be strengthened through instruction. What’s more, it can be strengthened in both fledgling and veteran doctors.

William Branch Jr., professor of medicine at Emory, led an effort in 2009 to assess a faculty development program designed to encourage humanism—seeing the value and goodness



in others and acknowledging common needs and concerns. Over 18 months, groups of physician-teachers met biweekly to discuss and write about things like listening, building relationships, and adopting caring attitudes toward patients.

At the study’s end, the physician-teachers who participated were

evaluated against a control group, and the former outperformed the latter across the board. “I was very surprised by the results,” Branch said at the time. “These skills can help physicians grow, not just in terms of knowing more but in becoming a more whole person.”

Another Emory-led study suggests that learning compassion is not only possible, it can be a powerful antidote to stress and burnout. “We saw that well-being was a real problem for medical students and residents, and we concluded that it must be the process of providing compassionate care that leads to burnout,” says Jennifer Mascaro, assistant professor of family and preventive medicine at Emory, who led the study. In fact, it appears to be just the opposite.

She looked to cognitively based compassion training (CBCT) for lessons in managing stress. CBCT was developed at Emory by Lebsang Tenzin Negi, co-founder and director of the Emory-Tibet Partnership. The training is derived from Tibetan Buddhism and designed to promote a deep sense of connectedness to others as well as insight into the causes of suffering.

Mascaro and colleagues randomly assigned volunteer second-year medical students to either 10 weeks of CBCT or to a wait list. Before and after the training, students answered questions related to their compassion levels, personal health, and well-being. The results were unequivocal—wait-listed students reported declines in compassion consistent with past studies, while students who received CBCT experienced no declines in compassion and reported less depression and loneliness. “It’s not the ability to be compassionate that leads physicians to suffer depression or burnout,” she says. “It’s the blocks to compassion and empathy that lead to suffering.”

RESTORE JOY

The annual Blue Ridge Academic Health Group report, which this year focuses on health professionals’ well-being, states: “We pay a staggering cost in lost productivity, risks to mental and physical health, eroding quality and safety, diminished patient satisfaction, staff turnover, and lost dollars. At the extreme [is the] personal toll of depression and suicide. ... When joy is lacking and burnout is present, the stakes are high.”

When a group of Woodruff Health Sciences Center leaders studied clinician and staff burnout this past year, the takeaway was that health care organizations and the medical culture itself must change, “transforming infrastructure and processes at the source.”

Everything from night shifts to break schedules, computer time to patient load, office procedures to information technology must be reexamined with an eye toward protecting physicians’ time, health, and well-being. “There is no amount of yoga that can help at night when you are 50 charts behind,” says group member and Emory emergency medicine physician Doug Ander. His department has instituted the use of scribes to gather and document patient information, which has helped physicians return more of their time to direct patient care and mentoring.

“Health care has traditionally emphasized the triple aim of patient satisfaction, quality, and cost-effective care,” the group concluded. “We need to add clinician satisfaction to those priorities.” ■

procedure was difficult, a member of the team made a mistake, and the patient died. With that began what he describes as “the inquisition”—a long, arduous investigation that “goes on and on



DR. KURT HEISS: “When something goes south, many of us self-isolate...but the isolation is a killer.”

and on, you tell the story again and again and again,” Heiss says. “And if you want to share the findings of the root cause analysis with the family, you have to go through even more.”

As he endured that ordeal, he turned to books on bouncing back from difficult experiences and discovered that resilience is not a trait but rather a set of thoughts and

behaviors that anyone can learn and develop.

These include attracting and giving social support, imitating resilient role models, focusing on mission and purpose, and holding to the belief that “adverse events are neither permanent nor pervasive.”

Heiss also took stock of the “culture of blame” that predominates in many medical environments, which singles out for reproach the individual who makes a mistake while ignoring systemic issues that can lead to unsafe behaviors. By comparison, a “just culture” supports learning over punishment and putting into place safeguards that can prevent errors.

Emory and Children’s have instituted a three-tiered response to second-victim syndrome that includes awareness training, peer support, and referrals to professional help. “When something goes south, many of us self-isolate,” he says. “We’re embarrassed, we’re reflective, and we’re thoughtful. And everyone assumes we want to be left alone. But the isolation is a killer, and that’s when it’s helpful for people to swarm us, to help us regain perspective.”

Providers can learn the skills to reach out to a colleague in need. “Our focus should be them and their feelings, to remind them of all the good things they’ve done in caring for their patients.” That said, he adds, everyone mourns differently. If a person doesn’t want to talk, “we have to honor that. The victory for us is in the invitation.”—Patrick Adams

'LIKE AN ICE PICK TO THE BRAIN'

Inside a migraine: This single photon emission computed tomography (SPECT) scan captures a patient's brain during a migraine attack. The horizontal brain scan indicates high brain activity in red and yellow and low activity in green and blue.



A breeze drifts across the restaurant patio, where diners are clustered around long tables in bright green chairs that match the park-like setting. As the group looks over the dinner menu, neurologist Gregory Esper cautions everyone to make their selections carefully.

“There are foods and drinks that can induce migraines,” says Esper, director of general neurology and neuromuscular diseases at Emory Clinic and associate professor at Emory School of Medicine. “The most common are processed meats, aged cheeses, and red wine. But you might be sensitive to a particular food not on the ‘list.’ I know one woman who would get a migraine if she had the artificial sweetener stevia. Aspartame in diet drinks can be a trigger as well.”

