BROWN MEDICINE

Volume 22 | Number 3 | Fall 2016

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The Elephant in the Room

What can these beloved animals teach us about cancer?

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LETTER FROM THE DEAN

Building on Distinction

In this issue of *Brown Medicine*, you'll read about three significant research grants that the Division of Biology and Medicine recently received from the National Institutes of Health. These grants are tremendously exciting. They will help build infrastructure and will foster the scientific progress that is needed to allow us to fulfill our strategic plan.

Even with this impressive NIH support, our plan can't come fully into fruition without the philanthropic support of our alumni, parents, faculty, and friends. *BrownTogether: The Campaign for Building on Distinction* has been launched, and we're excited to have received a number of gifts to support our plans to expand translational sciences and educational opportunities at the University. Brown Biomedical Innovations Inc. is also off to an exciting start, with $3 million in pledges toward commercializing research discoveries made at Brown. We are distributing our first round of funding to the most promising projects this fall.

BrownTogether is a comprehensive effort, which means all gifts made to Alpert Medical School—whether they are for the Brown Medical Annual Fund, a research fund, an endowed chair, or an endowed scholarship fund—count toward the Campaign. Our initiatives are the core of three of the Campaign's integrative themes:

- Deciphering Disease and Improving Population Health;
- Using Science and Technology to Improve Lives; and
- Understanding the Human Brain.

Last month, we paused to commemorate the fifth anniversary of the Alpert Medical School building, a tremendous advance in our ability to educate and a lasting symbol of the generosity of the Brown medical community. We also celebrated the increased number of medical students we have been able to educate, the new academic programs we have launched (including the MD/MPA joint degree you'll read about in this issue), and the faculty and staff who have joined our ranks. We are inspired as we look ahead to a future enriched by the initiatives we are advancing—such as the Brown Center for Biomedical Informatics—that provide new research opportunities for our students, and support efforts to translate our science into treatments and cures for patients.

I would say these are exciting times, but that doesn't quite capture the excitement and energy that we have here. I hope you'll join us on campus, or at upcoming events around the country, to learn more about what's happening at Alpert Medical School and the great things we can do together.

All the best to you.

Jack A Elias MD

Jack A. Elias, MD
Dean of Medicine and Biological Sciences

DAVID DELPOIO

"We need to think about this as a public health concern, rather than a moral failure."

—Heather Howard, ***page 34***

NICK DENTAMARO; DAVID DELPOIO; KAREN PHILIPPI

FEATURES

DEPARTMENTS

COVER

Christian Noni

National Geographic Creative

LETTER FROM THE EDITOR

Never Too Late

Living across the state line in Massachusetts, my work life in Providence rarely intersects with my home life. But this issue's feature story on what happens to infants born addicted to opioids led us to my hometown of New Bedford.

When the opioid epidemic started grabbing national headlines a few years ago, I had to scoff. We had been dealing with our own heroin epidemic in New Bedford since the 1980s. I saw classmates and even a member of my family trapped in the cycle of addiction that ultimately resulted in death. With the media and politicians finally paying attention to what is now a "crisis," people from inner city neighborhoods and lower socioeconomic groups have expressed some bitterness: no one cared until "good" kids from "good" families started dying. No one cared when it was happening to us.

But I don't waste time on recrimination. In the here and now, new health policies and laws are in place, both in Rhode Island and Massachusetts. The opioid task force convened by Rhode Island Governor Gina Raimondo, on which many Brown faculty members serve, created a new comprehensive website for monitoring and finding help for people who are addicted. And there are new programs and research, which you'll read about in this issue, to help vulnerable infants swept up in their mothers' addiction.

For its part, Alpert Medical School is educating medical students about proper prescribing practices and caring for patients who are addicted to opioids. In early October, a student-led symposium to discuss health disparities in the opioid crisis was held in conjunction with the School of Public Health. Earlier this year, we signed on to the Association of American Medical Colleges' pledge to provide instruction and training in opioid use and dependence, to promote research to direct how to respond within the context of policy and medicine, and to advance clinical innovations to combat opioid dependence. And last spring, the annual interprofessional workshop that brings together nursing, social work, and pharmacy students with our medical students to facilitate a team approach to care focused on addiction cases. The lesson was clear: addiction is a multifaceted issue, and it's going to take caregivers of all types to help these patients.

In the end, that's all that really matters.

Kris Cambra

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INBOX

LASTING TRIBUTE

Thank you so much for publishing a short obituary of my partner, Professor Richard A. Ellis, in your journal (Winter 2016).

He cared deeply about Brown University and bequeathed a significant part of his estate to his Brown scholarship. I was very happy to see his colleagues at the celebration of his life on August 14, 2016, and I also received notes and telephone calls from his students.

Thank you and my best wishes to all of you.

PhDr. Pavel Farkas
Prague, Czech Republic

YOU'RE INVITED

- **Healthcare in America Lecture Series**

  Health professionals from across the US speak on a wide array of topics, from health policy to technology to career opportunities. All are held at Alpert Medical School.

- **Paul Levinger Lectureship on the Economics of Health Care**

  Peter B. Bach, MD, director, Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center, will discuss the costs and benefits of personalized cancer drugs at Alpert Medical School on October 24 at 4 p.m.

Get more info and RSVP *at biomed.brown.edu/Events.*

READ. RESPOND.

Please send letters, which may be edited for length and clarity, to:

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Web Exclusives

Read these stories and more at brownmedicinemagazine.org.

- **What Would MD'16 Do?:** Alpert Medical School's newest grads share words of wisdom for the incoming class.
- **Study Describes New Brain Disorder:** Researchers identify mutations that cause a rare, unnamed neurological disease.
- **Who Ya Gonna Call?:** Med students are training undergrads to respond to emergencies on campus.
- **Scholarship and Service:** Two PLMEs join the MD Class of 2020—and the Army.

THE BEAT

WHAT'S NEW IN THE CLASSROOMS, ON THE WARDS, AND IN THE LABS

WHO KNEW?

SCHOLAR ATHLETE
Competing in the Olympics was "a once-in-a-lifetime opportunity," Pou says.

NICK DENTAMARO

From Brown to Brazil

A PLME student swims in the Olympics.

By the time Sovijja Pou '17 MD'21 was accepted into the Program in Liberal Medical Education (PLME), he had made the difficult decision to end the competitive swimming career he had pursued since age 5. With the daunting prospect of juggling athletics and academics in college, the dual citizen of Cambodia and the US planned instead to focus his energy in the classroom.

But after finishing his final high school swimming season strong and representing Cambodia at the 2013 FINA World Championships in Spain, he knew he wasn't quite ready to throw in the towel. "I loved practicing and I loved competing," Pou says.

That decision proved wise. Not only has Pou consistently been one of Brown's top swimmers, he was one of just two swimmers representing Cambodia in the 2016 Summer Olympics in Rio de Janeiro. He competed in the 100-meter freestyle competition August 9.

"It was such an unforgettable and indescribable experience to be able to represent Cambodia internationally," Pou

says. "I went into the Olympics without knowing what to expect and came back with a wealth of knowledge and inspiration."

Brown swimming coach Chris Ip says Pou epitomizes the amateur athlete ideal, balancing sports with his other responsibilities and interests. During the academic year, Pou spends 20 hours a week in the pool, yet maintains a stellar grade point average as a biology and applied math concentrator. While many athletes might focus solely on preparing for the Olympics, Pou trained this summer while also pursuing a full-time summer research project with Daniel Weinreich, PhD, associate professor of ecology and evolutionary biology, on the evolution of drug-resistant malaria.

"Sovijja is … not sacrificing any of his other goals," Ip says. "It's a pleasure to work with someone who has that balance—he wants to excel [in swimming] but not to the point where it's overtaking his whole life."

Pou, whose father is Cambodian and whose mother is Thai, says his passion for both swimming and academics are fueled by his Cambodian heritage. During the Khmer Rouge genocide, his father sought refuge in the US, ultimately landing in Portland, OR, where Pou grew up.

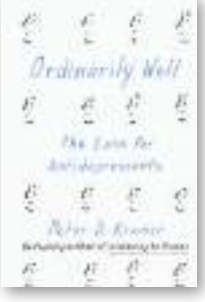
> Pou trained for Rio while pursuing a full-time summer research project on the evolution of drug-resistant malaria.

After medical school, Pou plans to practice in Cambodia, concentrating his efforts on fighting tropical diseases like malaria, which has impacted many of his family members who live in rural areas. Already, Pou has given back to the country. He travels there frequently, teaching English at his grandfather's monastery, advocating for the importance of oral hygiene and safe sex, and giving public swimming lessons to children in Phnom Penh.

—O'rya Hyde-Keller

BOOKSHELF

Ordinarily Well: The Case for Antidepressants



COURTESY FARRAR, STRAUS AND GIROUX

By Peter D. Kramer, MD
Farrar, Straus and Giroux, 2016, $27

"Denying the efficacy of antidepressants may begin well enough, with a love of psychotherapy and a respect for human complexity. But in time, the position becomes stigmatizing, too much in accord with the notion that depression is something other, something less than what research and practice find it to be: a progressive, destructive multisystem disorder fully worthy of medical attention."
—from **Ordinarily Well**

Kramer, a clinical professor emeritus of psychiatry and human behavior at Alpert Medical School, first waded into the psychopharmacology debate in 1993 with his book *Listening to Prozac*. Now, armed with two more decades of clinical experience, as well as scientific data and analysis, he takes on the latest charge, that antidepressants are no better than placebos.

Ordinarily Well offers a mostly chronological account of the history of the drugs and their development, interspersed with moving anecdotes of his patients and his own, evolving practice. Kramer acknowledges the "mixed blessing" of antidepressants' success—discussing cons like overprescribing and industry influence on medical practice and academic research—and explains the shortcomings of conventional drug trials, which he says don't reflect real-world patient encounters. Clinical experience, personal judgment, and "common sense," he argues, have a place in psychiatric treatment, alongside the statistics. "Could a doctor rely on randomized trials only and treat real people?" he asks. "What would that practice look like?" For Kramer, to rely on evidence-based medicine alone is to reduce his patients to mere data points, and to distrust his own eyes and ears. "[C]onsider what patients say," he writes: "On medication, they have come back to life." ***—Phoebe Hall***

Spread the word: *If you'd like your book featured in* Brown Medicine, *have your publisher send us a copy at Box G-R220, Providence, RI 02912.*

Facts + Figures

The MD Class of 2020, by the numbers.

Applicants: 10,675

8,916 applicants considered*

743
APPLICATIONS TO PRIMARY CARE-POPULATION MEDICINE COMBINED MD/SCM PROGRAM

24
ADMITTED

Total Matriculants: 144

* BASED ON *US NEWS* CATEGORIES: DIFFERENCE IS NUMBER OF COMPLETED SECONDARY APPLICATIONS RECEIVED IN AMCAS ROUTE.

72 MEN **72** WOMEN

24 AVERAGE AGE (RANGE 20-34)

REPRESENTING

29 US STATES AND WASHINGTON, DC

11 COUNTRIES (BIRTH OR CITIZENSHIP)

63 COLLEGES AND UNIVERSITIES

ROUTES OF ADMISSION

- AMCAS (STANDARD ROUTE OF ADMISSION) 90
- PROGRAM IN LIBERAL MEDICAL EDUCATION 45
- POSTBACCALAUREATE 7
- EARLY IDENTIFICATION PROGRAM 2

Wave the Flag

Alpert Medical School students, including twins Nichola Haddad '16 MD'20, left, and Jessica Haddad '16 MD'20, right, joined the rest of the University for Opening Convocation in September.

See more photos *from the day at flickr.com/photos/alpertmedicalschool.*

DAVID DELPOIO

POLITICS

Get Out the Vote

Med students across the US work to get their classmates to the polls in November.

You don't have to be a political junkie to be absorbed by election news this year. But even civically minded medical students, mired in exams and clinical rotations, may feel that voting should take a backseat to their studies.

Not so, says Aaron Shapiro MD'18, founder of the student group Citizen Physicians at Alpert Medical School. In the spring, they began the National Medical Student Voter Registration Campaign to register US medical students to vote in time for the November 8 election. So far 35 schools are participating, Shapiro says.

"Physicians—just like every other citizen—have a civic responsibility to vote," he says. "This is a very important election year and we want to make sure that medical students across the country are able to participate."

Citizen Physicians, which has chapters at five other medical schools, organizes voter registration drives for new students, answers questions about whether they should register locally or in their home states, and helps them get absentee ballots.

The group hopes students will make voting a lifetime habit. "Physicians vote significantly less than the national average," Shapiro says. "We heard from so many students across the country how needed this kind of programming is, which is why we decided to take this campaign to the national scale." ***—P.H.***

ASK
The Expert

Do No Harm

Would more melanoma screenings mean more unnecessary tests and treatments?

Malignant melanoma kills about 10,000 people in the US every year, but it can be cured if caught early. While some experts are calling for widespread training of primary care providers to screen patients during routine visits, others worry that could lead to misdiagnoses, overtreatment, and unnecessary patient distress. A team of researchers led by Martin Weinstock, MD, PhD, professor of dermatology at Alpert Medical School and chief of dermatology at the Providence Veterans Affairs Medical Center, studied what happened when PCPs in the University of Pittsburgh Medical Center system gained online training in melanoma screening and began looking for the skin cancers in 2014. They reported their findings in *Cancer* in July.

Weinstock's team reviewed the data from tens of thousands of encounters with patients 35 years and older both in the first eight months of 2013, before the training occurred, and after, in 2014. When they divided PCPs into three comparison groups based on how much training they received, they found that neither dermatologist visits nor skin surgeries increased substantially between 2013 and 2014 in any of the groups. Between the groups there was also little difference in how often those outcomes occurred.

The lack of major change was not because the training had no effect. Between 2013 and 2014, the group of providers with the most training produced a 79 percent increase in per-patient melanoma diagnoses, but the number of diagnoses was tiny (24 out of 11,238 patients in 2013, and 48 out of 12,560 patients in 2014). In the same group, in both years, skin surgeries numbered in the hundreds and dermatologist visits in the thousands. There are many reasons why both of those could occur independently of melanoma.

In other words, the newly diagnosed melanoma patients could well have received the proper follow-up care that their diagnoses warranted without radically changing the overall number of dermatologist visits or surgeries. And there was no sign that training PCPs to screen for melanoma had flooded dermatologists or surgeons with torrents of cases. ***—David Orenstein***

5 Things You Should Know

1 SECRET OF THE SEXES The evolution of gender required that gene expression be balanced between males' XY chromosomes and females' XX, but how does that happen? New research on fruit flies suggests the secret may be as simple as GAGAGA: a repeating DNA sequence that's crucial for binding the protein CLAMP to the X chromosome. Together with a protein called "male-specific lethal," CLAMP boosts gene expression of the single X chromosome so males can live. Erica Larschan, PhD, senior author of the study in *PLoS Genetics* and the Richard and Edna Salomon Assistant Professor of Molecular Biology, Cell Biology, and Biochemistry, says the same process is in play in some other flies; now she's trying to figure out if mammalian gender depends on GA repeats, too.

