

Mind Over Matter

After a devastating zip line accident, Aimee Copeland is forging ahead with grit, vision, and some high-tech hardware



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SPRING 2015

As her doctors told Paula how they were proposing to treat her seizures, her eyes grew wide. Her mother said, "Just listen to them, babe."

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Big Data is transforming critical care by using real-time, streaming analytics to predict which patients need extra attention—sometimes even before the crisis occurs.

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Saving Lives with Big Data



CHRISTIAN LARSEN
Dean, Emory School of Medicine
President, Emory Healthcare
Physicians Group

What if we could look into a crystal ball and predict which ICU patients were going to experience a life-threatening event in the next few hours or days?

We could intervene, possibly preventing the event instead of treating it after the fact.

Emory University Hospital is, in fact, using a pioneering model of predictive care for its most vulnerable patients. The new system can identify patterns in physiological data and instantly alert clinicians to danger signs, using real-time streaming analytics.

Big Data, which has revolutionized the airline, food, manufacturing, retail, and countless other industries, is also transforming health care. Huge databases of coded, aggregate information from past patients (with individual identifiers removed, of course) make this leap possible. A patient's vital signs can be compared not only with his or her own physiological data from an hour or a day ago but also to data from hundreds, even thousands, of others previously treated for the same condition.

"Everybody is different, sure, but if you record enough patients and enough information about each patient, you start to see similarities within subgroups," says biomedical engineer Gari Clifford, an associate professor of biomedical informatics who helps interpret Emory's data. "Then you can find a model that will be predictive for that individual and will allow you to recognize early warning signs."

Today's ICUs incorporate the best of design, functionality, and technology to create a nurturing, healing environment that is digitized, collaborative, and intuitive. (See the "Smarter ICU" infographic on page 12 and a Q&A with Dr. Tim Buchman, director of Emory's Critical Care Center on page 14.)

Emory's prototype, created in partnership with IBM and Excel Medical Electronics, uses software to collect and analyze more than 2,000 data points per patient per second.

This metadata can illuminate patterns that precede complications like pneumonia or that indicate imminent, life-threatening conditions like septic shock. It can even let us know that Mr. Z, who is being released from the ICU today, is 20 percent less likely to return if he receives this medication or that follow-up care.

As we get better at parsing and analyzing this wealth of data, we will also improve the efficiency and effectiveness of patient care—now and in the future. That's an algorithm we can all celebrate.



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Emory Medicine is published three times a year for School of Medicine alumni, faculty, and staff, as well as patients, donors, neighbors, and other friends of Emory Medicine. Produced by the Woodruff Health Sciences Center Communications Office, the magazine is made possible by support from the medical school dean and the Robert W. Woodruff Health Sciences Center Fund. © Emory University

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A Match Made on Facebook



WHEN GEORGIA POLICE OFFICER RALEIGH CALLAWAY PROGRESSED TO END-STAGE KIDNEY FAILURE, HE FACED AN ADDITIONAL CHALLENGE: AFRICAN AMERICANS ARE LESS LIKELY TO RECEIVE A KIDNEY FROM A LIVING ORGAN DONOR.

His wife, Kristi, decided to try to increase his odds by creating a Facebook page. The couple posed for photos with their two young daughters, who held signs reading, "Our Daddy Needs a Kidney."

Shortly after the post, nearly a thousand people contacted the Emory Transplant Center with offers to help. The overwhelming number of callers forced the center to shut down its phone lines and direct the calls straight to voicemail. "The response was really, really overwhelming," recalls Stephen Pastan, medical director of Emory's kidney-pancreas transplant program. "It's a big commitment to be a kidney donor."

More than 100 of the volunteers were evaluated as potential donors for Callaway, 49, whose renal failure was due to complications of type 2 diabetes and high blood pressure.

Chris Carroll, a 50-year-old health care consultant from Texas (below, with Callaway), ended up being an excellent match. "I've donated blood for most of my life but had never considered giving a kidney," he said. "When I saw this story, I felt God calling me to do it."

Callaway received his donated kidney on Sept. 25, after just two months on the donor list. Both men came through the operation successfully, and Callaway's condition improved almost immediately.

In response to the influx of calls, the Emory Transplant Center reorganized to shorten time between evaluations and referrals; it also added positions in both the living and deceased donor programs. Several of the callers were paired with others on the waiting list for kidney transplants.

The Emory Transplant Center has some of the highest successful kidney transplant rates in the nation. However, Georgia performs the lowest number of kidney transplants of any state. Close to 70 percent of dialysis patients in the Southeast are African American, nearly double the national average.

Emory researcher and epidemiologist Rachel Patzer leads a National Institutes of Health-funded community investigation on reducing disparities. Two years ago, the Carlos and Marguerite Mason Trust awarded \$1.1 million to the Emory Transplant Center to improve access to transplantation care for low-income Georgians. And Pastan leads the program Explore Transplants, which holds educational sessions for dialysis unit staff. The goal is to identify dialysis centers with the lowest transplant rates or highest racial disparities and to reverse the numbers.

"The number of patients referred to transplant centers has gone up a lot," says Pastan. "And not just at Emory but at other centers in Georgia."

Meanwhile, the Callaways hope to share their good fortune by profiling others still waiting for a kidney on their Facebook page. As for the family's message, it has been updated to read: "Our daddy found a kidney."—*Caroline Eggers*

At the Emory Transplant Center, around 220 kidney transplants are performed each year. Though the number of deceased donors is relatively fixed, the potential for live donations could increase substantially. The center's team normally performs between 60 to 65 live-donor transplants annually, although in 2014 it performed more than 80. "It's still fewer than we should be doing," says Stephen Pastan, program director. This year, he's hoping to break 100.



Thank you for the fine stories on Emory and Ebola. It is clear Emory has a lot to be proud of as an institution, and I shared in this pride as I watched the medical caravans proceed down Clifton Road outside my office window to Emory Hospital. Signature, high-profile, emotional events like this also provide an important opportunity to reflect. Here I raise just a couple types of ethical questions that arose in conversations I had in and around Emory during the time Ebola was here—questions not meant to condemn, but rather to provoke and use the momentum natural to such events for productive exploration. These are questions of attention and allocation of resources. In the case of Ebola, there was a great and enormous

response finally in this country only when white Americans got the disease—a disease from which only two people have died in the U.S., neither of whom contracted the disease here. Meanwhile, consider two other epidemics in the U.S.: (1) according to the CDC, 30,000 to 50,000 Americans die from the flu annually and (2) according to the *NY Times*, as many as two African Americans a week die at the hands of police. And of course the obvious question: how difficult is it for many, many Atlantans and other Americans to receive any kind of health care at all? Emory, according to our mission statement, is a community of scholars striving “to create, preserve, teach, and apply knowledge in the service of humanity.” We did this strikingly with Ebola; let’s continue to apply that same energy thoughtfully and effectively to all that needs doing.

Arri Eisen, PhD

Professor of Pedagogy
Biology, Institute of the Liberal Arts, Center for Ethics

I was enthralled by the storytelling in the latest issue—not just the reporting on Ebola, but also on neonatal care, Nadine Kaslow’s essay [“The Fear Factor”], just all of it. The Q&A with Aneesh Mehta had all the details about Ebola that I had been wishing national news outlets would dive into, and the illustration with the detailed breakdown of the Ebola virus structure was gorgeous. Plus Jack Kears’s photo of Kent Brantly giving high-fives was amazing.

Erica Endicott

Senior graphic designer, Institute Communications
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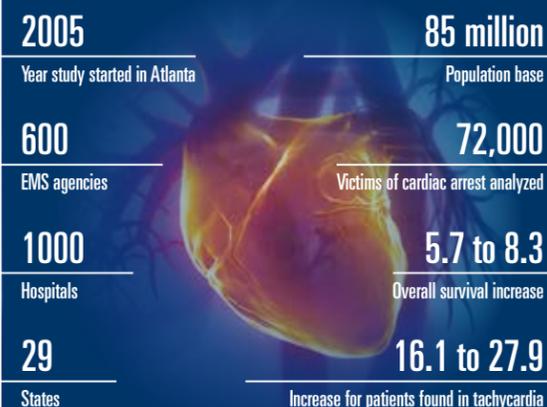
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By the Numbers

Survival rates for patients who experience “out-of-hospital” cardiac arrests have improved steadily over the past decade. Why? Because other people got involved. Bystander CPR and use of on-site automated external defibrillators contributed to the higher number of survivors, according to a study by Bryan McNally, associate professor of emergency medicine at Emory. “The study is about getting back to the basics and teaching community members to start CPR if someone is in need, rather than waiting on emergency personnel to arrive,” McNally says. ■



Slush Fund: The Ice Bucket Challenge raised \$115 million for the ALS Association. Jonathan Glass, who directs the Emory ALS Center, is one of the US investigators for Project MinE, an international genetic research program that will receive \$1 million in challenge funds. “In terms of a campaign, it was just extraordinary. We have money; we have awareness,” says Glass, who performed the challenge with his team. “Even my mother did it—and she’s 87 years old.” MinE will map the DNA of 15,000 people with ALS and compare these profiles with the profiles of 7,500 control subjects to identify genes that may influence whether and when someone will get ALS, how quickly it manifests, and how the disease affects the body.



Drs. Nicholas Boulis (left) and Jonathan Glass take part in the ALS Ice Bucket Challenge in front of the School of Medicine.

Use it or Lose it Teaching stroke patients to use their stroke-affected arm instead of their “good” arm has become a wide-spread physical therapy (PT) technique.

EXCITE (Extremity Constraint-Induced Therapy Evaluation)—the 2006 study that first proved it to be an effective technique—was selected by the Physiotherapy Evidence Database as one of the top 15 PT trials in the world. The study was led nationally by Steven Wolf, professor of rehabilitation medicine at Emory. Trials were selected for their significant impact in stroke rehabilitation and for setting the stage for many future trials.

The original trial enrolled 222 patients at seven sites who predominantly had suffered ischemic stroke. Patients had their less-impaired hand or arm restrained with an immobilizing mitt, then took part in behavioral therapy that included tasks such as opening a lock, turning a doorknob, or pouring a drink. Patients were evaluated using the Wolf Motor Function Test (named after Steven Wolf.)

“Often, stroke rehabilitation focuses on teaching patients how to better rely on their stronger limbs, even if they retain some use in the impaired limbs, creating a learned disuse,” says Wolf. “This trial focused on the impaired limb, which proved to be a valuable form of rehabilitation.”

Some 28,000 trials and manuscripts, going back as far as 1929, were reviewed for the honor. ■



A Better Chance More extremely premature infants are surviving than ever before, found a study published in the Jan. 22 issue of the *New England Journal of Medicine*. Prematurity is still a leading contributor to newborn deaths—one in four extremely premature infants (born at 22 to 28 weeks of gestation) does not survive beyond the birth hospitalization. Each additional week of gestation gives the baby a better chance. Deaths from immaturity or pulmonary causes and complications from infection or central nervous system injury decreased, but deaths due to necrotizing enterocolitis, an intestinal complication resulting from prematurity, increased. Ravi Mangal Patel, a neonatologist at Emory University Hospital and Children’s Healthcare of Atlanta, was lead author. ■



Field Clinics

The older migrant worker came to the mobile clinic complaining of chest pain. An Emory physician assistant (PA) student did a cardiac workup and screened for heart disease and blood pressure complications, but all tests came up negative. Then a physical therapy (PT) student asked the man what specific work he did. “I pick grapes,” he replied. The PT student told him, “You just need to switch sides, you have stretched your pectoral muscles.”

The annual South Georgia Farmworker Health Project clinics have broadened their scope and effectiveness by using teams of students and faculty from different School of Medicine programs—PA, PT, and MD, says Erin Lepp, director of community projects at Emory’s PA Program. Starting in 1996 with eight students, three faculty, and one physician under founder and PA alumnus Tom Himelick, the farmworker clinics have evolved into a service-learning project that includes more than 200 students, faculty members, and community volunteers. “We had this simple idea to try working truly collaboratively this year instead of in parallel,” says PT Assistant Professor Sara Pullen, “and the student feedback was overwhelmingly positive.”

While fruit and vegetable cultivation in Georgia brings more than a billion dollars a year into the state, pickers remain low paid, living largely in makeshift camps or seasonal housing with little access to health care. The clinic teams have treated people who have never seen a doctor before, women in labor, and workers with acute illnesses and chronic conditions. Sick patients can be transferred to emergency care, or follow-up appointments can be scheduled through community partners such as the state’s Farmworker Health Program. “What we’re doing is bringing the whole team to them,” Pullen says.

Rotating morning and afternoon clinics provide free care to 1,200 to 1,600 farmworkers and their families during 12 days in June and to an additional 300 seasonal workers over an October weekend. South Georgia locations include Valdosta and Bainbridge. Emory’s nursing school runs a similar clinic in Moultrie for farmworkers and their families.—*Sofia Kouninis*

Old drugs, new uses

It's a wonder new medications are ever developed at all. Taking a new drug from promising molecule to marketable drug can cost upwards of a billion dollars and take a decade or more. Oh, and the overall failure rate hovers near 95 percent.

Not surprisingly, the pharmaceutical industry has become interested in repurposing already approved drugs. These may be medications on the market for a different condition or those that didn't pan out for their original use.

Repurposing an existing drug can save developers years of time, preliminary clinical trials, and almost 40 percent in costs. "The amount needed to bring these drugs to market is often less, which is why smaller companies are interested: some of the risk has been taken out of the equation," says Cliff Michaels, senior licensing associate with Emory's Office of Technology Transfer (OTT).

Well-known repurposed drug success stories include the following:

ROGAINE, the hair regrowth treatment was developed from the oral blood pressure medication minoxidil after researchers noticed that hair growth was a common side effect.