Beyond migraines being a clinical interest, Esper himself suffers from them, as do each of the five guests. This is an opportunity to discuss migraine symptoms, triggers, treatments, and medications with an expert over a casual dinner. While



Esper can't offer specific suggestions in this situation, he can discuss generalities and answer questions broadly. “So, what constitutes a migraine as opposed to a headache?” Esper asks. “Well, it should be throbbing in nature, at least moderately

intense, and usually only on one side. In fact, the word is French for ‘pain in one half of the head.’ ”

Migraines can last from hours to days—most last 4 to 72 hours without treatment—and are sporadic. “If someone has a headache every day, that signals that it is not just a migraine,” says Esper. “Something else is going on.” In about 10 percent of cases of migraine-like headaches, the root cause is something else—a secondary condition.

The majority of migraine sufferers—60 percent to 80 percent—experience “common migraines,” in which the main symptom is the pain itself. “Classical migraines,” which include auras or other visual or sensory changes, can feel dangerous but usually are not, says Esper. “You might wonder



“I DON’T SEE AURAS, BUT SOMETIMES I SMELL ROSES”

if you’re having a stroke,” he says, “but a stroke is associated with a headache in only about 8 percent of cases.”

Migraine is both a genetic and an environmental disorder, Esper says: “Folks can be predisposed to having them, but triggers all around you can kick one off.”

The thinking is that, due to a stimulus and genetics, deep structures in the brain trigger activation of the “trigeminovascular system.” This causes blood vessels to dilate along the covering of the brain—the meninges—which is a very sensitive structure. Inflammatory mediators and neurotransmitters then seep onto the surface of the meninges, further dilating blood vessels and making them more “leaky.” These mediators and neurotransmitters excite the trigeminal nerve—the largest and most complex of the cranial nerves, responsible for sensation in the face and head—which stimulates the meninges to send signals to the part of the brain that senses pain.

“It becomes a vicious cycle,” Esper says, “which is why the pain can last a long time unless we cut it off with medications.”

When migraines start at a young age and are not treated correctly, they can change brain physiology. For some, migraines start at puberty and peak in middle age.

Others have experienced migraines since early childhood. For still others, migraines come on later in life, or after an event or injury.

One participant says his first migraine occurred after he fell in the night due to a spell of vertigo, and that he experienced a visual shift as well.

Sometimes, the participants say, they see flashing lights or feel strange before the headache’s onset—numb, tingly, or overly sensitive to stimuli.

“I don’t see auras, but sometimes I smell roses,” says one.

“Are there migraine-sniffing animals?” asks another. “My dog will come up to me and smell my eyeball and within an hour or two, I’ll have a migraine.”

“I don’t know about that,” says Esper, smiling, “but visual or sensory changes, and nausea or vomiting, are hallmarks of migraines.”

Most migraines involve a pulsing type of pain, which can migrate, says Esper. “Mine start at the back of my head and move forward. I can feel them coming on.”

“Mine feel like there’s an ice pick in my head,” says one participant. “Pain was just something I thought was normal.”

Preventing a migraine is far superior to trying to get rid of one that is full blown, says Esper.

“In the past 10 years, I have had tension-type headaches that, if controlled quickly with Fioricet, will go away,” says a participant who has had lifelong migraines. “If not, they will morph into a migraine in less than an hour.”

In general, Esper says, migraine pain is caused by vasodilation (expansion) in the cranial blood vessels, while headache pain is caused by vasoconstriction (narrowing) of the blood vessels.

Therefore, migraine medications are largely vasoconstrictors: first the ergots and then, in the 1990s, triptans, which are serotonin receptor agonists. These target a specific neurotransmitter receptor in the brain, 5-HT₁, thought to be associated with migraine pain.

Most at the table have tried a host of medications—Imitrex injections and pills, Treximet, Relpax, Maxalt, Zomig, Amerge, Fioricet. Triptans with naproxen sodium. Dilaudid with Phenergan injections (for migraines severe enough for an ER visit.)

“I take topiramate (Topomax) daily, which is designed to prevent migraines, and in the three years since I’ve been taking it, the number of migraines I have and their severity has gone down considerably,” says one participant. “I also take rizatriptan, a triptan that I call ‘the magic pill.’ It stops the bad feedback loop that leads to a migraine.”

Participants agree that taking medicine too late is useless. “I’m trying to learn not to be stingy with my pills and to take one when I feel the first symptoms, whether a light headache, or nausea, or an aura,” says one. “I keep up with my refills so I never feel like I’m going to run out.”

Several of the participants say they treat their migraines

with Botox. “It’s like I’m getting away with something,” says one. “The first time I didn’t have a headache after Botox, I couldn’t believe it. It’s 37 injections all over my head. I go every 90 days for injections, and I’m mostly free of migraines for the first time in my life. I didn’t know people were living like this, without pain.”

Esper makes a point to ask patients what is going on in their lives—relationships, work, diet, travel—since migraines can have environmental triggers. “An accountant comes to me every March to get ready for tax season,” Esper says. “Stress and sleepless nights can bring migraines on.”

One participant’s migraines had been misdiagnosed for 11 years as sinus headaches. Another went on vacation for 10 days and didn’t have one the entire time—she wasn’t sure if it was due to change of climate or less stress.

Estrogen, through hormone replacement therapy or oral contraceptives, can help or hurt, says Esper.

Some antidepressants are used to treat migraines—Es-

per recommends tricyclic antidepressants as first-line therapies. Other antidepressant drug classes may not work as well. “Cymbalta—it’s like putting my brain in a sling,” says one participant. “My knitting gets looser. I’m more relaxed.”

A “what if” question is posed: What if you had never had migraines? Some participants say they might have taken part in more activities, been more social, worried less.

