



What Scares You?

How fear and trauma
change the brain
and what can be done
to calm it **10**

A gift from the heart



JOHN FOX

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Transplant surgery is exceptional in that, not only does it require two skilled medical teams often working under intense time constraints, it also requires both a recipient and a donor. Living donors, such as 20-year-old Cindy Skrine, may make the generous decision to help a loved one. Cindy donated her kidney on March 5 to a recipient in California so her mother could receive a new kidney through Emory's paired donor kidney exchange, resulting in a lifesaving six-person kidney swap. Others make the choice to become an organ donor in the event of their death, knowing they will never meet the recipients who benefit from that decision.

When 68-year-old twins Jack and Joe Stott participate in the Transplant Games for Team Georgia, as the heart recipients have done every year since 1998, there is always a poignant moment when the athletes walk into the stadium to rousing applause from the donor families. Then the recipients applaud the families in turn. "Without them, the stadium would be empty," explains Joe, who wears a vest honoring his 19-year-old donor, Bryan, an ROTC cadet who was hit by a car while crossing a street by his high school. Joe remembers how, upon their first meeting after his 1996 transplant at Emory University Hospital, Bryan's foster mother put her head on his chest to hear her son's heart, beating anew.

Joe's identical twin, Jack, received his transplant 18 months later (the brothers are among those featured in a photo essay on heart transplant recipients that begins on page 22.) Raised with eight siblings on a 10-acre farm in Atlanta by nurse Mary Edna Willingham Stott, who worked on the pediatric floor of what was then Crawford Long Hospital, Jack and Joe consider themselves ambassadors for organ donation and Emory's transplant program. Jack, a field engineer, spreads the word to his customers and co-workers at GE Energy, and Joe hands out business cards that read "Heart Transplant Recipient" in large red letters. "I had cardiomyopathy and congestive heart failure," Joe says. "For me, it was a heart transplant or a pine box. I enjoy every minute of my second life."

The first heart transplant in Georgia was performed here at Emory. Since 1988, we have performed 648 heart transplants, 18 heart-kidney transplants, one heart-kidney-liver transplant, and one heart-liver transplant. We average 26 heart transplants per year. Pediatric heart transplants are performed by our Emory team at Children's Healthcare of Atlanta. Emory heart transplant recipients gather each spring at the Miller-Ward Alumni House to celebrate (this year's "Heart to Heart" group appears on the opposite page.) To quote David Vega, director of Emory's Heart Transplant Program: "It's a miracle every time."



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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 Healthcare. 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.

Please send correspondence to *Emory Medicine*, 1762 Clifton Road, Suite 1000, Atlanta, GA 30322; call 404-727-0161 or email mary.loftus@emory.edu.

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Heart disease is the No. 1 killer of women in the US. Knowing your individual risk factors could save your life.

An editorial by Gina Lundberg.

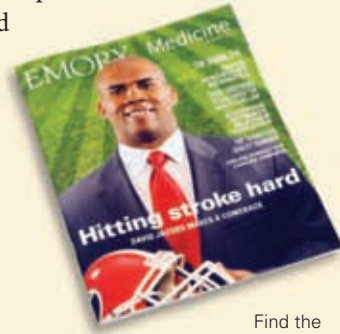


10

As I was recently visiting an old friend at your fine new Johns Creek location, I spied the Winter 2014 edition of *Emory Medicine* magazine, picked one up, and was quite impressed indeed. Within that issue on page 2 is an announcement of a new treatment for severe dry eye available at the Emory Eye Center. The new technology is called LipiFlow Thermal Pulsation and was actually invented by an optometrist I have met and taken many educational courses from over the years—Donald Korb, OD, PhD. He is known worldwide for his research talents in the ophthalmic field. I thought that your readers would like to know this.

Bill Sharpton

Emory College 1960
Lakemont



Find the Winter 2014 issue online emorymedicinemagazine.emory.edu

I have just finished reading the *Emory Medicine* magazine for Winter 2014, including the letters at the end about how patients viewed Emory’s caring and donation to the health care of so many. I am semi-retired and a cancer survivor of Emory’s Winship Cancer Institute. In 1996, I was diagnosed with stage I breast cancer. My local surgeon who did the first biopsy wanted me to see Douglas Murray at Emory for a second opinion. Dr. Murray was a very caring and wonderful physician and surgeon. After he did the lumpectomy, he referred me on to another physician, and I went through radiation treatments and five years of visits and tests. It was during these years that I had the pleasure of Joan Giblin’s care. Ms. Giblin, NP, who serves as director of the survivorship program, was my support and my guardian angel. On April 13, 2001, Joan released me to go forward as a healed cancer patient. What is important to me is on that day, Friday the 13th, Joan gave me a hug and we shed some tears together. She told my husband that this was a “woman’s thing,” but it wasn’t only a woman’s thing, it was a touch of love through the healing and knowledge of medicine, and a deeper knowledge of how to treat people. I will hold her in my memory until the day the Lord takes me home. I thank everyone who cared for me at Emory and the WCI, from the people who cleaned my room to the physicians: thank you for 18 years of survivorship.

Marlene Housworth

Buckhead

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

BY THE NUMBERS

Emory Transplant Center took part in the second-largest kidney swap in history through the kidney paired donor exchange program at Emory University Hospital. The program allows friends and family willing to donate who aren’t a match for their loved one to be matched with a stranger in need, and vice versa, until a kidney transplant chain is created. This particular swap, Chain 221, was initiated by an “altruistic” donor in Memphis in April, passed through Emory University Hospital where recipient Troy Milford, a former pastor, and donor Robert Poole, a friend and parishioner, had surgery on April 30, and ended in Cleveland five weeks later. ■

56
PARTICIPANTS

19
LOCATIONS

5
WEEKS

1
KIDNEY CHAIN

BEFORE YOU TAKE THAT PILL...



About half of pregnant women report taking at least one medication during pregnancy, but worry: **How will this medicine affect my baby?**

Emory School of Medicine’s MotherToBaby

Georgia is a free phone counseling service that can help. “Reliable information is often difficult to find, especially online,” says the program’s director Claire Coles, who also heads the Center for Maternal Substance Abuse and Child Development. “We wanted to be sure that pregnant women and health care providers knew that experts on the most cutting-edge research were readily available to them.” MotherToBaby is part of the Organization of Teratology Information Specialists (OTIS). The toll-free number is 866-626-6847, and calls are routed to local experts. ■



Parkinson's researcher Mahlon DeLong receives his \$3 million Breakthrough Prize from Anne Wojcicki (of 23andme) and Sergey Brin (of Google).

THE OSCARS OF SCIENCE

Scientists, not actors, were the honorees at this star-studded December event in the iconic NASA Hangar 1 in Silicon Valley. While plenty of VIPs were in attendance, including Kevin Spacey, Glenn Close, Rupert Murdoch, and Conan O'Brien, the 2014 Breakthrough Prizes in Life Sciences were awarded to celebrities of a different sort—scientists whose research is aimed at curing intractable diseases and extending human life.

Mahlon DeLong, William Timmie Professor of Neurology, received one of six Breakthrough awards for defining the interlocking circuits in the brain that malfunction in Parkinson's disease. His research laid the groundwork for treatment of the disease by deep brain stimulation.

"This is our effort to put the spotlight on these amazing heroes," said Facebook's Mark Zuckerberg, a founding sponsor. "Their work in physics and genetics, cosmology, neurology, and mathematics will change lives for generations."

Breakthrough sponsors read like a Who's Who of tech entrepreneurs: Sergey Brin, Anne Wojcicki, Jack Ma, Cathy Zhang, Yuri and Julia Milner, Mark Zuckerberg, and Priscilla Chan. Brin and Wojcicki presented DeLong's award for his research on Parkinson's, which afflicts Brin's mother. The \$3 million that comes with each award has no strings attached. "They should make at least a fraction of what some Wall Street trader makes," said Milner.

DeLong shared a few thoughts about his

Breakthrough Prize with *Emory Medicine*:

Is this award distinct from others you have received, and if so, why? Getting an award of this stature was an enormous honor. It was wonderful to meet the current and past awardees, a number of whom also have received the Nobel or other prestigious awards such as the Lasker Award or the Kavli Prize. But let me add, little happens in life without the efforts and support of others, from my students, fellows, and colleagues to my mentors and family.

Who were some of your mentors? My research career began at the National Institutes of Health in the remarkable laboratory and environment created by Edward Evarts, a true pioneer, who gave me the opportunity of a lifetime to work for five uninterrupted years in the uncharted waters of the basal ganglia, mysterious nuclei at the base of the brain.

Which celebrities did you rub shoulders with at the ceremony? I sat next to Rupert Murdoch and very much enjoyed meeting him. It was a star-studded occasion, done as if it were the Academy Awards. Meeting the founder of the Breakthrough Prize, Yuri Milner, was a once-in-a-lifetime experience. And the emcee, Kevin Spacey, was outstanding. I hadn't realized he started out as a stand-up comedian who specialized in doing imitations—several of which he did very well for us.

How cool was the NASA hangar? The setting was surreal, with a stage and room created in the middle of the hangar, a skeleton of the original hangar for blimps pre-WWII. I recalled it well from my undergraduate years at Stanford.

What are your plans for the \$3 million? First is sharing it with the IRS. I also want to support some of our ongoing efforts at Emory. [Indeed, DeLong immediately gave \$250,000 to fellow Emory scientists studying Parkinson's and other brain and movement disorders.]

What's next for your research? I am very involved with the deep brain stimulation program and the Emory Neuromodulation and Technology Innovation Center (ENTICE), a new collaborative enterprise with neurology, psychiatry, and neurosurgery to develop technologies for treating neurological and psychiatric

Am I a carrier? JScreen helps prospective parents determine risk

When Michael Chanin moved back to Atlanta from Dallas, his great-aunt set him up on a blind date.

“There’s a girl who just moved back to town,” she said. “You should meet her. She’s the granddaughter of one of my friends.”

Though Chanin was skeptical of his great-aunt’s matchmaking prowess, he agreed to meet Amanda Weinberg who, fresh from New York, agreed to meet him as well. “Our first date was phenomenal,” Chanin says. Two years later, they got engaged.

Chanin and Weinberg (right) started pre-marriage counseling at their synagogue with Rabbi Peter Berg. Along with discussing expectations, children, and potential areas of conflict with the couple, Rabbi Berg asked them to “get their JScreen.”

A nonprofit public health initiative based at Emory’s School of Medicine, JScreen is an at-home genetic screening program that allows individuals and couples to screen for more than 80 hereditary diseases, 19 of which are predominant in the Jewish community.