THALIDOMIDE, first positioned as a cure for morning sickness in pregnant women and taken off the market in 1961 after being linked to severe birth defects, was approved by the FDA

in 1998 for use in patients with leprosy and again in 2006 for those with multiple myeloma.

VIAGRA was developed to treat pulmonary arterial hypertension before gaining approval in 1998 to treat erectile dysfunction.

As the cost to develop drugs continues to go up, there is also an increased interest from the public and the federal government to make the most of drugs that have been approved. The NIH's Chemical Genomics Center recently opened its Pharmaceutical Collection database for public screening of nearly 27,000 active pharmaceutical ingredients, including 2,750 approved small-molecule drugs and all compounds registered for human clinical trials.

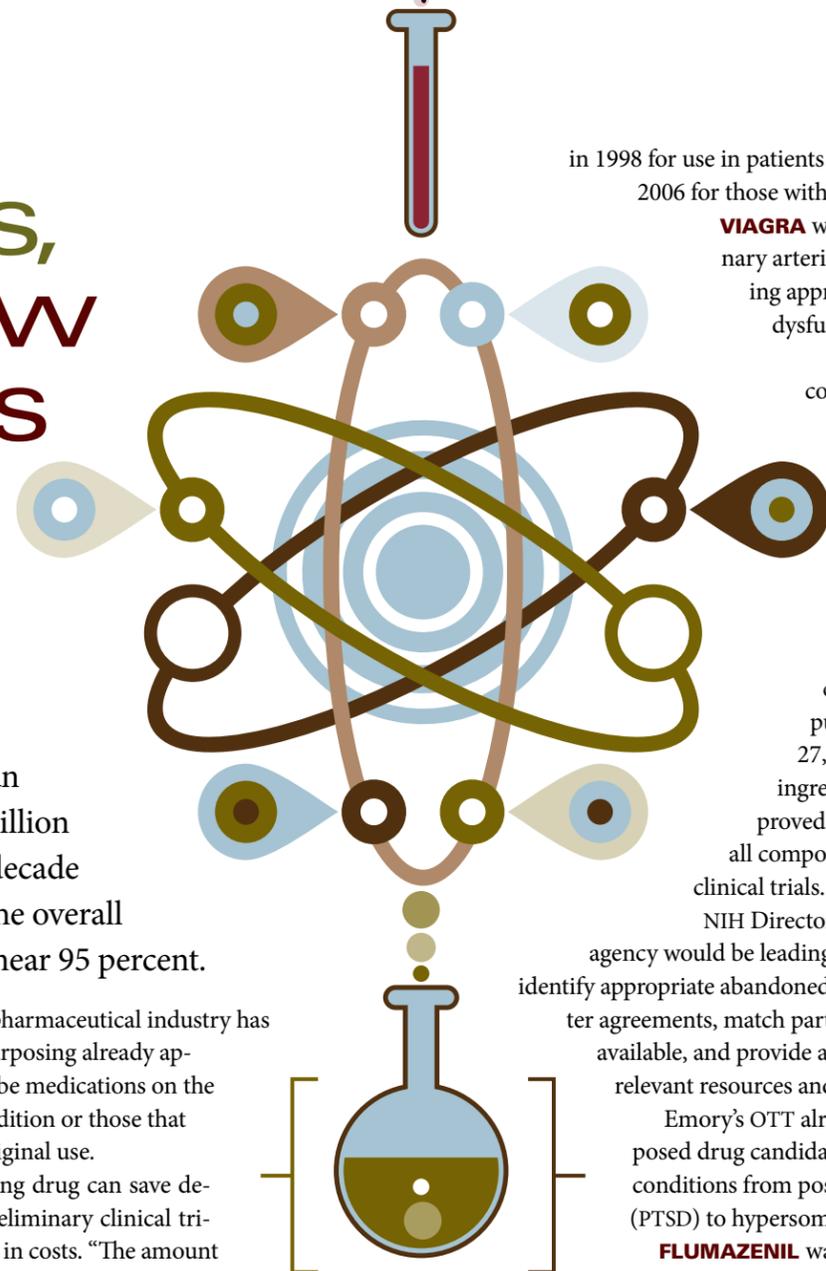
NIH Director Francis Collins said the agency would be leading a "comprehensive effort to identify appropriate abandoned compounds, establish master agreements, match partners, make data resources available, and provide a central access point to relevant resources and expertise."

Emory's OTT already has several repurposed drug candidates in development to treat conditions from post-traumatic stress disorder (PTSD) to hypersomnia to stroke.

FLUMAZENIL was developed for treating overdoses of benzodiazepine sedative hypnotics but was found by Emory School of Medicine sleep researchers David Rye and Andrew Jenkins to be useful for patients with hypersomnia, or excessive sleepiness—even those who hadn't responded to traditional treatments like stimulants.

RAPAMYCIN was originally developed as an antifungal agent but was discovered to have potent immunosuppressive and anti-inflammatory properties and has been used to prevent rejection of transplanted organs. School of Medicine Dean Christian Larsen, Emory Vaccine Center Director Rafi Ahmed, and colleagues at the Emory transplant and vaccine centers found that the drug could also boost T cell immunity from immunizations.

Repurposing an existing drug can save developers years of time and almost 40 percent of the cost of bringing a drug to market by eliminating the need for additional assessments.



METFORMIN, used to treat type 2 diabetes, may be effective in treating nephrogenic diabetes insipidus as well, found researcher Jeff Sands. People with this rare condition (which is related to diabetes only in name) can't regulate water in their body versus urine output. Sands, chair of nephrology, says these individuals may produce gallons of urine over 24 hours, which makes life difficult during the day but even harder at night. Children with this genetic condition can make up to a liter of urine per hour, and must also drink that much to rehydrate.

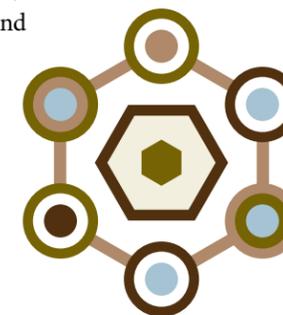
Nephrogenic diabetes insipidus can also be a side effect of chronic lithium use, so it is sometimes seen in adults being treated for bipolar disorder. The drug has proven effective in mice. Larry Greenbaum, of pediatric nephrology, is doing a pilot study to see if what has been observed in animals can be duplicated in humans.

OSANETANT was first tested to treat schizophrenia but did not show a clear advantage over traditional treatments and was abandoned. Yerkes National Primate Research Center scientists Kerry Ressler, Raúl Andero Galí, and Brian Dias discovered that osanetant made memories of frightening events less durable in mice by blocking the pathway involved in fear learning and the consolidation of fear memories. The drug may prove to be therapeutic for people with anxiety or fear disorders, such as PTSD.

A combination of **RAPAMYCIN** and the drug **IMATINIB** (Gleevec), used in the treatment of chronic myeloid leukemia, was found by researcher Jack Arbiser in dermatology to be highly effective in decreasing tumors in mouse models of tuberous sclerosis, a genetic disorder that causes non-malignant tumors to form in many different organs, primarily the brain, eyes, heart, kidney, skin, and lungs.

TAK-242 a Japanese drug that was originally developed to treat sepsis, went through safety trials but didn't show efficacy. Researchers Fang Hua, Donald Stein, and Iqbal Sayeed, in emergency medicine, found that TAK-242 could be used as a non-surgical treatment for ischemic stroke by blocking inflammation and lessening brain injury.—

Mary Loftus



You be the doctor

Attack of the Empañadas?

Some puzzling illnesses remain mysteries, or misdiagnosed, for decades. Take the case of a 16-year-old girl from Erie, Pennsylvania, who received a scholarship to study abroad in the village of Concepción in Tucumán, Argentina.

Having developed a fondness for the local culinary fare, she overindulged one evening in some scrumptious empañadas prepared by her host family. A day later, her gastrointestinal tract declared complete treason. Accompanying this intestinal distress was a dramatic dermatologic conversion— she turned a disconcerting yellow.

Sponsored as she was by the International Rotary Club, great consternation ensued in the members of this service organization responsible for her welfare. Worried looking representatives lined her bedroom in the humble dwelling. The local physician was summoned, and, after due deliberation with him, the Rotary president declared with authority, "Señores, esta niña no tiene hepatitis. Tiene empañaditis." (The child does not have hepatitis. She has empañaditis.) Recovery was uneventful.

Over the years, that intrepid world traveler—Karen Stolley, chair of Emory's Department of Spanish and Portuguese—has recounted that humorous tale of her high school study-abroad days many times to colleagues.

But when Clyde Partin, director of Emory Special Diagnostic Services, heard it, he became interested in some of the case's discrepancies. "The sage advice of the local doctor was correct. He recognized a transient, non-threatening illness and provided the needed reassurance," Partin says. "But what created diagnostic dissonance for me was explaining the time course of why Karen turned yellow so acutely."

Can you take a guess, careful reader, as to his revised diagnosis?

Hepatitis A, acquired some weeks prior, that happened to manifest itself just after the empañada immoderation. "The empañadas are probably innocent of the foodborne illness accusation," Partin says, "and should be acquitted." ■

A New Weapon Against the Measles



With the recent outbreak of measles at Disneyland a week before Christmas, resulting in at least 70 cases that spread across California and beyond, there has been a renewed focus on the “childhood disease.”

The CDC reported 644 cases of measles from 27 states last year, the largest number since 2000.

Before measles vaccines became widespread in 1963, an estimated 3 million to 4 million Americans a year contracted the disease, and 400 to 500 died of it.

Most of the people who contracted measles in the latest outbreak were not vaccinated, raising another public health cry for universal MMR immunizations. But at least five of the patients were fully vaccinated, which may be even more alarming.

Researchers from the Institute for Biomedical Sciences at Georgia State, the Emory Institute for Drug Development (EIDD), and the Paul-Ehrlich Institute in Germany have developed a novel antiviral drug that may keep people infected with the highly contagious, airborne virus from getting sick—as well as preventing them from spreading it to others.

The drug works by blocking the replication of the pathogen. Richard Plemper, from the Institute for Biomedical Sciences, and colleagues from the EIDD said the drug could be used to treat friends, family, and other social contacts of a person infected with measles who have not developed symptoms yet but are at risk.

While animal studies have been encouraging, more research is needed before the drug can be used in people. “The emergence of strong antiviral immunity in treated animals is particularly encouraging, since it suggests that the drug may not only save an infected individual from disease but contribute to closing measles immunity gaps in a population,” Plemper says.

Researchers emphasized that the drug is not envisioned as a substitute for vaccination but as an additional weapon. ■

Nurse Amber Vinson Grateful

Looking composed and happy, Texas nurse Amber Vinson—one of the first two health care workers to acquire Ebola in the U.S.—sat beside Dr. Bruce Ribner at Emory University Hospital as he announced her discharge from the Serious Communicable Disease Unit on Oct. 28.

“The team is extremely pleased with Ms. Vinson’s recovery, and we were inspired by her courageous attitude and the strong support of her family and health care colleagues in Dallas,” said Ribner, director of the unit. “As fellow members of the health care community, we greatly admire her dedication. Nurses are on the front lines 24 hours a day.”

Vinson, 29, was one of the nurses who cared for patient Thomas Eric Duncan, a Liberian man who became ill with Ebola while visiting family in Dallas and who died Oct. 8

at Texas Health Presbyterian.

Vinson and nurse Nina Pham, 26, both became ill after caring for Duncan. They were the first health care workers to acquire Ebola while caring for a patient in the U.S.

Vinson arrived at Emory on Oct. 15 by private jet. Pham was

treated at the National Institutes of Health Clinical Center in Bethesda, Maryland. Both have recovered.

“I am so grateful to be well and, first and foremost, I want to thank God. While the skill and dedication of the doctors, nurses, and others who have taken care of me have obviously led to my recovery, it has been God’s love that has truly carried my family and me through this difficult time and has played such an important role in giving me hope and the strength to fight,” Vinson said. “And I’d like to thank my family for being there every minute, every day.”

She also thanked Dr. Kent Brantly and Nancy Writebol, “both of whom were successfully treated here at Emory, for your donations of plasma for me and other patients, and thank you for your leadership in helping to educate the public about this difficult but treatable disease.”

While calling it “a day of celebration and gratitude” for her, Vinson asked that “we not lose focus on the thousands of families who continue to labor under the burden of this disease in West Africa.”—M.J.L.



Amber Vinson, above, on the day of her discharge, with her Emory health care team.

The Long, Extraordinary Recovery of Ian Crozier

The most critically ill of Emory’s four patients with Ebola was admitted to the Serious Communicable Disease Unit on Sept. 9, after becoming infected while treating patients in Sierra Leone. His identity remained confidential throughout his stay, at his request.

Spending more than a month in Emory University Hospital’s isolation unit, he was placed on a ventilator and had kidney dialysis (a first for a patient with Ebola). Doctors in charge of his care feared he would die or suffer brain damage.

“He was by far the sickest patient with Ebola virus that we’ve cared for at Emory,” said infectious disease specialist Jay Varkey. After 40 arduous days, he was determined to be virus-free and was quietly discharged on Oct. 19.

In early December, Ian Crozier broke his silence and went public about his experience with Ebola and his rough, unmarked road to recovery.

Crozier, 44, was born in Zimbabwe and moved at the age of 10 to the United States, where he became an American citizen. He went to medical school at Vanderbilt University, then trained in internal medicine and infectious diseases.

As Ebola spread in West Africa, he volunteered with the World Health Organization (WHO) at the Ebola Treatment Unit in Kenema, Sierra Leone, in August, planning to stay for a month or so.