2 WHAT DOES THE FOXO SAY? Worms, flies, mice, and humans share 46 genes regulated by the same family of FOXO proteins that play roles in metabolism, DNA repair, and other processes important to aging and longevity. The data could help researchers develop hypotheses about human FOXOs, which in turn could improve our lifespan, or at least our healthspan, says Ashley Webb, PhD, assistant professor of molecular biology, cell biology, and biochemistry and lead author of a recent paper in *Aging Cell*. "If we want to enhance tissue function in the elderly, we need to first know how a normal healthy cell functions, and why it becomes dysfunctional with age," she says.

3 ONE EYE OPEN Bad sleep on your first night in a new place may be a hardwired, evolutionary fact of life. In a paper in *Current Biology*, researchers in Brown's Department of Cognitive, Linguistic, and Psychological Sciences reported that the brain's left hemisphere remains more awake than the right during deep sleep—likely an adaptation that helps us stay alert in case of trouble.

4 TRANSPLANT TRACKER Gastroenterologist Colleen Kelly, MD F'06, assistant professor of medicine, received a $2.8 million grant for the Fecal Microbiome Transplant National Registry from the National Institute for Allergy and Infectious Diseases. As a co-PI she will follow fecal transplant donors and recipients for up to 10 years to assess the short- and long-term safety and effectiveness of the transplants, which have been highly successful in treating severe *Clostridium difficile* infections (see *Brown Medicine*, Spring 2016).

5 DIGITAL HEALTH DIDACTICS Alpert Medical School began offering a digital health preclinical elective this fall, under the guidance of Megan Ranney, MD RES'08 F'10 MPH'10, assistant professor of emergency medicine and founder and director of Brown's Emergency Digital Health Innovation program (see *Brown Medicine*, Winter 2016). The course introduces students to an array of topics and discusses how tech innovations can improve care—as well as safety, privacy, and other issues. Course coleader Margaret Thorsen '15 MD'19 says the elective will "provide students with the frameworks and concrete skills to critically evaluate digital health innovations and develop and implement their own ideas."

OVER HEARD

"I shook his hand for so long he said, 'You've got to let go now.'"

—ERIKA EDWARDS, *PhD, associate professor of ecology and evolutionary biology, on meeting President Obama at the White House when she received the Presidential Early Career Award for Scientists and Engineers*

COOL TOOL

High and Dry

A simple score is the best way to assess dehydration severity in kids.

Skin and tears, breath and behavior: all readily observed in a child, and assessed together, a reliable indicator of dehydration.

The four-symptom DHAKA score—which notes a child's general appearance, breathing pattern, skin elasticity, and volume of tears—is the quickest, most accurate way to assess the severity of dehydration, according to a study in *The Lancet Global Health*.

> "From an evidence-based medicine point of view, it is better than anything else out there."

"The DHAKA score now has better evidence for its performance in assessing dehydration in a specifically low-income country setting than any other scale," says lead author Adam Levine, MD, MPH, associate professor of emergency medicine. "From an evidence-based medicine point of view, it is better than anything else out there."

In a side-by-side comparison, the study, which assessed 500 kids in Dhaka, Bangladesh, found that DHAKA (Dehydration: Assess Kids Accurately) was a significantly better predictor of dehydration severity in children under age 5 than the current guidelines provided by the World Health Organization.

Levine and colleagues derived the score in 2014 by statistically analyzing the cases of 770 children with diarrhea in Dhaka and determining which clinical signs at intake best predicted dehydration severity. In the new study, they validated the score by testing it with a new patient population.

"Not only is this the first score to be derived and validated in a low-income country setting, but the DHAKA study is also the largest study ever of dehydration assessment of kids anywhere," Levine says.

Next spring he'll run more tests, in rural Bangladesh, in order for DHAKA to earn the WHO's endorsement as a new diagnostic standard in resource-limited settings. ***—D.O.***

COURTESY WATSON INSTITUTE

ACADEMICS

Medicine + Policy = Health

Brown launches a joint MD/MPA degree program.

A doctor can diagnose a patient and prescribe life-saving treatment only to find that it's not covered by insurance, or may have insight into how policies could provide better health outcomes for patients, but no experience navigating the system that institutes them.

Brown's new dual-degree Doctor of Medicine/Master of Public Affairs program aims to train students in both medicine and health care policy and create the next generation of leaders in those intersecting fields.

"This degree program was developed knowing what knowledge and skills students will need if they want to effect change in health care moving forward," says Paul George '01 MD'05 RES'08, assistant dean of medical education. "It was important for us that students have an idea of what shapes health policy and gain practical experience in this arena, so that they would be facile in promoting health policy changes during their careers."

ON-THE-GROUND EXPERIENCE: MPA students learn about global policy at a nonprofit in India.

This is the first integrated program of its kind in the US, in which students are able to complete their degree program in four years and take courses taught by both Medical School and public policy faculty.

Students will be able to "see patients, identify issues directly related to health policy, and then learn about those issues with the patient's context in mind," George says. In addition, he says, the design of the program

enables a cross-disciplinary approach as students encounter issues related to health policy in clinical settings.

The four-year program begins in June, and students must be admitted to Alpert Medical School before opting for the dual-degree track.

In the first year, students take courses in health systems science and public organizations management. They also begin a four-year Policy in Action consultancy, spending a half-day per week in a health care system, foundation, or non-governmental organization, shaping and implementing a project with a real-world client. In subsequent years, students engage in a longitudinal clerkship with a mentor physician (see page 12).

> "To do health care well, decision makers must bridge traditional disciplinary divides."

In the third year, they gain global policy experience, meeting with elected officials, entrepreneurs, and lawmakers to examine how policy is constructed in other countries. Past sites for these immersion programs have included Sweden, Brazil, India, and Cambodia.

"The delivery of health care is a fundamental public good, something that governments worldwide are expected to ensure through policy," says Edward Steinfeld, PhD, the Howard R. Swearer Director of the Thomas J. Watson Institute for International and Public Affairs. "Our joint MD/MPA program reflects the basic fact that to do health care well, decision makers must bridge traditional divides between the social sciences, the sciences, and the humanities. That only Brown today offers a program like this reflects the University's fantastic strengths in interdisciplinary scholarship, education, and public outreach."

Asked what roles he envisions MD/MPA students taking on in their professional lives, George says he hopes that "graduates of this program continue seeing patients to some extent, as I think it is important to stay involved in clinical care as one is shaping health policy. That being said, my hope is that [they] seek out opportunities to lead health policy change in government, generate innovative ideas in health policy think tanks, conduct research in academia, or act as key consultants to those shaping health policy."

—Gillian Kiley

ANATOMY OF A MICROSCOPIST

Fine Focus

Childhood seemed pretty idyllic for Geoff Williams, MS. Sure, the Seattle native was a "struggling musician's kid," but he always had a camera, played the violin with his family, and rode his bike everywhere. "We grew up on a dead end road, and we had a hill," he says. "We'd ride down the hill and crash at the bottom." He's still riding (and only rarely crashing) his bike, logging thousands of miles year-round on his daily commute; on punishingly long routes around southern New England; and racing cyclocross, a steeplechase-type, mostly off-road (and usually muddy) event that mixes pedaling, running, and obstacle jumping at relentless speeds. It's a high-octane contrast to his day job in the sedate, dark labs of Brown's Leduc Bioimaging Facility, where, as the manager, he keeps a dozen microscopes up and running and teaches students and faculty how to use them. For Williams, microscopy labs are more than a place to indulge his mechanical mind or, as a botanist, to observe the minutest details of the plant world; they're also an art studio. Whenever he has a few minutes to spare, he zooms in on everyday objects—bike parts, insects, kitchen scraps—to explore their aesthetic possibilities; he prints his favorite images and occasionally displays them in local galleries and exhibits. Examining pollen and other hidden treasures of a tiny juniper specimen in a scanning electron microscope (SEM), he says, "It's a different world inside here that you don't see everywhere else."

—P.H.

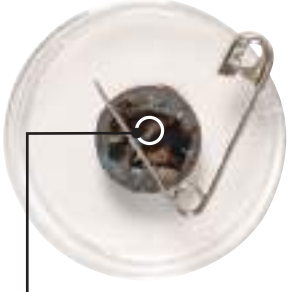
MR. FIX-IT

In his spare time Williams, a certified bicycle mechanic, gets cyclists rolling again at a Providence bike shop.

ADAM MASTOON

DAILY BREW

A coffee pot in his office keeps Williams fueled throughout the day.



READY TO SCAN

To visualize this beetle wing with an SEM, Williams mounted it on a metal cylinder and coated it with gold, which enhances the scope's electron signal (see magnified image, page 52).

ALONG FOR THE RIDE

This water bottle has traveled with Williams more than 4,000 miles so far this year.

RAW MATERIALS

Williams imaged hops, yeast, and malt from his friend's brewery, Independent Fermentations in Plymouth, MA, for his latest SEM photography project.

KITCHEN CONFIDENCE

Though he has several knives, Williams only uses this Wüsthof to prepare the family meals.

THE BETTER TO SEE

A Zeiss 63x objective lens "has been on every confocal [microscope] I've used since '91," Williams says.

STRINGS ATTACHED

Williams, a classically trained violinist, got this instrument when he was 10 years old. He still performs at his family's Celtic Yuletide concert in Seattle every year.

ADAM MASTOON (8)

ESSAY

BY DIVYA DETHIER MD'17

Stand Up to Cancer

An integrated clerkship provides students with new insight into their patients' lives.

During my first few weeks as a third-year student on the medicine wards, we admitted a patient I'll call R. She had multiple myeloma. When I first met R, she was sitting in her hospital bed reading the sports section of the newspaper. She had a cast on her right arm. Despite feeling sick and weak, she was smiling. She told me the Red Sox were her favorite team, and she wanted to be sure to keep up with the scores even when she was in the hospital. She had even chosen a red cast in support of her team.

I looked forward to visiting her and her husband every morning. During the weeks she was hospitalized, her stomach was bleeding and we could not determine its etiology. There were times our team thought we may not figure it out in time to help her recover. With the help of my attending, R and I had a conversation about her life goals. What is important to you? How do you define a "good death"? What do you want to happen before you leave this earth? She responded, "I want to be home and feel my dog sleeping in my lap again."

Throughout the next few weeks, R had a partial gastrectomy to stop the bleeding. Although she improved and was able to leave the hospital to a rehabilitation center, new problems arose. Her right arm was healing, but a new bone lesion appeared in her left. Her delicate femur fractured just from sitting down on the toilet.

As part of the longitudinal integrated clerkship (LIC), I continued to follow R throughout my third year. During the LIC, medical students follow a panel of patients throughout the year, seeing the continuum of total health from outpatient appointments and hospitalizations to personal crises and changes in their social histories. It allows students to see how health unfolds for patients, and become advocates for them as they navigate the complex health care system.

I was with R as she prepared for surgery to fix her femur. I accompanied her to a radiation appointment, where she received palliative treatment for bone pain. I was able to be with her before and during a subsequent surgery to fix her left arm. I visited her during a dialysis session, one of the three she goes to every week. Her husband updated me every step of the way.

> Those small steps represented one of the most special moments in my medical training.

Finally, at the end of August, R was able to go home. Before she and her husband left for Florida for the winter, I paid them a visit. It was a very special feeling to see R in her own home, her dog by her side, just as she had wished.

A few days before Christmas, I got an email from R's husband. It had a video of her walking several steps on her own, with a walker, and then sitting down in a chair, smiling as always, dog at her side. In the six months I had known her, I had never seen her walk on her own. Those small steps represented one of the most special moments in my medical training.

In the LIC, I learned a lot about each field of medicine; I gained more knowledge than I thought possible. But R helped me learn something more abstract, about the power of remaining optimistic and hopeful in the face of the enormous adversity of disease that, as health care providers, we easily lose sight of.

To this day I get regular updates about R's health, the obstacles that present themselves, and her continual resolution to push past them. I am convinced her recovery from these obstacles is due in large part to her tenacity and positivity. I am grateful to the longitudinal integrated clerkship for giving me the opportunity to learn so much from R, and witness the way health care extends from the hospital to impact the smallest, most intimate and important parts of our patients' daily lives.

***Divya Dethier** is a fourth-year medical student applying to obstetrics and gynecology residency programs. She grew up in Washington, DC, attended Middlebury College as an undergraduate, and spent a gap year in Mauritius before starting medical school.*

RESIDENT EXPERT

BY AMANDA FANTRY, MD RES'16 F'17

BLAIR THORNLEY

No Apologies

To succeed in a male-dominated field, be yourself.

I carry a pink briefcase. Not a subtle pink, but a vivid, intense, practically bubble-gum pink. I set it down each morning among the ubiquitous black backpacks, drab brown briefcases, and camouflage baseball hats. I finish rounds and attend morning lecture, where the speaker invariably scans the room and identifies me as the only female in a sea of male orthopedic residents.

When I first arrived at Brown, in 2011, I was the fifth woman in the program, and at 16 percent female, our program matched the national average for orthopedics. However, as each successive Match Day yielded six men and no women, that number fell. And finally, as a fourth-year resident, I was the lone woman in the annual orthopedic residency photo, standing proudly in fuchsia high heels.

In medical school, senior attendings in multiple specialties tried to convince me that orthopedic surgery was for male jocks and athletic has-beens, and a female orthopedic resident told me that the only way to fit in was to chest bump my way through residency and "act like a man." I questioned my choice. During residency interviews I was frequently asked what sort of things I did with my hands. Could I play the ukulele? Could I build a shed? Did I whittle wooden animal figurines? After I stared back blankly for a few seconds, I quickly endorsed my ability to shop for shoes online and my penchant for baking. Did participating in stereotypically female gender role activities make me unable to do orthopedic surgery? Despite my hesitance, I matched into orthopedics, believing in my passion for the patients, the surgeries, and their outcomes.

In the last five years, I have been called into my program director's office because I have been easily identified as "the lady doctor," for both the good and the bad (thankfully more frequently for the good). I have been told I'm too young or too pretty to be a surgeon, and that's when I'm not mistaken for the nurse, physical therapist, or dietary aide. Yet I would choose it all again. The satisfaction of fixing fractures, restoring quality of life, and improving a patient's pain and disability has far outweighed any of the perceived, or actual, negatives. I embrace being a woman in a department that has embraced me. I learned how to succeed while contributing a much-needed female perspective in a male-dominated field.