Rather than predicting an individual’s own health risks, JScreen helps prospective parents learn about their risk for passing devastating and sometimes lethal genetic conditions on to their children. In addition, JScreen, which launched last fall, offers education and counseling to help people understand their results, says Karen Grinzaid, an instructor in Emory’s Department of Human Genetics and JScreen’s senior director of outreach initiatives.

Almost 80% of babies with a genetic disease are born to parents with no known family history. For Ashkenazi Jews like Chanin and Weinberg, the risk for genetic disease is higher than for the general population. Nearly one in four Ashkenazi Jews carries a gene for a serious genetic disease.

According to an Emory survey, an estimated 75% of American Jews of

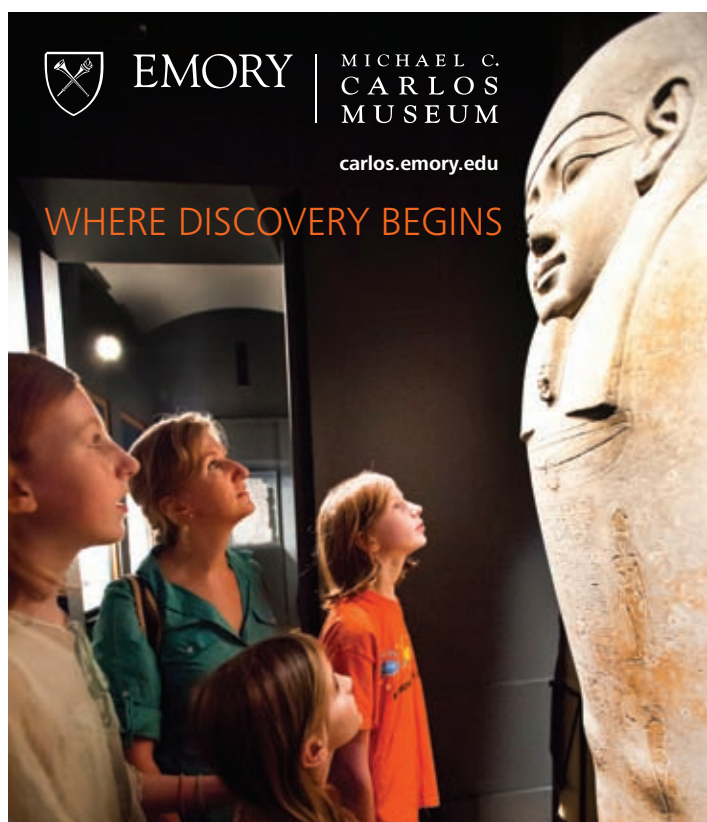
reproductive age have not been tested for genetic disease, and 24% aren’t aware they have an elevated risk of having a child with a genetic disease.

“Many women don’t think about screening until they are pregnant, and that is a stressful time to screen and make decisions,” says Tricia Page, director of Emory’s Genetic Counseling Services and JScreen senior director. “There are two ways to find out if you are a carrier—to screen or to have an affected child. Our goal is pre-conception screening, which gives people the opportunity to plan.”

The first online carrier screening program, JScreen allows people to request kits, learn about hereditary diseases, and speak to genetic counselors. While the program is focused on the Jewish population, those with mixed ancestry or even no Jewish ancestry can also be screened.

“It was easy,” Weinberg says. “I filled out my name and insurance on the website and within a couple of weeks there was a package at the door.” She did the saliva test and sent the kit back to the lab. Upon getting the results, Weinberg reviewed them with a genetic counselor over a private teleconference. She found that she was a carrier for Fanconi anemia and Niemann-Pick disease. “Jessica was wonderful,” Weinberg says of her counselor. “I appreciate the time she took to discuss the diseases and answer my questions. It made the process as painless as possible.”

Chanin also was tested, and found he was a carrier for Joubert syndrome. Because Chanin and Weinberg carry recessive genes for different diseases, the probability is that they would not have a problem. “It was a relief,” Chanin says. “We can look forward to having kids with the comfort of knowing that we don’t have to worry about genetic disease.” — *Yael D Sherman*



Free from diabetes Islet transplant recipients thriving a decade later

Rob Allen had brittle diabetes, meaning he'd had type 1 diabetes for so long that he lost the ability to sense when his glucose level was dangerously low. He had no islets, the pancreatic cells that release insulin, which regulates blood sugar levels and allows people to get energy from food.

"Until you've been through an insulin reaction, you really can't appreciate it," says Allen (below right), who was diagnosed at 17 after experiencing extreme weight loss, fatigue, and thirst. As a hydro-logic technician for the US Geological Survey, he was often alone in the woods checking water levels in wells. "Passing out was

a huge concern," he says.

After decades of insulin injections, an insulin pump, occasional seizures, and his wife, Lisa, standing by with glucagon in case his levels dipped too low, Allen was desperate to try something new. He volunteered to receive an islet transplant as part of a clinical trial at Emory Transplant Center in 2004. He has been free of all symptoms of diabetes for a decade now. Allen and Laura Cochran, a mother of four

from Columbus diagnosed with type 1 diabetes at 27, were among the first to have islet transplants in Georgia. "I had several severe hypoglycemia incidents while I was with my

children, and that was scary," Cochran says.

They received two islet cell transplants each, a few months apart, from deceased donors. Hundreds of thousands of donor islet cells were slow-dripped by an IV into the liver. After the transplants, Allen and Cochran's abilities to produce insulin naturally were restored.

"We transplanted just two teaspoons of islet cells into these patients 10 years ago, and they no longer need insulin injections," says Christian Larsen, transplant surgeon and dean of the School of Medicine. "Our work is about making this possible for others."

Nineteen patients have received islet cell transplants in four clinical trials at Emory. FDA approval of islet cell transplants would mean that the surgery would no longer be considered experimental. ■



PHOTO BY SARAH L. O'NEILL

DDT exposure potential risk factor for Alzheimer's



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US soldiers demonstrate DDT hand-spraying equipment.

DDT was used extensively after World War II in agriculture and for mosquito control until it was banned in the US in 1972. Now researchers have found that patients with Alzheimer's disease have significantly higher levels of DDE, the long-lasting metabolite of the pesticide DDT, in their blood than healthy people.

Researchers found that DDE levels were almost four times higher in serum samples from Alzheimer's patients than in controls. DDE levels in the highest third of the sample range increased the

risk of Alzheimer's by a factor of four, according to a study published in *JAMA Neurology*. "This is one of the first studies identifying a strong environmental risk factor for Alzheimer's disease," says coauthor Allan Levey, director of Emory's Alzheimer's Disease Research Center and Betty Gage Holland Chair of Neurology. "The magnitude of the effect is strikingly large—it is comparable in size to the most common genetic risk factor for late-onset Alzheimer's."

The researchers identified a plausible mechanism for DDE's effects. Cultured neural cells exposed to high levels of the pesticide produced more of a protein that is a precursor to beta-amyloid, the main component of plaques found in the brains of Alzheimer's patients.—Quinn Eastman

IN THE NEWS

Alzheimer's disease may be a much more common cause of death than previously thought.

Alzheimer's is under-reported on death certificates and may, in fact, be the third-leading cause of death after heart disease and cancer, say researchers at Rush Alzheimer's Disease Center in Chicago. The CDC attributed about 84,000 deaths to Alzheimer's in 2010, but the new study shows the disease may actually be responsible for more than half a million deaths a year among those 75 and older. Death certificates often record only the immediate cause. "Pneumonia, urinary tract infection, heart attack, those are the things that are obvious, and that's what a doctor will frequently list on the death certificate," says Emory neurologist Allan Levey.

Magnetic nursing care



Emory University Hospital and Emory Saint Joseph's Hospital have achieved Magnet recognition from the American Nurses Credentialing Center for nursing professionalism, teamwork, and quality in patient care. (This is Emory Saint Joseph's fifth consecutive Magnet designation.) Magnet recognition is earned by less than 7% of US hospitals, and signals benefits to both patients and staff, including lower mortality and hospital-acquired infection rates, higher patient satisfaction, and higher job satisfaction among nurses. John Fox, Emory Healthcare president and CEO, describes Magnet status as the "unequivocal national and international gold standard for nursing quality."

Do you see what I see?



Following another's gaze or looking in the direction someone else is pointing are examples of receptive joint attention, a key nonverbal communication skill.

Researchers at Yerkes National Primate Research Center found that these behaviors have a genetic basis, which could have important implications for autism spectrum disorders (ASD).

Determining that the ability to pick up on these communicative cues may be an inborn trait led the researchers to the vasopressin receptor gene, known for its role in social bonding.

Yerkes researchers Larry Young and Bill Hopkins, coauthors of the study in *Scientific Reports*, say that receptive joint attention is important for developing complex cognitive processes, including language and theory of mind. Poor joint attention abilities may be a core feature in children with or at risk of ASD.

"Chimpanzees are an excellent animal model for exploring the role of the vasopressin receptor on social behaviors because of their similarities to humans," says Young, director of the Center for Translational Social Neuroscience at Emory, Timmie Professor of Psychiatry and Behavioral Sciences, and a newly elected member of the American Academy of Arts and Sciences.—*Lisa Newbern*

YOU BE THE DOCTOR ...

The mysterious case of the saxophone lungs

A 68-year-old man sought treatment from the asthma, allergy, and immunology team at Emory Clinic. He complained of coughing and wheezing that had lasted more than a year.

His chest X-rays showed blockages with mucus and a calcified lymph node.

The man's symptoms hadn't responded to any typical treatments, including inhalers, steroids, and antibiotics.

He mentioned in passing that he performed with a Dixieland band, and that he had played clarinet for more than 30 years. "He was playing very frequently, several nights a week," says Marissa Shams, one of the Emory physicians who treated the patient.

Doctors originally thought he had allergic bronchopulmonary aspergillosis, a type of fungal reaction. Indeed, tests showed the man was allergic to several types of fungi. He was given oral steroids but didn't get any better.

What was causing his illness, and if it was an allergic reaction, how was he being exposed to the fungi?

Yep, you guessed it, the clarinet was the culprit.

Exophiala, a fungus usually found in decaying wood and soil, was discovered inside his clarinet and on its reed. "There was very impressive fungal growth on those," Shams says. The musician admitted that he hadn't thoroughly cleaned his instrument in years.

The diagnosis? "Saxophone lung," a rare type of hypersensitivity pneumonia. "Basically, he was breathing in this fungus and developed an allergic reaction," Shams says.

Once the musician started sterilizing his instrument regularly, he improved substantially.

Shams and colleagues David Berkowitz, Frances Lee, and Jennifer Shih presented the case at the annual meeting of the American College of Allergy, Asthma, and Immunology.