He encountered an overwhelmed health care system with an overflowing ETU and patients who feared they had Ebola traveling there from all over the country.

On clinical rounds in early September, he developed a fever and headache, and drew his own blood for a diagnostic test, hoping he had malaria. The next day, he found out he was positive for Ebola.

WHO flew him back to the U.S., and he was taken straight to Emory Hospital for treatment. Although Crozier doesn’t remember much of his time in the isolation unit, his doctors realized early on that he was severely ill. The viral load in his blood was more than 100 times that of the other patients with Ebola that Emory had treated. “The general dogma in July was that if Ebola patients needed dialysis or a vent, they would invariably die,” says Bruce Ribner, director of the unit. “I think we have shown that is certainly not the case. We’ve changed the algorithm for how aggressive we are going to be in caring for patients with Ebola.”



Dr. Ian Crozier with a group of Ebola survivors and a nurse at the Kenema Government Hospital in Sierra Leone. He contracted Ebola but survived after intensive care at Emory, including dialysis.

Ribner also believes that Crozier’s age may have worked against him. “Both nurses who acquired Ebola were young and recovered fairly quickly,” he says. “It seems that younger patients do better. And the higher the virus load that you’re infected with, the worse your infection will be.”

Crozier’s family and girlfriend kept a vigil outside his room at the isolation unit, reading to him through an intercom and giving his nurses personal photos to tape on his wall. A nurse who had also been infected in Kenema flew to Emory from England and donated several units of plasma for a transfusion.

Crozier’s virus levels began dropping, but his kidneys failed.

He started having heart arrhythmia. In all, he was on a ventilator for nearly two weeks and on dialysis for just over three weeks. “The really tough part was the thought that he was going to die and that I was not going to be able to touch him before he left the earth,” his mother told reporters.

Finally, his viral levels dropped and his condition stabilized enough for him to be quietly discharged from the unit. He went to Phoenix with his family to recover.

He emerged from the

hospital 30 pounds lighter, and has since struggled with fatigue and deconditioning as well as inflammatory eye disease. “Though I have struggled with some clinical setbacks in December and January, I’m feeling much better and getting stronger more recently,” Crozier says. “My appreciation for the kind of care I was privileged to receive then and now at Emory continues to grow. I will always be grateful for the way this remarkable Emory team fought tooth and nail for me when I could not, and continues to fight for me now.”

Lessons learned in caring for Crozier and the other Ebola patients continue to ripple through the medical community. For example, doctors now have a model for safely and effectively providing dialysis to Ebola patients who experience kidney failure, which involves special, extensive training for ICU nurses performing the dialysis. The Emory team reported this protocol at the annual meeting of the American Society of Nephrology in Philadelphia, and it was published online Nov. 14 in the *Journal of the American Society of Nephrology*. “One of the things Ian taught us was, you can get sick enough to need these types of interventions, and you can still walk out of the hospital,” Ribner says. “I think it has sent a message to our colleagues around the world.”—M.J.L.

Cross-Country Training

Emory Medicine is teaming up with the Centers for Disease Control and Prevention (CDC) to provide training, educational resources, and consultations for 48 U.S. medical centers that have been designated Ebola treatment centers.

Emory has hosted three Ebola-preparedness training conferences, which focused on managing specialized treatment units, and doctors and nurses have been going on site visits.

“It is our mission to pass on what we have learned to other health care providers and hospital staff, so they can ready themselves to care for patients diagnosed with Ebola,” says Bruce Ribner, director of Emory’s Serious Communicable Disease Unit. ■



Therapeutic Gold?

The Defense Advanced Research Projects Agency (DARPA) has awarded Emory a grant for up to \$10.8 million over three years to determine if the blood of Ebola survivors contains antibodies and immune cells that could help doctors fight Ebola infections in others.

A team of researchers will begin answering this question as it applies to four patients with Ebola who were treated at Emory University Hospital.

The 10-institution national team will be led by Rafi Ahmed, director of the Emory Vaccine Center and a Georgia Research Alliance Eminent Scholar, and Aneesh Mehta, assistant professor of medicine, and includes laboratories from the University of Wisconsin-Madison, Rockefeller University, Aaron Diamond AIDS Research Center, Vanderbilt University, Scripps Research Institute, Stanford University, and the University of Pennsylvania. ■

Ebola Survivor Nancy Writebol: Giving back and looking forward



With a television crew following them, Nancy and David Writebol returned to Emory University Hospital on Feb. 3, holding hands and chatting with the staff about a new grandchild who was expected to be making his arrival later that day.

Writebol, a missionary who contracted Ebola while working at a Liberian hospital for SIM, has gotten used to a certain degree of celebrity



unit in August, Writebol was found virus-free and was discharged. She left the hospital quietly, with family, to continue her recuperation. After growing stronger, she has given multiple interviews and returned several times to Emory to donate plasma. “I am thrilled to be able to help others who might contract Ebola,” she says. “And it makes it special to be here at Emory and to catch up with the doctors and nurses who became like family to me.”

Emory Healthcare is collecting plasma from Writebol and the small group of other American Ebola survivors, banking it for the possible needs of future Ebola patients.

David Writebol, who was doing mission work with his wife in Liberia but did not contract Ebola, is taking part in an Ebola vaccine trial at Emory’s Hope Clinic. He had his blood drawn right after Nancy’s plasma donation. “They are measuring the

progress of the antibodies,” he says. “We are happy to give back and to share our joy and hope.” ■

After spending 17 days in Emory Hospital’s special isolation

Watch an interview with Nancy and David Writebol at bit.ly/ebolaplasm.

“We really take an all-cause, all-infections approach because we know that whatever comes is likely going to be something we didn’t plan for.”—Dr. Bruce Ribner, *TIME* magazine.

Ebola Fighters: Ribner among those honored as *TIME*’s Person of the Year

WHEN *TIME* MAGAZINE SELECTED THE EBOLA FIGHTERS AS ITS PERSON OF THE YEAR, IT DID SO TO HONOR “THE HERO’S HEART,” SAID MANAGING EDITOR NANCY GIBBS.

“Ebola is a war, and a warning. The global health system is nowhere close to strong enough to keep us safe from infectious disease, and ‘us’ means everyone, not just those in faraway places where this is one threat among many that claim lives every day,” she wrote. “The rest of the world can sleep at night because a group of men and women are willing to stand and fight. For tireless acts of courage and mercy, for buying the world time to boost its defenses, for risking, for persisting, for sacrificing and saving, the Ebola fighters are *TIME*’s 2014 Person of the Year.”

Among the Ebola doctors selected was Bruce Ribner, medical director of Emory University Hospital’s Serious Communicable Disease Unit. “In the process of getting our patients better, we are learning a great deal about the virus, which we hope feeds back to our colleagues in Africa, so that perhaps they can no longer have such high fatality rates,” said Ribner, in the article. “I am surprised we haven’t had more patients. We are prepared for more patients



with Ebola, and we’re ready for other diseases, too. We really take an all-cause, all-infections approach because we know that whatever comes is likely going to be something we didn’t plan for.”

Missionary doctor Kent Brantly, the first patient with Ebola treated at Emory (and in the U.S.) was pictured on one of the five alternate covers of the magazine, as well as being recognized as an Ebola fighter. He and Ribner were two of five Ebola doctors selected. “I’ve had time to reflect on what happened to me,” Brantly says, in the *Time* piece. “I chose a career in medicine because I wanted a tangible skill with which to serve

people. And so my role as a physician is my attempt to do that. I’ll probably get tired of talking about my experience some day, but I went to Liberia because I long felt it was my vocation to spend my career as medical missionary. Deep in the core of my heart, I still think that’s my calling. I don’t want to go on with life and forget this.”

The issue also included coverage of aid worker Nancy Writebol and Dallas nurse Amber Vinson, who were also successfully treated for the disease at Emory. ■

Banking Plasma from Ebola Survivors

PLASMA FROM PEOPLE WHO HAVE SURVIVED EBOLA MAY PROVE EXTREMELY VALUABLE, BOTH FOR THERAPEUTIC AND RESEARCH PURPOSES.

To that end, Emory is collecting plasma from the small group of Ebola survivors in the U.S., and storing it for future needs.

Many of these survivors were themselves given “convalescent plasma” from other Ebola survivors, based on the thought that people who survive an illness have antibodies and immune cells that will recognize and fight against the virus, and that this can be transmitted to another by transfusion.

But no careful research has been done concerning this practice with Ebola.

“Donating is a completely voluntary process,” says Anne Winkler, the Emory pathologist overseeing the study.

Patients can choose to donate when they are at Emory for follow-up visits.

In total, Winkler says, the hospital has collected 18 units of plasma from six donors.

Of the 10 Ebola patients treated in the U.S., Emory University Hospital treated four in its special isolation unit:

- Dr. Kent Brantly and Nancy Writebol, missionaries infected in Liberia
- Dr. Ian Crozier, infected while working for WHO in Sierra Leone
- Amber Vinson, infected while caring for an Ebola patient at a Dallas hospital.

British nurse and Ebola survivor William Pooley flew to Emory to donate plasma to Crozier during his illness. Doctors used their own judgment in determining how much plasma to give.

“Some patients have received two units and some patients have received more,” Winkler said. “We don’t know the optimal dose.” Doctors also don’t know if the plasma



transfusions have been effective therapeutically.

Questions like these are ones that Winkler hopes Emory’s plasma bank will be able to help answer.

A similar trial is being conducted with Ebola survivors’ plasma at the ELWA2 hospital outside Monrovia.

The goal is to establish a network of such facilities in the U.S. and abroad. ■

THE SMARTER ICU

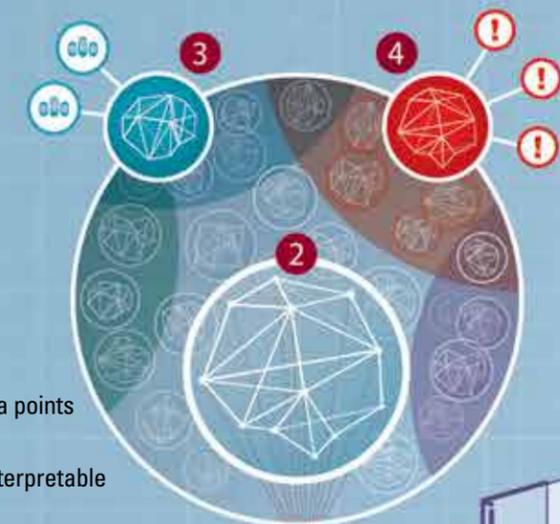
Illustration by DAMIEN SCOGIN

Harnessing Big Data for Better Results

In a typical ICU, a dozen different streams of data light up the monitors at a patient's bedside, including heart physiology, respiration, brain waves, and blood pressure. Currently it's up to doctors and nurses to rapidly process and analyze this constant feed of vital signs to make important medical decisions. Emory University Hospital is using software from IBM and Excel Medical Electronics (EME) for a pioneering collaboration to create advanced, predictive medical care for critically ill patients through real-time streaming analytics. Emory is testing a system that can identify patterns in physiological data and instantly alert clinicians to danger signs in patients.



Coined in aviation community after WWI, Situation Awareness is the perception of elements in the current environment, the comprehension of their meaning, and the projection of their status into the near future—a paradigm that applies to critical care as well.



INTERCONNECTED PHYSIOLOGY | Harvested information and real-time analysis and display of data allow nurses and doctors to detect how vital organs are interacting with each other

HOW IT WORKS

1. Smarter ICUs harvest 1000-2000 data points per second from every patient.
2. Real-time analysis leads to easily interpretable displays.
3. Most patients under surveillance are doing well.
4. Early detection of anomalies and rapid intervention trigger early and effective responses.

NATURAL LIGHT AND A LARGER FLOORPLAN

Mobile care columns and a large floor plan make it possible for patients to be turned toward windows. The natural light/dark cycle encourages rest for patients and families.

STREAMING TELEMETRY

Sensors on patients and on support devices convey both patient and alarm data to multiple locations and software programs. These enable a harvesting of "big data" for real-time analysis.

REMOTE MONITORING

Critical Care nurses and ICU attending physicians continually monitor data and provide in-person consultation to Emory hospitals and other partner hospitals.

BRIEFING ROOM

The semi-opaque windows allow the professionals to be seen from the hallways, but not the patient data displayed on the screens. The caregivers can reorder rounds in order of patient need.

VIDEO CONFERENCING

High-resolution, two-way conferencing engages patients, families, and bedside caregivers into rounds and discussion. Participation of remote caregivers promotes situation awareness.

INTEGRATED DATA

Data about the patient's physiology, lab results, and medications are displayed around the patient and family on the center screen to promote a holistic view of the patient's condition and discussion of treatment options.

FAMILY FRIENDLY SPACE

Families are encouraged to stay with the patient in separately lighted sleeping, sitting, and working areas. Wi-Fi is provided and in-room conference phones are available.

UP CLOSE AND PERSONAL

Virtual presence using the two-way audio-visual system means that families can conference with an attending ICU physician around-the-clock.

CLINICIAN WORKSTATION

Large displays and windows into rooms make it possible for busy clinicians to complete their tasks while staying close to their patients. Integrated blinds (louvers between two panes of glass) can be closed for privacy.



THE SMARTER ICU Q&A

Professor of Surgery and Anesthesiology **Tim Buchman**, founding director of Emory's Critical Care Center, is in charge of integrating ICUs throughout Emory Healthcare. He also has been an airplane pilot for more than four decades.

What are the primary ways intensive care units (ICUs) are going to change during the next decade? ICUs will focus on

providing the "right care, right now, every time" by engineering consistency and reliability into every process. Standard communications, evaluations, treatments, and assessments form the foundation of high-reliability care. This is the same approach that has been used in other high-stakes human endeavors, such as commercial aviation and nuclear power plant operation.