Esper, who first experienced migraines in medical school and residency when he was under pressure and getting little sleep, says his migraines have one upside: “They have given me more empathy and compassion for my patients.” ■

Windows of Opportunity

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Dinner with a Doctor participants:



Wendy Darling
communication specialist
First migraine at 11 or 12

► **Usual symptoms:** Pain on one side of face, often at temple or eye socket, like a spike through my head or a rock pressing against it, pain in the back, lower neck, nausea, feeling “floaty” or dizzy, hard time focusing.

► **What helps:** Topiramate and Rizatripan, and hot showers with water directed at my face and head.



Andrew Thompson
lawyer
First migraine about 6

► **Usual symptoms:** Often begins with a pulsing headache on one side of forehead, usually the right, with pain and behind right eye. The migraine will spread from the forehead to the base of the skull, close to the neck, on the same side. “The migration may take a day or two until I eventually become very sensitive to light.”

► **What helps:** Lots of sleep, eliminating dark chocolate, wine, and other foods and beverages with tannins from my diet. As far as medicines, Excedrin migraine and sometimes an Imitrex when one is at its worst.



Claire Hennessey
fundraising director
First migraine at 13

► **Usual symptoms:** Intense pain at base of neck and behind left eye, nauseous, very sensitive to smell and light, unable to focus.

► **What helps:** “I have tried every Triptan in the book, nerve blocks, Eastern and Western medicine—what’s working for me now is the use of two preventive daily medications, Botox injections every three months, and Imitrex when I get a migraine.”



Susan Scarbrough
executive assistant/editor
First migraine: “I have never not had migraines.”

► **Usual symptoms:** In the last decade, pain either unilateral (right frontal) or bilateral. Sometimes I feel like my right ear needs to pop.

► **What helps:** Imitrex injections, Imitrex pills, Treximet, Relpax pills and dissolvables, Maxalt pills and dissolvables, Zomig dissolvables, Amerge pills, Fioricet. Triptans always perform better for me in combination with naproxen sodium. In the ER, Dilaudid with Phenergan piggyback injections.



John Johnston
English professor
First migraine: adult

► **Usual symptoms:** Visual shift in perception, pain.

► **What helps:** Relaxing, being in a dark room, medications.

Learning *from* Lampreys

*An ancient immune
system provides insights
into our own*



BY Quinn Eastman ■ ILLUSTRATION BY Andrew Bannecker

Lampreys are described as primitive predators, aggressive flesh feeders, and piston-tongued parasites. To watch a lamprey attach itself to the glass of an aquarium or dangle off the side of an unfortunate fish causes an involuntary shudder.

In the Great Lakes region, lampreys are viewed as fish-killing pests and an invasive species and are regularly poisoned to control their numbers. In Europe during the Middle Ages they were considered a delicacy.

But in immunologist Max Cooper's Emory Vaccine Center lab, researchers see lampreys as windows into the distant past and biomedical treasure troves that may contain disease-fighting secrets from another eon.

Lampreys and their close cousins, hagfish—both jawless vertebrates—are early offshoots on the evolutionary tree, having diverged from jawed fish and sharks and, ultimately, humans, hundreds of millions of years ago.

“Our studies led to the discovery that two very different types of adaptive immune systems have evolved in vertebrates,” says Cooper. Adaptive immune systems can “remember” and target certain pathogens they have encountered before.

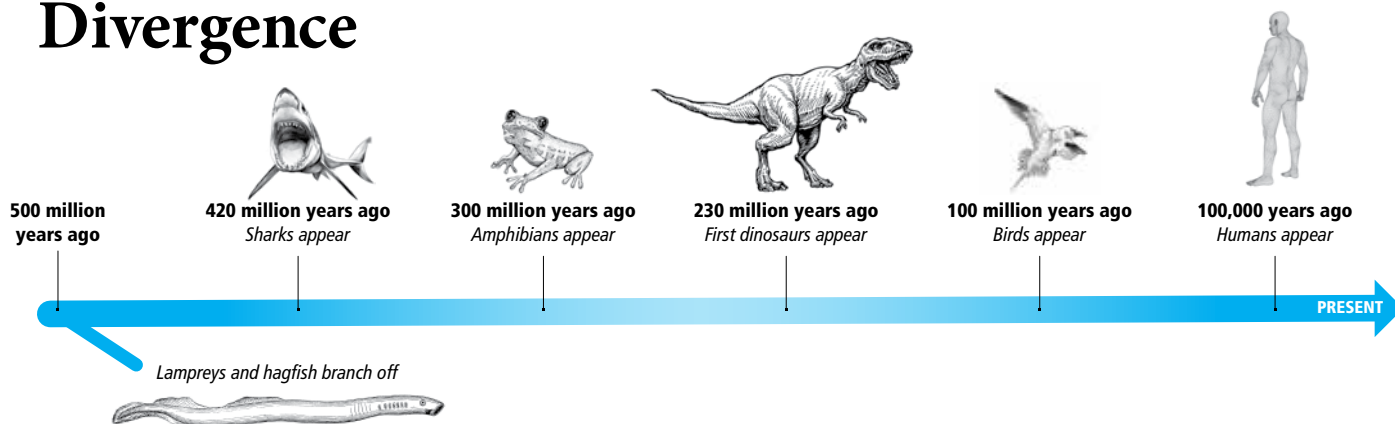
While lampreys may look primitive, like parasitic tubes with teeth, they have sophisticated immune systems, which is why Cooper is interested in them.