"We were happy to help him," Shams said. "This is not the typical allergy and asthma patient that we see in our clinic." ■



When less is more

Reducing oxygen to mountain-peak levels benefits patients with spinal cord injuries

Friday the 13th did prove unlucky, even devastating, for Danny Jackson. On March 13, 2009, the North Carolina sheriff's deputy was responding to a call when his car went off the road and hit a tree. Since then, he had been confined to a wheelchair.

While undergoing physical therapy in Atlanta, he heard about an Emory study for people with incomplete spinal injuries, in which participants might improve their walking ability by temporarily reducing their oxygen supply. It sounded counterintuitive to Jackson. "I said yeah, right," he says. "But it changed everything—dramatically. I wish this treatment was FDA-approved."

For patients with spinal injuries that are not absolute, pathways in the nervous system are capable of functioning but often work only minimally, making for modest gains in mobility. Most do not return to walking unassisted even after years of physical therapy.

Jackson, 32, and other participants breathed 90 seconds of reduced oxygen (9%) followed by a minute of normal oxygen, repeated 15 times for five days, and did walking therapy. (The 9% rate of oxygen is the equivalent of standing on Mount McKinley at 26,000 feet.) The lack of oxygen causes the brain to release serotonin, which acts on receptors within the spinal cord. The



receptors help increase the production of an important protein, brain-derived neurotrophic factor, which in turn increases the excitability of neurons in the leg muscles, causing movement, and in the diaphragm muscle, increasing the patient's breathing capacity.

Of the 19 participants, 70% walked faster and farther after the treatment, including Jackson, who now uses a walker instead of a wheelchair. "Functional recovery after spinal injury is slow, variable, and frustratingly limited," says Randy Trumbower, a researcher in Emory's Division of Physical Therapy, who led the study. "There is a need for therapies that can help patients be more independent. Even small improvements that enable someone to stand, walk within the home, or negotiate spaces not accessible to wheelchairs can translate into significant health benefits and improved quality of life."—*Kay Torrance*



GEORGIA RESPONDS

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To register please go to
www.GeorgiaResponds.org



Q&A WITH CARDIOLOGIST PETER WILSON GUIDELINES FOR TREATING CHOLESTEROL

By QUINN EASTMAN



Newly revised guidelines for treating cholesterol to reduce cardiovascular disease risk were released in November by the American Heart Association (AHA) and American College of Cardiology (ACC). The new guidelines de-emphasized achieving target numbers for LDL-C (low density lipoprotein cholesterol), the harmful form of cholesterol. Emory preventive cardiologist Peter Wilson served on the AHA/ACC task force that formulated the new guidelines. He drew on a wealth of research experience, including 20 years as director of laboratories at the Framingham Heart Study in Massachusetts, as well as clinical experience at the Emory Clinic and the Atlanta VA Medical Center Lipid Clinic.

Why did an update become necessary?

Cholesterol-lowering medications had become more potent over the past decade. More information on their safety and efficacy was available, but that evidence had not been integrated into the recommendations. Many statins have recently gone off patent, so their cost has gone down—atorvastatin [Lipitor] is a prominent example of a lipid-lowering drug that now costs much less. And we needed to evaluate the results of clinical trials involving statins—statins vs. placebos, low dose vs. high dose, statin plus a second drug vs. statin alone.

In addition, several questions about testing and evaluation had come up. Doctors want to know: "How low does cholesterol need to go? Do you need to do a CRP (C-reactive protein) test? What about coronary artery calcium (CAC) testing?"

The NIH Heart, Lung, and Blood Institute directed us to use the Institute of Medicine approach, which is sort of a "guideline for guidelines." They have a hierarchy of evidence, with randomized controlled clinical trials carrying the greatest weight, and a mandate to limit the number of recommendations that are "expert opinion."

What is considered expert opinion?

For example, the advice to get some patients' LDL-C below 70 mg/dL. When that was promulgated in 2004, there was no hard evidence for it. There was one study with data on people who had LDL lower than 70 mg/dL, where you could infer some possible benefit. A lot of providers jumped on that and said, "I'll get everybody under 70 if I can! If it's safe and tolerated, why not?"

How will the new guidelines affect patients with different profiles?

Let's take a high-risk case—a middle-age male smoker with high blood pressure. His LDL-C level is 130 mg/dL. This is an "average Joe" LDL. He had a heart attack and is sent home from the hospital on a statin. Before, the goal was to get the patient's LDL-C below 100 mg/dL. The doctor would say, we'll see you in six weeks. When the patient came back, the doctor would ask about statin side effects and look at the LDL-C levels. If there had been some progress, the patient would be told to keep up the good work. But this reflects a short-term focus. Sometimes you see people at six months post-heart attack and they're not on their medicines. Patients ask: "Is this lifelong?" Well, yes, unless there's a big change. Unless you become a low-fat, low-cholesterol vegetarian, you're probably not going to be able to make great progress in lowering LDL-C without medicine. Now, let's take that same man under the new guidelines. An LDL-C of 130 is clearly too high, so he'd be put on a high-potency statin. A post-heart attack patient would probably get rosuvastatin (Crestor) or atorvastatin (Lipitor). If he can't tolerate either of those, we'll move on to other options.

One of the biggest changes is that there are no hard targets for patients' LDL-C. How will you determine success?

The key element of success is that the patient takes the medicine. If that same patient we just

talked about comes back in a few months and his LDL-C level is 140 mg/dL, I get the feeling he is not taking it. Some experts say they want patients to take medicines and see if LDL-C gets better. I say, probably the most important thing is for you to take the medicine and follow other preventive advice like cutting down on smoking, eating a heart-healthy diet, and reducing weight if needed.

Let's consider another patient, someone with different risk factors. She is diabetic and a smoker, but has not had a heart attack. All diabetics are now considered to be at high risk for cardiovascular disease, especially if they are over 40. Should we wait six months before giving lipid medication? No, we treat her more aggressively.

Now let's take a trickier case. We have a 50-year-old, no risk factors, but a family history of heart disease. He's concerned. The calculated 10-year risk is about 5%. LDL-C is 110 or 120 mg/dL. He might say, "Doctor, what you say is comforting but I'm wondering if we're doing enough." This is where you have the risk discussion, and where some of the newer tests (CRP and CAC) come into play as discriminating factors. I may bring up a low-dose statin as a preventive, perhaps pravastatin 40 mg per day. It's very easy to tolerate.

Why not just take a daily, low-dose aspirin?

It's not clear that you need to take both aspirin and a statin. Most of the trials that showed the benefit of taking a daily aspirin were completed before the modern era of statins. There is a trial going on at NIH that is evaluating the role of aspirin in the elderly.

One of the main effects of the new guidelines is that there will probably be less cholesterol testing in patients on lipid medications. In the past the patient would return to clinic every three months and progress would be marked by looking at the patient's LDL-C level. Now, the most important thing is to keep taking the medicine, as tolerated.

Are there diminishing returns with cholesterol-lowering drugs after some point?

Yes, for those with LDL-C 70 compared to 90 mg/dL. The data suggest that lower is better for your cardiovascular health, but the evidence is not as strong as some physicians would like to think. The next frontier is LDL 40 compared to 80 mg/dL.

An LDL-C of less than 50 mg/dL is more achievable than ever before. There are new medicines coming online, such as PCSK9 inhibitors, which can accomplish that. The question is, is there a benefit? Is it appropriate? We don't know yet.

Are there any gaps in the guidelines?

Statins are of little or no benefit where there is already lots of calcification. You see that in people with calcified aortic valves. You also see it with patients who are on dialysis because of kidney disease. When you see the more calcified lesions, it's probably too late for statins. Statins won't do harm, but there may be little benefit.

If there is a gap in the guidelines, it's what to do with young people with familial high cholesterol levels. What do I do with a 20- or 30-year-old with very high LDL and no other risk factors? They should be on very aggressive treatment. It may seem obvious, but often physicians will give them one medicine and will stop there. These patients really should be referred to a specialist.

Media coverage of the new guidelines may have given the public the impression that almost everybody should take statins at some stage in their lives. They do identify more people to take statins because of the risks and benefits. We knew that in 2001, but the treatment threshold was put higher, somewhat arbitrarily. At that time, recommending statins was more apt to be considered inappropriate because the cost of treatment would be substantial. That's no longer the case. In terms of cost, statin therapy is starting to look very similar to blood pressure control, which can be done inexpensively.

In the new guidelines, did you reach a conclusion about the value of tests such as CRP and coronary artery calcium (CAC)?

These tests are a research issue that many of us are interested in, but it's still unclear whether we need to have them done for every patient. I would advise patients not to run out and get a coronary artery calcium test. Cost is an issue and, with CAC scoring, radiation exposure is a concern if the patient has the test multiple times.

Stepping back, some of these tests may be helpful for patients with intermediate risk. They may help us decide whether to treat more or less aggressively. If you're having a risk discussion

with a patient about family history and other risk factors but the patient is reluctant, that's where additional testing might help and a positive test might tip the balance toward a more aggressive treatment.

So, how long should a patient be on statins? What age should you start?

It's hard to say because there are very few heart disease events in men younger than 45 or women younger than 55.

Let's talk about statin side effects. What are the most common ones?

Between 5% and 15% of people who take statins will get muscle aches. It's not like cramps that appear at night—it feels like soreness after exercise. There is no blood test to shed light on this symptom, and there are no obvious signs of muscle inflammation.

The three main items to monitor for safety are muscle symptoms, liver enzymes, and creatine kinase for kidney function. The rule of thumb is this: monitoring is good to do when starting treatment or when changing dose. You don't need to do the tests all the time, but maybe once a year is appropriate. More frequent monitoring may be needed for some of the newer drugs.

The risk of developing diabetes while taking statins is real but relatively small: 1% or 2% greater risk. It is dose dependent and related to the potency of the statin. You have to balance that against reducing the risk of a heart attack.

What should be done if the patient does not tolerate the statin medication?

There are a lot of statins you can try. But it's problematic if someone needs a high-potency statin over the long term. Let's take someone who was sent home with a prescription for atorvastatin (Lipitor) 80 mg/day. He tries it for three weeks and stops because of aches. Doctors will probably try switching him to a different drug. But an overlooked strategy is to simply use the same statin at a lower dose. Patients can take the statin every other day, and gradually work their way up to a dose they can tolerate. Plus, it's OK to take a statin holiday for a few days when, say, you have the flu and feel horrible.



The Anatomy of Fear

Understanding the biological underpinnings
of anxiety, phobias, and PTSD

By MARTHA NOLAN MCKENZIE ■ Illustration by BRIAN STAUFFER

Fear in a mouse brain looks much the same as fear in a human brain.