What does Big Data have to do with critical care? Making the best decision for each patient involves early detection that something is amiss and choosing the intervention with the best benefit/risk profile for that particular patient. Both depend on Big Data. Clinicians need computers to assist here for two reasons. First, no person can possibly interpret the several thousand data points each patient generates every second. Computers do this well. Second, we have selective memory. We are very good at remembering our most recent patient, less good at remembering what happened when we treated a similar patient four years ago. Big Data balances those memories and provides a much more accurate picture of how a current patient compares with all the other patients with seemingly similar conditions, allowing more personalized care.

You talk a lot about situation awareness (SA), a concept that originated in the aviation community after WWI. How does this apply to medicine? Situation awareness is about forming the best possible basis for a decision through perception, comprehension, and projection. My favorite illustration is the way my dad used to drive and the way I drive. He had the same information, but he had it on a paper map, an odometer, and so on. We got lost—a lot. Today, I have a GPS navigator in the car and on my smartphone. I get a bird's-eye view of the car overlaid onto a map, along with traffic, weather, and turn-by-turn directions that represent the computer's best suggestion of what to do next. None of this threatens my authority as a driver—in fact, it frees me up to ask, "Do I really want to take this route to my destination?" We need to do the same thing for patient care: Perceive all of the data—history, physical exam, lab data, images, current treatments,

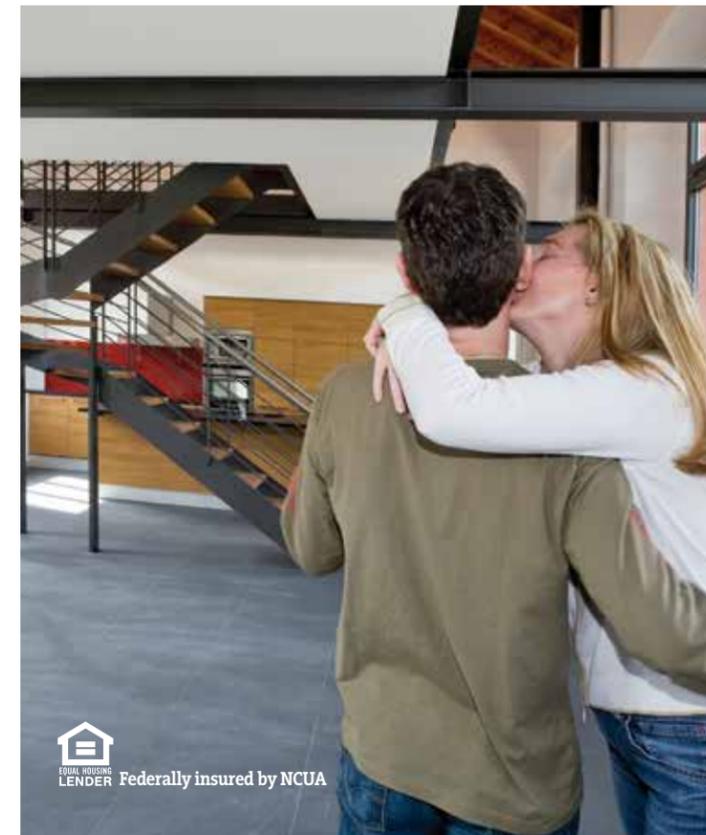
and the patient's physiology. Accurately comprehend the data to form a "picture" of the patient's overall condition. And finally, use the data to predict the future in various scenarios—if no changes are made, if a test is ordered, if a treatment is started or stopped.

We have seen hospitals in the past several years strive to create a more relaxing, aesthetically pleasing, healing environment in their ICUs. Is there still more to be done? Definitely. We need to make sensors less invasive and obtrusive. We need to move the alarms away from the bedside and get them to the caregivers who will act on them. We need to know when our treatments are not helping and, worse, when they are causing harm. And we need to optimize how critical care improves lives not just in the hospital but also once a patient and family go home.

You had a personal experience with being in critical condition. What did you learn? When I was a physician in training, I was in an automobile collision—another driver "T-boned" my car. I ended up being a patient in my ICU. There were three key lessons I took from that experience: First, life is fragile. One must live strong and live well. You never know when it's going to be your turn to be the patient. Second, human touch and kind words are the greatest comfort. And third, there is no safety device better than a well-trained ICU nurse, just as a well-trained pilot is the best safety device in an airplane.

Recently, Emory doctors had the experience of caring for Ebola patients in Emory University Hospital's Serious Communicable Disease Unit, which is at its core an isolated, self-contained ICU room. What did critical care learn from this experience? We learned that it really does take a team to get the best care possible to the patient while maintaining the highest achievable safety for the caregivers. Care of the Ebola patients included several complex therapies that could not have been done safely or successfully without tight team integration.

What most excites you about recent advances made in ICUs? Advances in monitoring are helping us act more quickly and advances in treatment are helping us act more precisely. Together, those make for shorter ICU stays, better outcomes and happier patients. ■



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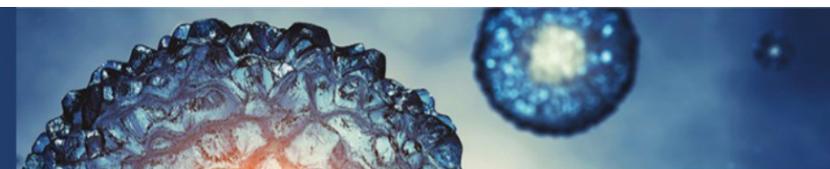
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Critical Training for Critical Issues.

Highlights of Emory's Master of Arts in Bioethics program:

- ◆ Ethics faculty scholars across clinical, research, and policy arenas, including neuroethics and biotechnology, religion and bioethics, and public health ethics
- ◆ Part-time study is available
- ◆ Innovative Practicum sites: CDC, NASA, etc.
- ◆ Two track options: Thesis or Exam



The Master of Arts in Bioethics program at Emory University's Center for Ethics provides rigorous, advanced, and interdisciplinary training for professionals and students interested in social and ethical challenges in health care and the life sciences. Students in the program are connected with a dynamic network of experts, scholars, and resources in order to prepare themselves to constructively address ethical issues in biomedicine.



Current MA-Bioethics student and Emory anesthesiologist, Dr. Joel Zivot, says, "My experience as an MAB student with the Emory Center for Ethics has been extremely positive. The Center is very supportive and the experience thus far has left me feeling intellectually refreshed. I have had opportunities to lend my voice to important ethical issues as the MAB has given me the confidence and credibility to join these debates. I would strongly recommend the program to practicing physicians."

To learn more, visit our website at ethics.emory.edu/mabioethics and join the conversation.



Electrodes, insulated wire, and a battery-powered pulse generator.

These are the components of deep brain stimulation, a technique being used to lift depression, still movement disorders, and calm epileptic seizures. Even the researchers who developed and refined it still don't know exactly how it works.

Welcome to brain hacking.

Surgery photos and illustrations by MICHAEL KONOMOS



A team including neurologist Helen Mayberg and neurosurgeon Robert Gross prepare for deep brain stimulation surgery on a patient with treatment-resistant depression at Emory University Hospital.

FLIPPING THE SWITCH

Targeting depression's neural circuitry

By SYLVIA WROBEL

The darkest day of Marjorie Stowe's depression came when her long-time psychiatrist told her she obviously was choosing to resist the healing effects of one medication after another, psychotherapy, electric shock. "You must be getting some emotional payoff that prevents you from letting your depression go," he said. "Secretly, you must enjoy being this way."

What's left when your own psychiatrist gives up on you? During the day, praying helped her hold on. At night, she prayed not to wake up.

Growing up in Franklin Springs, Georgia, the youngest of a Pentecostal minister's six children, Stowe was a serious, unsmiling child. She graduated from hometown Emmanuel College, took pre-pharmacy courses at the University of Hawaii, and earned a PharmD from Campbell University in North Carolina. She managed it all—school, then work and marriage—with the help of antidepressants.

Her plunge into suicidal darkness began at 39, after the birth of her daughter. Could it be hormonal? Her gynecologist shook her head, then told Stowe about an Emory neurologist named Helen Mayberg she had just read about, who was doing a special type of brain surgery with electrodes for treatment-resistant depression, with promising results. You have a physical illness of the brain, the gynecologist said. This might be your best hope.

Fifteen percent of Americans have clinical depression during some portion of their lives. A third of those have major depression: suicidal thoughts, a sense of disconnection from the world. For a few of those, the entire arsenal of traditional treatments—therapy, medications, even electroconvulsive therapy—doesn't work. These are the patients Mayberg sees.

Stowe was a model case. Indeed, her long-term depression was so severe, it made it difficult for her to gather the required docu-

mentation and go through the long psychiatric interviews.

The day of surgery, Emory neurosurgeon Robert Gross implanted very thin wires with tiny electrodes in two small lobes deep at the midline of Stowe's brain.

Mayberg stood beside Gross, quietly talking to Stowe, guiding her through the process as she often does with patients. Gross was the surgeon, Mayberg the architect and team leader. Precisely where Gross placed the electrodes was based on Mayberg's extensive brain maps, both of activity in different regions of the brains of depressed patients and of the neural cables that connect these regions, allowing communication between them. Stowe was awake to report any sensations when the electrodes were activated. (It's not as bad as it sounds, since the brain has no pain receptors.)

The electrodes' job is to deliver a small amount of electrical current to the specific region of the brain Mayberg discovered is overactive in people with depression. This region, Area 25, serves as a kind of junction box, so adjusting activity here is like tuning the entire depression circuitry. The electrodes are connected to an implantable pulse generator (IPG), a pacemaker-like device placed under Stowe's collarbone. The IPG keeps a steady stream of low voltage flowing into the patient's brain.

As the electrodes are tested in the OR, patients often report an emotional weight being lifted instantaneously—one way the team knows the electrode is in the right place. Within a week after surgery, with the electrical current flowing continuously, Stowe began to notice sunlight, birdsong. Her sense of humor returned. Her boss didn't recognize her on the phone, so changed was her voice.

Two years later, Stowe says the procedure has been transformative. "It brought me out of the pit," she says. "People who haven't been there can't understand what a gift it is to feel joy.



After three decades of severe depression and trying nearly every treatment, deep brain stimulation helped Marjorie Stowe (above with daughter, Maddie) reclaim her life and regain the ability to feel joy.

I always loved my family. Now I enjoy them."

Her 5-year-old daughter, Maddie, doesn't remember the mommy who cried every day, only the happy one involved in her life. They enjoy horseback riding, playing in the park, and getting mani-pedis on girls' days out. Before deep brain stimulation (DBS), Stowe felt completely dependent on her husband, Jeff, a Home Depot project manager. After the procedure, she feels like an equal partner—and it's fun, she says: "Laughing like we used to, motorcycles, camping, Georgia Tech football, happy times with my daughter and stepsons, Joshua, Sean, and Zachary."

She recently started training for a 5-K race, determined to be as healthy physically as she now feels mentally. Jeff refers to her as "the new and improved version."

This major shift in mood and energy level took some getting used to, however. "After 30 years in a kind of prison, it was a big adjustment to suddenly be well," says Stowe. "I didn't know what to do, what to feel." The research team's responsibility doesn't end in the OR, says Mayberg. Stowe receives ongoing treatment from behavioral therapist Cynthia Romero, psychiatrist Patricio Riva Pose, and the rest of the DBS research team.

Now that Stowe's brain is able to focus, thanks to the "reset" of DBS, she is learning to enjoy the moment, to not dread the future, and—hardest of all, she says—to let go of the guilt about what her family went through during her illness.

Making the map As a neurologist, Mayberg's territory is the brain, and her maps are the neural circuits that go awry in depression. She's also a dedicated clinician, determined to retune those circuits and give patients back their lives.

Entering medical school in the late 1970s, Mayberg planned to become a psychiatrist. At the time, however, psychiatry had not fully embraced the genetic and neural underpinnings of mental illnesses, focusing instead on causes like maternal neglect or suppressed anger. Inspired by a mentor, Mayberg switched to neurology and began investigating how faulty neural communications might contribute to mental disorders.

Positron emission tomography (PET) was starting to make it possible to actually see brain activity. Mayberg took extra training to learn this new nuclear technology, inside and out. She worked first with stroke, then Parkinson's patients, but began to hone in on depression. "Some clinical decisions just call to you," she says.

As a research fellow at Johns Hopkins, Mayberg worked down the hall from neurologist Mahlon DeLong, who had discovered pathways in the basal ganglia, a part of the brain associated with movement and cognition—pathways that he believed could

explain the symptoms of Parkinson's disease. DeLong was interested in the patient's movement problems, but what interested Mayberg was the depression experienced by some, but not all, Parkinson's patients. The severity of the movement disorder seemed to have no bearing on which patients became depressed. Mayberg asked herself if the depressed patients could be wired differently. Working with many of DeLong's patients and drawing on his model of distinct patterns of brain activity related to movement problems, she used her new imaging skills to find the answer.

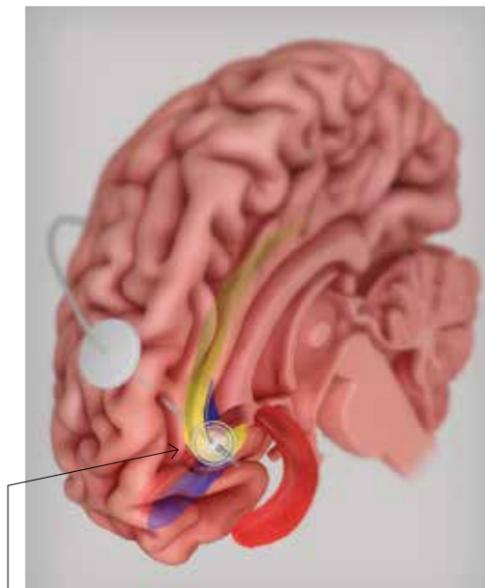
In PET imaging, a tiny amount of radioactive material is attached to glucose molecules and given to the patient intravenously. Glucose is the brain's biggest source of energy, so the brain grabs the molecules from the circulating blood to fuel its various activities. The most active regions show up as brilliant red or yellow, the less active in muted green, blue, or black.