According to AAMC data, orthopedic surgery residencies and fellowships across the nation rank behind only interventional radiology and interventional cardiology for the lowest percentage of women. I have two female mentors among more than 30 attending surgeons in our department, both of whom are strong advocates for women in orthopedic surgery. Together we have spoken at interest groups, held workshops, and invited medical students to spend time with us, all in an effort to prove that orthopedic surgery is an amazing, fulfilling career for anyone.

Until these efforts translate into an increase in female orthopedic residents, there is significant work left to do. For now, I will continue to answer questions about what it's like to spend my days surrounded by male colleagues (a little smellier and messier) and gently remind patients that my junior resident is not their surgeon despite his Y chromosome. I will then take my sparkly lead to the operating room, use a collection of power tools, and fix one more patient. When that patient walks into my office at follow-up, I will have a smile of satisfaction on my face. And maybe some delicious baked goods.

Amanda Fantry *is an orthopedic trauma fellow at Brown. She will pursue an additional fellowship in foot and ankle surgery at Baylor University Medical Center.*

BY JAYSON MARWAHA '14 MD'18

A New Dimension to the Duty Hours Debate

Are we asking the right questions?

ISTOCK PHOTO

Not too long ago in the history of medical education, the resident workweek was an almost completely uncharted territory. Until just over a decade ago, there were no national rules governing how long residents could be kept in the hospital by their training programs—so they rarely ever left. Residents, regardless of specialty, worked longer hours (120 hours was not an uncommon workweek), took more calls, and had fewer, shorter breaks than they do now.

That all changed in 2003 when, after a high-profile case of a young woman in New York dying in the hands of fatigued and overworked residents, the governing body overseeing resident education (the Accreditation Council for Graduate Medical Education, or ACGME) restricted all residents to an 80-hour workweek. Then in 2011 the ACGME issued another set of rules specifying how those 80 hours could be used—how long shifts could be, how many hours would be given in between shifts, and so forth. Both announcements from the ACGME were followed by heated national debate. Proponents of the duty hour restrictions claimed that the policy decreased resident fatigue, thereby reducing medical errors that could cause harm to patients. Critics argued that a limit on resident work hours would not only decrease resident experience and education, but would also increase the number of transitions of patient care between residents

as shifts became shorter; these "handoffs" are widely recognized as a major source of error in hospitals.

Researchers have conducted dozens of massive studies analyzing the impact of this policy over the years and almost all have come to the exact same conclusion: the ACGME's duty hour limitations have not affected patient outcomes at all. No significant changes in broad, nonspecific markers of patient care such as mortality, length of stay, or readmissions are associated with the new duty hour rules.

This is fantastic news: we have not hurt patient care in the process of trying to make a safer working environment for residents. But it's also not entirely unexpected news. There are many systems of checks and balances in hospitals—such as attending physician supervision of all residents—to ensure that minor errors like ordering unnecessary medications or tests are avoided or caught early, before they cause any significant harm. These safeguards are a layer of insulation that protects broad metrics of hospital performance like mortality, readmissions, and length of stay from skyrocketing in the face of not just the new duty hours policy, but also the countless other changes happening daily in the teaching hospital environment.

LESS IS MORE

In fact, these metrics are influenced by so many other factors in a hospital that they may not be the best ones by which to gauge the impact of this policy. Studying major patient outcomes alone may not uncover more subtle underlying changes in quality, cost, or efficiency of care. Yet this is all we know about the effect of the duty hours policy, largely because this is all we've asked.

In the June issue of the *Journal of the American College of Surgeons*, faculty members at Rhode Island Hospital and I investigated these more subtle changes. We gathered historical data on all patient admissions to the hospital's trauma center in the four years before and after the 2011 duty hour reform—more than 11,700 patients—and compared the care of those admitted before the reform to those admitted after. In addition to studying the same major outcomes as previous studies, we looked at the amount of resources used for each patient (such as OR visits) and the rates of many specific complications (such as chest cavity infections after chest tube placement). As expected, no major outcomes exhibited meaningful changes.

However, we uncovered a surprisingly strong trend of changing resource utilization habits linked to the time that the policy took effect: after the reform, patients were being taken to the OR more often, getting more x-rays and CT scans, more lab tests, more fluids and meds: on average, more things were being done to each patient without any corresponding improvement in outcomes (and they weren't any sicker than the patients before the reform, either).

It's hard to explain why these changes occurred in association with the duty hour reform without much more information. However, one possible explanation is that, compared with their pre-reform counterparts, post-reform residents are less experienced on the floor—or perhaps less informed about their patients, more of whom are now being handed off from shift to shift—and therefore are ordering more unnecessary tests and interventions. Regardless of the true explanation, the results of this study are strong evidence for the existence of more nuanced policy effects. In fact, changing resource use patterns may be a sign that duty hour reform has affected the cost of care in ways that should be studied further.

> Duty hour reform has affected the cost of care in ways that should be studied further.

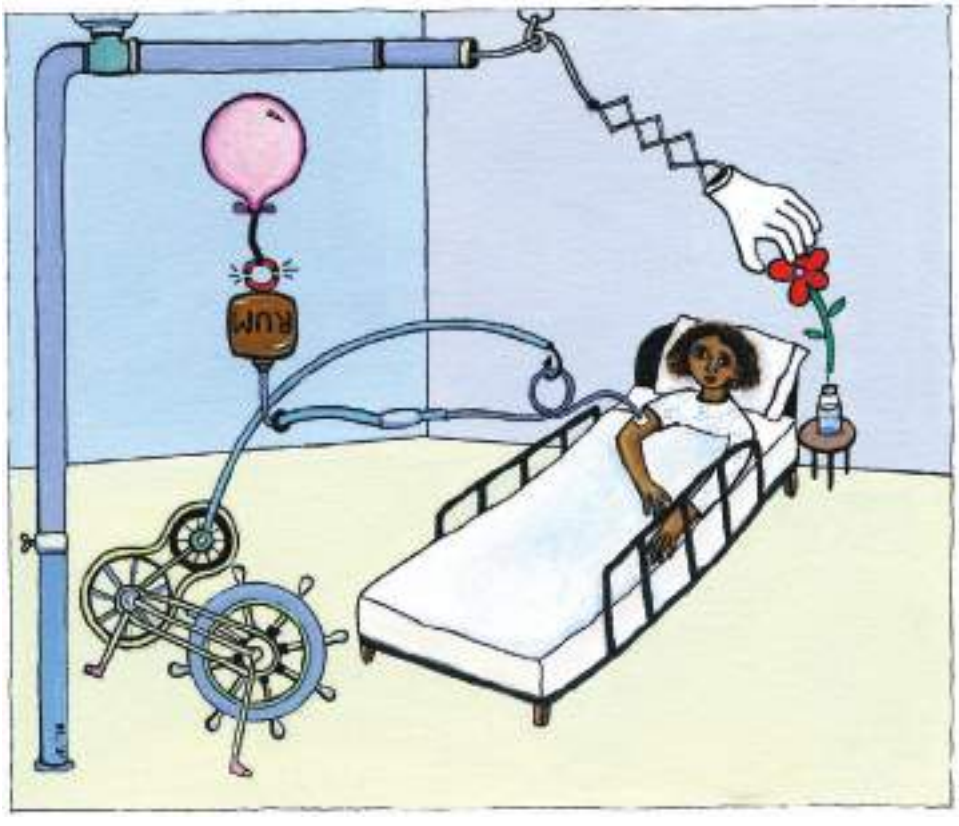
We don't yet know enough to decide on the fate of the 80-hour workweek; an understanding of the policy's effects beyond high-level patient outcomes is a huge part of what we're missing. Even the FIRST Trial—an ongoing national study being used to guide policymaking on the issue—is not using any new metrics to evaluate the policy's impact. To be fair, it's unreasonable to expect large trials to collect data as granular as ours. But having several more retrospective studies like ours—ones that leverage hospitals' detailed historical records to examine unexpected effects of the policy—would be tremendously valuable to this debate. Without them, we may end up making many of our decisions on duty hours in the dark.

Jayson Marwaha *is a third-year medical student whose research and writing interests include data, finance, and safety in health care. He's on Twitter @Jayson_Marwaha.*

BY SARAH NORTON MD'17

When the World Calls

By turning to local resources and know-how, surgeons can improve global access to care.



JESSICA DEANE ROSNER

My relaxing morning on the beach came to an abrupt end when a foray into the water resulted in searing nerve pain in the tibial and peroneal distribution of my right foot. The culprit: an exotic sea creature. The place: San Juan del Sur, Nicaragua. As I applied pressure to dull the pain and stop the bleeding, some locals swung to the rescue; they knew what it was that had stung me (some relative of a stingray) and, more importantly, how to treat it. My foot was thrust into a bucket of water and a shot of rum appeared in my hand. Local resources and knowledge endemic to place saved the day.

I was in Nicaragua on Alpert Medical School's new, monthlong surgical endoscopy elective, led by Andrew Stephen, MD, assistant professor of surgery (trauma), and Milton Mairena, MD, a general and endoscopic surgeon at Hospital SUMEDICO in Managua. For this international health rotation, a classmate and I scrubbed in on general and trauma surgeries and observed surgical endoscopies at three hospitals in the capital city of Managua: Hospital Antonio Lenin Fonseca, one of the public teaching hospitals and trauma centers with incredibly high emergent and surgical volume; Hospital SUMEDICO, which has more advanced endoscopic and laparoscopic facilities and equipment, and accepts both private and Social Security Institute (INSS) patients; and the police hospital, a center for surgical endoscopy and general surgery that serves law enforcement personnel as well as INSS patients.

A resident at Lenin Fonseca described the provision of health care in Nicaragua as an "effort to practice evidence-based medicine in low-resource settings." I was struck time and again by the ways physicians in Nicaragua advocate for their patients to receive the care that they need, as well as their refusal to admit defeat when resources fail to materialize. Their pride, knowledge, and ingenuity are tangible and endemic resources.

In each hospital I sought to understand the limitations (and corresponding innovations) that come with practicing medicine in a setting with far fewer resources than the Rhode Island operating rooms to which I'm accustomed. The differences range from mundane frustrations to startling omissions to novel workarounds. Masks and surgical caps are often absent from the supply closets in the public hospital; endoscopies are often done without anesthesia;

and it is not unheard of for a resident to go to a local hardware store to craft a negative pressure system to help with wound closure.

The care conversations during rounds resembled those we have in the States, but required some local contextualization and consideration of what to do in the absence of resources. One morning, we discussed a septic patient who had been referred after a complicated jejunostomy. She had a frozen abdomen and there was no way to surgically treat the infection; antibiotics were continued. More pressing was that she was wasting in front of us. Her care team requested TPN (total parenteral nutrition), but the IV formula often takes weeks to materialize from the government stock. A long conversation followed regarding a creative substitute to TPN, with some even offering to make it.

CALL TO ACTION

Local differences in surgical approaches and resources are finally garnering the attention of the global health field. In a 2015 article in the *World Journal of Surgery*, Charlie Mock, MPH PhD '77 MD'80 RES'88, a professor of global health and of surgery at the University of Washington, highlights the importance of understanding these differences. Worldwide, he writes, upwards of 5 billion people do not have access to safe, affordable surgical and anesthesia care when needed; only 6 percent of the surgeries done each year are performed in the world's poorest countries. Emphasis should be placed on "surgical care that addresses conditions that have very large health burdens and for which there are surgical procedures (and related care) that are highly cost effective and that are feasible to promote globally," such as complications of pregnancy, injury, surgical emergencies, and congenital anomalies.

Mock also quotes a resolution by the World Health Assembly to strengthen emergency and essential surgical care and anesthesia. The resolution seeks to "raise awareness of cost-effective options to reduce morbidity, mortality [...] through improved organization and planning of provision of anesthesia and surgical care that is appropriate for resource constrained countries," he writes. Both the number of specialists and the surgical volume need to increase; in so doing, the perioperative mortality rate will decline. Global surgery now has an agenda.

In Nicaragua, I saw firsthand why making surgery a main focus of global health is of utmost importance. Our patients ranged from law enforcement agents needing endoscopic diagnosis of *H. pylori*, to people with end-stage pancreatic cancer seeking surgical intervention or hospice care in the private sector, to shooting and stabbing victims who had no insurance or ability to pay. In each instance, and to varying degrees, physicians asked: what OR or endoscopic suite space is available? What personnel are in place to perform the surgery? Are there enough anesthesiologists? What anesthetic medications are available? We rarely have to ask these questions in Rhode Island; we take for granted that these basic surgical needs are met and care conversations proceed from there. In an increasingly globalized world, and with calls for greater global equity in surgical care, surgical training and practice must consider the nuances of time and place.

> I saw firsthand why making surgery a main focus of global health is of utmost importance.

But awareness isn't enough. Mock writes that, unless physicians respond to the global call to action to increase access to surgical care, all of the studies are at "risk of becoming academic exercises and wasted effort." My background in medical anthropology and qualitative research teaches me that individual stories speak volumes and inform statistics. My clinical training illustrates the breadth and depth of potential that physicians have to enhance standards of existence. As I figure out my path in medicine, of one thing I am sure: I have the obligation and privilege to take the stories I have heard and translate my knowledge into action. Be it as a surgeon in the OR, an emergency physician working to stabilize and triage patients from the field, or an internist managing patients with a surgical history, I will combine this call to action with local resources and knowledge endemic to place to help these academic exercises impact global health.

Sarah Norton *is in South Africa this year for the Doris Duke International Clinical Research Fellowship through the Yale School of Medicine. She earned a master's in medical anthropology at the University of Colorado at Denver and completed her postbac at Bryn Mawr.*

BY SUMMER E. ALLEN PHD'12
PHOTOGRAPH BY SCOTT KINGSLEY

Open Mind

Neurologist **KAREN FURIE** has devoted her career to understanding and preventing stroke.

Karen Furie has always been a reader. As the daughter of a nurse and a dentist growing up in Queens, NY, she would marvel at the medical textbooks she pulled off her parents' shelves, particularly the parts about tropical diseases and brain parasites.

And it was her love of literature that drew her to apply to the Program in Liberal Medical Education at Brown while attending Stuyvesant High School, a science- and math-focused magnet school.

"I always had a passion for literature and English, and coming to Brown enabled me to be an English major while fulfilling all the premedical requirements," says Furie, MPH '87 MD'90 RES'94 F'95, P'19MD'23, now the Samuel I. Kennison, MD, and Bertha S. Kennison Professor of Clinical Neuroscience and chair of the Department of Neurology at Alpert Medical School.

Today if you sit next to Furie on a train or a plane, you might catch her in one of her guilty literary pleasures: reading mystery novels (her current favorites are by Deborah Crombie and Louise Penny). "I read them like popcorn," she says. "That's the way I relax and unwind." But even her favorite pastime is intimately connected to her true passion: neurology.