When a frightening stimulus is encountered, the thalamus shoots a message to the amygdala—the primitive part of the brain—even before it informs the parts responsible for higher cognition. The amygdala then goes into its hard-wired fight-or-flight response, triggering a host of predictable symptoms, including racing heart, heavy breathing, startle response, and sweating.



THE *take-away*

Nearly one-third of us will experience an anxiety disorder at some point in our lives. **Why do some people overcome their fears while others become incapacitated?** The answer might be in our genes.



Psychiatrist **Kerry Ressler** studies the molecular and cellular mechanisms of fear learning and extinction to determine the role biology plays in placing people at risk for anxiety disorders, phobias, and post-traumatic stress disorder (PTSD); he's also researching the genetic transfer of fears and phobias across generations.

The similarities of fear response in the brains of mice and men have allowed scientists to understand the neural circuitry and molecular processes of fear and fear behaviors perhaps better than any other response. That understanding has spurred

“There’s a patient I’ve seen who was attacked in a dark alley. Initially it just felt dangerous to go out at night, but after a while she grew afraid of men and couldn’t go to that part of town. Then she couldn’t leave her house, and finally, her bedroom. The world got more and more dangerous.”

breakthroughs in treatments for psychiatric disorders that are underpinned by fear.

Anxiety disorders are one of the most common mental illnesses in the country, with nearly one-third of Americans experiencing symptoms at least once during their lives. There are generalized anxiety

disorders and fear-related disorders, which include panic disorders, phobias, and post-traumatic stress disorder (PTSD).

Psychiatrist and researcher Kerry Ressler is on the front lines of fear-disorder research. In his lab at Yerkes National

Primate Research Center, he studies the molecular and cellular mechanisms of fear learning and extinction in mouse models. At Grady Hospital, he investigates the psychology, genetics, and biology of PTSD. And through the Grady Trauma Project, he works to draw attention to the problem of

inner city intergenerational violence.

“If you look at Kerry’s work, it can seem like it’s all over the place—he’s got so many studies going on, and he collaborates with so many other scientists,” says Barbara Rothbaum, associate vice chair of clinical research in psychiatry and director of the Trauma and Anxiety Recovery Program at Emory. “But they are all pieces to the same puzzle. All his work, from molecular to clinical to policy, fits together and starts telling a story.” A Howard Hughes Medical Institute investigator,

Ressler was recently elected to the Institute of Medicine—one of the highest honors in the fields of health and medicine. He was named a member of a new national PTSD consortium led by Draper Laboratory. And he recently appeared on the *Charlie Rose* show’s brain series.



Panic attacks seem to tie the fear-related disorders together, he explained on *Charlie Rose*. Everyone experiences fear, which evolved as a survival mechanism, but it only rises to a clinical level when people are unable to function normally in the face of it. For instance, PTSD includes not only intrusive thoughts, memories, nightmares, and startle responses, but also the concept of avoidance, which may extend to other areas of the individual's life.

"There's a patient I've seen who was attacked in a dark alley," Ressler shared on the show. "Initially it just felt dangerous to go out at night, but after a while she grew afraid of men and couldn't go to that part of town. Then she couldn't leave her house, and finally, her bedroom. The world got more and more dangerous."

AMYGDALA-BASED ANXIETY

Ressler wanted to see if he could identify genes that could explain why some people (about 20%) develop PTSD after a trauma while others are resilient.

He traumatized a group of mice—immobilizing them by strapping them to wooden boards for two hours. A week later, he put both the traumatized group of mice and a control group that had not undergone trauma through a common fear-conditioning regimen. Mice received a slight shock on their feet at the same time that a tone sounded. Days later he played the tone without an accompanying shock, and some of the previously traumatized mice exhibited PTSD-like symptoms. They startled more dramatically and were unable to "extinguish" their fear—to learn that the tone was now safe and no longer signaled a shock.

When the region of the brain responsible for creating and storing fear memories, the amygdala, was examined afterward through autopsies, Ressler and Raul Andero found that one gene, *Oprl1* (opioid receptor-like 1), was switched on in the mice that had experienced prior trauma and had PTSD-like symptoms. "From that finding, we hypothesized that if we could activate the *Oprl1* pathway within the brain, it would prevent the over-learning of the fear response, which is at the crux of the PTSD syndrome," says Ressler.

Agoraphobia—intense fear and anxiety of any place or situation where escape might be difficult, leading to avoidance of situations such as being alone outside of the home, in a crowded area, or traveling in a car, bus, or airplane.

Lifetime prevalence—1.4% of US adult population; average age of onset, 20 years.

Generalized anxiety disorder (GAD)—excessive worry about a variety of everyday problems for at least 6 months. For example, people with GAD may excessively worry about and anticipate problems with their finances, health, employment, and relationships. They typically have difficulty calming their concerns, even though they realize that their anxiety is more intense than the situation warrants. **5.7%; 31 years.**

Panic disorder—unexpected and repeated episodes of intense fear accompanied by physical symptoms that may include chest pain, heart palpitations, shortness of breath, dizziness, or abdominal distress. **4.7%; 24 years.**

Post-traumatic stress disorder—develops after exposure to a terrifying event or ordeal such as a violent personal assault, natural or human-caused disaster, accident, or military combat. People with PTSD have persistent frightening thoughts and memories of their ordeal, and may experience sleep problems, feel detached or numb, or be easily startled. **6.8%; 23 years.**

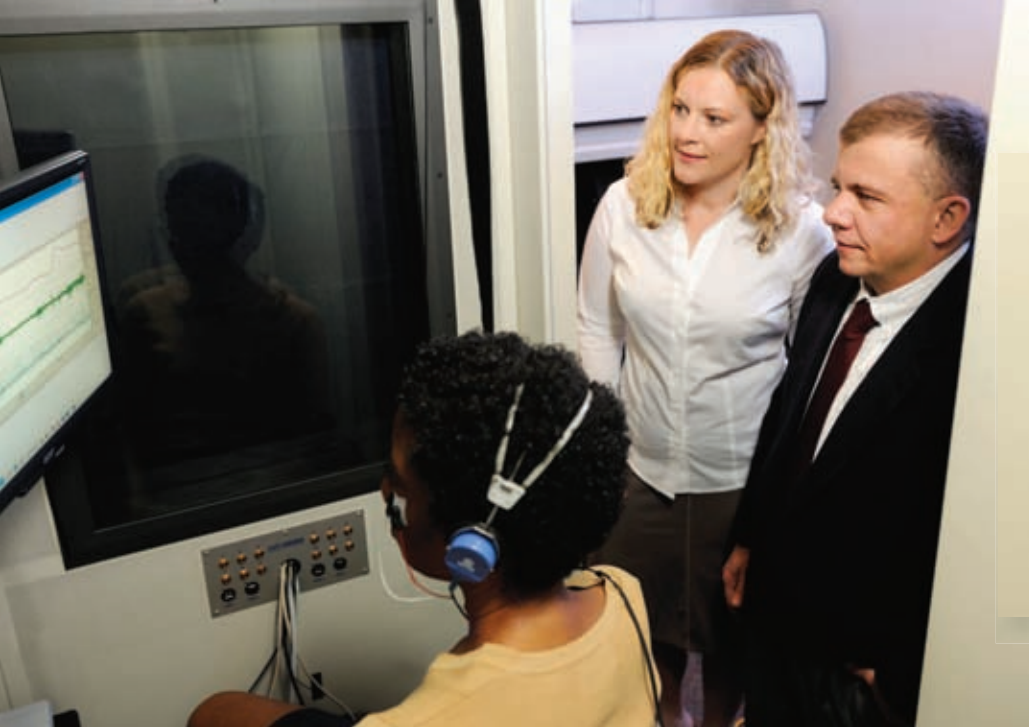
Social phobia—intense and chronic fear of being watched and judged by others and feeling embarrassed or humiliated by their actions. This fear may be so severe that it interferes with work, school, and other activities and may negatively affect the person's ability to form relationships. **12.1%; 13 years.**

Specific phobia—persistent fear and avoidance of a specific object or situation, including but not limited to the fear of heights, spiders, and flying. **12.5%; 7 years.**

Obsessive-compulsive disorder (OCD)—intrusive thoughts that produce anxiety (obsessions), repetitive behaviors that are engaged in to reduce anxiety (compulsions), or both. While many are concerned about germs or leaving their stove on, people with OCD are unable to control their anxiety-producing thoughts and ritualized behaviors. **1.6%; 19 years.**

Source: National Institutes of Mental Health





Shown here at the “startle booth” at the Atlanta VA Medical Center, **Tanja Jovanovic**, assistant professor of psychiatry, and **Bekh Bradley**, co-founder of the Grady Trauma Project and director of the PTSD treatment program at the VA, are collaborating with Ressler on a research study involving highly traumatized mothers with and without PTSD, and their children. “We are looking at psychological, physiological, and genetic components of both the mothers and their children and then following them over time,” Jovanovic says.

A literature search revealed only two papers looking at this gene and its pathway in humans, and Ressler happened to know the author of one from Scripps Research Institute. He contacted Scripps and found that its institute, along with University of Miami, had developed a drug called SR-8993 that targets the Oprl1 receptor. The pathway is part of a family of opioid receptors that allow brain cells to receive signals from opioid drugs as well as natural opioids produced by the body. Scientists, however, believe that the euphoric and analgesic effects of opioid drugs mainly come from triggering other members of the opioid receptor family, not Oprl1. As a result, Scripps was looking at the drug as a possible treatment for drug and alcohol addiction.

Ressler’s team repeated all the steps from the first mouse study, but this time they administered SR-8993 after fear conditioning. The previously traumatized mice that got the drug did not develop any of the PTSD symptoms. They behaved like their control kindred.

“We think SR-8993 is helping promote a natural process that occurs after trauma, preventing fear learning from becoming over-represented and generalized,” Ressler says. “Our model is that in PTSD, the Oprl1 system is serving as a brake on fear learning, but that brake is not working if prior

trauma had occurred. This is an important step toward developing a treatment to possibly prevent the onset of PTSD symptoms.”

Previous studies in Ressler’s lab, in collaboration with Michael Davis, emeritus professor of psychiatry, showed it was possible to prevent the development of PTSD-like fear memories in rats by doing extinction training immediately after a trauma, since a memory doesn’t become permanent, or consolidated, right away. So directly after going through the shock/tone fear conditioning, the rat is repeatedly exposed to the tone without the shock and doesn’t learn to fear the tone.