Mayberg's findings were stunning:

Parkinson's patients who were depressed all had less brain activity in the frontal and limbic regions responsible for thinking, emotion, memory, and learning. She broadened her investigation. Depressed Huntington's patients had the same pattern. So did depressed stroke and epilepsy patients. So did depressed patients with no neurological disease.

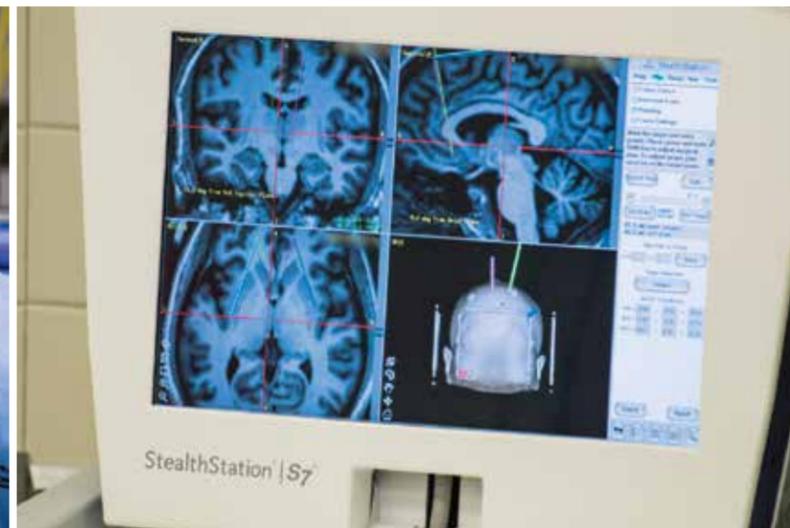
Then things got even more interesting. When depressed patients took Prozac or other antidepressant drugs and improved, their depressed frontal lobe activity corrected, rising again. But activity lowered in a different area of the brain, Area 25.

When healthy, non-depressed research subjects were told to



Junction Implanted electrodes deliver a small amount of electrical current to a specific part of the brain that is overactive in people with depression. This region, Area 25, serves as a kind of junction box, so adjusting activity here is like tuning the entire depression circuitry.

"After 30 years in a kind of prison, it was a big adjustment to suddenly be well," says Stowe. "I didn't know what to do, what to feel."



The deep brain stimulation (DBS) team stands at the ready behind the patient's skull, planning the surgical target for the electrodes that will be connected by a thin wire to the battery-powered pulse generator implanted under the patient's collarbone. Neurologist Helen Mayberg (above), who pioneered the use of DBS for patients with treatment-resistant depression, speaks with the patient, who is awake and alert and providing feedback. Many times, as soon as the device is turned on in the operating room the patient will feel an immediate lightening of mood—an indication that the electrodes are in the right place.

“If we couldn't talk depression down, couldn't drug it down, couldn't shock it down, then I believed we could go directly to Area 25 of the brain and tune it down,” says Mayberg.

think about sad memories, activity in the frontal cortex went down and activity in Area 25 rose. When the subjects switched to happier thoughts, activity in Area 25 dropped and activity in the frontal cortex increased to normal.

Clearly this was a clue into how treatments worked. But for certain patients, activity in Area 25 stayed high and activity in the frontal lobe remained low, despite treatment. Mayberg believed that in these “treatment resistant” patients, a brain glitch was preventing signals from traveling between Area 25 and the frontal lobe, trapping the person in a kind of depression loop. She had found her target. “If we couldn't talk depression down, couldn't drug it down, couldn't shock it down, then I believed we could go directly to Area 25 of the brain and tune it down,” Mayberg says.

Some might call this a daring leap, but when Mayberg proposed placing electrodes in Area 25 to her University of Toronto colleague Andres Lozano in 2003, where she was then professor of neuropsychiatry and neurology, she viewed it as simply the next logical step. “I have never been a risk-taker,” she says. “I was following 20 years of evidence I and others had gathered about how brain circuitry works in depression and where an electrode might need to be placed if we wanted to change that circuitry in severely ill patients.”

Lozano and other surgeons already were inserting electrodes into the basal ganglia of patients with intractable movement symptoms, based on DeLong's work. But even when these procedures were successful in reducing the rigidity and uncontrollable body

movements of Parkinson's, they did nothing to affect depression.

Depression, as Mayberg had discovered, hid in a different region of the brain. With funding from the Brain and Behavior Research Foundation, Mayberg and Lozano began a pilot study. Of 20 patients who received the DBS procedure in Toronto under Mayberg's direction—patients for whom all other treatments had failed—12 experienced significant clinical benefit. People who had been suffering profoundly, some of whom were suicidal, were now describing feelings of rejuvenation, of looking forward to something new and exciting. Colors were more intense. One spontaneously recalled the beauty of seeing a crocus blooming in spring. Hope, for the first time in a long while, was budding inside them.

DBS surgery was proving successful beyond Mayberg's most optimistic estimates.

Marking the trail Mayberg came to Emory in 2003 because of her belief in a multidisciplinary approach to depression, which dovetailed perfectly with the growing neuroscience initiative at Emory (headed by her former colleague, DeLong) that was bringing together researchers from a dozen departments and the Yerkes National Primate Research Center. She commuted back to Toronto to finish her work with the first cohort of DBS patients.

At Emory, Mayberg and Robert Gross began a larger research trial of DBS, including patients with treatment-resistant bipolar II depression (a form with no manic episodes) as well as those, like

Stowe, with severe unipolar depression. The first surgery was done at Emory University Hospital in 2008. Cases now number more than 30, with ever-increasing precision of electrode placement and, correspondingly, higher rates of clinical success. “Doing research like this takes a team,” says Mayberg, the Dorothy C. Fuqua chair in Psychiatric Neuroimaging and Therapeutics. “We keep progressing because we have been successful in leveraging expertise across Emory, Georgia Tech, and labs worldwide.”

Recently, Mayberg and her team have turned their attention to understanding not if but how DBS achieves its effects. “I never thought depression was just about Area 25,” she says. “It's always been about communication between multiple brain regions.” A recent paper from her lab identifies three connections in the brain that must be affected for patients to improve. “Now,” she says, “we understand better how to stimulate the entire depression circuit.”

No one knows why some depressed patients respond to one type of therapy and others to another type. Failing one treatment, trying another, failing, trying again, until something works—or finding that no treatment works long-term—is costly, agonizing, and even, given the suicide rate in depression, deadly. Understanding subtle differences in the brains of severely ill, treatment-resistant patients may identify the subgroup that can most benefit from DBS and even point to adjustments in target or intensity of stimulation

that can convert non- or slow-responders into full responders.

Mayberg's team is now able to read the brain signatures of people with depression who respond to different therapies. A new study is testing whether these patterns can guide treatment choices. The goal is to create evidence-based guidelines that will allow clinicians to select the best treatment for each individual with depression, much as now happens for breast cancer patients, whose type of treatment depends on their genetics and other biomarkers.

Even newer studies focus on the “brain radio,” an extra component built into the standard IPG pacemaker device. The radio continuously measures activity in depression-related areas of the brain—data researchers can use to tune stimulation up or down as needed, with a special magnet held against the patient's chest. They believe such precise tuning will lead to faster and longer-lasting recoveries.

“I realize every day what DBS has given me,” says Stowe, a pharmacist in Carrollton, where she, Jeff, and Maddie live. When Stowe's mother died after a prolonged illness recently, Stowe was able to be there for her and to handle her own grief in a way she couldn't have imagined before surgery.

“I truly would have been paralyzed with depression before,” she says. “Now, whether it is enjoying the good things or coping with the stress and loss that everyone experiences sooner or later, DBS lets me do life.” ■

Fine-tuning the Brain With a “pacemaker” that sends electrical impulses to electrodes surgically implanted in targeted brain regions, deep brain stimulation (DBS) has been able to reduce or eliminate the symptoms of depression, epilepsy, and movement disorders like Parkinson's, essential tremor, or dystonia. While not a cure (symptoms return if the implanted pulse generator is shut off), DBS does often result in remarkable recoveries in people whose lives had been severely disrupted by their illness. The departments of neurology (Mahlon DeLong, Thomas Wichmann), psychiatry (Helen Mayberg), and neurosurgery (Robert Gross) came together to form the Emory Neuromodulation & Technology Innovation Center (ENTICE) to advance the understanding and effectiveness of this therapy. The Neural Engineering Center at Georgia Tech is also a partner. “We are harnessing the synergy of basic scientists, engineers, clinical researchers, and industry to interact in an open, collegial, and creative environment.”

CALMING THE STORM

Reducing epileptic seizures

By QUINN EASTMAN

As her doctors told Paula Moreland how they were proposing to treat her seizures, her eyes grew wide. Moreland's mother, who was with her at the appointment, said, "Just listen to them, babe."

A surgeon would implant an electrical stimulation device deep within her brain. The device would deliver current to calm the storms of signals that would sometimes erupt and cause her to lose consciousness. Moreland had already seen several neurologists and tried a variety of anti-seizure drugs. At one point, she was taking seven different medications. "They didn't seem to work, and they made me sick," she says. "I went to talk with one doctor, and he threw up his hands. It was like he was saying, 'I give up.'"

Epilepsy seemed to have come into her life out of nowhere, Moreland recalls.

A divorced mom, she was traveling often for her job at a telecommunications company. Her doctors hypothesized that a car accident in Florida may have stirred up the seizures, but a precise cause was never pinned down.

Twice, seizures occurred while she was driving. She doesn't remember the accidents that followed, but she does remember the odd feeling (sometimes called an "aura") that preceded them. She once lost consciousness after a seizure at a bible study meeting.

Her family suggested that she see doctors at Emory, where she underwent diagnostic procedures, including surgery, that kept her in the hospital for a month and led to painful swelling. Her daughter started crying when she saw her with a shaved head. "I laugh about it now, but it was hurtful then," Moreland says.

Loss of control Thomas Henry, the former head of Emory's epilepsy program, described deep brain stimulation to her. It may have seemed risky to try an experimental procedure, but Moreland was willing to take the risk. "If I had to choose between the epilepsy and having only one leg or one arm," she says, "I would not choose epilepsy, because of the loss of control."

At that point, the only tested-and-proven measure against drug-resistant epilepsy was surgery to remove the part of the brain

where seizures originated. In Moreland's case, that region was the hippocampus: the same region she depended on for remembering words and forming memories.

"That's the reason why we thought she was a good candidate [for deep brain stimulation] and why she was enrolled," says neurosurgeon Robert Gross. "The only other option at that time was to resect the temporal lobe on her language-dominant side. If she experienced negative effects, we could simply shut the current off or even take the device out if it was completely ineffective."

Two wires were inserted under the skin of her head and carefully positioned through two small drill holes that lead to the region of the brain called the thalamus. The wires run down her neck and are connected to an electrical stimulator with a battery implanted

under her collarbone. Now, several years after surgery, Moreland is nearly seizure-free. She continues to take the anti-seizure drug carbamazepine. She says there are some effects of the stimulation on her short-term memory. "I need to write things down," she says. "I can remember things from 20 years ago, but sometimes my family needs to remind me about something I did just a little while ago."

Moreland is an active community volunteer and writes, directs, and produces gospel plays. Still, it took seven years before she had the confidence to drive again, and she does not go long distances. She says she is blessed to have a large group of supportive friends and relatives. Her plays have been performed at community venues such as Big Miller Grove Baptist Church, where she is a member, and at her alma mater, Liberty University. She also appears as an extra in the film *Selma*. "I feel like a walking miracle," she says.

Daring treatment The basic idea underlying Moreland's treatment is this: if electric stimulation with the right frequency can restrain activity in a key bottleneck area, seizures won't spread. Many patients with drug-resistant epilepsy have seizures that begin in the temporal lobe. The anterior nucleus of the thalamus (or ANT) appears to serve as a highway on-ramp connecting the hippocampus and other temporal lobe structures to the rest of the brain.

where seizures originated. In Moreland's case, that region was the hippocampus: the same region she depended on for remembering words and forming memories.



Feeling liberated from epileptic seizures by deep brain stimulation, Moreland has thrown herself into writing and directing gospel plays. She volunteers at local schools and senior centers, as well as with the Rockland County Sheriff's Department.



Neurosurgeon Robert Gross (above, talking with neurologist Helen Mayberg) conducts a majority of the deep brain stimulation surgeries performed at Emory, in patients with epilepsy, movement disorders, or severe depression.

These observations led to small studies of the effects of stimulating the ANT in patients with drug-resistant epilepsy as early as the 1960s. Subsequent success with deep brain stimulation in Parkinson's, along with experiments with animal models of epilepsy, led to further studies of ANT stimulation in epilepsy patients in the 1990s.

The first multi-center controlled trial, which Moreland participated in, didn't start until 2003. SANTE (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) was sponsored by the medical device company Medtronic. Most of the 110 participants saw a reduction in the frequency of their seizures of at least 50%, but that effect built up gradually over two years. Only a few were seizure free for six months or more. About a quarter of participants reported noticing some memory impairment, like Moreland.