"When I think of neurology, I see all the patients and the problems as mysteries to be worked through," she says. As a neurologist and researcher, Furie has spent her career un-

MEDAL CEREMONY: Karen Furie was inaugurated as the first Samuel I. Kennison, MD, and Bertha S. Kennison Professor of Clinical Neuroscience in 2014.

winding the mysteries of one of the most common and debilitating neurological afflictions: stroke.

STOKED BY STROKE

Furie's fascination with stroke was ignited by the first person to hold her current position, J. Donald Easton, MD, Brown's inaugural chair of neurology. "He was a stroke neurologist before there even was such a thing," Furie says. She was especially inspired by Easton's ability to balance seeing patients with research into how best to prevent and treat stroke. "It was so exciting," she says, "trying to answer all of the many questions that were still unresolved."

She left a similarly strong impression on Easton. "It was obvious that she was really smart, driven, and going to be a future success," he says.

In medical school, Furie took an elective at Massachusetts General Hospital with J. Philip Kistler, MD, director of the MGH Stroke Service. "He was an amazing mentor," she says. "He is an incredibly dedicated clinician and he had a roll-up-your-sleeves-and-do-the-work attitude toward things."

> "It was obvious that she was really smart, driven, and going to be a future success."

During her elective, Furie and Kistler determined that the drug warfarin (Coumadin) can help prevent stroke in patients with atrial fibrillation. Their finding is now so fundamental that it's taken for granted as the course of treatment. "He had recruited patients from hospitals all around Boston and he would get in his truck with a little portable centrifuge," Furie says. "We'd go to people's kitchens—quite literally—and draw their blood and spin it."

When it was time for Furie to pursue her residency, Easton encouraged her to consider Brown's program, which was then only four years old. "She was, of course, top of her class, and that was an attraction to having her join us, but it became pretty obvious that she was a risk taker and had great self-confidence," says Easton, who's now a professor emeritus of neurology. "She just jumped right in and decided she was going to thrive here. And she sure did."

After completing her fellowship at Rhode Island Hospital and earning a Master of Public Health from Harvard, Furie joined the faculty at MGH's Stroke Service. Besides treating stroke patients there and at Spaulding Rehabilitation Hospital, Furie joined Kistler on another clinical trial—this time looking at clotting propensity and blood markers for cryptogenic stroke (stroke of unknown cause).

Furie wrote a career development grant from this work, seeking to identify genes that put people at risk for developing thrombosis, or blood vessel clotting, which can lead to stroke. In addition to identifying potential risk genes, she created a unique database of well-characterized stroke patients that included a blood biobank, genetics bank, and clinical database complete with imaging data. It's a major part of Furie's MGH legacy: "There are still papers being written on that database," she says.

STROKE AROUND THE WORLD

Furie has had a hand in dozens of clinical studies related to preventing and treating stroke. "She's really moving along in the field, nationally and internationally, because she's recognized to be intelligent, knowledgeable, and very easy to work with," Easton says.

In February, Furie and others published in the *New England Journal of Medicine* the results of a decade-long international study on the effects of the diabetes drug pioglitazone on stroke survivors with insulin resistance. "You can reduce the risk of heart attack and recurrent stroke by 24 percent," she says. "That's pretty dramatic."

As the primary neurologist for the study, Furie traveled extensively, to the UK, Germany, Israel, and Australia. She also got to explore her childhood interest in tropical medicine when she went to Brazil to study Chagas disease, a parasitic infection that can cause inflammation of the heart and brain.

"Neurology, and stroke in particular, is a major problem globally," she says. "We're fortunate in the US to have so many resources at hand, but when you travel to other places in the world, you realize how much there is to be done."

HOMECOMING

As the head of Alpert Medical School's neurology department since 2012, Furie is traveling a lot less these days. But she couldn't be happier.

DISTINGUISHED ALUMNA: Furie delivered the 26th Annual Ruth Sauber Lecture during Reunion Weekend 2016.

FRANK MULLIN

"When the opportunity came up, I got emails from multiple people who knew me from my time at Brown saying, 'Oh, this was the job you always wanted,' and it's true," she says. "It felt so right—that desire to come back to this environment and the culture of Brown."

"This community nurtured us for a dozen years," adds Furie, who met her husband, neurosurgeon Marc Friedberg '87 PhD'91 MD'93, P'19MD'23, as an undergraduate. "There was this sense of coming home." Brown feels even more like home these days, since one of their two sons, Adam Friedberg '19 MD'23, enrolled as a PLME.

In four short years at the helm, Furie has implemented some big changes in the department, including a required neurology clerkship for all medical students, an increase in the number of residency spots in neurology from 15 to 18, and the requirement of a clinical research project as part of resident training.

Furie marvels at just how different training for these residents is now, thanks to advances like the invention of the stent retriever, a mesh tube that can remove large clots from blood vessels in the brain. The device has changed clinical outcomes for some of the most poorly off stroke patients.

"They would often be left unable to move one side of their body, unable to speak, unable to swallow, unable to return home to any type of an independent lifestyle," Furie says. Now these patients can go home "virtually normal" in a matter of days. "It's really been a transformation of our whole field," she says.

LOOKING AHEAD

But there's still much to be done. "We really still don't understand completely how the brain recovers from injury and how we can augment that," Furie says. "That's the question that patients who are left with any deficits want to know: how can I improve my language function? How do I help get my weak arms strong again?" She has been working to get FDA approval to test a new drug that may preserve brain tissue that's injured by the lack of blood flow during an acute stroke.

Developing treatments for brain recovery—whether pharmaceuticals, stem cell therapy, or brain stimulation—will require coordinated efforts between basic and clinical researchers. Furie says this is something that Brown is uniquely situated to foster, with collaborations between the Brown Institute for Brain Science, the VA Center of Excellence for Neurorestoration and Neurotechnology in Providence, and the Norman Prince Neurosciences Institute at Rhode Island Hospital, of which she is coclinical director. "That's the real joy of Brown: thinking outside the box and forming unconventional partnerships to solve problems," she says.

Meanwhile the already blossoming neurology department will continue to grow under her watch. "We've gained about six new positions and we'll probably add that many again in the coming year. Lots of good things are happening in neurology," she says.

Despite the administrative demands, Furie still makes time for her patients. "Karen Furie is everything you'd like your doctor to be like—smart, knowledgeable, nice, concerned about you," Easton says. "As busy as she is and as involved in as many things as she is, she's still able to stop when she's at the bedside and talk to the patient and put those other things out of her mind. She's a winner."

Summer E. Allen *is a freelance writer based in Rhode Island. Originally from Portland, OR, she studied biology at Carleton College and completed her doctorate in neuroscience at Brown. Read more of her work at sciencebysummer.com.*

Think Big

In elephants' cancer-resistant genes, an oncologist sees new hope for people.

BY PHOEBE HALL

PHOTOGRAPHS BY AUGUST MILLER

BLOOD DRIVE: Josh Schiffman gets a sample from an African elephant's ear at Utah's Hogle Zoo. The zoo draws blood every week to check the animals' health, and gives some to Schiffman to study their tumor-suppressing genes.

DREAM TEAM: Schiffman goes to Utah's Hogle Zoo almost every weekend with his three kids. He collaborates with the zoo's elephant keepers in his cancer research.

A few years ago pediatric oncologist Joshua Schiffman '96 MD'00 learned an astonishing fact. Elephants have an extraordinarily low rate of cancer, despite their enormous size and long lifespan.

An investigator at Huntsman Cancer Institute at the University of Utah, and a childhood cancer survivor himself, he'd dedicated his career to understanding why people get cancer and to caring for sick and dying kids, like the doctors who'd once cared for him.

He'd been studying human hereditary cancer syndromes, focusing on a tumor-suppressing gene that, when absent, heralds a nearly 100-percent cancer risk. Elephants, Schiffman learned, have 40 copies of the gene. "I almost fell out of my seat when I heard that," he says. Over its lifetime, an elephant's chance of dying from cancer is less than 5 percent.

The finding turned his research on its head. "What if we focus on who's getting less cancer, not who's getting more?" he asked himself.

Still, he didn't see how this quirk of elephant genetics could translate into anything useful for humans. "People

always would say, how will you actually use this discovery to help people?" Schiffman says. "I would say there's not really a way to do that. Maybe one day we'll find a drug that mimics the effects, but there's no way of actually putting an elephant gene into people."

That was before he met Avi Schroeder, PhD, a nanotechnologist in Israel. Their labs have since joined forces, and their goals are not small. "I want a world where no one has to go through what I went through, or what my patients go through," Schiffman says. "Maybe one day, we can prevent cancer."

PERSONAL TOUCH

Many physicians are spurred into the field of medicine by a personal encounter with disease; many others because they have a doctor in the family. Schiffman first was inspired by his dad, Fred Schiffman, MD, a hematologist/oncologist and the Sigal Family Professor of Humanistic Medicine at Alpert Medical School. "He's always there for his patients and his colleagues," Josh Schiffman says. "When he goes kayaking, he puts his phone in a pouch so patients can reach him, or another physician can call him up."

When Josh was diagnosed with Hodgkin's lymphoma, at age 15, Fred initially sought help from his colleague Edwin Forman, MD '56, P'92, who practiced pediatric hematology/oncology at Rhode Island Hospital, and then Hasbro Children's Hospital, for more than 40 years. Josh, who ultimately was treated at Dana-Farber Cancer Institute, in Boston, survived his illness "very determined to be like Ed Forman," he says. "I wanted to learn to be a good doctor humanistically and spiritually—to sit on the bed, hold a patient's hand, and look them in the eyes."

Schiffman enrolled at Brown in the Program for Liberal Medical Education, studying biology, psychology, and animal behavior as an undergraduate and spending his summers as a camp counselor, including working with seriously ill kids at the Hole in the Wall Gang Camp. In medical school he took an elective with Forman. "[Josh] was just wonderful with patients. Obviously he could identify with the patients and the families," says Forman, now a professor emeritus of pediatrics at Alpert Medical School who still sees hematology patients at Mount Sinai and Elmhurst hospitals in New York City.

But Forman says he also witnessed Schiffman's "terrific curiosity and independent creative thinking." He recalled a 5-year-old patient who appeared to have a bone marrow disease, yet Schiffman insisted that because the boy had recently been bitten by a tick, they should order a blood test for ehrlichiosis instead of a marrow biopsy. "So we did both. The marrow came back normal, and the ehrlichiosis was positive," Forman says. "A paper came out of it," in the *Journal of Pediatric Hematology/Oncology*, in 2001.

> "What if we focus on who's getting less cancer, not who's getting more?"

"His aggression is not the kind that would ever turn anyone off," Forman says, chuckling as he remembered Schiffman's persistence. "It's, hey, can we think about this in a different way?" He adds, "He's always giving credit to others. ... He credits me with more than I deserve."

Schiffman says, "Ed Forman and my dad taught me your patients guide your career. You'll learn more from your patients than from any medical textbook." After graduating, Schiffman moved across the country for a residency and pediatric oncology fellowship at Stanford. During his first year as a fellow he saw a 4-year-old girl who had acute lymphoblastic leukemia and Li-Fraumeni syndrome, an inherited disorder that dramatically increases the risk of developing cancer, often at a young age. "I'd never heard of it," he says.

As long as Schiffman could remember, he'd wanted to become a pediatric palliative care physician. But in that young patient, and her rare genotype, he found a new calling—at the start of life, instead of the end. "I wanted to know who is at risk for cancer," he says, "and could there be a way to intervene?"

FAMILY MATTERS

Even if you don't know Schiffman's name, you may have heard about the elephant study. Published in the *Journal of the American Medical Association* last October, it was the second most popular *JAMA* article of 2015, according to Altmetric, and thrust Schiffman, its corresponding author, into an international media spotlight. Virtually every major news outlet covered it, in dozens of languages, and he says he's still fielding reporters' calls.

Elephant genetics came to Schiffman's attention because of his studies of Li-Fraumeni syndrome. Affected individuals have only one working copy of the gene TP53, instead of the usual two inherited from both parents. TP53 codes for a protein, p53, that plays an essential role in cancer prevention by monitoring for genetic anomalies during cell division. "If a DNA mutation occurs in a cell, p53 stops the cell from dividing so it can repair the damage, and if it can't fix it, it kills the cell," Schiffman says.

> "One person with cancer is one person too many."

A lack of p53 has been observed in about half of human cancers, including breast, colon, lung, and prostate cancers. Without p53, there's nothing to prompt the malfunctioning cells to self-destruct and halt their development and metastasis. "Also, as we age, p53 naturally stops working as well as it used to function," Schiffman says. Even with two copies of TP53, half of men and a third of women will get cancer in their lifetimes. For people with Li-Fraumeni syndrome, the incidence is more than 90 percent.

In 2008 Schiffman, his wife, their two sons (they now have a daughter, too), and their Bernese mountain dog, Rhody, moved to Salt Lake City. There he sees patients at Primary Children's Hospital, runs a translational research laboratory at Huntsman Cancer Institute at the University of Utah, and serves as medical director of the High Risk Pediatric Cancer Clinic and professor of pediatrics and of oncological sciences. Schiffman has helped to implement a protocol for early cancer detection in children and families with Li-Fraumeni syndrome, and he's overseeing an effort to sequence the genome of every pediatric cancer patient in Utah to identify risk factors and develop therapies.

Schiffman's work followed him home and back to the lab again when, shortly after they moved to Utah, Rhody died of cancer. "What are the odds the dog of an oncologist gets cancer?" he says. Unfortunately, pretty good, he learned: purebred dogs develop cancer at 11 times the rate that humans do, and certain breeds, such as Rhody's, are particularly prone. The loss sparked an interest in comparative oncology—the study of the genomics of human and other animal tumors—and evolutionary medicine.

The evolution of cancer risk "went hand in hand with my focus on familial cancer," Schiffman says. It was at an evolutionary medicine conference in 2012 that he learned that elephants, which have many times more cells than humans, and many times more cell divisions, can live up to 70 years yet almost never get cancer.

"From an evolutionary perspective, they must be protected against cancer," Schiffman says. Not only do elephants have 20 times more TP53 genes than humans do, he discovered that when cell division goes awry, rather than stop the process and try to repair the DNA, elephant cells preferentially commit suicide, halting cancer before it can start.

His goals shifted again: "How do we take 55 million years of evolution of cancer resistance [in elephants] and turn it into medicine for people?"

PROTEINS WITH A PUNCH

In 2015 Schiffman traveled to a pediatric oncology conference in Haifa, Israel, to deliver a lecture on elephants, p53, and cancer resistance. In the audience was Avi Schroeder, an assistant professor of chemical engineering at the Technion–Israel Institute of Technology who specializes in novel drug delivery. Schroeder made a note to himself that he had to meet this oncologist from Utah.