In collaboration with Rothbaum and Debra Houry, vice chair for research in emergency medicine and director of the Emory Center for Injury Control, Ressler set out to see if the same window of time existed in humans. Patients admitted to the ER following a trauma—a car wreck, gunshot wound, rape—received imaginal exposure therapy. “We asked them to talk about what happened to them in a therapeutic way,” says Rothbaum. “We know this type of cognitive behavior therapy works very well for people with chronic PTSD. Here we were applying the same technique before the fear memory was consolidated.”

The results were encouraging. Three months after their trauma, PTSD incidence in patients who received the intervention was

half that of patients who did not receive it.

“This is significant because some earlier studies had shown that psychological debriefing could actually make people worse, which scared people off from early interventions,” Rothbaum says. “The fact that our intervention worked so well may help reopen early intervention efforts.”

PREDICTING AND PREVENTING PTSD

Ressler and his team are taking this study a step further, collecting blood samples from trauma victims in the ER and searching for genes and other biomarkers that would identify people who are at increased risk for developing PTSD following trauma.

So far pilot data from the study agree with findings reported in two recent papers—people who get morphine immediately after a trauma are less likely to develop PTSD. Many assume that’s because morphine is an analgesic, so the patients who get it do not experience the pain as severely and therefore are less likely to develop PTSD. But Ressler hypothesizes that morphine’s protective powers stem from activating the Oprl1 gene pathway in the amygdala.

“In the same way we found these brain-based biomarkers in mice that changed right after a trauma or fear conditioning, we are getting blood from people right after they come into the ED and looking for biomarkers that are predictive, within the first hours after suffering a trauma, of later development of PTSD,” says Ressler. “The vision would be to develop the equivalent of a stroke protocol or a heart attack protocol in the ED for psychological trauma.”

Based both on answers to a set of psychological questions and on blood-based biomarkers, he says, predictions could be made about who is at highest risk of developing PTSD. With early pharmacological or psychological therapeutic intervention, possibly even in the emergency department, preventing PTSD might be possible.

People tend to equate PTSD with combat trauma, and, in fact, most PTSD research, treatment, and funding is focused on returning veterans. Yet Ressler and his colleagues have found that low-income, inner-city residents suffer from the disorder as much as or more than combat vets.

Ressler and his colleagues have found that low-income, inner-city residents suffer from PTSD as much as or more than combat vets.

“One of the reasons we created the Grady Trauma Project and continue to work on it is to shine light on an extremely underserved and underappreciated problem, civilian inner-city trauma,” says Ressler. “Within the Grady Hospital population, we’ve found that 80% to 90% have experienced a severe trauma, and 30% to 35% have gone on to develop PTSD. That rate is higher than for combat vets, yet this is something that most people are not aware of. We think it is an epidemic problem, and we believe that the inner-city cycle of violence and poverty can be explained in part through the effects of trauma on residents’ brains.”

The Grady Trauma Project is now in its seventh year, and DNA, historical, and psychological data have been collected on more than 6,000 Grady medical clinic outpatients. “These are not patients from the ED or from psychiatry,” says Ressler. “We wanted a cross-sample of the general Grady patient population.”

Ressler and his team are examining subjects’ genomes to look for PTSD risk factors. “We currently understand what a few hundred of the genes in the brain do,” he says. “But that’s only about 2% of the

brain’s expressed genes. We don’t know how the vast majority of these work. Looking at the entire genome likely will allow us to identify other important genes involved.”

The Grady project may also shed some light on the intergenerational nature of PTSD. In collaboration with Tanja Jovanovic, assistant professor of psychiatry, and Bekh Bradley, co-founder of the Grady Trauma Project and director of the PTSD treatment program at the Atlanta Veterans Affairs Medical Center, Ressler is looking at highly traumatized mothers with and without PTSD and their children. “We are looking at psychological, physiological,

and genetic components of both the mothers and their children and then following them over time,” Jovanovic says.

Scientists know that about 30% to 40% of the

risk for PTSD is inherited. They speculate that genes shared between parent and child may be one mechanism for this inheritance, or that traumatized parents could increase their children’s likelihood of developing symptoms environmentally, through psychological and parenting processes.

Another interesting answer could lie in the new science of epigenetics. “A mother’s stress could alter gene expression from her own DNA through experience-dependent chemical ‘tags’ on her DNA, which she could then also pass down to her child,” says Ressler. “So we think evidence is building that experiences in one generation could affect how genes are expressed in the next generation.”

FEARS OF OUR FATHERS

Ressler’s lab at Yerkes is following up on some of these ideas in powerful mouse models of epigenetic transfer

of fear across generations.

Ressler and fellow researcher Brian Dias trained mice to become afraid of an odor by pairing exposure to the odor with a mild electric shock. They then measured how much the animal startled in response to a loud noise alone, and then in conjunction with the odor.

Surprisingly, they found that the naïve adult offspring of the sensitized mice also startled more in response to the particular odor that one parent had learned to fear, despite the fact that they had never been exposed to the odor/shock combination. In addition, the younger mice were more able to detect small amounts of that particular odor.

A third generation of mice also inherited this reaction, as did mice conceived through in vitro fertilization with sperm from males sensitized to the smell.

These offspring were not more anxious in general; in separate experiments not involving odors, Dias found that the mice were not more afraid to explore the bright, elevated areas of a maze.

Dias also discovered that the DNA from the sperm of the smell-sensitized father mice is altered. This is an epigenetic alteration, found not in the letter-by-letter sequence of the DNA but in its packaging or chemical modifications.

Knowing how the experiences of parents influence their descendants helps us to understand psychiatric disorders that may have a transgenerational basis and possibly to design therapeutic strategies, Ressler says.

“Practicing medicine reminds us of why the research we do is so important for our patients, who are suffering every day,” he says. “And if we find ways to treat these adults, it may very well help their children and grandchildren as well.” ■

🔗 **want more?**



YOUR BRAIN AND FEAR To see Kerry Ressler speak about the neuroscience of emotion at TEDx Peachtree 2012, go to tedxpeachtree.com/tag/kerry-ressler/.

To see Ressler on the Charlie Rose show’s brain series, go to charlierose.com/watch/50059537.



THE *take-away*

Battling glioblastoma takes a combination of powerful tools—including genomic analyses, targeted therapies, and imaging techniques that **make the cancer cells glow bright pink.**

A Different Beast

Confronting the most aggressive, evasive, and cunning of all brain tumors

Cody Mahan and his family didn't think they would have to deal with cancer again so soon.

After graduating college, Mahan, 23, had earned a prestigious Department of Defense SMART scholarship and had just started working at Warner Robins Air Force Base. He was looking forward to a promising engineering career.

In December, he started to experience headaches and then pain in his neck. His family took him to a hospital close to where they lived in Tennessee, suspecting meningitis. Doctors discovered a tumor on the right side of his brain. "It was quite a shock," says Cody's mother, Lisa. "It was the furthest thing from our minds when we went to the ER."

They had thought cancer was behind them. As a teenager, Mahan had ALL (acute lymphoblastic leukemia) and had received full cranial radiation as part of his treatment. At the time, this was a standard prophylactic for patients with ALL. The radiation, his family suspects, may have led to the development of the brain tumor. In fact, radiation exposure is one of the only known risk factors for developing a brain tumor.

Mahan is fighting a different beast this time. Five-year survival rates for children with ALL are reaching 80%. Five-year survival rates for glioblastoma, the most

common and most aggressive malignant brain tumor, are around 10%.

Glioblastomas are especially frustrating, often striking adults in the prime of their lives. They quickly spread within the confines of the skull, destroying normal brain cells. The tumors are heterogeneous, containing a mix of cell types, and are supported by a large system of blood vessels. And they can slip past barriers that oncologists have tried to put in their way, such as newer "targeted" therapies.

As daunting as this sounds, progress is taking place. For a time, it was not clear from clinical trials if chemotherapy lengthened survival times with glioblastoma. But the drug temozolomide appeared to make a difference. Since the Food and Drug Administration (FDA) approved temozolomide in 2005, the five-year survival rate has tripled.

"We want to turn glioblastoma into a chronic disease, so that it's possible to keep it at bay for a decade, like with some other forms of cancer," says Jeffrey Olson, co-director of Winship Cancer Institute's brain tumor program. "So far, there have been incremental improvements in treatment, but no home runs."

Turning tumors pink

At the outset, a factor that sets the course for the rest of the patient's journey is how

much of the tumor can be removed in surgery. But glioblastomas are especially tricky to remove cleanly—a task that has been compared to removing chewing gum tangled in hair. "Glioblastoma is the most challenging type of tumor we deal with," says Winship neurosurgeon Costas Hadjipanayis. "At the margin of the tumor, cancer cells infiltrate into normal tissue, and that region is very difficult to see during surgery."

The cancerous cells often extend several centimeters into normal tissue, making removal of the entire tumor impossible. But surgery usually can alleviate symptoms, and if surgeons can remove 92% to 98% of the tumor, a patient's survival can be extended.

Led by Hadjipanayis, Emory has been testing an imaging agent that turns cancer cells pink during surgery, allowing neurosurgeons to discern tumor boundaries more effectively. Before surgery, the patient drinks a cocktail containing 5-aminolevulinic acid (5-ALA) to illuminate the cancer cells. Compared with healthy cells, cancer cells soak up more of this substance and then convert the 5-ALA into a chemical that shines pink when viewed through a special microscope.

In Europe, surgeons using 5-ALA found that it helped them remove the brain tumor more completely, as determined by MRI brain scans, and prolong progression-free survival by several months.

5-ALA, which was approved for clinical use in Europe and is known commercially as Gliolan, is still undergoing evaluation by the FDA. Emory was the first medical center in the United States to use Gliolan and has been one of the top sites in surger-



Cody Mahan, above, volunteered for a clinical trial that may improve surgical results by making his tumor more visible.



Winship Cancer Institute's **Costas Hadjipanayis**, **Jeffrey Olson**, **Alfredo Voloschin**, and **Daniel Brat** (above, left) are finding new ways to battle an old foe—glioblastoma. Radiologist **Hyunsuk Shim** (above, right) is using magnetic resonance spectroscopy to detect changes in cancer metabolism.

ies performed using the imaging agent. Hadjipanayis has trained surgeons at other medical centers to use it as well.

This effort to improve the surgery's success rate appealed to Mahan—enough that he took special steps to be able to join the study. To prevent leukemia recurrence, he was taking the anticancer drug Gleevec, which barred him from participating in the 5-ALA trial. He offered to go off Gleevec before the surgery so he could take part. [In March 2014, Mahan was about halfway through treatment with radiation and chemotherapy with temozolomide.]