Even after generally encouraging results from SANTE and a narrow vote in favor from an advisory panel, the FDA did not approve Medtronic's application in 2010, citing concern over safety and side effects. The device is approved in Europe, Canada, and elsewhere. Medtronic has reapplied to the FDA, armed with more long-term data on SANTE participants.

In 2013, the FDA did approve another deep brain stimulation (DBS) device as a treatment for drug-resistant epilepsy. The Respon-

sive Neurostimulation System, made by Neuropace, targets a different region of the brain: the actual site of onset of the seizures in the cortex, including, in half the patients, the hippocampus itself. It is programmed to sense an oncoming seizure and respond with a burst of electricity.

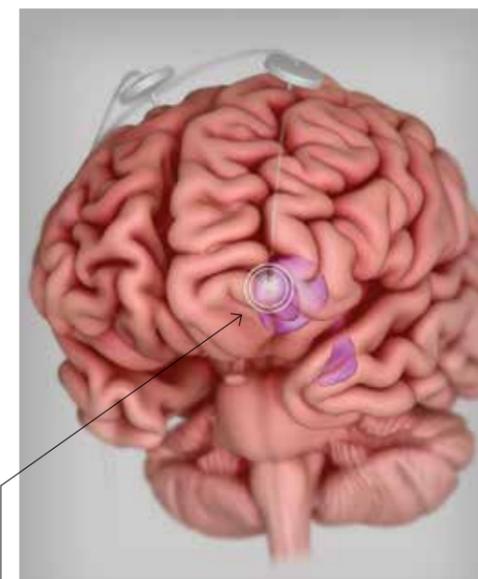
Gross is not yet satisfied with the reduction in seizure frequency seen in published clinical trials of DBS. "This is not a cure; this is a first step," he says.

Exactly how electrical stimulation works is poorly understood. Researchers first thought that high-frequency stimulation simply shut down some circuits in the brain but now believe its effects are more complex. The gradual improvement seen in trials suggest that the brain's circuits are remodeling in response to the stimulation.

Gross sees opportunities to refine electrical stimulation as technology advances. Industry scientists have developed finer electrodes with more contacts, making it possible to "steer current where we want it to go." Better MRIs can allow more precise electrode placement. Newer DBS devices can record electrical signals from inside the brain over time. And a better understanding of how seizures spread in the brain could make it possible to design treatments

for patients whose seizures originate outside the temporal lobe.

"My concern is that the field will settle for something that is just good," Gross says. "The question now is, how do we make this therapy great?" ■



Blockade: The anterior nucleus of the thalamus appears to serve as a highway on-ramp connecting the hippocampus and other temporal lobe structures to the rest of the brain.

CAPPING THE OVERFLOW

Easing dystonia symptoms

By MARY LOFTUS

Michael Richardson first experienced symptoms of dystonia, a movement disorder characterized by involuntary muscle contractions and spasms, when he was 13.

“When I walked, I would put the toe of my left foot down first. My dad would say, ‘Walk right,’ but I couldn’t change it. Over time, it got worse. My foot contorted. I finally had to use crutches, then a wheelchair on and off,” he says. “My arms became involved—my biggest struggle was with writing. I couldn’t write at all with my dominant hand, so I learned to write left-handed.”

When Richardson tried to make the small, precise movement required for writing, his arm would move back and forth in wide, sweeping motions.

These exaggerated movements are called “overflow”—a common occurrence among dystonia patients, says Mahlon DeLong, William Timmie Professor of Neurology at Emory’s School of Medicine.

For example, if dystonia patients are asked to wiggle a toe, their whole leg will start moving. Or if they try to tap their index finger and thumb together, their arm will swing.

“Imagine trying to force two positive magnets together,” says Richardson. “The more intent I was on writing, the worse it became.” He had the same problems when trying to bring a cup to his mouth, or using a fork to eat.

The son of American missionaries, Richardson spent his teenage years in Mexico, where a pediatric neurologist treated his symptoms with Botox shots and oral medications. This allowed him to walk, but there were side effects to the medication, such as drowsiness.

“Cold, stress, being tired could all be triggers, and the symptoms would get even worse,” he says.

Dystonia is the third most common movement disorder, says

DeLong, after essential tremor and Parkinson’s. “It doesn’t get as much recognition because it can occur in so many different ways and locations,” he says. “Generalized dystonia is most common in children and young adults, whereas focal dystonias show up later in life and can affect virtually any part of the body—neck, eyelids, jaw, hand . . .”

When focal dystonia does get attention in the media and elsewhere, it is often associated with musicians and artists who can no longer perform the fine motor skills necessary for their craft—violinists, pianists, guitarists, flautists, even visual artists. (Cartoonist Scott Adams, of Dilbert fame, developed focal dystonia in his right hand, which hampered his ability to draw.)

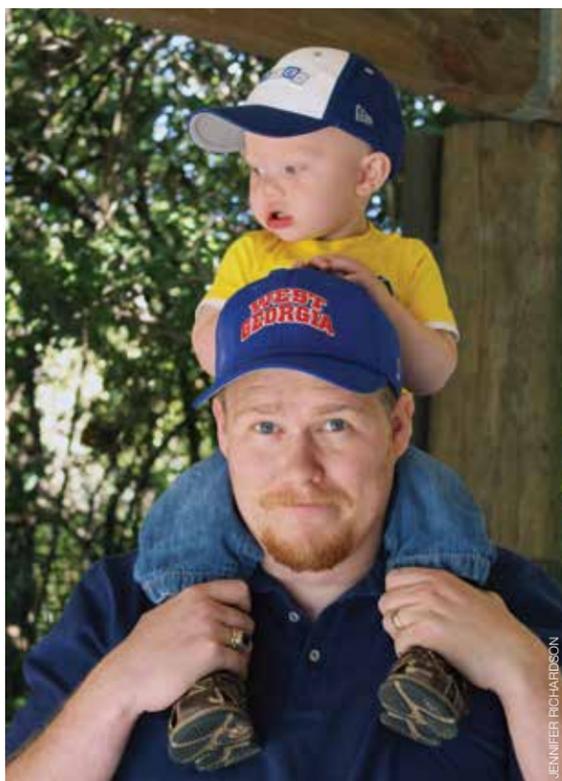
Richardson moved back to the US for college. After graduation, while working for Verizon, he would often find himself typing in phone numbers incorrectly. Even with Botox shots every three months and baclofen, an oral muscle relaxer and anti-spastic agent, he had to use a wheelchair for longer distances and crutches inside the house.

That’s when his doctor told him about a surgery available at Emory. Doctors could put electrode leads into his brain and, using a battery, provide deep brain stimulation (DBS) that could reduce or eliminate his symptoms. He decided to go through with the surgery in February 2007.

“They laid it all out, that my head would be bolted to the table,

that I would be awake for the whole thing,” says Richardson, who lives in Douglasville. “My wife, Jennifer, was pretty stressed out. She stayed up all night doing laundry. I tried to get some sleep.”

At 6 a.m. the morning of the surgery at Emory University Hospital, the operation started with a pre-op MRI as reference, and the frame being fitted over his head. “There was a shield above my head so there would be no contamination. Dr. Bob



Dystonia patient **Michael Richardson** enjoys hiking with his son, Eddie—one of many activities that wasn’t possible before his DBS surgery.

Gross and the other surgeons were on that side [performing the brain surgery] and Dr. DeLong was by my side, giving me commands, asking me questions, and mapping my responses.”

During this phase of Richardson’s surgery, the leads were placed in the correct spots inside his brain—the basal ganglia, specifically the globus pallidus internus (which regulates voluntary movement.)

Over four decades of discovery about the mysterious basal ganglia and its role in movement and movement disorders, DeLong has become a celebrated neurologist and researcher. Last year, he received the Breakthrough Prize in Life Sciences (the “Oscar” of science) from a cluster of tech titans in Silicon Valley, including Mark Zuckerberg. He also received the Lasker-DeBakey Clinical Medical Research Award, among the most respected science prizes in the world, which he shared with Alim Louis Benabid of France.

At his acceptance speech for the Lasker in September, he said, “A growing fascination with how the brain controls behavior led me to medicine and then to neurology. This took a clear direction when I found a choice research position at the NIH in the laboratory of renowned researcher Edward Evarts. Because the other obvious brain regions were already assigned to other fellows, I was asked to work on the basal ganglia, a cluster of poorly understood brain structures, and to determine their role in the control of bodily movement.”

This chance assignment evolved into promising treatments for Parkinson’s disease, essential tremor, and dystonia, all of which emerge from the same motor network and are circuit disorders. “With deep brain stimulation, we’re not curing or treating the disease, we’re targeting the network,” he says. “It’s the circuit we’re after.”

Profound change Disrupting the circuit eases or eliminates symptoms, which is a miraculous thing to witness, says DeLong. “Sometimes it takes a few weeks to achieve the full effect, but the surgery for dystonia is one of the best and most satisfying,” he says. “Dystonia is a non-progressive disease—patients usually reach a level plateau. It is a pure movement disorder without any other components. After DBS, the change is profound.”

In Richardson’s first surgery, DeLong “mapped” his brain to discover the exact areas for placement of the microelectrodes. “The target lies close to the motor and visual pathways, and we’re

talking about a matter of millimeters, so we need a fair amount of precision,” DeLong says. Advances have allowed researchers to do this now with an MRI scanner while the patient is under anesthesia, through direct visualization, but Richardson experienced the traditional way: providing feedback while awake and alert as different areas of his brain were stimulated.

The neurologists were also determining Richardson’s stimulation thresholds, finding the best amplitude for the neurostimulator. “Too high and you have side effects, like movements or optic disturbances, which we don’t want,” DeLong says. “In the initial mapping, we gain a lot of information that helps us place the permanent electrode, four contacts and the lead, that is going to remain.”

Richardson recalls one test where the amplitude was ramped up until he had facial spasms, and then taken back down just below that level.

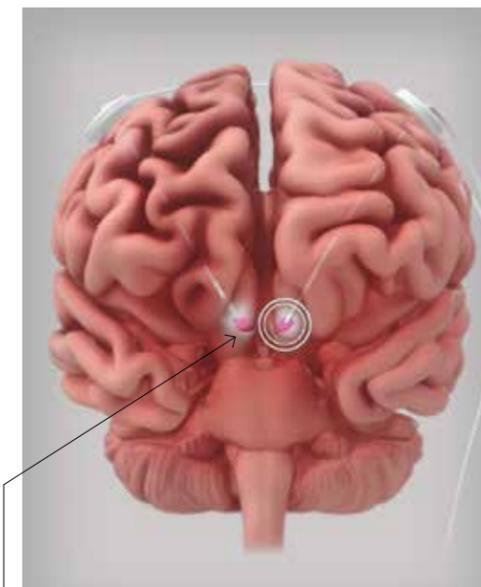
The wires were left unattached and coiled under Richardson’s scalp. In a second surgery a few weeks after the first, the neurostimulator was connected to the battery, which was inserted under the skin just below his collarbone. The battery is about the size of a deck of cards, and lasts three to five years before needing replacement (rechargeable batteries are now available, as well). “It took awhile getting used to the wire that ran down the side of my neck,” he says.

Richardson had to return for fine-tuning. “There was immediate improvement, but it took about two years to achieve the full benefit because of a setting that needed to be changed,” he says. He estimates he is about 97% improved from before DBS surgery. “On bad days, 95%,” he jokes.

When his son, Eddie, was born, he had a vivid reminder of how much the surgery has helped. “I started to feel tired, but I thought it was just from having a new baby and not getting much sleep,” he says. In fact, his battery had failed, and he regressed to being in a wheelchair in a matter of weeks, says Richardson. After a new battery was put in, he quickly returned to his “new normal.”

“Before I married Jennifer, I warned her that I might not be able to work by the time that I was 30 and that if she wasn’t able to deal with that, we shouldn’t get married,” he says.

Now Richardson works full time as an accounting and logistics consultant, is youth pastor at his church, Colonial Hills Baptist in Lithia Springs, and enjoys carrying Eddie on his shoulders during hikes through the mountains. “I can do anything anyone else can do,” he says. “Most people don’t even know I have dystonia. The risk was completely worth the benefit.” ■



Disruption: In patients with dystonia, the leads are placed in the globus pallidus internus, the part of the basal ganglia that regulates voluntary movement.

The Evolution of Aimee Copeland

By MARY LOFTUS • ILLUSTRATION BY STEPHANIE DALTON COWAN

A freak accident on a sunny spring day may have disrupted her life, but with grit, determination, and some high-tech hardware, Aimee is resuming the adventure

The zip line wasn't the fancy kind you see at resorts or parks, with safety straps and secure buckles. It was more of the homemade variety—bicycle bars sliding over a dog-runner cable.

Aimee Copeland, an athletic, adventurous graduate student in humanistic psychology at the University of West Georgia, was the first one to spot it.

Copeland had just finished her last final for her last class of the semester, and was ready to relax. After working the breakfast shift at Sunnyside Café in Carrollton the morning of May 1, 2012, she was hanging out with friends next to the Little Tallapoosa River, which ran right through the backyard of one of their houses.

“School was out, I was waitressing and bartending at night. I had just gone rock climbing with my boyfriend in Alabama a few days before,” she says. “I was living the dream.”

The group took turns on the zip line, skimming over the riverbed while hanging about six feet above the shallow water. On Copeland's second pass, the line snapped and she fell onto the rocks below. She could see her leg muscle through the deep, crescent-shaped cut in her leg, and passed out when the ambulance arrived. At the local ER, the wound was stapled up and she was sent home.

Four days later, after increasing pain

and several more ER visits, she was on a life-flight to the JMS Burn Center in Augusta, diagnosed with necrotizing fasciitis—commonly known as “flesh-eating bacteria”—which was spreading rapidly through her body.