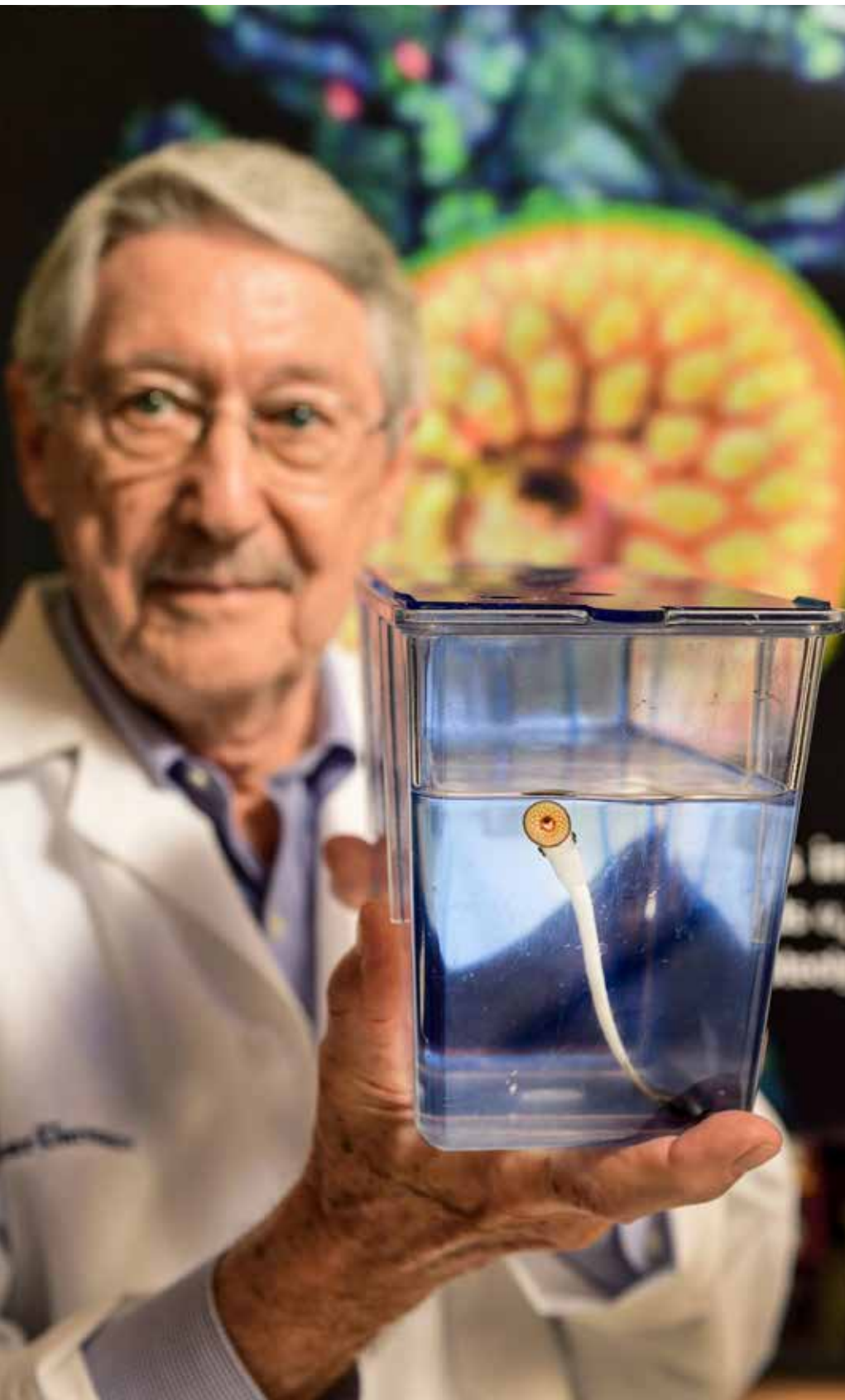
To defend themselves against microbes, lampreys' immune cells produce proteins that grab onto foreign substances, much the same as our own antibodies. But these proteins don't look anything like the antibodies found in mammals, birds, and jawed fish.



Professor of Pathology and Laboratory Medicine Max Cooper discovered B-cell and T-cell systems in the 1960s, laying the groundwork for modern immunology.

Divergence





Max Cooper, a Georgia Research Alliance Eminent Scholar, is interested in the lamprey's unique immune system, which separated from our own about 500 million years ago. Here he holds a juvenile lamprey.

So studying these creatures provides scientists a glimpse of where the human immune system came from—as well as how ours might have looked if evolution had taken a different path.

While vertebrates went on to develop jaws, and eventually evolved into mammals, primates, and humans, vertebrates without jaws (lampreys and hagfish) stayed similar in form to their genetic forebears.

Mature lampreys attach themselves to fish and feed on their innards or their blood. While adults can extend as long as your arm, Cooper's lab studies the finger-sized larvae. In the wild, these lamprey larvae feed on the muck at the bottom of streams and rivers for a few years before getting big enough to go foraging. "We work with the juveniles, which are like teenagers if humans became adults at age 50," says Jonathan Rast, senior scientist.

In Emory's animal facilities, scientists keep lampreys in tubs and feed the larvae brewer's yeast. Cooper's lab gets its lampreys from biologists in the Midwest, who catch lampreys by first stunning them with electricity.

"We used to do the same kind of thing when I was growing up in Mississippi," Cooper says. "It was called 'telephone fishing' because someone would crank the magnet from a telephone."

The story of why lampreys came to attract Cooper's attention, however, begins more than five decades ago—not with fish, but with fowl.

INVADER ALERT

Two main types of white blood cells, or lymphocytes, drive our adaptive immune responses: T cells, which use cell-to-cell contact, and B cells, which produce antibodies.