Walking a tightrope

Gary Gelb, a pharmaceutical sales manager, lives in Atlanta with his wife and daughter. He was making a presentation to colleagues at a business meeting in Las Vegas in 2010 when he was distracted by a distasteful odor. Later that day, he found himself unable to speak. Both events were symptoms of a seizure caused by a tumor seen on CT scan when he was taken to a local hospital. The tumor was above his left ear in the temporal lobe, a region of the brain important for language.

Gelb's case illustrates the tightrope neurosurgeons must walk in removing as much of the tumor as possible without compromising brain function. After his first surgery, Gelb impressed doctors and nurses with his ability to walk the hospital corridors, and he was able to go home in just two

days. He continued working on his motor skills and balance by climbing stairs and taking walks, but the surgery had affected his short-term memory. "When I fell asleep, I felt like my mind was going through flash cards of words and pictures," he says. "Dr. Hadjipanayis said my brain was reconnecting the left and right sides."

Concerned about possible side effects, Gelb declined treatment with temozolomide. Because his tumor was not a full-blown glioblastoma, he was able to exercise some discretion; studies show temozolomide does not give patients with less aggressive tumors a clear survival boost. "I was back at work and leading a team within 60 days," he says.

Three years later, the tumor came back, and Gelb participated in the Gliolan study. Where Gliolan helped, Hadjipanayis says, was in differentiating tumor from brain tissue that had been irradiated and treated with chemotherapy. During part of Gelb's second surgery, he was awake, and Hadjipanayis asked him to identify pictures of animals on a laptop to test whether the surgery was interfering with the regions of the brain controlling language.

After this surgery, Gelb opted for temozolomide, and he's also taking an anticonvulsant medication to avert seizures.

Treatment strategies for some other types of cancer have been transformed by the discovery of "targeted therapies," directed specifically against the genetic mutations

that drive tumor growth. But so far these strategies have been relatively unsuccessful with glioblastoma, Olson says.

For example, about 40% of glioblastoma tumors have extra copies of the EGFR (epidermal growth factor receptor) gene, which provides a pedal-to-the-metal growth signal and is known to play a role in driving the growth of lung and colon cancers as well. But drugs targeted against EGFR that have extended patient survival in lung cancer have shown disappointing results with glioblastoma. "It comes from the germ-like nature of glioblastoma," Olson says. "It changes so quickly, like antibiotic-resistant bacteria. It isn't that the drug doesn't work or the science was bad, it's that the tumor becomes resistant."

Similarly, clinical trials have shown no overall survival benefit for the drug bevacizumab (Avastin), which targets blood vessel growth, in newly diagnosed glioblastoma. While it has been shown to lengthen survival in other types of cancers, the efficacy of bevacizumab in glioblastoma remains a topic of debate among oncologists.

Olson and the Winship brain tumor team have begun a clinical trial that combines the drugs bevacizumab, bortezomib, and temozolomide, with the rationale that glioblastoma cells will find resisting three drugs at once more difficult.

And Hadjipanayis and his colleagues in the lab have been exploring the use of tiny iron oxide particles covered with an

antibody that preferentially sticks to brain tumor cells. Injected before surgery, the particles would provide a prominent signal on MRI scans and could even be used to heat the tumor with magnetic fields, thus proving useful for both imaging and treating the tumor.

Using genomics

Because of its lethality, glioblastoma was the first brain tumor to be analyzed by the Cancer Genome Atlas, an NCI-supported megaproject. Scientists cataloged genetic aberrations in 91 glioblastomas and then divided the cancer into four molecular subtypes. (Winship was one of the largest contributors of patient samples to the study.) Each subtype responds differently to aggressive treatment. “We are firmly in the era of brain tumor diagnosis that incorporates molecular genetic findings, sometimes at the level of the whole genome, for each patient sample,” says Dan Brat, professor of pathology and laboratory medicine and director of Winship’s cancer tissue facility. Already, glioblastoma tumors are routinely probed for whether the MGMT (methylguanine DNA methyltransferase) gene is active or silenced. Multicenter studies have shown that if a tumor’s MGMT gene is active, the tumor is more resistant to temozolomide because it repairs DNA damage more quickly. But if it is silenced, the patient has a better chance of responding well to temozolomide.

The sooner a doctor can get feedback on how a tumor is responding to chemotherapy and radiation treatment, the better. But this is trickier to determine than it might seem. Research by radiologist Hyunsuk Shim, a Georgia Research Alliance Distinguished Scholar, focuses on a perplexing problem in neuro-oncology: a CT or MRI scan does not always accurately depict what is happening. “I have a patient who seems to be doing great, but the MRIs come back every time and indicate that she has a possible progression,” says Winship oncologist

Will Read. Radiation treatment can cause inflammation that looks like tumor progression in scans. Also, oncologists suspect that treatments that target blood vessels, such as bevacizumab, can make the tumor appear smaller on brain scans, without much actual

have his tumor evaluated in this way, was attracted to Shim’s imaging study because he wanted to take an aggressive stance. “I felt like I knew how the standard game played out, and I didn’t want to go out without kicking,” he said.

The first sign of Sowles’ tumor was numbness in his fingers, which he thought might be carpal tunnel syndrome. At the time, he was studying business at Georgia State while working as CFO of a business equipment firm. A couple of months later, Sowles began to have trouble spelling and doing calculations. He started to have focal seizures, in which the feeling of numbness would rush up his arm to his face. A probable tumor was located in his left parietal lobe, close to the brain region that controls the sense of touch.

After his diagnosis was confirmed, Sowles traveled to Duke for surgery. He returned to Atlanta for radiation and chemotherapy, and met with Read, who told

Sowles about Shim’s study. “They never treated me like I was a terminal patient,” he said. “That was really important to me psychologically.” His response to vorinostat appeared strong, and after continuing treatment with temozolomide, Sowles returned to work, although not with the same punishing schedule as before. He was aware that every month was precious. In May 2013, he was able to greet his son’s baby, Lucas. “I set a goal to be there for him,” he said. “I became a grandfather because of the treatment I received.” Sowles’ tumor returned several months later, and he died at the end of December.

Some glioblastoma patients live much longer than the average 15 months, although they are rare. Winship neuro-oncologist Alfredo Voloschin has a patient who was diagnosed at 35 and has survived more than ten years. “I don’t pat myself on the back for keeping someone alive for a decade,” Voloschin says. “There is no cookbook approach. Every patient

Detecting mutations without biopsy

Winship researchers led by Erwin Van Meir and Hui Mao have developed a technique to use imaging to detect an “oncometabolite,” a chemical produced by some brain tumors’ warped metabolism that provides insight into a tumor’s particular genetic mutation.

“This is a significant advance, in that we can have a glimpse into the human brain without actually having to do brain surgery,” Van Meir says. “The technique offers the possibility of following the patient after surgery to see if the treatment is working by monitoring the decline in levels of the oncometabolite.”

effect on the growth of the tumor itself.

Shim has been examining the effect of temozolomide combined with an experimental drug, vorinostat. In tumor cells, genes that normally prevent runaway growth have been silenced. Vorinostat is thought to help reverse this silencing as well as making tumor cells more sensitive to the DNA damage provoked by temozolomide.

She is testing whether magnetic resonance spectroscopy (MRS) can detect changes in cancer metabolism, which may indicate how fast the tumor is growing, shrinking, or dying. Her study, funded by a \$4 million grant from the National Cancer Institute (NCI), uses MRS in an effort to detect whether vorinostat is having its desired effect after just two weeks. “Our hope is that this technique could be used to assess responses to other drugs besides vorinostat,” Shim says. “It is better to figure out as early as possible which patients any given drug is working for.”

Allen Sowles, one of the first patients to



Talking **the talk**

By KAY TORRANCE

THE *take-away*

Through role playing and expert coaching, new doctors are becoming more skilled in having difficult conversations with patients' families.

Be clear and straightforward, but preserve hope.

Palliative Care Center Director Tammie Quest, an emergency medicine physician, is coaching a group of fourth-year medical students on how to have difficult conversations with patients' families about their medical condition.

It's all part of prepping these soon-to-be physicians in the art and science of palliative care, a burgeoning subspecialty that focuses on providing patients relief from symptoms of serious or life-threatening illness.

As residents, most of them will be called on to lead such meetings, which are difficult even for seasoned physicians, Quest concedes. Many doctors now call Emory's palliative care physicians to handle the uncomfortable task. "That's why we have 6,000 palliative care consults each year," she says. "We're often called to pick the family up off the floor after a diagnosis has been made. Family meetings will come to you over and over in your career."

Quest has spent her career perfecting the language she uses to converse with families, and teaching others how to do the same. She became interested in palliative care after graduating from medical school at UC-San Francisco and realizing that no one had versed her in how to tell someone that their family member had died.

"In medicine today, we've moved away from the idea that good communication skills are inherent—that because you are a kind, sensitive person you must be a good communicator," she says. "Now there is a fundamental belief in medicine that communication skills are not inherent, they are taught."

Quest started the first palliative care service at Grady Hospital in 2005 and is director of the Emory Center for Palliative Care, formed in 2010 to integrate palliative care across Emory Healthcare and its affiliates, and to foster research in the field. The center now

has palliative care programs in five Emory or Emory-associated hospitals and has received \$4.2 million in research funding.

Numerous studies have pointed to better outcomes for patients under palliative care—they often undergo fewer aggressive and expensive treatments, yet have longer survival times. In one three-year study at Massachusetts General Hospital, advanced lung cancer patients were randomly assigned to either standard oncology care or standard oncology care and palliative care. The palliative care patients had fewer symptoms of depression and a 2.5-month longer median survival rate.

Palliative and hospice (end-of-life) care are slowly making inroads as medical centers look to reduce costs in the wake of health care reform. Today 33% of hospitals have a palliative care program. The bigger the hospital, the more likely it is to offer palliative care—80% of hospitals with more than 300 beds have such programs. The field began forming in hospitals about 20 years ago and became an official subspecialty of medicine in 2008. Still, confusion persists. “Not all physicians separate palliative care from hospice care, but when they understand our role they will work with us,” says Emory palliative care physician Alyssa Majesko. “We are a consistent face in an often overwhelming system.”

Palliative medicine is integrating into the fabric of medicine, Quest says. Nursing, social work, and chaplaincy have already embraced palliative care concepts, and even emergency departments are using palliative care services. Emory, for example, began screening all cancer patients who come into the ED for palliative care needs in 2009.

“During the past century of therapeutic advances and training paradigms that codified a never-give-up ethos, we lost some of the compassion of medicine,” says School of Medicine Dean Christian Larsen, also a transplant surgeon. “Tammie and the palliative care team’s efforts are helping us reclaim this vital aspect of patient-centered care.”