“It could have been any of us, but it was me,” Copeland says, in her typical, direct manner. “You can't

live your life being paranoid, or in a bubble. The truth is, things like this happen when you least expect it.”



“This has made me grateful for what I do still have. I’m newly thankful for things like my elbows and my right knee.”

A father’s pride

Copeland doesn’t remember much of the next few weeks, although her father, Andy, kept a heart-rending blog of her time in the hospital.

Her left leg up to the hip was amputated immediately to stop the spread of the infection. She went into cardiac arrest on the operating table but was revived. The first night, her lactic acid levels dipped below the survivable range, she was in renal failure, and a ventilator was helping her breathe.

Her parents and sister kept vigil by her bedside, driving in from their home in Snellville. They played her favorite music, including Bob Marley tunes. Her condition would stabilize, then worsen. By May 8, doctors told them: “Aimee’s survival chances are ‘slim to none.’ She continues to experience a major shutdown of all five major organs.”

Against steep odds, Copeland pulled through, her body, aided by medications, drawing resources from her extremities to protect her vital organs. But there was a cost. Two weeks after her left leg was amputated, doctors decided they must also amputate both her hands and her right foot.

Her father told her. First, he let her know she had become a symbol of strength and hope around the country, that AJC Pulitzer-Prize winning cartoonist Mike Luckovich had drawn an editorial cartoon about her bravery (above), and that messages of support were coming in from friends and fans the world over. “Aimee’s eyes widened and her jaw dropped. She was amazed,” Andy Copeland wrote.

He told her that more amputations were necessary to save her life, and had her look at her damaged hands. She nodded, then said, “Let’s do this.”

The comment brought her father to tears. “I wasn’t crying because Aimee was going to lose her hands and foot,” he wrote. “I was crying because in all my 53 years of existence, I have never seen such a strong display of courage.”

After several months of healing, she was moved to the Shepherd Center in Atlanta to learn how to use her electric wheelchair and begin to regain her independence. She went through a

period of depression and grief.

And then she got on with it.

“This has made me grateful for what I do still have,” Copeland says. “I’m newly thankful for things like my elbows and my right knee.”

The tao of eating a tortilla

A little more than two years later, Copeland lives in an apartment adjoining her parents’ home, drives her retrofitted van with ease, and uses an iPad to keep up with friends, grad school research, speaking engagements, and rehab appointments like this morning’s occupational therapy (OT) session at Emory Rehabilitation Hospital off Clifton Road.

OT focuses on life skills and daily tasks, says therapist Melissa Tober, so the focus here is often on Aimee perfecting the use of her high-tech prosthetic hands. “There are so many everyday challenges, and Aimee faces them with patience and grace,” she says.

The prosthetics can be awkward, heavy, and hot.

Sometimes they malfunction. This is frustrating for Copeland, since she can do so much without her prosthetics. Sometimes, using them seems more cumbersome than not using them. “But she just perseveres,” Tober says.

Copeland smiles wryly. “As much as I love my parents, I don’t want to live with them for the rest of my life. I want to move out and be independent,” she says, “so this is all pretty important.”

Today’s session focuses on eating a lunch Copeland has brought with her from Moe’s—a burrito, a drink, chips, guacamole. “I want to get more confident about eating in public,” Copeland says. “Eating is such a messy thing anyway.”

She’s had some issues with her prosthetics, with the fingers sticking on some of her finer movements and her thumb hyperextending.

Rob Kistenberg, co-director and coordinator of prosthetics at the School of Applied Physiology at Georgia Tech and an adjunct faculty member in Emory’s Division of Physical Therapy, is sitting in on the session. He’s making minor adjustments to



In occupational therapy, Aimee Copeland focuses on learning to perform life skills and daily tasks with her prosthetic hands, such as eating lunch from Moe’s: holding the Styrofoam cup, taking off a lid, and picking up a chip. The i-limbs have rotating thumbs, fingers that bend at the natural joints, and “grip chips” that use Bluetooth technology. They respond to tiny movements and chemical and electrical reactions in her residual limbs. Still, learning to control them is a challenge. “It feels like my hand is in wet concrete that has almost completely dried,” she says, “and I have to try to move it.”



“One of the hardest things about this is that I love cooking and cleaning and entertaining. I’m kind of OCD about it,” says Copeland. “I like to nurture other people. Not be the one asking for help.”

her prosthetic hands, the i-limb ultra revolution manufactured by Touch Bionics in Scotland, on his computer.

Copeland gets annoyed when people think her “bionic hands” are controlled by her mind—that she can just think what she wants them to do, and they will automatically do it. “It’s a lot more complicated and harder than that,” she says. “It feels like my hand is in wet concrete that has almost completely dried, and I have to try to move it.”

Basically, she says, she concentrates on moving the muscles of her phantom hand, which translates to tiny movements and chemical and electrical reactions in her residual limbs that signal her prosthetic hands.

“Sometimes it feels like bending my wrist backward, or a double-pulse, or flicking water off my fingers,” she says.

These signals are very subtle, Kistenburg says, but electrode sensors placed in the forearms of her prosthetics are sensitive enough to read them through the skin.

Tober encourages Copeland to start unwrapping the burrito, and the aluminum foil—which has stuck to the warm tortilla shell—provides the first challenge. After several attempts, Copeland is able to separate the foil from her veggie burrito.

“A lot of OT is just troubleshooting,” says Tober. “Aimee will tell me about something that is frustrating her, things she’s having a hard time doing, and we’ll brainstorm different ways to make them easier.”

Copeland appreciates Tober’s female sensitivity as well. “I was talking with another therapist, who was male, about wanting to be able to put my hair back in a ponytail, and he said, ‘Just cut your hair,’” she says, shaking her head in disbelief. “No offense, Rob.”

“None taken,” says Kistenburg, laughing. “I have daughters and am the sole male in my household, so I can do ponytails. I understand the importance.”

Prosthetic hands need different types of coverings and accessories to make them practical—touch-screen friendly fingertips, for instance, to be able to use devices like tablets. “My iPad is my connection to the world,” Copeland says. “I use it for

school, my papers, all my books, social networking, email. It controls the lights, fans, and thermostat in my house and is my remote control.”

Today’s efforts to eat the Moe’s meal, including opening the chip bag, taking out a chip without crushing it, hinge on fine-tuning her grip. This is made immeasurably harder without the sense of touch. Kistenburg experiments by programming several different options into the prosthetic hands—there are 24 grips available.

“One of the hardest things about this is that I love cooking and cleaning and entertaining. I’m kind of OCD about it,” says Copeland. “I like to nurture other people, not be the one asking for help.”



ANDREW DAVIS TUCKER, UNIVERSITY OF GEORGIA

Forward momentum

Copeland remains active—she’s been kayaking, does strength training, and has even been back on a zip line. And she’s looking forward to taking up more sports, such as horseback riding and cycling via a custom bike.

But mostly, she wants

to spend more time walking and less in her electric wheelchair.

“I don’t really need my prosthetic hands, I have silly, creative methods I’ve devised,” she says. “But I can’t walk without legs. That’s my main goal—to get rid of the obstacles this wheelchair produces.”

During a physical therapy (PT) session at Emory, she works on going up and down steps, stairways, and ramps with physical therapist Beth Fordyce in the hallway of the Rehab hospital, wearing her leg prosthetics and blue Puma sneakers.

“I find it’s better when I don’t stare at my feet,” she tells Fordyce, taking careful steps down the stairs. “It feels like if I get too much forward momentum, I could fall.”

“You’ve got to train your muscle memory,” says Fordyce. “But steps are different heights, so it’s hard to know what to expect.”

One of Copeland’s prosthetics includes a waist strap and an artificial hip joint that mimics human hip movement; the other fits onto her calf just below her knee. Gel liners, medical-grade silicone, and five-



Stairs and ramps are difficult to navigate with two prosthetic legs, requiring incredible strength and balance. Building up her endurance is a large part of physical therapy, and Copeland can do 200 crunches in seven minutes, as well as 400 leg lifts, side planks, push-ups, and more. “It’s all about the core,” she says. “I can do more crunches now than I ever could before, but I’m still sweaty and exhausted after an hour or so of walking.”



Excerpt from Aimee Copeland’s dad’s blog about her PT

“I hate my physical therapist.”
 “arghh”
 “My therapist hates me.”
 “gasp”
 “She’s a sadist.”
 “grunt”
 “Just watch and see.”
 “ermm”
 “She loves to see me grimace in pain.”
 “arrghh”
 “She says my torture is my own gain.”
 “ooof”

All right, I know what you’re thinking: “Oh my goodness, that poor Aimee! She hates her therapist? What are they doing to that poor child?” Not quite. The above is a brief glimpse of a typical moment of rehab.

These workouts serve a great purpose for Aimee. She is conditioning her body to be strong enough to shift her weight so that she can maneuver in and out of her chair onto any surface [and to use her prosthetic legs, which takes an incredibly strong core].

I must add one important factor: Aimee loves her physical therapist.



Prosthetist Rachel Schmidt of ProCare Prosthetics adjusts Copeland's leg, which has a microprocessor in the knee with angle and load sensors that analyze her gait while she's walking as well as how much weight she puts on her toe and heel. Alignments are made by linking the knee through Bluetooth to the computer, but Schmidt can also make manual adjustments.

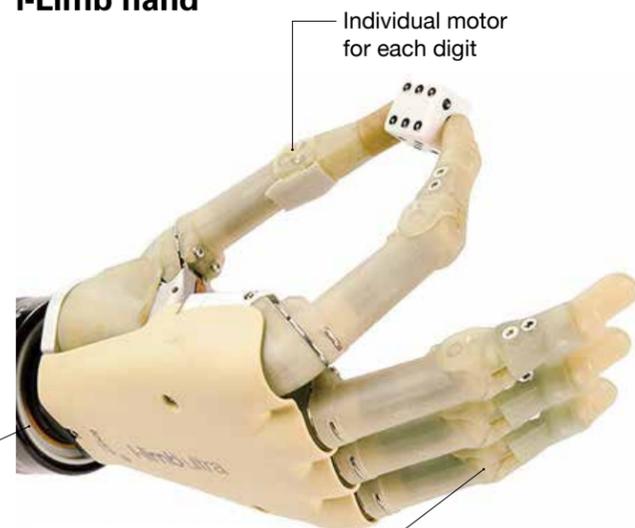
From bronze cast to bionic limbs



In ancient Egypt, prosthetics were developed more for cosmetic reasons than for functionality. Some mummies had prosthetics made of leather and wood and were buried with them so they would be "whole" in the afterlife. The first true prosthetics, in the sense that the term is used today, were made during the Greek and Roman period, usually to replace limbs lost in battle. These were often

bronze or iron, with a wooden core and leather straps. French surgeon Ambroise Pare's mechanical hand, "Le Petit Lorrain," from the 16th century, was operated by catches and springs. Now, prosthetic hands have motorized digits and look and move more like natural hands. For example, i-limbs can be programmed to individual specifications and controlled by mobile apps. Prosthetic legs have made similar advances, with robotic legs, sports legs designed for speed and impact—from running blades to swimming fins, and high-fashion designer legs. "Bionic" limbs can be moved by neurosignals sent from existing muscles.

i-Limb hand



Sensors in socket pick up myoelectric signals from arm muscles to make full range of movements

Individual motor for each digit

Fully articulated joints

ply and three-ply socks keep the skin from chafing, in theory, but dealing with blisters and bone bruising is unfortunately still a common occurrence.

Fittings are always a challenge, says Copeland's prosthetist Rachel Schmidt of ProCare Prosthetics, due to the fact that leg prosthetics are weight bearing, the complications of joints, and scar tissue.

Copeland's prosthetic has a microprocessor in the knee with angle and load sensors, which analyze her gait while she's walking as well as how much weight she's putting on her toe and heel. "When we're initially aligning, we link the knee up through Bluetooth to the computer," says Schmidt. "But we also can make manual adjustments."

Copeland's PT appointments often involve a killer workout in the hospital's gym. "It's all about the core," she says. "I can do more crunches now than I ever could before, but I'm still sweaty and exhausted after an hour or so of walking."

She isn't kidding—Copeland can do 200 crunches in seven minutes, as well as 400 leg lifts, side planks, pushups, and almost any other core-strengthening exercise you can think of. This has been the focus of her PT at Emory for several years, since much of Copeland's mobility—getting in and out of her wheelchair, walking on prosthetics—relies on her abdominal muscles.

"Being outdoors and adventurous has always been vitally important to me, and I'm not going to compromise on that," she says. "I'm not going to be going on five-mile hikes anymore, but I don't want to be stuck inside either."

Into the wild

In Copeland's dreams, some of the time she is like she was before, and other times, she has been through the amputations. "My essential 'self' is the same," she says, "but I'm definitely not as idealistic as I used to be. I've become hardened by the realities of life. It's not all puppies and rainbows anymore. I've learned to cultivate deeper strengths."

Copeland believes, more than ever, that it's

essential to teach girls that they are more than just their physical bodies and appearances. And she now has the platform to do that: She has appeared on the *TODAY Show*, *CNN Headline News*, and *Good Morning America* and receives constant invitations to be a motivational speaker, especially to student groups.

She drives to Valdosta State once a month to meet with professors in her second graduate program and has started an internship in social work. And she does lots of advocacy work, serving on the advisory council for Tools for Life and the board of Friends of Disabled Adults and Children, pushing for accessibility and inclusion.

"I was super spoiled before. I relied on being charming and attractive to get what I wanted. Now, I'm more mentally focused. I have to be more clever, to use my intellect," she says. "But my experiences

have also bred compassion. When you lose a large part of your body, you have to go deeper."