T cells shuttle through our bodies ready to respond to invaders—think K-9 sniffers. Some T cells can target and kill cells that are infected by viruses because tiny traces of the invader are found on the target cells' surfaces.

In contrast, B cells are like factories designed to make bombs (antibodies)

that will blow up one specific enemy.

We know about B cells and T cells because of pioneering work done by Cooper in the 1960s with Robert Good at the University of Minnesota that helped lay the foundation for modern immunology.

Cooper started his career as a pediatrician and became interested in children with inherited immunodeficiencies. One group of kids had trouble fighting viruses, while others had trouble making antibodies.

This led him to study birds, because in the 1950s, researchers at Ohio State had already had some success modeling antibody deficiency in chickens.

B IS FOR BURSA

B cells are named after an organ found only in birds, called the bursa of Fabricius. T cells are named after the thymus, where they develop in both birds and mammals.

Cooper and Good were the first to demonstrate that the B cells needed for antibody production develop in the bursa, and that B cells and T cells develop in different places.

“The effect of this accomplishment is difficult to overstate,” wrote Alexander Gitlin and Michel Nussenzweig in the journal *Nature*. “Through their discovery of the B and T cell systems, Cooper and his colleagues set in motion a series of landmark findings... As these discoveries continue to affect human health, it remains important to remember their origins in an experiment performed 50 years ago, by Cooper, in chickens.”

In humans, the precursors of B cells and T cells begin in the bone marrow but develop along different paths, reuniting in the spleen and lymph nodes, where they collaborate to mount immune responses and take down pathogens.

In the 1970s, the discovery of B cells gave birth to monoclonal antibody technology. Basically, this allowed researchers to make clones of antibodies that target particular cells or proteins.

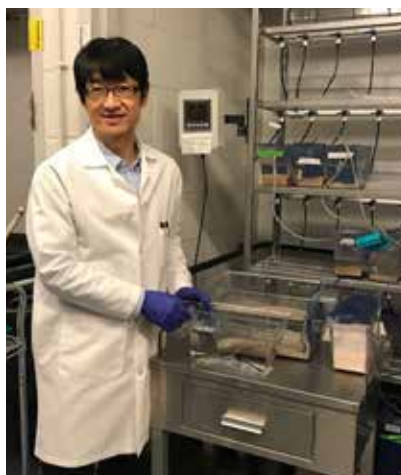
Over the past few decades the FDA has approved more than a dozen monoclonal antibodies to treat cancers. Because they can more specifically target cancer cells, antibodies aren't as destructive to healthy cells as chemotherapy or radiation.

More recently, monoclonal antibodies have been enlisted to fine-tune the immune system. The drug that enabled former President Jimmy Carter to beat metastatic melanoma? A monoclonal antibody.

Researchers have created antibodies for even more diseases, such as inherited high cholesterol, rheumatoid arthritis, multiple sclerosis, and Ebola.

DISEASE-FIGHTING CLUES

Cooper had begun studying lampreys and their immune systems to figure out which came first, B cells or T cells. The secondary benefits of this research are still unfolding: What kinds of disease-fighting clues and cures might lamprey antibodies contain?



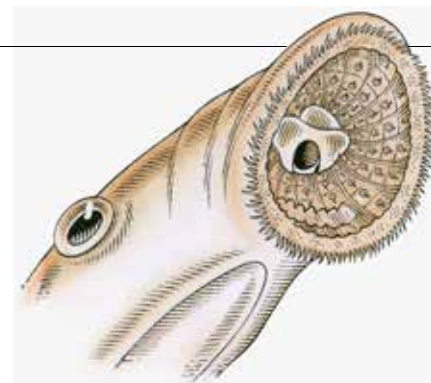
Masa Hirano, assistant professor of pathology and laboratory medicine, is investigating new lymphocytes (B and T cells) in lampreys.

Lampreys' antibody-like molecules are called “variable lymphocyte receptors” or VLRs.

When Cooper and colleagues first discovered VLRs at the University of Alabama-Birmingham, the scientists recognized that they might also have potential as diagnostic tools



Lamprey trivia: In some European countries, lamprey meat was regarded as a delicacy—King Henry I of England is said to have died from consuming a “surfeit of lampreys.”



Engineering immune cells to treat cancer

One way lamprey antibodies are being weaponized is by using CAR-T (chimeric antigen receptor T cell) technology, which was recently approved by the FDA to treat some forms of leukemia and lymphoma. In CAR-T, immune cells are removed from an individual, “retrained” by giving them extra genes, and infused into cancer patients. This approach has shown dramatic success in eliminating cancer, with less harsh side effects than other treatments. But manufacturer Novartis projects costs upward of \$500,000 per patient. Researchers around the world are trying CAR-T on other types of cancer; success could eventually mean lower costs.

or cancer-fighting drugs.

When Cooper came to Emory in 2008, his team continued to explore how to harness lamprey antibodies' unique properties. VLRs could offer some advantages over standard, mammalian antibodies that are currently used against cancer and autoimmune diseases. As proteins, VLRs are sturdy and don't need to be refrigerated. And they are simple—they come in one piece and are easier to engineer genetically.

"In every case we've tested, VLRs were more specific than a standard antibody," Cooper says, citing experiments in which lamprey antibodies were isolated after the lampreys were immunized with anthrax spores. "Even when VLRs recognize the same target as a conventional antibody, they recognize it differently. I think it's because their structure is simpler and more rigid."

And possibly, a whole lot older.

500 MILLION YEAR ADVANTAGE

Lamprey antibodies are relative strangers to certain modern pathogens. When fighting disease, this lack of antibody familiarity allows doctors a leg up.