Then Schroeder spoke about his work synthesizing proteins and delivering chemotherapy and other drugs via

nanoparticles, microscopic spheres that are one-one thousandth the diameter of a human hair, into metastatic tumors. Schiffman wrote a similar note that he must talk to the nanotechnologist. "When we met, we immediately saw this was meant to be," Schroeder says.

Nanomedicines "create accuracy that cannot be attained using larger systems because they are actually able to penetrate into the cancer site," Schroeder says. (Or as Schiffman puts it, they target the tumor "like heat-seeking missiles.") About 40 nanotechnology cancer therapies, such as Doxil and Abraxane, are in wide use. But they could do more, Schroeder says. "In cancer medicine we've improved a lot," he says. "The length of life has increased, but today, looking at quality of life in cancer patients, it isn't as good as you'd actually aspire to have."

A year of "exciting sleepless nights" has followed that initial meeting, Schiffman says, as he and Schroeder negotiate the nine-hour time difference to collaborate via Skype. "The technical challenge was, could we actually deliver these proteins to the cells of humans that are suffering from cancer and maybe … add functionality to these cancer cells so they would self destroy?" Schroeder says.

They believe they can, and the potential was too exciting to leave to the pace of academic research. "Industry and commercialization move faster than academics," Schiffman says. "One person with cancer is one person too many. I don't want to wait 20, 30 years to see this discovery impact people."

OFFICE OF THE SPOKESPERSON, TECHNION

THE VISION: "Our dream is really a world without cancer," says Avi Schroeder, Schiffman's collaborator on a new nanomedicine.

Together, they have founded a startup, PEEL Therapeutics ("peel" is the phonetic spelling of the Hebrew word for elephant), spun off through the University of Utah and Technion. They have synthesized elephant p53, or eP53, proteins and begun to encapsulate them in nanoparticles, and shown proof of concept on human cancer cells in vitro. If they have success in preclinical trials, on animals with cancer, they may release the drug for veterinary use as well. "We have great interest from people who have dogs and pets at home with cancer," Schroeder says.

(They both stress repeatedly that their labs are not experimenting on elephants, and certainly aren't giving cancer to elephants, of which they've been accused, Schiffman says. "We're not even asking for any extra blood draws," he says; the blood they analyze comes from routine draws by veterinarians at Utah's Hogle Zoo and the Ringling Bros. and Barnum & Bailey Center for Elephant Conservation, in central Florida, whose owner, the Feld Family, is helping to fund their academic research.)

Now the challenge is determining which elephant proteins make the best medicine. "There is something about the individual eP53 proteins and the increased number of eP53 genes turned into proteins that makes them more robust than the two copies of human p53," Schiffman wrote in an email. "We are trying to learn these answers so that we can choose the correct eP53 protein, or combination of eP53 proteins." He and Schroeder estimate they're three to five years away from human clinical trials.

Ed Forman likens the nascent field of nanotechnology to the development of immunotherapy and targeted gene therapy, both of which "exploded" over the course of his career treating cancer patients. "Nano is going to explode," he says. "It's a can't-miss field."

Schiffman tries to be circumspect. For one thing, he knows that many new drugs will never reach the clinic. "As a clinician, I never want to overpromise and underdeliver to my patients," he says. "I don't want to make that claim that I think we have found the wonder drug, the silver bullet, the cure for cancer. What I am claiming is that elephants have figured it out, and now it's our job to figure out how to apply this to our patients."

COMPUTATIONAL BIOLOGY

$11.5 million

TOTAL FUNDING, OVER FIVE YEARS.

PRINCIPAL INVESTIGATOR:
David Rand, PhD

4+

JOBS CREATED

5

PROJECT LEADERS

BIOLOGY OF AGING

$9.7 million

TOTAL FUNDING, OVER FIVE YEARS.

PRINCIPAL INVESTIGATOR:
John Sedivy, PhD

3

PARTNERS

- Brown University
- New York University
- University of Rochester

CLINICAL AND TRANSLATIONAL SCIENCE

$19.5 million

TOTAL FUNDING, OVER FIVE YEARS.

COPRINCIPAL INVESTIGATORS:
James Padbury, MD, and
Edward Hawrot, PhD

10+

JOBS CREATED

4

PILOT PROJECTS TO BE FUNDED EACH YEAR

6

PARTNERS

- Brown University
- University of Rhode Island
- Care New England
- Lifespan
- Providence VA Medical Center
- Rhode Island Quality Institute

BY DAVID ORENSTEIN

RESEARCH BOOM

UNPRECEDENTED FUNDING EXPANDS THE DIVISION'S PROFILE.

As federal grant funding goes, the past year was one for the record books. An $11.5 million Center for Biomedical Research Excellence (COBRE) in computational biology was followed closely by $19.5 million to launch the Rhode Island Center for Clinical and Translational Science. Then in August, a $9.7 million Program Project Grant boosted research efforts related to the biology of aging. The new investments from the National Institutes of Health were a major boon for the Division's strategic initiative to increase clinical and translational research.

Life sciences writer David Orenstein explains what these grants mean for Brown, Rhode Island, and the patients who may someday benefit from their resulting discoveries. *—Kris Cambra*

COMPU WHAT?

"There's data and then there's information," says David Rand, PhD, the Stephen T. Olney Professor of Natural History, chair of the Department of Ecology and Evolutionary Biology (EEB), and director of the new COBRE. "Turning data into information you can use for something is what computational biology is all about."

The five-year, $11.5 million NIH grant will expand Brown's research in computational biology and launch the center, which will support five early-career faculty members as they tackle the genomics underlying diseases such as cancer, preeclampsia, and severe lung infections.

NEW PROJECTS, NEW CAPABILITIES

To date, computational biology researchers have had to develop their own in-house technical capabilities, but the COBRE will build a research core where expert staff will be able to code technical implementations for the center's researchers, freeing valuable time and resources in their own labs. This data analysis core will be codirected by associate professors Casey Dunn, PhD, from EEB and Zhijin (Jean) Wu, PhD, from the Department of Biostatistics in the School of Public Health.

The center will directly fund research of five teams of scientists in which younger faculty members will pursue studies related to human disease under the mentorship of two more senior professors: one with expertise in computing and mathematics and another with expertise in biology and medicine. An administrative core will support new seed projects to increase the breadth of users across the University.

THE FIVE PROJECTS:

- **Amanda Jamieson**, PhD, assistant professor of molecular microbiology and immunology (MMI), will study bioinformatics data to identify the genomic and cellular mechanisms underlying tolerance of viral and bacterial coinfection in the lung.
- **Nicola Neretti** PhD'01, assistant professor of biology, will use bioinformatics screening of a fruit fly model to identify new drug targets for extending healthy lifespan.
- **Sohini Ramachandran**, PhD, Manning Assistant Professor of EEB, will develop new computational and analytical methodologies to identify risk genes for leukemia that differ in incidence across ethnic groups and genders.
- **Alper Uzun**, PhD, assistant professor of pediatrics (research), will test the hypothesis that variants in a refined set of gene candidates underlie the complex basis of preeclampsia.
- **Shipra Vaishnava**, PhD, assistant professor of MMI, will study the spatial variation in the gut microbiome in response to antimicrobials and immunity pathways that can inform aspects of human irritable bowel disease.

MIKE COHEA (2); STEPHANIE EWES; D. ECE GAMSIZ UZUN; ADAM MASTOON

AN AGE-OLD PROBLEM

Over the last few years, scientists—including a team at Brown—have produced mounting evidence that mobility within the genome of potentially harmful DNA snippets, called retrotransposable elements, may cause health problems associated with aging (see *Brown Medicine*, Winter 2016).

With a new $9.7 million, five-year NIH grant, researchers at Brown, New York University, and the University of Rochester will collaborate to further strengthen the evidence and to advance toward the goal of applying the findings medically.

"There are a lot of provocative data and a lot of very cool ideas, but the issue now is how to nail this down," says John Sedivy, PhD, the Hermon C. Bumpus Professor of Biology and principal investigator of the grant. "Let's take the bull by the horns and see what's really going on. Is this a legitimate mechanism of aging and can we control it for therapeutic purposes?"

John Sedivy, PhD

JOHN MACIEL

"Let's take the bull by the horns and see what's really going on."

Previous studies have shown that as cells become senescent, they lose their ability to prevent retrotransposable elements from spreading into new places in the genome. In three new projects supported by two core facilities, the grant will spur the study of how retrotransposable elements function in cells and how their activity might cause specific diseases, and test possible ways of suppressing that activity.

The researchers will work with not only human cells but also mice and fruit flies (*Drosophila*), where they can ask more direct questions, obtain faster answers, and therefore better inform eventual interventions for people.

The results could shed important light on the health consequences of retrotransposable element activity, Sedivy says. Experiments demonstrating the best interventions could then be translated into future human clinical trials.

THE GRANT WILL FUND THREE PROJECTS:

- "Regulation of Retrotransposable Element Activity in Cellular Senescence and Aging," John Sedivy;
- "Regulation of Retrotransposable Element Activity in *Drosophila*," Stephen Helfand, MD, professor of biology;
- "Repression of Retrotransposable Elements by the Longevity Gene SIRT6," Vera Gorbunova, PhD, University of Rochester;

AND THREE CORES:

- Retrotransposon Engineering and Genomics Core, led by Jef Boeke, PhD, New York University School of Medicine;
- Mouse Intervention and Aging Core, led by Andrei Seluanov, PhD, University of Rochester; and
- Administrative Core, led by John Sedivy at Brown.

"Through RI-CCTS we will be better positioned to bring discoveries from the lab to the clinic, we'll have new tools to analyze and improve patient care, and we'll endow young scientists and clinicians with the skills to ask the most pertinent questions and to find the answers." *—Jack A. Elias, MD, dean of medicine and biological sciences*

LET'S GET CLINICAL

A Center for Translational Research grant from the NIH's National Institute of General Medical Sciences will establish the Rhode Island Center for Clinical Translational Science (RI-CCTS).

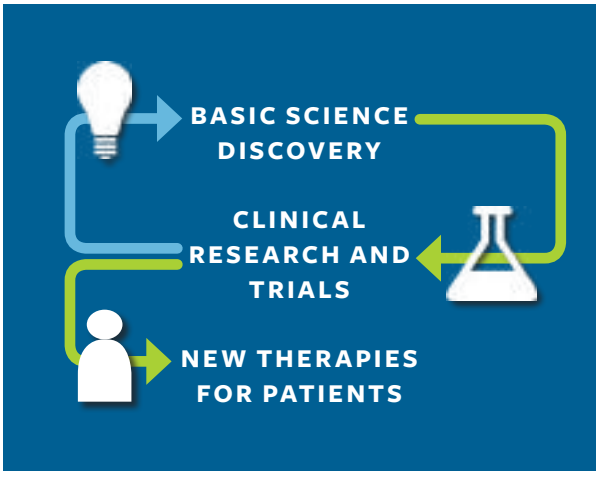
In this statewide collaboration, scientists can deliver the benefits of discoveries more quickly to health care providers and those clinicians can pose more pertinent questions to scientists when they work together closely with broad, deep, and cohesive services and support from their academic medical institutions. That's the vision for RI-CCTS.

When a biologist discovers how one protein interacts with another to cause disease and a biochemist synthesizes a compound to block it, those advances still need to be translated into a safe and effective drug therapy to help patients with the disease. But similarly, if an epidemiologist analyzing statewide health records notices that many people who have one disease also seem to have another health problem, the question of how those might be related can be translated back to scientists who can study the molecular biology at play.

The grant will allow RI-CCTS to create the educational and technical infrastructure needed to spur Rhode Island researchers to design, conduct, and analyze more medical studies, including treatment trials, that build on basic research. The center will also expand the access that medical and public health researchers have to population health data by working with the Rhode Island Quality Institute (RIQI).

To achieve those aims, RI-CCTS will create a robust foundation of services and supports and fund dozens of pilot projects and training grants to catalyze new clinical research, says James Padbury, MD, principal investigator and program director of the new center.

"This is an infrastructure grant," says Padbury, the William and Mary Oh–William and Elsa Zopfi Professor of Pediatrics for Perinatal Research at Alpert Medical School



and pediatrician-in-chief at Women & Infants Hospital. Rather than targeting a specific disease area, the grant provides the means to target a wide range of opportunities.

"Nonetheless, with these resources we will be able to support the kinds of advances that have already been taking place in our own research community," Padbury says. These include new therapies for asthma and muscular dystrophy, technology for cardiac regenerative medicine, methods for pain management, national trials on hormone therapy for menopause, malaria vaccine development, measuring the effect of home-delivered meals on loneliness in the elderly, and identifying the link between the mechanisms underlying preeclampsia and Alzheimer's disease.

THE GRANT WILL CREATE SEVEN CORES AND PROGRAMS:

- **Administrative Core:** Led by Padbury; Ed Hawrot, PhD, associate dean of biology and Alva O. Way University Professor of Medical Science; and Helen Leffers, MS, the core will manage, coordinate, and supervise RI-CCTS operations.
- **Pilot Projects Program:** Led by medical professors and Providence VA Medical Center physicians Sharon Rounds, MD, and Michelle Lally, MD, the core will provide 20 seed grants to multidisciplinary teams of junior researchers and mentors to do new clinical research. At least one project each year will be a clinical trial.
- **Biomedical Informatics Core:** Led by medical science professors Neil Sarkar, PhD, and Elizabeth Chen, PhD, this core will provide expertise, training, and technological resources to allow for big data analyses of medical and genomic data. Sarkar says the grant will accelerate the ability of the Brown Center for Biomedical Informatics to establish a multi-institutional framework for using electronic health data from Lifespan, Care New England, and the Rhode Island Quality Institute to enable novel biomedical research opportunities and to support enhanced patient care.
- **Clinical Research Design, Epidemiology, and Biostatistics Core:** Led by School of Public Health biostatistics professor Chris Schmid, PhD, and Lifespan Biostatistics Core Director Jason Machan ScM'98 PhD'02, this core will create a central "storefront" of statewide resources and services, mentoring and training, and tools and methods development for conducting well-designed clinical research.
- **Professional Development Core:** Led by Ira Wilson, MD, chair of health services, policy, and practice in the School of Public Health, the core will provide Mentored Research Awards to three scholars each year. It will also create training programs and develop a statewide mentoring network for clinical and translational research.
- **Clinical Research Resources and Facilities:** Led by Rhode Island Hospital Clinical Research Center Medical Director and Associate Professor of Medicine Bharat Ramratnam '86 MD'93, this core will unify the many successful clinical research enterprises among partner institutions (encompassing 700 researchers) into a general Clinical Research Center to share best practices and gain cost efficiency.
- **Tracking and Evaluation Core:** Led by University of Rhode Island pharmacy professor Cynthia Willey-Temkin, PhD, and Anthony Hayward, PhD, adjunct professor of pediatrics at Brown, this core will ensure that the center's work is aligned with program goals and community needs and uses resources wisely. The core will also track the center's output and monitor progress and practices.