One of the reasons she was pursuing humanistic psychology at a graduate level, even before the accident, was to investigate the purpose and

meaning of life on her own spiritual quest. Now, she says, it has become essential in giving her the ability to deal with what she's facing. "My whole life has led up to this moment," she says. "That's never been more clear."

Copeland is studying eco-psychology and wilderness therapy, with the intent of bridging the gap between nature and accessibility. After she graduates in 2016, she intends to become a licensed clinical social worker and start a private practice.

Her larger vision is to get "a big chunk of natural land," and build a sustainable, off-the-grid community open to people of all ages and abilities, with wide trails, adaptive yoga, outdoor sports, raised campsites—and a staff of nurses, therapists, and instructors, where all visitors' needs would be met.

Already, people have contacted her about donating land. "I want to create a place where the wilderness can be available to anyone," she says. "And I will live there. And it will be totally awesome." ■



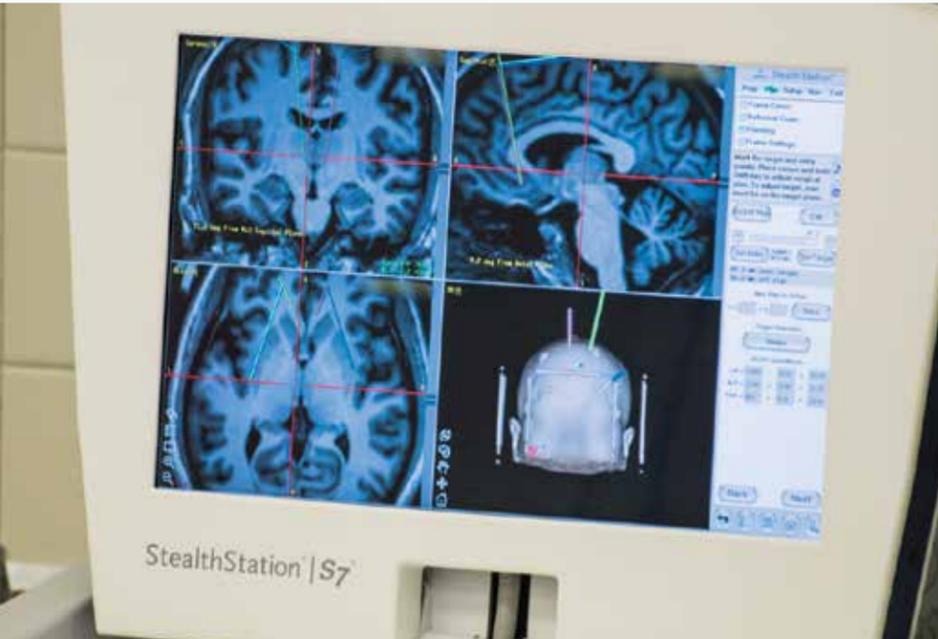
Copeland has made several television appearances and is frequently asked to speak to student and community groups about her experiences.

"Being outdoors and adventurous has always been vitally important to me, and I'm not going to compromise on that."

windows

OF OPPORTUNITY If you've been touched by a story or stories in this issue of *Emory Medicine*, these windows can open up ways for you to turn your inspiration into action. Here you'll see how you can invest in the people, places, and programs you're reading about. Gifts to Emory produce powerful, lasting returns; they help create knowledge, advance research, strengthen communities, improve health, and much more.

Find your window.



PAGE **16** FINE-TUNING THE BRAIN

Brain health is a top priority at Emory University. Neurosurgeon Robert Gross, MD, PhD, has developed a novel electrical stimulation approach that controls the activity of the brain to prevent epileptic seizures. Neurologist Mahlon DeLong, MD, winner of the 2014 Lasker-DeBakey Clinical Medical Research Award for his pioneering research in Parkinson's disease, has developed a microelectrode brain mapping system that can pinpoint and eliminate overactive and troublesome cells in patients suffering from tremor disorders like Parkinson's. And the Emory deep brain stimulation for depression research team led by Helen Mayberg, MD, continues to fine-tune a procedure that produces positive outcomes for patients with treatment-resistant depression who receive electrical modulation to Area 25.

For more information or to support these areas of research at Emory, contact Katie Dozier, director of development, at 404.712.2211 or katie.dozier@emory.edu.

PAGE **26** PUSHING THE LIMITS

After a fall from a zip-line resulted in a near-deadly infection from necrotizing fasciitis bacteria, Aimee Copeland is adjusting to her bionic limbs and pushing her limits with physical therapy at Emory's Rehabilitation Hospital. She has already beaten the odds and is working with a team of physicians and therapists to achieve—and surpass—her goals.

To support advances that allow injured patients the chance to return to activities important for healthy, productive lives, contact Courtney Harris, associate director of development, at 404.727.5282 or courtney.harris@emory.edu.



PAGE **5** CULTIVATING HEALTH ON GEORGIA'S FARMS

Although migrant workers in Georgia help the state's farming industry bring in more than a billion dollars, many of these laborers do not receive regular medical care. Emory's Farmworker Health Project is working to close this gap. Students seeking careers as physicians, physical therapists, and physician assistants team up with interpreters to help migrant workers receive physical exams, health education, and hygiene kits. Your generous gifts can grow this healthy partnership.

To support degree programs in the allied health professions, please contact Andrew Christopherson at 404.727.8253 or andrew.christopherson@emory.edu.

GIFTS OF NOTE

A significant gift from the **Montgomery Foundation II** will support new outpatient programs at the Emory Palliative Care Center and create the George and Nancy Montgomery Endowed Lecture in Palliative Care. The new outpatient services will launch in spring 2015, and the lecture will feature a nationally respected speaker in this field. Emory is a leader in palliative care, which can reduce patients' anxiety, better control their symptoms, make care plans more realistic and consistent with patients' preferences, and lower conflicts about use of life-sustaining treatments.



The new director of Yerkes National Primate Research Center, R. Paul Johnson, has received funding from the **Bill & Melina Gates Foundation** to study gene expression in T-cells infected with SIV, the cousin of HIV. His goal is to uncover information that helps experts design new treatment strategies. The funding is part of the Gates Foundation's Grand Challenges Explorations program, which supports innovative, early-stage research projects in more than 60 countries.

Funding from the **Fuqua Family Foundation** and **Mary and John Brock** supports the Emory Child and Adolescent Mood Program (CAMP). Its staff of more than 15 faculty members and trainees conduct a thriving research program and clinical practice now based at the Emory Brain Health Center at Executive Park. Philanthropy has helped CAMP advance the understanding of mood disorders, provide prevention and treatment interventions, and expand a model program that offers relief for young people struggling with psychiatric, psychological, and developmental disorders, including children from families who could not otherwise afford adequate care. CAMP's goal is to determine which patients will respond best to particular treatments by identifying neurobiological, genetic, familial, and personality factors that predict outcomes.



A team of physicians and engineers from Emory University and Georgia Tech is receiving \$500,000 from the **National Football League, GE, and Under Armour** for winning the Head Health Challenge, a competition for new ideas to diagnose and treat concussions. The team will use the funding to advance their work with **IDTECT**, a quick, easily administered system to improve assessment after brain injuries sustained during athletic events or military conflict. The Emory/Georgia Tech team was among seven winners chosen from more than 500 submissions worldwide.

To learn how you can make a major gift to the health sciences at Emory, call 404.712.4483. To make a gift online, please visit emory.edu/give.

From the Woodruff Health Sciences Center

Changing lives



WRIGHT CAUGHMAN
Executive Vice President for Health Affairs

Here at Emory we celebrate our faculty who are doing particularly high-impact research with the designation "Game Changers."

These are the scientists and physicians whose innovations and discoveries have profoundly transformed the understanding and practice of medicine worldwide.

Two of the faculty members who have been honored with the title,

Dr. Mahlon DeLong and Dr. Helen Mayberg, are featured in this issue of *Emory Medicine*. These pioneers, along with their colleagues, are using deep brain stimulation (DBS)—sending electrical impulses to electrodes surgically implanted in targeted areas of the brain—to reduce or eliminate the symptoms of conditions such as treatment-resistant depression, movement disorders, and epilepsy. As you've seen in the DBS feature earlier in the magazine, their advances are returning hope to patients whose chronic conditions had formerly seemed hopeless.

Across the Woodruff Health Sciences Center (WHSC), we have the great fortune to be surrounded by many pioneers who meet the "Game Changers" criteria, even if they haven't yet been officially honored as such. In the Nell Hodgson Woodruff School of Nursing, the Rollins School of Public Health, the Winship Cancer Institute, and Yerkes National Primate Research Center, and Emory School of Medicine, our faculty are discovering and perfecting novel methods for preventing, detecting, and treating conditions that take far too much from far too many. In fields such as cancer, cardiovascular health, transplant, neuroscience, orthopedics, child health, and many others, WHSC faculty are developing high-impact research that will ultimately benefit not only the people we serve here at Emory, but also people in need around the world.

For the patients they serve, Drs. Mayberg and DeLong, and all the investigators on the Woodruff Health Sciences Center faculty, aren't just game changers; they're life changers.

Into the Fire

By QUINN EASTMAN

Before coming to work at Emory, I was a newspaper reporter in Southern California. My time there was bookended by two episodes of huge wildfires, one in 2003 and one in 2007.

Although I started work at the *North County Times* after the 2003 Cedar and Paradise fires, a large part of my writing concerned San Diego County's recovery from and response to these disasters, which destroyed thousands of homes and killed 17 people.

But by the time the 2007 wildfires came, I had already given notice. My wife and I had started to pack for our upcoming move to Atlanta. Our apartment came through unscathed, but we stayed with a friend near the beach for a night just in case.

Later, while I was driving from California to Georgia, an editor called me on my cell phone and asked me to come back and work on a freelance basis. I will always regret not turning the car around.

[My wife was still in California finishing a work project.] It's partly for the selfish reason of having missed out on "the action" but also having abandoned the team and community I was part of.

That feeling of regret is what drove me to volunteer for a clinical trial testing an experimental vaccine against Ebola.

I don't want to compare the Ebola outbreak and California's wildfires too closely. They're different in scale and lives lost,

certainly. But reading news about the Ebola outbreak made me feel the same way I did when we watched the sky above our apartment slowly fill with smoke. I could think, "Not my problem anymore," and drive away, or I could get involved somehow.

Many people in the Emory/CDC community are more directly engaged in learning about and fighting the Ebola outbreak. I don't have training that would make me especially useful in West Africa, but

I can offer up my shoulder for a shot.

Working in California, I met people whose family members had died trapped in cars overrun by flames. I talked with veteran firefighters and ranchers whose properties had been covered in ash. I heard some harrowing stories, but the smell of smoke was gone by the time I arrived. My articles covered more prosaic questions, such as insurance reforms, building permits, and taxes to support more firefighters.

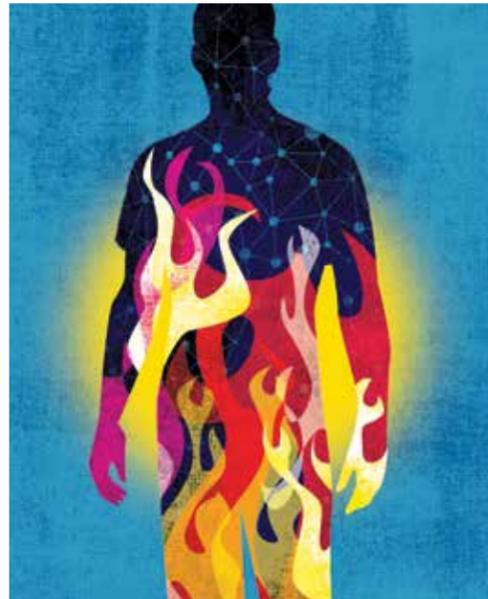
Similarly, the hard work of figuring out how to fight Ebola has just begun. The study Emory is participating in will inform how vaccines will be deployed against the virus in Africa. The vaccine I was given is also being tested at the National Institutes of Health and the University of Maryland. I and the other volunteers received our shots at Emory Vaccine Center's Hope Clinic. Director Mark Mulligan is overseeing the Hope Clinic's part of the study, which is expected to enroll around 100 people.

The GlaxoSmithKline/NIH vaccine consists of the shell of a chimpanzee cold virus, with the external protein from the Ebola virus glued on. It has already been tested extensively in monkeys. I tell friends who look alarmed that "it's really more a vehicle than a virus," since it can't replicate or cause infection.

I received my shot one morning in November. Then all I had to do was come back regularly to provide a few vials of blood; I won't come anywhere near the live virus.

The information gained about the vaccine's safety and whether immune responses are long lasting is expected to be important as the vaccine moves into frontline testing in Africa early in 2015.

This time instead of driving away, I'm sticking around. ■



Quinn Eastman, PhD, is a science writer in research communications at Emory and writes the blog *Lab Land*. He and his wife, Edith, have two daughters, 5-year-old Maia and 2-year-old Carolina.

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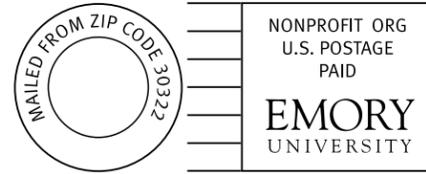




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This is my legacy.

Susan Shapiro
*Associate Chief Nursing Officer for
Research and Evidence-based Practice
Emory Healthcare
Associate Dean for Clinical
and Community Partnerships
Nell Hodgson Woodruff School of Nursing*



“AT EMORY I have found a spirit of excellence that I have not seen anywhere else. That spirit is very alive at Emory Healthcare and the school of nursing, where we are helping to build a culture that is based on constant inquiry and improvement. Emory students are going to transform health care for the benefit of patients, and I want to help them. My bequest will support nursing education programs at Emory Healthcare and the nursing school.”

Have you planned your legacy?

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