Because VLRs come from vertebrates so far removed from humans, they can be used to target important molecules that have persisted in similar form through millions of years of evolution—so-called "conserved antigens."

Our immune system generates vast libraries of potential antibodies, but the ones that react against "self" (something already in the body) are generally muted or edited out. If they weren't, our immune system would be in perpetual overdrive, similar to what occurs in autoimmune diseases.

If researchers are trying to make antibodies against something in mice, they can get around this muting response by immunizing and collecting antibodies from different animals—say, rabbits or goats—instead. But what if they are dealing with a molecule that's common to almost all mammals? That's where lampreys come in. "It's hard to generate a classical monoclonal antibody against

a conserved antigen," Cooper says. "But if you are separated by 500 million years of evolution, like lampreys are, you may have a better chance."

One example of an immune target that has been difficult is plasma cells, the bone marrow cells that churn out antibodies. In a sense, plasma cells are specialized, fully mature B cells; the healthy counterparts to multiple myeloma cells.

Former Cooper lab member Goetz Ehrhardt, now at the University of Toronto, immunized lampreys with bone marrow from a multiple myeloma patient. Scientists were able to pick out a VLR that reacted specifically with plasma cells and myeloma cells. The VLR they found targets the same molecule as a recent FDA-approved treatment for multiple myeloma—proof that lamprey antibodies could be useful.

"Because of the unique origins of lamprey antibodies and their radically distinct protein architecture, these molecules may be able to recognize structures that conventional antibodies cannot," Ehrhardt says.

WEAPONIZING ANTIBODIES

A biotech company called NovAb, formed with the help of the Georgia Research Alliance, aims to commercialize lamprey antibodies. NovAb created a "weaponized" version of the same antibody that recognizes plasma cells and has shown good results in the lab. In mice, this version works just as well as standard treatments, says company CEO Ed Cannon.

In Emory's Department of Pediatrics, Associate Professor Trent Spencer and graduate student Robert Moot have also been experimenting with lamprey antibodies for possible use against leukemia or neuroblastoma, a common form of tumor in children.

Looking ahead, Cannon and Cooper say that lamprey-derived molecules may have special roles to play that ordinary antibodies can't. "We are not interested in reproducing or replacing existing drugs," Cannon says. "We are more interested in targeting molecules against



Cover Worthy: Max

Cooper's work with lampreys has been featured in some high-profile journals, such as *Nature* and *Nature Immunology*.

which conventional antibody technology has been often unsuccessful."

One possible target: brain cancer stem cells.

While the potential anticancer weapons proliferate, Cooper's lab continues to unearth more of lampreys' basic biology.

Despite the progress of the last decade, how lampreys slice and dice their genes to create a huge variety of antibodies is still mysterious.

And, perhaps because of lampreys' status as pests, little is known about the viruses that lampreys' immune systems are called upon to fight. "Viruses played a huge role in shaping the evolution of the vertebrate immune system," says virologist and cell death expert Ed Mocarski, an Emory Woodruff Professor in microbiology and immunology. "If more is known about viruses that infect lampreys, it could unlock other molecular details about lamprey immunology."

Lamprey antibody technology also could be applied against HIV, influenza, and other infectious agents.

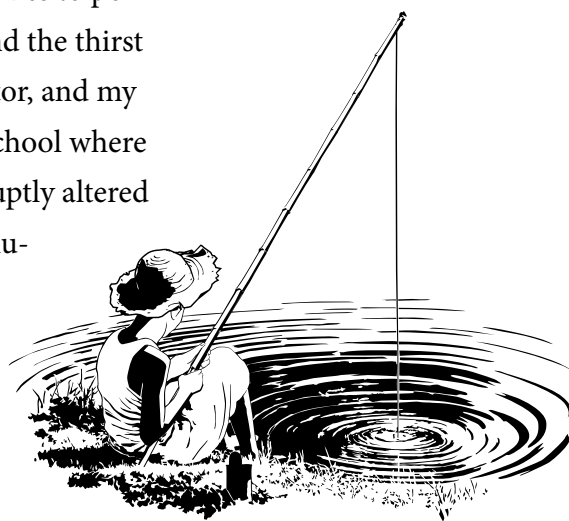
Although ancient in origin, lampreys could become the foundation for the next generation of immunotherapy weapons, able to boost our body's own ability to fight disease.

That's enough to make these toothy parasites seem downright valiant. ■

“ONE OF THE MOST REMARKABLE THINGS ABOUT A CAREER IN BIOMEDICAL RESEARCH IS THAT YOU CAN START ALMOST ANYWHERE AND END UP IN THE MOST UNFORESEEN PLACES, BEING CONSTANTLY AMAZED BY WHAT YOU ARE LEARNING ALONG THE WAY.”—Max Cooper

Max Cooper on Becoming a Physician Scientist

Little did I imagine while growing up in rural Mississippi in the 1930s that I would eventually pursue a research career in immunology. My childhood was rich in unfettered time, space to roam freely, woods and streams to explore, an uncontaminated view of starry night skies to ponder, and an abundance of books to read. The treasure of books and the thirst to read them were gifts of my father, a mathematician and educator, and my mother, also a teacher. We lived on the campus of the 12-grade school where my father was the superintendent. The tranquility of life was abruptly altered in 1941 by U.S. entry into World War II. Older boys in the community were drafted into the military services, my mother began to work in an underground munitions plant, and, in 1945, my older brother joined the Marines at age 17, just before peace was declared. As a high school senior obsessed with sports, hunting, and girls, I began to realize that reaching my stated goal of becoming a doctor would require a great zeal for study and a long time in school at a high cost. The tragic death of my wonderful and adventurous older brother in an automobile accident abruptly changed this equation for me. He had made me the beneficiary of his service insurance policy. During this time of intense family grieving, my father took me aside to tell me that I now must do what my brother and I both would have done. Although my interests did not change overnight and my study habits failed to undergo any miraculous transformation, I began the well-prescribed course to becoming a doctor. My fascination with caring for patients and understanding the pathophysiology of their diseases grew at each step along this career path. It became more and more obvious that I had stumbled into an endless wonderland of challenging problems. ■



Windows of Opportunity

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To find out more, contact Ashley Michaud, senior director of development, at 404.778.1250 or ashleymichaud@emory.edu.