James Padbury


Edward Hawrot

COURTESY WOMEN & INFANTS; PETER GOLDBERG

As more and more infants are born dependent on opioids, hospitals and researchers are working together to chart the best path to recovery.

Baby Steps

BY PHOEBE HALL
PHOTOGRAPHS BY KAREN PHILIPPI

Caitlyn O'Brien has been here before. That doesn't make it any easier.

It's mid-August, and the slim 29-year-old is eight months pregnant with her third child, and first son. She shifts uncomfortably in a floral-patterned chair at Women & Infants Hospital, her partner, Perry Fedorak, 26, by her side. They're preparing, for the second time, to bring a baby into the world dependent on opioids.

TEAM EFFORT: Perry Fedorak, Caitlyn O'Brien, and their children, Hailie and Bentley, at Women & Infants Hospital. Maternal-infant bonding can help speed a baby's recovery from neonatal abstinence syndrome.

"I'm scared," O'Brien says. "It sucks that he has to go through this for the decisions I made."

The medical director of the Newborn Nursery, Adam Czynski, DO, has a different take.

"It would be worse if you weren't taking medication," he says, referring to the methadone O'Brien needs to recover from an addiction to Percocet. If she'd detoxed, he says, she could have gone into withdrawal. "You'd be at risk of delivering preterm. Any parental stress can be bad," Czynski says. "You're making sure that his home is perfect."

But when he's born on August 25, after 38 weeks of daily methadone, Bentley Fedorak will go cold turkey. Then they'll wait for signs of withdrawal, such as fever, diarrhea, or tremors. The constellation of symptoms indicates neonatal abstinence syndrome (NAS), and it extends an infant's hospital stay by days or weeks as clinicians assess the severity of the withdrawal and administer an opioid—usually morphine or methadone—to ease the symptoms and wean the newborn off the drug.

"His body is making changes based on hormones and chemicals he's seen," Czynski tells the anxious couple. "Then when he's born, we'll tweak it. We'll slowly let him readapt back."

O'Brien and Fedorak saw this firsthand in January 2015, when their daughter, Hailie, was born. She stayed at Women & Infants for two weeks as doctors helped her taper off the opioids in her bloodstream.

"That was the hardest thing when I had Hailie, when my dad asked, why are you still here?" O'Brien says. "It felt like forever."

But she says it helped that Hailie is participating in a longitudinal study at Brown and Women & Infants, which O'Brien and Fedorak are doing again with their son. Though children have been born dependent on opioids for years, no one agrees on the best way to wean them off, so every hospital that treats NAS babies has its own standard of care. The trial now underway is assessing treatment strategies and long-term effects, an attempt to define a no man's land of personal experience, observational studies, and anecdotal evidence.

"If we can be of assistance to other people, if I could save someone else from going through the unknown, help find the best way to make sure the baby's comfortable, the mother's comfortable…" O'Brien trails off.

"Nobody wants their child to have to go through this."

OLD PROBLEM, NEW FACE

The escalating opioid epidemic has claimed millions of victims. In 2014, the Substance Abuse and Mental Health Services Administration reports, there were 1.9 million people in the US with a substance use disorder involving prescription pain relievers, and nearly another 600,000 involving heroin. Hundreds of thousands more use an opioid replacement therapy, such as methadone or buprenorphine, to treat their dependence.

"There was so much hatred and anger in this country against these women using drugs."

The sheer scale of the tragedy has done much to raise awareness about the disease of addiction, and that it can happen to anyone. That includes pregnant women. The rate of babies born in the US with neonatal abstinence syndrome has skyrocketed along with opioid use: from 2000 to 2012 it nearly quintupled, to 5.8 per 1,000 hospital births. According to a 2015 analysis in the *Journal of Perinatology*, that's 21,732 infants diagnosed with opioid withdrawal every year.

It's a distinctly regional issue: in New England, the NAS birth rate is 13.7 per 1,000, while in the Pacific states it's 3.0. "This is the only place I've encountered with a specific NAS unit in the nursery," instead of in the NICU, says Czynski, an assistant professor of pediatrics at Alpert Medical School who moved to Rhode Island from southern California in March. "In California, it's all methamphetamines," he says. "Here, everything's opioids, opioids, opioids."

Thirty years ago, it was cocaine. Barry Lester, PhD, professor of psychiatry and human behavior and of pediatrics at Alpert Medical School, has been studying the effects of drug use during pregnancy for decades. Babies exposed to cocaine in utero are born with the drug in their system, and right away they may have a high-pitched cry, tremors, and other symptoms that look like mild opioid withdrawal; as

the newborn metabolizes the cocaine, the symptoms go away.

But how did cocaine affect these children long term? Many people—doctors, lawmakers, the general public—were sure they suffered developmentally for it. "People didn't understand the consequences of prenatal cocaine exposure," Lester says. "There was a knee-jerk reaction: cocaine equals inadequate mother equals take the infant away and put it in foster care."

From 1993 to 2011 Lester ran the NIH Maternal Lifestyle Study, which followed almost 1,400 kids nationwide to document the long-term effects of prenatal cocaine exposure. Their findings suggested that poverty and other chronic stresses, not just prenatal drug exposure, adversely affected those children's behavior, educational achievement, and other factors.

"There was so much hatred and anger in this country against these women using drugs, which has improved, I have to say," Lester says. "Research has shown that addiction is a disease of the brain. ... This is not about women willfully doing harm to their babies. It has helped dispel myths and deep-seated prejudices and shift policy from punitive to treatment approaches."

WHAT IS BEST?

Around the time Lester began recruiting for the Maternal Lifestyle Study, neonatologist Mara Coyle MD'86, P'15ScM'16 became the director of the level II nursery at St. Luke's Hospital in New Bedford, MA. Right away Coyle was caring for patients with NAS, whose mothers had taken heroin or methadone. "Prescription opiates were not an issue yet," she says. Twenty years later, "the face of opioid dependence has changed"—and so has treatment.

NAS is related to exposure in the latter stages of pregnancy; what opioid a woman is taking at that time—street drugs, replacement therapy like methadone or buprenorphine, or a prescription—will impact the degree to which the newborn will experience withdrawal.

But there's no recognized standard of care for NAS treatment, leaving hospitals to figure it out on their own. Most use morphine or methadone; diluted tincture of opium (DTO) has fallen out of favor. Some administer sedatives like phenobarbital or clonidine to reduce opioid dosage. How much medication infants receive, and for how long, depends on the results of a scoring system that attempts to quantify NAS symptoms to standardize treatment, yet which every hospital interprets differently.

"It's not because there's been an absence of research," Coyle says of the varied approaches. "There have been dozens of studies attempting to define which is the best treatment strategy for a standard of care. But what is 'best'? Cut the length of stay? You can quantify that. Or is it long-term outcome? We don't have the information, we don't have good follow-up data, which ultimately is the more important issue."

Coyle, a professor of pediatrics (clinical) at Alpert Medical School, who considers Lester a mentor, has published numerous papers since the early 2000s on treatment strategies for moms and babies and their effect on the newborns' symptoms and length of hospital stay. For the double-blind, multisite MOTHER study, published in the *New England Journal of Medicine* in 2010, Coyle evaluated neonatal outcomes for exposure to buprenorphine and methadone, the more widely recommended treatment. In an earlier trial, in *Pediatrics*, she investigated whether phenobarbital alleviated NAS symptoms.

"I don't think newborn treatment should be one-stop shopping," Coyle says. "It's not the exact same dosing strategy for each patient, because they have different levels of dependence." She found that giving babies phenobarbital helped wean them off opioids, and go home, sooner. Meanwhile the MOTHER trial showed that infants who had been exposed to buprenorphine needed less morphine and the duration of treatment was shorter than those exposed to methadone.

"That's important information [for mothers] to have," says Coyle, who now sees patients at Women & Infants. "But they're not the same drugs. ... Buprenorphine has a ceiling of effect, meaning more drug doesn't mean more opioid effect, so if you're seriously addicted you may not be a candidate for buprenorphine because you could go into immediate withdrawal. So it's not a replacement for methadone."

A key part of Coyle's work is prenatal consultation, to counter misinformation about replacement therapy and NAS. Most women don't want to be on any drug when they find out they're pregnant, she says; they want to quit then and there. "They don't want their baby to go through withdrawal," Coyle says. While some recreational users may be able to quit, she says the majority will relapse, which is why she recommends replacement therapy; piling the agony of

detox onto the normal discomforts of pregnancy is simply unrealistic for most women.

"The first thing I tell a patient is congratulations for being in treatment. It's far better to be in treatment than to be using," Coyle says. As for NAS, she tells moms, "It's a medical condition, it's short lived, and we're going to help your baby get through that."

Coyle focuses on the certainties of NAS during prenatal consults: withdrawal symptoms, how they're assessed and treated, how long treatment might take, the benefits of breastfeeding. While opiate-exposed newborns have a greater incidence of complications, like low birth weight and respiratory problems, she says she doesn't discuss these because not all babies will experience every problem.

A 2015 retrospective study in the *Journal of Perinatology* that Coyle co-authored with developmental pediatrician Jo-Ann Bier, MD RES'88 F'90, an assistant professor of pediatrics at Harvard Medical School, noted smaller head circumferences and lower motor skill development among infants exposed to high doses of maternal methadone. "This shouldn't be interpreted as causal, but merely an observation of a select group of opiate-exposed newborns," Coyle wrote in an email. "A prospective blinded study to specifically look at these outcomes would better confirm these findings."

"It's a medical condition, it's short lived, and we're going to help your baby get through that."

The need for such research is critical, Lester says. "There are no studies in the literature of the long-term developmental outcome of babies who went through NAS. Period," he says. "One of my PowerPoint slides says, 'Summary of outcome studies for NAS kids,' and there's nothing on the slide."

TEAM APPROACH

Now an outcome study is underway. Lester is coprincipal investigator, with Jonathan Davis, MD, professor of pediatrics at Tufts, of an NIH-funded, double-blind, randomized controlled trial at several US hospitals (including Women & Infants, where Czynski is the site PI) to compare methadone versus morphine for the treatment of NAS; tease out long-term effects of prenatal opioid exposures; and look for genetic, epigenetic, and newborn neurobehavioral markers that could predict susceptibility to and severity of withdrawal symptoms.

"At least 20 to 25 percent of opioid-exposed kids do not develop NAS. Why not?" Lester says. "To some of us, that's the most interesting question."

Pregnant women enrolled in the study are taking methadone, buprenorphine, or pain medication; their babies will be treated with either morphine or methadone if they develop NAS, and researchers will follow the children for 18 months to document developmental milestones. They hope their findings will help guide clinical practice by determining the short- and long-term effects of these treatments.

"There's a lot of regionalization in what people use to treat NAS," Czynski says. "In California we used methadone, morphine, opium—personally, I've treated kids with everything." What's more important than the type of medication is that a hospital adheres to a standardized treatment protocol, rather than letting provider preference guide each child's care. Researchers at six Ohio children's hospitals demonstrated that in a paper in *Pediatrics* in 2014: whether they used morphine or methadone, protocol-based weaning cut the treatment time nearly in half and the infant's hospital stay by a third.

Onset of withdrawal symptoms may take one day or several, and it begins abruptly. "Everything's great and suddenly it's not," Czynski says. Hospitals use a tool—usually based on the Finnegan scoring system—to rate, at regular intervals throughout the day, the severity of various central nervous system, respiratory, gastrointestinal, and other symptoms, and tally the Finnegan scores; a total of 8, Czynski says, "is the beginning of the gray zone; 12 is clearly the zone of withdrawal."

At that point the baby starts receiving medication, with dosage depending on his weight and how long it takes to "capture" him, meaning withdrawal symptoms cease and he's stable for 48 hours; then weaning can begin. "The poster child for withdrawal will wean down in a predictable fashion," Czynski says. But things don't always go as planned: if symptoms return, dosage is increased until the baby is captured again, and the taper restarts. Though most babies go

home after two or three weeks, a few may be stuck in the hospital for a month or more.

Bentley Fedorak showed signs of withdrawal, including tremors and mottling, the day after he was born, says his mom, Caitlyn O'Brien. "He didn't want to be not held. A normal newborn can soothe themselves. But he would just be upset until you picked him up again," she says. It took two weeks for him to stabilize, so the taper could finally begin. "It was a roller coaster to get him where he needs to be."

Close maternal involvement benefits all parties: mom, baby, and hospital staff. "If a mother can be part of the team, she can give information to nurses about how the baby is doing," Coyle says. When families see withdrawal symptoms for themselves, "they want the baby on medication. Having them here and witnessing helps them understand."

Citing a recent *Pediatrics* study that demonstrated reduced costs and length of stay when moms could room in with their infants, Coyle adds, "All of us are working to find space to keep mothers and infants together."

ALL IN THE FAMILY: Adam Czynski, with Bentley Fedorak at Women & Infants, says mothers are the "most important" members of the NAS care team.

A few years ago, Women & Infants began offering private rooms, at no charge, to some mothers of NAS infants. "Caring for these babies can be challenging," nurse manager Donnalee J. Segal, MSN, says. "This model of care allows for mom to care for and learn about her baby under the guidance of our nursing staff." Nonpharmacological interventions like rooming in, skin-to-skin contact, and breastfeeding not only aid bonding, they may delay onset and reduce severity of NAS symptoms. "We feel that the best thing for these babies is to keep them together" with their mothers, Segal says. "Our hope is that babies will require less medication and go home sooner."

Kimberly Pelletier, of Central Falls, RI, got a private room at Women & Infants with her son, Preston, who was born in July. "Now that I've been with him every day I just feel so much better," she says, cradling the sleeping 10-day-old on a loveseat near the nursery. She says when a nurse

had told her Preston was having a rough day, "he saw me, I picked him up, and he was fine within a minute." Pelletier strokes his face. "I think he just knows it's me. He really does."

Since Czynski joined the hospital earlier this year, he's instituted NAS rounds, every afternoon at 1:30, with the core group of caretakers: physicians, nurse practitioners, social workers, occupational therapists—and families, if they can. "The most important person in the whole entire spectrum is the mother," Czynski says. "She can really tell us the subtleties of their child. If she tells you there's something different about their child, there's something different about their child, and we need to respect that."