Back in patient exam training rooms on the third floor at the School of Medicine, fourth-year students are practicing talking

STEPS TO A SUCCESSFUL FAMILY MEETING

- 1 Lead physician should set the stage—introduce all in attendance, establish medical goals and the family’s goals, set amount of time for discussion.
- 2 Physician should first clarify with relatives what they currently understand about the patient’s medical condition.
- 3 The family should then be given clear information about the patient’s illness, treatments, and prognosis.
- 4 Everyone at the meeting should have a turn to ask questions or address concerns.
- 5 Relatives may be asked to make care decisions based on the goals of the patient and family. Any recommendations made by the care team should be fully understood.
- 6 The meeting should end with both the care team and the family understanding the next steps in the patient’s care.

PALLIATIVE CARE / HOSPICE CARE: What’s the difference?

PALLIATIVE CARE focuses on providing patients who have serious illness with relief from symptoms, pain, and stress, and is appropriate for patients in all disease stages, including those undergoing treatment for curable illnesses and those living with chronic diseases.

HOSPICE CARE is a philosophy regarding end-of-life care, though it is often confused with a place. Hospice services can be provided in the patient’s home or at a hospice center, nursing home, or hospital and is designed to keep the patient comfortable and improve quality of life while the patient is dying. It does not speed up or prolong the dying process.



Tammie Quest, above, was named the first Roxann Arnold Professor of Palliative Care Medicine this spring.

to actors who are playing the role of a patient’s family member. One group is holding a “family meeting” with the wife and son of a 60-year-old man who suffered cardiac arrest and whose condition is declining. “Sometimes we can hedge and be more

optimistic when we don’t know the answer to a family’s question. First-year residents often hedge. Don’t hedge,” Quest counsels.

Being clear and straightforward, however, doesn’t mean being insensitive or destroying hope. “We are teaching empathic communication,” she says, “not blunt or overly direct communication.”

Another group must ask the family if they want to institute a do-not-resuscitate order. One student starts to say, “What do you want us to do if...” and then backtracks, having already been advised by Quest to avoid that phrase, as it has no context.

Doctors, Quest says, are there to make an assessment and recommendations.

“As physicians, we have a hard time living in the gray, where things are not settled,” Quest says. “Three-fourths of palliative care is about the phrases you use. The hardest part is getting the language correct.” ■

BRAVE HEARTS

Your heart weighs about 10 ounces and is the epicenter of your body. A muscle shaped like a pear and protected by a cage of ribs, it pumps more than a gallon of blood through your circulatory system every minute. Electric signals make your heart contract and relax, contract and relax, 60 to 100 times a minute. Its beat responds to your level of exertion and your emotions—faster with fear, slower with contentment. An average lifetime measured in heartbeats: 2.5 billion. The people you are about to meet—ranging in age from 3 to 79—are well aware of the importance of this muscle.

Through illness or genetics, their hearts gave out,
and through a generosity beyond imagin-
ing, they were given another chance.

As you will see, they are making
every beat count.

“Two months after Owen was born,
he had to have a heart transplant.
The whole day was a blur, and
I was a mess. But he did great.”

Maranda and Owen Burr, 3, transplant 2011





“There are a lot of emotions right before surgery. It’s like being reborn, but you also realize that somebody else had to die.”

—son, Michael Haynes, 45, transplant 2011

“I was so sick before the transplant that afterward I couldn’t sleep because I could actually feel my new heart beating, it was that strong.”

—mother, Alice Haynes, 67, transplant 2012

“I was three weeks old, so I don’t really remember. I don’t even pretend to understand how it works when they plug everything back in, I’m just glad it does.”

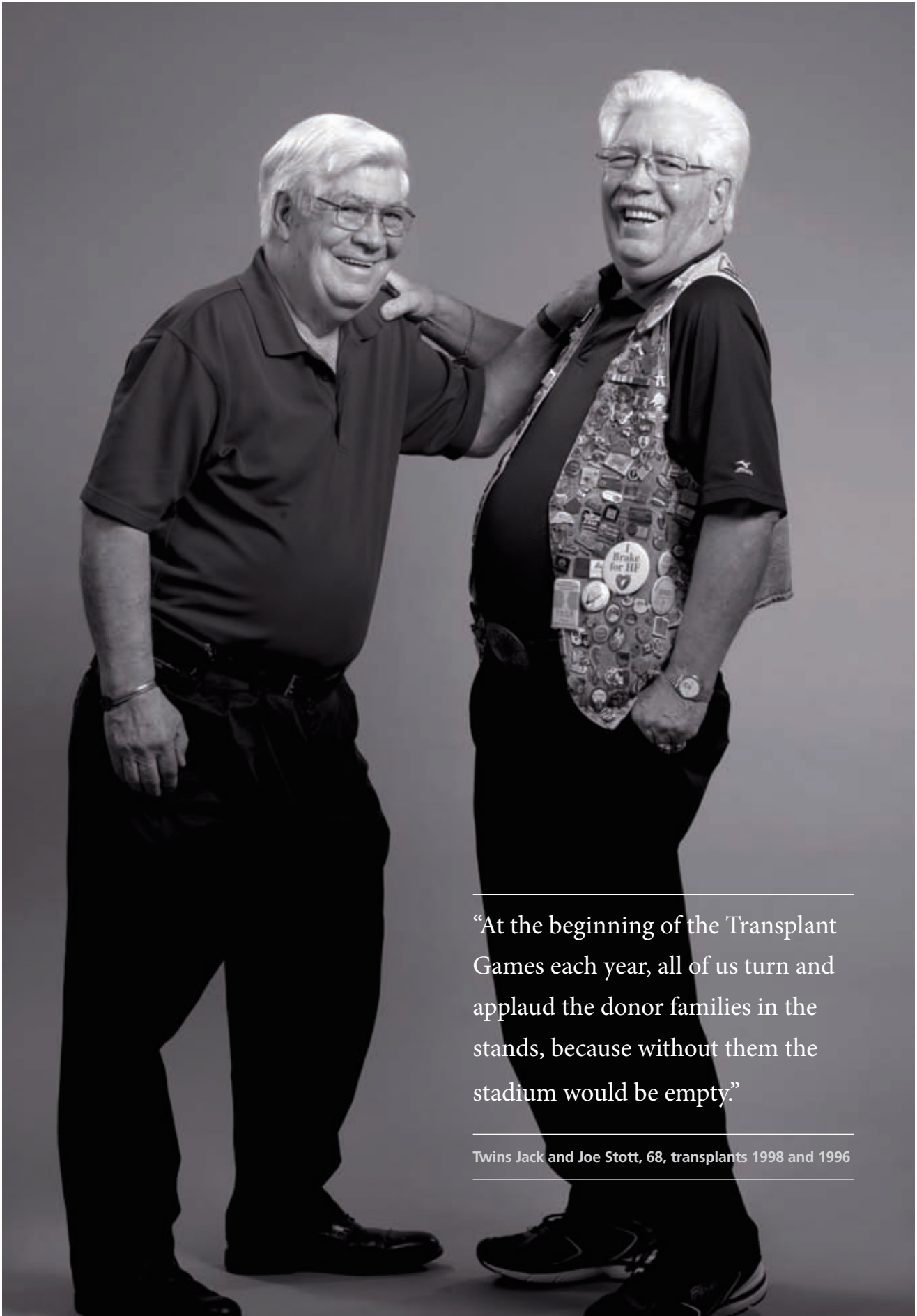
David Williams, 19, musician,
transplant 1994



“My 16-year-old donor’s mother and I speak to groups of students, it’s an incredible relationship we have. She calls me kiddo, and gets mad if I don’t eat my vegetables. By being a donor, Clayton helped 43 people including me.”

Beverly Williamson, 79, ballet teacher, transplant 1996





“At the beginning of the Transplant Games each year, all of us turn and applaud the donor families in the stands, because without them the stadium would be empty.”

Twins Jack and Joe Stott, 68, transplants 1998 and 1996



“Even though it is a simple thing, the most significant difference now is I am able to carry our daughter up the stairs when she falls asleep to put her to bed.”

Ketan Thanki, 45, transplant 2010



“My students all have theories about how the transplant happened, like the one who asked if the doctors took my heart out through my throat.”

Nicole Tyler, 40, special education teacher, transplant 2012



“Just before his second birthday, he got his transplant. On his first day of school, I thought I’d cry my eyes out, but then I realized, you know, I prayed for this. And now, he’s getting married.”

Nick May, 24, transplant 1991

 [want more?](#)



BRAVE HEARTS Find out more about Emory heart transplant patients at bit.ly/emorygiftoflife2014

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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** **BATTLING BRAIN TUMORS**

Glioblastoma is the most aggressive and common form of brain tumor, but physicians and researchers at the Brain Tumor Center at Winship Cancer Institute are working to change that. You can support their efforts to develop new drugs and drug combinations, pioneer new imaging techniques, and decode each tumor's genome to customize therapy.

To join the fight against brain tumors, contact Jennifer Daly, director of development, at 404.778.4270 or jdaly@emory.edu.



PAGE **22** **LISTEN TO MY HEARTBEAT**

Emory physicians performed Georgia's first heart transplant in 1985. Since then, the team has given second chances to more than 700 people, such as Ketan Thanki (below, with daughter Ariha.) Leading the way in transplant immunology research, Emory physicians are creating and perfecting therapies that improve outcomes, including strategies to keep the body from rejecting transplanted organs.

You can invest in heart transplantation research and advanced training opportunities. To learn more, contact Alicia Kanjira, director of development, at 404.727.3989 or alicia.kanjira@emory.edu.



PAGE **4** **HEALTHY CHILDREN**

Amanda Weinberg and Michael Chanin know their chances of having a healthy child, thanks to JScreen. Based at Emory Medicine, JScreen provides genetic screening and counseling for 80 devastating hereditary diseases that could be passed to children. JScreen gives couples the tools they need to plan for healthy children. You can help safeguard the next generation.

To support JScreen, contact Gabrielle Stearns, director of development, at 404.727.2512 or gabrielle.stearns@emory.edu.



PAGE **5** **TEAM TRANSPLANT**

Ten years ago, Emory patients Rob Allen and Laura Cochran entered a clinical trial for type 1 diabetes. The outcome has been exceptional: Both have been diabetes free since. Credit goes to islet cell transplantation through a clinical trial at the Emory Transplant Center. Type 1 diabetes occurs when the body's immune system attacks islets, clusters of cells in the pancreas. Islets make insulin, which is required to absorb and use glucose. When the islets die, diabetes patients must take insulin multiple times a day to live. An islet transplant renews the body's ability to regulate its own glucose levels.