This is an excerpt from an essay by Max Cooper that first ran in the *Annual Review of Immunology*.

55 words

Fifty-five word stories are brief pieces of experiential writing that use elements of poetry and prose to encapsulate key experiences. Hughes Evans, vice chair for education in the Department of Pediatrics, uses the technique with her medical students and residents. “We often pare down our stories to be clinical, but that leaves out other aspects that have emotional resonance, parts that are funny or poignant,” she says. “These speak to a part of being a doctor that doesn’t always get its due—about death, making mistakes, or other things that are hard to deal with.”

Andrew McReynolds

Letting Go

24 years old. Blue jeans, white shirt. Credit card, driver’s license in a small black wallet. Bloodied, bruised, broken in pieces. A crumpled piece of paper in there. You want what’s best for your family. How did it feel, before you fell, to let go? Are you feeling better now? We picked up the pieces.



Rachel Buckle

Rush Delivery

2 am, an urgent call when we show up, her sheets are already soaked
a chaotic rush to delivery translator yelling through the phone.
I have never seen so much blood.
I only know enough to be paralyzed.
She only knows enough to push through.
One still moment
Dad pleads, “Baby?”
With sharp wailing, baby answers.

Divya Kishore

Nobody Left

The 20-year-old in cardiogenic shock said she had nobody. Her hobbies included playing games on her phone, and watching TV. Her mom and sister had died and she’d been through foster care. Her dad couldn’t raise her so he left. Through tears she asked us to please leave her alone before her right heart catheterization.



Kristen Balkam

Comedian at 7

Seven years old.
He came in having swallowed a quarter.
It was stuck. Endoscopy needed in the morning.
He smiled at me as I examined him.
I placed my stethoscope on his abdomen.
He wiggled his body back and forth.
He asked,
“Can you hear it? ... I’m a piggy bank.”
Kids say the darnedest things.

Lia Phillips

The Conversation

Baby boy in for VSD repair.
Surgeons can’t pass the Foley.
Heart repair postponed. Parents expect a fixed baby, instead are learning to change an ostomy.
In recovery, new organ defects discovered every day. Hope of having a normal child is gone, parents are grieving. Am I really the best person to start this conversation?

Erica Smearman

Passing On

I remember the human body, splayed open, organs now removed. Sitting next to a liver packaged in a box for the trip back. Surgeons await. I pass it over. An insurmountable gift.
Through a death I helped finish, to the chance at life for another.
The joy. The heartbreak.
Wildly, beautifully,
tied together as one.



Lizzy Robertson

First Week

Code blue, what do I do?
 Jumbled resuscitation algorithms
 in my head
 Heart racing, what room again?
 Pager drops on the floor and breaks
 Keep running, out of breath
 Don't know where that room is
 Think I went down this hall already
 Left or right? Which way?
 Lost in the hospital
 Code canceled!
 Thank God.

Nathan Yarnell

Todo Está Bien

New diagnosis. AML. Poor prognosis.
 Mom confident. Prefiere espanol. Play-
 ful, curly black locks. A real lady-killer
 at 12 months. Su fe en El Dios. Chemo-
 therapy. Good PO. Broken Spanish. Está
 bien. New rash. Hopeful spirit. Está
 bien. Restricted from the garden. Está
 bien. Curly black locks fall to the floor.
 Está bien. Todo Está bien.



Omar Shakeel

Curveball

Healthy boy with new onset seizures,
 Diagnosed with AVM, successfully
 resected, prognosis good,
 We anticipate a quick recovery.
 Curveball
 Increased ICP. EVD continues to drain.
 Pentobarb coma.
 Three weeks pass,
 we expect the worst.
 Parents refuse to give up...
 Just when your mind is made up,
 his mind wakes up.
 Never give up on miracles.

Uriel Castaneda

Uncle Doctor

4 a.m. 3-year-old niece in Egleston ED.
 Bowel telescoping explains her shrieks.
 Uncle is here! What can he do? Explain
 diagnosis, bring popsicles, play Frozen
 the movie, interpret, advocate. He's
 tired. Is he doing enough? Pain subsides
 with reduction. No surgery, thank God.
 How will I be remembered? Will my
 niece remember me as the doctor
 or the uncle?

Rob Gonsalves

13 Years

It wasn't long ago that I was the one
 in a hospital bed. A new diagnosis.
 Finger-sticks and insulin injections.
 A long and bumpy road that undoubt-
 edly led to my career in medicine.
 Now I am the one in the white coat.
 Making the diagnosis. Breaking the
 bad news. Offering hope. It's come
 full circle.



Courtney Charvat

Monday Morning Quarterback

Back on service
 Kid with rash may have Middle Eastern
 Respiratory Syndrome
 ... Cool!
 Mom says visited Dubai, rode camels.
 Dr. Miller super excited!
 Health crisis! CDC called, lab emergent-
 ly opened.
 MERS negative.
 Mom acts weird, goes to ED because
 nonresponsive.
 Call grandma who says, "He's never left
 Georgia. No camels. Momma crazy."
 Discharge diagnosis ... rash.