O'Brien—who has two daughters at home, Hailie, now a toddler, and Alexis, 10, who's just starting fifth grade—can't stay in her cozy private room with Bentley every night. But she and Perry Fedorak try to attend daily NAS rounds. "Sometimes it's a lot of people filing into this tiny little room," she laughs.

The regular access to so many experts helped them understand why their son needed phenobarbital to calm his withdrawal symptoms. "I always looked at it like, if he's not having seizures, why give him a seizure medicine?" O'Brien says. "It wasn't until we gave him the phenobarbital, that's when you could tell it was that little bit he needed to really be better."

But close involvement can be challenging for some women on opioid replacement therapy, who visit a clinic every day to take their medication and attend counseling sessions. Furthermore few hospitals have the facilities to care for NAS infants, so some mothers have a long drive to get to their home clinic. O'Brien has to go to Woonsocket, a half-hour drive, every day; other women travel greater distances. "A lot of times, these patients take buses," Segal says. "They could be gone three-quarters of the day just to get their medication."

Pelletier, who was used to a daily 45-minute bus trip from home to her South Providence methadone clinic, had a much shorter ride while Preston was in the hospital. "I don't want to get back on the bus," she says. "Especially when you just had a baby and—I'm not healed, you know?" But reflecting on the long bus commutes she's had over the past four years, when she's lived even farther from the methadone clinic, she adds, "These are the sacrifices you have to make, unfortunately."

Segal and Czynski want to minimize those sacrifices. They're working to partner with a nearby clinic that could administer women's medication while they're staying at Women & Infants. "You help facilitate their recovery while also caring for their child," Czynski says. "The mother and baby collectively are one team. You have to maximize treatment because that's the best thing for the baby."

Jo-Ann Bier's patients at her Boston Children's Hospital developmental follow-up clinic in North Dartmouth, MA, include children exposed to prenatal opioids. Several years ago she applied for, but didn't get, a grant to offer a developmental follow-up program at a local methadone clinic. "We would have had a great show rate," she says. She agrees with the comprehensive approach Czynski is advocating. "If you can take care of mothers and their babies together, and their fathers if they're involved, that would be helpful," Bier says. "These families benefit from intensive support."

"The changes that Dr. Czynski is making at Women & Infants are truly sea changes that could very well provide a new model of care for the entire country," Lester says.

CULTURAL SHIFT

In his longitudinal studies of prenatal exposure to cocaine and other drugs, "if there's one thing we learned, it is that the environment has as much to do with the outcome of these kids as these drugs," Lester says. "The environment that some of the current NAS kids are growing up in can be quite positive."

Lester draws a contrast between pregnant women using illicit drugs and those on opioid replacement therapy. "You're not taking street drugs, you're taking care of yourself," he says of the latter group. "A lot of women in methadone maintenance go to the clinic, they take their dose, they go to work. They can live normal lives and provide better environments for their kids."

"Lots of data show that women on methadone are healthier, have a lower incidence of infections and complications, are more compliant, and are more likely to get prenatal care," Coyle says. But many states, including Rhode Island and Massachusetts, require hospitals to report to child welfare services any substance use during pregnancy, including replacement therapy or an opioid prescription deemed medically necessary. For women who aren't in treatment or are concealing their substance use, and haven't learned about NAS and that their baby won't go home right away, she says, "It's like they're hit between the eyes with a two-by-four."

Heather Howard, PhD, LICSW, works with families of

NAS infants at Women & Infants to make sure they have the support they need when their children go home. "There are no studies that say if you have a positive tox screen, then you can't parent," she says. But guilt, coupled with fear of the child welfare system, "which is very real," may deter mothers from seeking prenatal care.

"When a woman becomes pregnant, she becomes more ... treatment ready," Howard says. "It's a great window to help someone." As a patient advocate, she supports mothers who want to stay with their babies, makes sure they're getting the treatment they want, and connects them with programs like Healthy Families America, which sends trained staff to families' homes to model positive parenting and, she says, helps more parents and children stay together.

"There are no studies that say if you have a positive tox screen, then you can't parent."

Despite those interventions, Howard says she sees child welfare services separate mothers from babies up to three times each week. She talked about one woman who was on methadone maintenance and staying with her newborn son at Women & Infants this summer as he recovered from NAS. "She's doing everything she needs to do, she's bonded with the baby," Howard says. But in August, the woman temporarily lost custody of her son.

"We need to think about this as a public health concern, rather than a moral failure," Howard says. "That's going to take a major cultural shift." She, Coyle, and Segal are members of Rhode Island's NAS Task Force; among its goals are to standardize treatment protocols at all birthing hospitals in the state and to recommend screening of all pregnant women for opioid use.

The task force also wants to rekindle the Vulnerable Infants Program (VIP), a hospital-based program that Lester developed in the late 1990s to coordinate drug treatment plans with a special Family Treatment Drug Court and keep more families together. The VIP was supported by grants, yet despite its success the state didn't step up when the funding ran out. "You can't sell prevention. We've been trying to do that for years and years," Lester says. He's helping the task force develop a similar program specific to the opioid epidemic, write supportive legislation, and ensure a permanent funding mechanism.

"There are still plenty of women being prosecuted," Lester says. "There's still a fair amount of prejudice and hatred." But judicial bias against mothers rarely serves the children the courts are aiming to protect. "If the kid is in foster care and they go from one foster home to another, that kind of disruption has a really big impact—especially as attachments are developing, as emotional lives are developing," he says.

Czynski envisions a comprehensive NAS unit at Women & Infants that better engages and prepares families for the transition home. "There's work in progress for more of a multidisciplinary approach ... to get them plugged into mental health, medical, and social services support," he says, such as group counseling at the hospital and home visitation programs like Healthy Families America. "The medical side doesn't capture the complete needs of a family," Czynski says. "We're just one time point in this child's life and journey."

FAMILY TIES

When Hailie Fedorak comes to the hospital in early September to visit her new brother, Bentley, she toddles around the room and out into the hallway, intent on inspecting everything and every person in the vicinity, her parents patiently steering her back to the room when she strays too far. But when she's with Bentley she stops and leans close, taking it all in, this new little person.

"It's funny to watch her with the baby. She's trying to figure him out," Caitlyn O'Brien says. She says she was pleased at Hailie's 18-month evaluation for the longitudinal NAS study, where she demonstrated above-average problem solving and word acquisition abilities. "She's a thinker. Nothing gets past her," her mom says.

"I got pregnant with Hailie four months after I got clean. That kept me going," O'Brien says. Now she's also going to Narcotics Anonymous meetings, finding shared experiences with other people and focusing on her recovery. "Nobody wants to be in the situation I'm in," she says. "But the fact of the matter is I'm in it and there's nothing I can do but push forward."

ALUMNI ALBUM

CHECKING IN WITH BROWN MEDICAL ALUMNI

COMMENCEMENT
Greg Walker MD'16 accepts a warm hug on his big day.

DAVID DELPOIO

CLASS NOTES
ALUMNI

1975

Arthur Horwich '72 ScMD'14 hon., the Sterling Professor of Genetics and professor of pediatrics at the Yale School of Medicine, and two other researchers received the 2016 Albany Medical Center Prize in Medicine and Biomedical Research for their complementary discoveries related to the mechanisms of protein folding. Arthur has studied ALS for several years, focusing on protein quality control mechanisms. He also is an in-

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vestigator for the Howard Hughes Medical Institute and a member of the National Academy of Sciences and the Institute of Medicine. He has received numerous honors, including the 2011 Lasker Award for Basic Medical Research and the 2012 Shaw Prize in Life Science and Medicine.

1976

David Brooks was named a 2016 Distinguished Clinician of Brigham and Women's Hospital at a ceremony in February. David is a senior surgeon specializing in gastrointestinal and general surgery and an associate professor of surgery at Harvard Medical School.

1978

Roy Poses '74, a clinical associate professor of medicine at Alpert Medical School, published an opinion piece, "How Employed Physicians' Contracts May Threaten Their Patients and Professionalism," in *Annals of Internal Medicine* in March. Roy, an internist, is the president of the Foundation for Integrity and Responsibility in Medicine.

1979

Preston Calvert '76 and Margaret Guerin-Calvert '76 announce the marriage of their daughter, Kate Guerin-Calvert, to Farzad Sharafi in September. Preston is past president of the Brown Medical Alumni Association board of directors and serves on the board of the North American Neuro-Ophthalmology Society.

Yul D. Ejnes was appointed to the board of directors of the American Board of Internal Medicine.

1983

Ralph Panos '80 advises on COPD for the clinical and medical advisory board of a drug to treat antibiotic-resistant infections in lungs at Arch Biopartners of Toronto. Ralph is chief of medicine at the Cincinnati Veterans Affairs Medical Center and a professor of medicine, pulmonary, critical care, and sleep medicine at the University of Cincinnati College of Medicine.

1985

Yul D. Ejnes '82 RES'89, an internal medicine specialist and clinical associate professor of medicine at Alpert Medical School, was appointed to the board of directors of the American Board of Internal Medicine. A cofounder of Coastal Medical, a private practice in Cranston, RI, he has served on the ABIM's Internal Medicine Specialty Board and in leadership positions on numerous other national and state professional organizations.

Robert Kim, MBA '82 was named chief medical officer at Apellis Pharmaceuticals, a clinical stage biopharmaceutical company in Crestwood, KY. Bob has worked at several firms in the life sciences industry, most recently as CMO and head of R&D at Vision Medicines. He's also an associate clinical professor of ophthalmology at the University of California, San Francisco, where he continues to see patients.

1986

Tina Cheng, MPH '83 was named the Given Foundation Professor of Pediatrics and director of the Department of Pediatrics at the Johns Hopkins University School of Medicine; pediatrician-in-chief of The Johns Hopkins Hospital; and codirector of the Johns Hopkins Children's Center. Her clinical work, teaching, and research focus on child and adolescent health disparities. She has been the principal investigator on numerous federal and foundation grants, and has conducted randomized trials of primary care and emergency department-initiated interventions to promote positive youth development and family health.

Robert W. Panton '83 MMS'86 was re-elected vice speaker of the Illinois State Medical Society. An ophthalmologist, he practices in Elmwood Park, IL, and serves on the medical staffs at Gottlieb Memorial Hospital, Rush Oak Park Hospital, Westlake Hospital, and West Suburban Hospital Medical Center. He's a member and past president of the Chicago Medical Society.

CAROLINE GOLLUB

OPENING CELEBRATION: Governor Gina Raimondo received the W.W. Keen Award from the Brown Medical Alumni Association.

ALUMNI ALBUM

1988

Thomas Bledsoe, clinical associate professor of medicine at Alpert Medical School and a primary care physician at the Governor Street Primary Care Center of University Medicine in Providence, was elected to the board of regents of the American College of Physicians in May.

1992

Roger Waltzman '88 is the chief scientific officer of Jaguar Animal Health, a San Francisco-based company that develops gastrointestinal products for pets, horses, and other animals. A medical oncologist, he also worked in drug development for Novartis Pharmaceuticals, most recently as head of development for antimalarials. At Jaguar, Roger will lead development efforts for drugs to treat equine gastric ulcer syndrome and chemotherapy-induced diarrhea in dogs.

1993

Galen Henderson was named a 2016 Distinguished Clinician of Brigham and Women's Hospital at a ceremony in February. Galen is the director of the Neurocritical Care and Neuroscience ICU and an assistant professor of neurology at Harvard Medical School. He is also president-elect of the Brown Alumni Association and sits on the board of the Brown Medical Alumni Association.

Albert Woo is the chief of pediatric plastic surgery at Hasbro Children's Hospital.

COMMENCEMENT: Associate Dean for Medical Education Allan R. Tunkel, MD, PhD, left, and Associate Professor of Medicine Dominick Tammaro '81 MD'84 line up for the procession.

DAVID DELPOIO

1995

Sara Fazio '91 was elected chair of the board of the Alliance for Academic Internal Medicine, the national umbrella organization representing academic departments of medicine. She is the associate director for Innovation in Medical Education and an associate professor of medicine at Harvard Medical School. Sara practices general internal medicine at Beth Israel Deaconess Medical Center.

John Pezzullo RES'00 was elected president of the board of directors of Rhode Island Medical Imaging. A radiologist who specializes in body imaging with an emphasis on MRI, John has been on the board since 2007. He is also a clinical associate professor of diagnostic imaging at Alpert Medical School.

1997

Geoffrey Gilmartin is the chief development officer at Proteostasis Therapeutics in Cambridge, MA. Previously a clinical research physician for Global Medicines Development at AstraZeneca, Geoff is an attending at Beth Israel Deaconess Medical Center's ICU, where he has served on the pulmonary leadership team, and an instructor in the Division of Sleep Medicine at Harvard Medical School.

1999

Albert Woo '95 RES'05, a plastic and reconstructive surgeon who treats children and adults affected by a variety of facial and body malformations, is the chief of pediatric plastic surgery and director of the Cleft and Craniofacial Cen-

COOKE LECTURE: David M. Carlisle, PhD MD'81, president and CEO of Charles R. Drew University of Medicine and Science, presented the Commencement Forum "Health Care 5.0."

ter at Hasbro Children's Hospital. He is on the faculty of the Department of Surgery and director of the craniofacial program at Alpert Medical School.

2002

Amar Desai, MPH '97 rejoined DaVita HealthCare Partners Inc. in June as president for HealthCare Partners California–Coastal Region. He returned to DaVita, where he'd previously served in other executive roles, after more than two years as CEO of the University of Southern California Medical Group and Ambulatory Services. Board certified in internal medicine and nephrology, Amar is an associate clinical professor of medicine at the Keck School of Medicine of USC.

2003

Barrett Bready '99 retook the helm last year as CEO of Nabsys, a genomics firm in Providence, which he founded in 2005. He is an adjunct assistant professor of molecular pharmacology, physiology, and biotechnology at Brown, where he teaches biotechnology management, and a commissioner on the I-195 Redevelopment District Commission in Providence. In August, Barrett and his wife, **Alma Guerrero** '09 MD'15 RES'18, hosted Sen. Tim Kaine, the Democratic candidate for vice president, at a fundraiser at their home in Newport. Alma is completing Alpert Medical School's internal medicine residency program at Rhode Island Hospital.

Terrance Healey '98 RES'08 was elected secretary of the board of directors for Rhode Island Medical Imaging. An assistant professor of diagnostic imaging at Alpert Medical School and the director of thoracic radiology at Rhode Island Hospital, he's been a member of RIMI's board since 2014.

2004

Dara Huang '99 MMS'04 is a culinary medicine specialist whose first book, *The Culinary Medicine Cookbook*, will be published in spring 2017. She practices internal medicine and nephrology in New York City, where she is affiliated with Mount Sinai, Beth Israel, and

COMMENCEMENT: Front, left to right, Bethany Gentilesco, MD, and Nicolette Rodriguez '11 MPH'16 MD'16. Back, Fred Schiffman, MD, and Amanda Dowden '12 MD'16.