For more information or to support the Emory Transplant Center, contact Stacia Brown at 404.727.9030 or stacia.brown@emory.edu.

GIFTS OF NOTE



From left: Allan Levey, Alzheimer's Disease Research Center director; Jamie Kennedy; Barbara Kennedy Harty, "A Family Affair" chairs Sarah and Jim Kennedy; and event honoree David Weinschenker of the Department of Human Genetics.

When **Sarah Kennedy's** father was affected by Alzheimer's disease, she decided to take action. She and **Jim Kennedy**, her husband, became passionate supporters of the Emory Alzheimer's Disease Research Center (ADRC). Chairing "A Family Affair," they helped raise more than \$800,000 to support research at the center. The dinner brought in the most money ever raised by an Emory event. The Kennedys also are supporting a clinical trial of a new drug therapy for patients with mild cognitive impairment, which often precedes Alzheimer's.

The **James B. Pendleton Trust** made a \$250,000 gift to physician Paul Spearman to support pediatric HIV research. The funds are being used to purchase imaging technology, which will enable pioneering research on virus assembly and replication. Seeing how the virus works at the molecular level is key to creating a vaccine.



Dana and Tom Curtis of Decatur (left, with daughters Haley Curtis Stevens and Hannah Marie Curtis), have made a generous donation for Parkinson's disease research. The gift will be used to

fund a three-year study of freezing of gait, a phenomenon that affects a majority of Parkinson's patients. People with the condition describe it as feeling as if their feet are glued to the floor. Tom Curtis, who has Parkinson's disease, is a patient of Stewart Factor, Vance Lanier Chair of Neurology and director of Emory's Parkinson's Disease and Movement Disorders Program.



Georgia has one of the highest death rates for newborns. **Bernard Taylor** is helping to change that. He gave \$25,000 to the Global Collaborating Center in Reproductive Health, which works with community health providers in Georgia to improve maternal health and reduce fetal and newborn deaths. Directed by Emory pediatrician Alfred Brann, the center develops low-cost but effective inter-

ventions. Supporting this work makes a profound difference in the lives of mothers and babies.

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

Much to celebrate



WRIGHT CAUGHMAN

Executive Vice President for Health Affairs

Each year, I have the wonderful opportunity to get together with the faculty, staff, and students of Emory's Woodruff Health Sciences Center (WHSC) to discuss the "State of the WHSC." Together we reflect on the triumphs of the past year and focus our collective energy and will on the opportunities and challenges of the year ahead. In the past year, in spite of unprecedented external

challenges, the people of the Woodruff Health Sciences Center achieved more than ever before in our history.

Our schools of medicine, nursing, and public health continue to educate and train students who are not only among the world's brightest, but who also have a deep commitment to leading positive transformation in the world and having a meaningful impact on the lives of others. Our research funding remains consistently impressive in spite of a challenging funding environment, reflecting the strength of our investigators and the lifesaving breakthroughs they work so hard to pioneer. And our extraordinary health care team earned the nation's top honors for quality and safety this past year—Magnet designation and recognition by the University HealthSystem Consortium as the No. 2 and No. 3 hospitals in the nation—without ever losing focus on the care and compassion that our patients and their families deserve.

As you've seen from the stories in this issue of *Emory Medicine*, from advances in brain tumor treatment and understanding the biology of fear to life-affirming palliative care and cutting-edge heart transplants, the Woodruff Health Sciences Center and all the people it serves have much to celebrate. Thanks as always to our faculty, staff, students, alumni, and friends for the outstanding year past and for all the outstanding years to come.

Knowing your risk can save your life

By GINA LUNDBERG



During my early years in private practice, I found that women were requesting a female cardiologist, and I was getting many new referrals.

I began to see inadequacies in the way women were treated for chest pain. I would get furious when a female patient would tell me how her doctor had dismissed her symptoms and told her she was just stressed. I heard story after story of women getting a pat on the head and being given an antidepressant or benzodiazepine for chest pain. I continued to see women get diagnosed late in their cardiac disease because their doctor did not request testing for heart disease.

THE *take-away*

Despite heart disease being the No. 1 killer of women in the US, little attention has been paid. **Doctors, and women themselves, need to focus on prevention and early intervention.**

Cardiovascular disease (CVD) is the single largest killer of women in the United States—one woman dies of cardiovascular disease every minute. While one in 30 women will die of breast cancer, one in three women will die of cardiovascular disease. CVD deaths in women surpass deaths from all forms of cancer, lung disease, and Alzheimer's disease combined.

African-American women are 40% more likely to die of CVD compared with white women. Yet, awareness of CVD as the No. 1 killer of women is lacking in African American and Hispanic women.

Two-thirds of women who die of heart disease have had no prior symptoms, compared with half of men having no prior symptoms. And more women than men will have a second heart attack after their first heart attack.

While deaths from heart disease in men were declining in the US between 1979 and 2003, deaths from heart disease in women remained unchanged. Only recently have we seen

declines in heart disease deaths in women.

I decided to specialize in women and heart disease, with a focus on prevention, founding the first women's heart center in the state in 1998 and the first hospital-based program in 2001.

In the years since then, I have seen a 24-year-old woman who suffered an acute anterior myocardial infarction that unfortunately was misdiagnosed in the ED as gastroenteritis because she presented with nausea, vomiting, epigastric pain, and diaphoresis. Because of her age, no one ordered an EKG or cardiac enzymes. But her past medical history showed that she was a smoker on birth control pills who had low HDL cholesterol, central obesity, and elevated triglyceride levels—all known risk factors for cardiovascular disease. Sadly, her infarction progressed before I was consulted, and she now has a low ejection fraction (a measure of heart failure) and a defibrillator.

I have seen a 45-year-old woman who complained for 10 years of epigastric pain,

fatigue, and shortness of breath on exertion. She finally came to me for consultation, and her EKG revealed left bundle branch block, meaning her left ventricle was contracting later than her right ventricle. Her echocardiogram confirmed dilated cardiomyopathy with an ejection fraction of 25%, when over 55% is normal. She is doing much better now with proper medical therapy and a biventricular pacemaker with resynchronization therapy.

And I've seen a 75-year-old woman with chronic angina who suffered from Parkinson's disease. Medical therapy for her angina had failed, and no one would attempt heart catheterization because she could not lie flat or stop shaking with tremor. But one of my interventional colleagues gave in to my pleading and took her to the cath lab. With sedation, she had a reduction in her tremor, and he opened her nearly totally blocked right coronary artery. She lived pain free another 10 years. She and her family were extremely grateful that we had been very driven to improve the quality and quantity of her life.

Of the more than 600 women screened at the Emory Saint Joseph's Heart Center for Women, about 40% were recommended to a cardiologist for further evaluation. Twenty percent of the screened women established care with a primary-care physician, 43% needed further evaluation for a sleep disorder, and up to 10% were recommended to follow up with a psychologist or psychiatrist for significant signs of depression. Nearly 10% were sent for further evaluation of peripheral artery disease. Using the 2011 ACC Guidelines on Prevention of Heart Disease in Women, 12% of the women screened were high risk, 43% were at risk, 43% were low risk, and less than 2% were found to be ideal risk (no risk factors.)

The Emory Women's Heart Center (EWHC) was developed in 2013, and now has six locations: Emory University Hospital, Emory East Cobb, Emory Johns Creek, Emory Midtown, Emory Decatur, and Emory Hillandale. Susmita Parashar, Ijeoma Isiadinso, Alexis Cutchins, and Farheen Shirazi are the EWHC site physicians,

One in three women will die of cardiovascular disease.

Two-thirds of these women will have had no prior symptoms.

Diet, exercise, screenings, and education can reduce your risk.

Ideal is defined as no risk factors. This means systolic blood pressure of less than 120/80, blood glucose less than 100, HDL greater than 50, LDL less than 100, triglycerides less than 150, BMI less than 25 and waist size less than 35 inches.

(AHA/ACC prevention of heart disease in women guidelines.)



Gina Price Lundberg is founder and director of the Heart Center for Women at Emory Saint Joseph's Hospital. She serves on the American College of Cardiology Foundation Prevention of Cardiovascular Disease Committee and is an American Heart Association national spokesperson.

and four nurse practitioners provide screenings, CVD evaluation, and education of our patients.

The goals of the center are to screen and educate women on their individual risk. We also strive to educate the regional medical community about the latest information and treatment of heart disease in women. August 16, 2014, will be the eighth annual Women and Heart Disease Conference at Twelve Atlantic Station. In addition to promoting awareness and education, we encourage participation in clinical research so we will have the best evidence for treatment of heart disease in women. Women need to understand the symptoms and risk factors that can be unique to them.

The EWHC team is continuing the rich history of Emory's dedication to heart disease in women. Cardiologists Nanette Wenger, professor emeritus of medicine at Emory who received the Lifetime Achievement Award from the American College of Cardiology, and Leslee Shaw, professor of cardiology and co-director of Emory's Clinical Cardiovascular Research Institute, are pioneers and leaders in the field of heart disease in women. Both have been essential advisers to the center, and Shaw is its research director.

Most heart disease is preventable, so we want to reach women before 60 years of age, evaluate their individual risks, and educate them on risk reduction. We counsel patients on weight loss, exercise programs, diet, and other lifestyle changes, as well as help them understand how stress, obesity, depression, and menopause may impact their hearts.

I also recommend fish oil supplements to most of my patients after 50, not just for the triglyceride-lowering and cardiovascular benefits, but for the powerful antioxidant and brain-power benefits as well.

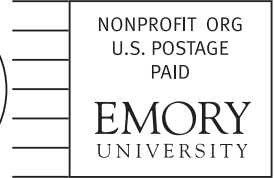
We are busy—busy at work, at home, taking care of kids and aging parents, keeping up with friends, and a million other commitments. Days and weeks fly by, without much thought to our own well-being. But your heart deserves a bit of your attention. Don't wait until it demands it. ■



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Have a plan.

They grew up in the same Decatur neighborhood, but Barbara Alford Reed 57N 79N and Bob Reed 57C didn't connect until they were at Emory. Their lives have been entwined with Emory ever since. They wed after their sophomore years and she worked for decades as a clinical faculty member at the Nell Hodgson Woodruff School of Nursing. She also was a nurse at Emory University Hospital, where both of their sons were born. Longtime Emory supporters, they have made a bequest to create an endowed scholarship in nursing. "Emory gave me what I had always wanted, and that was to make a difference through nursing," she says. He adds, "And Emory gave me Barbara."

Learn how you can include Emory in your estate plans. Visit www.emory.edu/giftplanning or call 404.727.8875.

Plan to champion what you love.



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