Brian Winn

Why My Child?

Hot summer day, middle of June. EMS
 calls in 5-year-old drowning, in asys-
 tole. We beat on her chest, give many
 rounds of epi surrounded by noisy
 chaos. All the while she stays cool,
 dark and dusky. The attending finally
 ends the madness. Mom asks "Why my
 child?" I reply, "I wish I knew."

Allison Gay

First Time

Hughes Clinic, intern year. Newborn
 visit. First-time mom, full of questions.
 I feel overwhelmed too, but we make it
 through. 2-week visit, 2 months, then 4.
 Always bigger, always happier.
 9-month visit now, big laugh, bigger
 cheeks. Mom holds him up, whispers
 in his ear, "Look bud, it's your doctor!"
 Small victories.



Marie Duftumukiza

Unresponsive

Notification—2-month-old by EMS—
 cardiac arrest. Heart thumps! Nervous!
 Eyes on attending. "What do I do?"
 "CPR." Sigh of relief. I can do this. Baby
 arrives, unresponsive. Start compres-
 sions. Praying under breath. Mother
 stands in corner with tears, 5, 10, 15
 minutes, nothing. "Time to call it."
 I look up, lump in throat.

Laura Wilson

Quiet Soldier

18-year-old with terrible disease. Dialy-
 sis dependent. Listed for transplant. Fi-
 nally gets the call. Initial course is rocky
 but almost ready for home. "My back
 hurts. I don't feel so good." Crash. Code.
 Arterial anastomosis blown. Transplant
 is lost. Depression sets in. "I shouldn't
 have survived." Epiphany occurs. He is
 strong. Relisted once again.

The Other End of the Stethoscope

I receive a call from my father. His voice heavy and calm, he says my name as I pick up the phone. Am I someplace where I can talk?

There is news, unfortunately. A mass. He speaks with the same quiet reserve and scientific openness to fact that have made him a good physician. There is courage in his maintenance of this stance even as he finds himself on the other end of the stethoscope.

The surgeon, Viraj Master, has already called. It calms my father to know that Dr. Master advises the World Health Organization on renal cancer. They will meet tomorrow.

I bite my lip through the call, not wanting to burden him with my own fear at the thought of losing the man on the other end of the line.

The air in Atlanta is warmer than the air I left behind in New York. As I enter my father's room, he sees me first. My mother is asleep in the chair beside him. He pulls me close, holds my head to his chest for a long time. He is still groggy, not long post-op, but he wants to show me his scars. He lifts his gown with pride to reveal three small holes, one for each trocar, and a large incision in the midline.

At 3 a.m., I awake uncomfortably in the chair beside him to the squeaky wheels of the phlebotomy cart. At its helm is a tiny woman cloaked in headscarf and accent and night. Anonymous, ageless, she is a gentle ambassador from a faraway place, destined to wander dim halls into dark rooms to draw the blood of the sick of this place. "You've done this before," he tells her. I hear her smile in the darkness.

In the morning, the residents are nervous, untucked, their confidence and unquestioned authority unsettled by the presence of a senior member of the medical faculty in the bed before them.

When Master arrives, he is crisp, pressed, and wearing deep blue suit pants beneath his white coat. My father is in the chair. Master asks to sit on his bed. A foot below my father, he looks up at him to ask how he's feeling. He proceeds to cite four articles in five minutes, one on the benefits of ice after abdominal surgery, another on postnephrectomy kidney function. He wants the same thing from my father the residents did, but is better equipped to get it. When he leaves, my father turns to me, wants to know if I caught that—how Master sat below him on the bed, approaching from below to put him at ease.

Later I return from the cafeteria to the sound of my father's voice. He is on the phone with his nurse's aide, calls her by name. He wonders if she's free to take a walk. Of all the people on the floor, he has connected most with her, the

lowest-paid member of the team, with the least training. By a twist, she is the one least afraid of him.

"They told me you would be trouble because you're a doctor," she tells him, "but you're OK."

They walk slowly, IV pole in tow. She insists he hold the wooden railing while she remains firmly at his other side. The first lap is enough.

But he is ready again an hour later. Two laps, then four.

I catch snippets of their conversation as they pass his room. She hopes to go into speech pathology if she can afford the training. "You'll be good at that," he tells her.

He begins to push himself to break his own record, a moving goalpost scrawled on the whiteboard in his room. Twenty laps to a mile.

Thirty laps. Forty laps. Home.

My father is back at work now. His scans are clear three years out.

I am in my fourth year of medical school. As I walk the halls of my hospital, I often think of those nights I spent with him in his. I think, too, about what I'm looking for in medicine.

I enjoy the dynamic strength of its methods—the double edge of its empiricism—which damns it to abandon its most sacred truths as soon as still holier evidence comes to light. But I know that I am here for something loftier than a certain methodology and the mechanisms it illuminates.

I want to find, in the depth of a fluorescent night or the stillness of a linoleum day, some understanding of life and death, my own life, my own death, your life and your death.

I believe I have come to medicine looking for a kind of peace and purpose. I do wonder whether it lives here. What my father showed me—as he was learning to be a patient for the first time in a life full of patients—is that it does. ■



Evan Joiner is a medical student at Columbia University's College of Physicians and Surgeons. His father, Emory Professor of Pediatrics Clinton Joiner, is director of the hematology program. This essay first appeared in the New England Journal of Medicine.



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