CAROLINE GOLLUB; DAVID DELPOIO

Lenox Hill hospitals. Before medical school, Dara earned a culinary arts degree at the California Sushi Academy and worked as a sushi chef. Learn more about her work at culinarymednyc.com.

2005

Paul George, MHPE '01 RES'08 is assistant dean for medical education and an associate professor of family medicine at Alpert Medical School. Paul is the director of the second-year curriculum and the Primary Care-Population Medicine Program. He holds a master's degree in health professions education from the University of Illinois College of Medicine.

2007

Scott Zimmerman, cofounder and CEO of Xola, which develops booking and marketing software for the tours and activities market, announced in April that the company had raised $5 million in a Series A funding round, led by the Japanese firm Rakuten Travel.

2009

Marie Audett '05 and Adam Knapp were married May 15 at the Ocean Cliff Hotel in Newport, RI. Marie is a general surgeon at the Wright-Patterson Air Force Base Medical Center in Dayton, OH, where Adam, a former staff sergeant in the US Air Force, is a radiation dosimetrist. They live in Beavercreek, OH.

2011

David Washington '07 RES'15 and his wife, Emma Welch '07, welcomed their first child, Aurora Mae, in August 2015. Dave is an instructor of medicine at Boston University School of Medicine.

2012

Shilpa Gowda, MPH '08 is completing her clinical fellowship in occupational

REUNION DINNER: Uzoma Ukomadu '00 MD'06, Antonio Cruz MD'06 RES'10, and Keith Corl MD'06 RES'10, left to right, represent the 10th Reunion class.

Front row, left to right, Dan Medeiros MD'86; Andree Heinl '83 MD'86, PMD'15, '18; Marlene Cutitar '83 MD'86 RES'92; Hon Lee '82 MD'86, P'17MD'21, '18. Back row, Diane Scott '75, P'05MD'09, '09MD'13; Mark Scott '75 MD'86, P'05MD'09, '09MD'13; Robert Panton '83 MMS'86 MD'86; and Blaze Lee '17 MD'21.

Left to right, Yeuen Kim '92 MD'96, Victoria Reyes-D'arcy '92 MD'96, Meg Rydell MD'96, and Melissa Gaitanis '92 MD'96.

CAROLINE GOLLUB (3)

and environmental medicine at the University of Washington, where in June she earned her Master of Public Health. She received the Outstanding Master's Student Award from the Department of Environmental and Occupational Health Sciences. She has presented her master's thesis, on ambient air pollution and lung cancer risk, at national and regional conferences. This fall she began work as a health hazard evaluation physician for the National Institute for Occupational Safety and Health.

Jay Levin '08 RES'16 F'17 and his wife, **Michal Ganz**, MD F'17, welcomed Joseph Ganz Levin to the world on February 26. As a neurology resident at Alpert Medical School, Jay was chosen by his peers to receive the 2016 Humanism and Excellence in Teaching Award. He is now completing his clinical neurophysiology fellowship, while Michal is a gastroenterology fellow at Alpert Medical School.

2013

John Luo '09, president and founder of Doctor's Choice, an organization that helps patients select Medicare coverage, was named to the *Providence Business News* 40 Under Forty list for 2016.

Kartik Venkatesh '06 PhD'11, an obstetrics/gynecology resident at Harvard Medical School, was named one of five 2016 Quilligan Scholars by the Pregnancy Foundation of the Society for Maternal and Fetal Medicine. The two-year program offers mentoring and educational opportunities for residents who show potential to be leaders in the field of maternal-fetal medicine. Kartik's interests are antidepression treatment and preterm births, postpartum depression in adolescent mothers, and the progression of HIV/AIDS treatment in resource-limited settings in India.

John Luo was named to the *Providence Business News* 40 Under Forty list for 2016.

COMMENCEMENT: Michael Allen '11 MD'16 shows off his diploma.

President of Tougaloo College Beverly Wade Hogan was on hand for graduation.

DAVID DELPOIO (2)

ALUMNI ALBUM

COMMENCEMENT: Will Mangham MD'16 walks through the Van Wickle Gates and into his future as a physician.

2015

Alma Guerrero '09 RES'18. See **Barrett Bready** '99 MD'03.

Joy Liu '11 and **Jovian Yu** '12 MD'16 were married June 4 in Newport, RI. Joy is in her second year of her medicine residency at Beth Israel Deaconess Medical Center; Jovian began his internal medicine residency at Yale-New Haven Hospital in June.

2016

Jovian Yu '12. See **Joy Liu** '11 MD'15.

2017

Sean R. Love and Laura E. Thompson were married April 30 in Chapel Hill, NC. The couple met as undergraduates at the University of North Carolina. Sean is beginning his fourth year at Alpert Medical School and Laura is an associate director at Year Up in Boston.

RESIDENTS

1983

David E. Wazer, MD, is the new director of the Lifespan Comprehensive Cancer Center. He is also radiation oncologist-in-chief at Rhode Island Hospital, The Miriam Hospital, and Newport Hospital, and professor and chair of the Department of Radiation Oncology at Alpert Medical School.

1998

Christine Emmick, MD, joined the Center for Breast Care at University Surgical Associates in Providence. A general surgeon for 18 years, she focuses on patients with malignant and benign breast disease. She also sees patients at The Miriam Hospital and is a clinical assistant professor of surgery at Alpert

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DAVID DELPOIO

Medical School. Christine; her husband, **Michael Belanger**, MD F'99, a partner at the Center for Orthopaedics in Johnston, RI, and a clinical assistant professor of orthopaedics at Alpert Medical School; and three children live in Cumberland, RI.

David Holub, MD, received the Distinguished Physician Award at Highland Hospital in Rochester, NY. The honor is presented annually to a physician whose work is "exemplary and extraordinary." David is an assistant professor in the Department of Family Medicine at the University of Rochester School of Medicine and Dentistry and the associate director of the Family Medicine Residency. He and his wife, Eva Galka, MD, a surgeon, have two children.

2003

Peter Evangelista, MD, was elected treasurer of the board of directors for Rhode Island Medical Imaging. A specialist in musculoskeletal imaging at RIMI, he joined the board in 2013. He is an assistant professor of diagnostic imaging at Alpert Medical School and the director of musculoskeletal radiology at Rhode Island Hospital.

2007

Melinda Hooton, MD, became medical director of Providence Community Health Centers in June. She worked in community-based primary care programs in California and Boston before returning to Rhode Island, where she was medical director at Rhode Island Hospital Center for Primary Care before assuming her new role. Melinda is a clinical associate professor of medicine at Alpert Medical School.

Taro Minami, MD, director of simulation and ultrasound training and fellowship site director for pulmonary and critical care medicine in the Division of Pulmonary, Critical Care, and Sleep Medicine at Memorial Hospital of Rhode Island, received the division's Teacher of the Year Award at the Brown Chest Conference in June. Taro is a clinical assistant professor of medicine at Alpert Medical School.

Corey Ventetuolo, MD, MS, is the director of clinical research for the Division of Pulmonary, Critical Care, and Sleep Medicine at Rhode Island Hospital and The Miriam Hospital and an assistant professor of medicine and of health services, policy, and practice at Brown. This year she also received the Beckwith Teaching Award and the Internal Medicine Award as a teacher of the year. She studies the influence of gender and sex hormones on pulmonary vascular and right heart function, as well as unique predictors of right ventricular function. Corey lives in Bristol, RI.

2009

Asma Latif, MD, joined the staff of Sturdy Hematology & Oncology Associates in Attleboro, MA. A specialist in breast cancer and gynecological oncology, including ovarian, uterine, and cervical cancers, she previously worked at the Memorial Sloan Kettering Cancer Center. She completed her hematology and medical oncology fellowship through Mount Sinai School of Medicine.

Sean R. Love and Laura E. Thompson were married April 30 in Chapel Hill, NC.

DAVID DELPOIO

COMMENCEMENT: Deborah Lee '11 MD'16 gets ready to march.

FELLOWS

2006

Vivian Sung, MD MPH'06, a urogynecologist at Women & Infants Hospital and an associate professor of obstetrics and gynecology at Alpert Medical School, was named president of the Society of Gynecologic Surgeons in May. The Providence resident is also the principal investigator of the Pelvic Floor Disorders Network grant at Women & Infants.

2009

Nicole Alexander-Scott, MD MPH'11 was elected to the board of directors at Crossroads Rhode Island, a homeless services organization. She is the director of the Rhode Island Department of Health as well as an assistant professor of pediatrics and of medicine at Alpert Medical School and of health services, policy, and practice at the Brown School of Public Health.

2017

Michal Ganz, MD. See **Jay Levin** '08 MD'12 RES'16.

2018

Kristin Jacobs, MD, a fellow in the Department of Urogynecology and Reconstructive Pelvic Surgery at Women & Infants Hospital, was elected president of the Steering Committee for the Fellows' Pelvic Research Network of the Society of Gynecologic Surgeons. She will oversee the administrative logistics of national, multisite research conducted within the network by gynecology fellows from more than 20 participating US medical centers. Her research focuses include painful bladder syndrome, the female urinary microbiome, and patients' knowledge and preferences regarding hysterectomy procedures.

OBITUARIES

FACULTY

CHARLES MALONE, MD

Charles "Charlie" Malone, 88, died April 24. A professor of psychiatry and human behavior at Brown and the medical director at Bradley Hospital, he devoted his career to training mental health practitioners and delivering services to disadvantaged individuals and families.

Born in Paterson, NJ, he grew up in Manhattan and attended Oberlin College, where he majored in chemistry. After graduating from Cornell University Medical College he completed his residency in child psychiatry at Boston University Medical Center and the Worcester State Hospital and his psychoanalytic training at the Boston Psychoanalytic Institute, where he was an analysand of Helene Deutsch (herself an analysand of Sigmund Freud).

While at the University of Pennsylvania Medical School, where Dr. Malone was a professor of clinical child psychiatry, he cowrote *The Drifters*, a landmark study of severely deprived children from disorganized and impoverished families. He then spent a decade at Case Western Reserve University before moving to Brown, where he remained for 20 years. He was appointed professor emeritus in 1997, though he continued to supervise child and adolescent psychiatry and triple board residents and remained active in his ongoing research projects.

Dr. Malone returned to Ohio after his full retirement, where he helped develop the state's Core Competencies for Early Childhood Mental Health Professionals for the Ohio Department of Mental Health. He remained active politically and became very interested in community-based health care for elders. He was instrumental in establishing on-site nursing care at an independent living community in Cleveland.

He loved his family, food, dancing, traveling, jazz, and the Giants. He is survived by three children, three stepchildren, four grandchildren, and five stepgrandchildren. "In lieu of flowers," Dr. Malone's family wrote in his obituary in the *Cleveland Plain Dealer*, "please consider donating to a candidate or cause of your choice, or, better still, get out and pound the pavement. He did."

LYMAN PAGE, MD

Lyman Page, 84, died July 3 in Scarborough, ME. A graduate of Yale University and the Columbia College of Physicians and Surgeons, he practiced pediatrics for 15 years in Maine, and was the first board-certified pediatric endocrinologist in the state. He then moved to Waterbury, CT, where he was the chief of pediatrics at two hospitals. As a professor of pediatrics at Yale University, he led a program in Riyadh, Saudi Arabia, at King Faisal Hospital. He returned to practicing pediatrics in Providence with Jay Orson, MD, and joined the faculty at Brown's medical school. He also served as a pediatrician for the Mission Evangelique Baptiste Bethesda in Haiti. After retiring to Kennebunkport in 2002, Dr. Page volunteered with local environmental organizations, sang in his church choir, sailed, skied, and shared laughs with friends and family. He is survived by his wife, Gillet Thomas Page, two sons, a daughter, and five grandchildren. Gifts in his memory may be made to Hospice of Southern Maine, US Route One, #1, Scarborough, ME 04074; or the Mission Evangelique Baptiste Bethesda/UCC, 600 Fall River Ave., Seekonk, MA 02771.

S. FREDERICK SLAFSKY, MD

S. Frederick Slafsky, 83, died January 8 after a fall. A general surgeon who practiced in Providence for 38 years, he

was one of the first surgical appointees to the Brown University School of Medicine, serving as a clinical associate professor of surgery from 1986 to 2002 and named surgeon emeritus when he retired in 2004. He was a compassionate physician and a dedicated and committed teacher who built strong bonds with his patients, students, and professional colleagues.

A native of Gloucester, MA, where he spent summers working on the docks, Dr. Slafsky retained a love for the ocean and fishing throughout his life. He earned his bachelor's and medical degrees at Cornell University and completed his surgical residency at Boston City Hospital and then St. Vincent's Hospital in Manhattan, where he received the Spiedel Award from Cardinal Cushing for research on portacaval shunts. As a research fellow and instructor of surgery at Peter Bent Brigham Hospital, he worked in the animal laboratories of pioneering transplant surgeon and future Nobel Prize winner Joseph E. Murray, MD.

At The Miriam Hospital Dr. Slafsky was the first director of the Surgical Intensive Care Unit. He served on many hospital committees and the board of directors of the Rhode Island State Review Organization, and participated in multiple levels in the development of Lifespan. He had clinical appointments at Roger Williams Medical Center and Women & Infants Hospital. He was president of the board of Mosshassuck Medical Center, where he maintained a clinical practice for more than 30 years.

Dr. Slafsky leaves his wife, Joan Temkin Slafsky, two sons, and four grandchildren. Gifts in his memory may be made to The Miriam Hospital, 164 Summit Ave., Providence, RI 02906; and WaterFire Providence, 101 Regent Ave., Providence, RI 02908.

COURTESY SLAFSKY FAMILY

S. Frederick Slafsky, MD

LOUIS VINCENT SORRENTINO, MD

Louis V. Sorrentino, 93, died June 12 in Amherst, MA. He attended Princeton and, after serving in World War II, graduated from Boston University Medical School. After residency, he served for five years as a medical missionary in Japan. He then completed psychiatric training at Boston State Hospital and began his psychiatric practice in Rhode Island in 1960. He was a member and past president of the Rhode Island Psychiatric Society, the American Medical Association, and the Rhode Island Medical Society. He was active for many years on the Rhode Island Medical Society Physician Health Committee and the Rhode Island Group Psychotherapy Society, of which he was a founder. He was on the staff of Rhode Island Hospital and Butler Hospital and a clinical assistant professor of psychiatry at the Brown University School of Medicine. Dr. Sorrentino was predeceased by his wife, Rosemary Pierrel Sorrentino, and is survived by a daughter, a son, four grandchildren, and eight great-grandchildren. Donations in his honor may be made to the Dean of Pembroke College Endowed Visiting Professorship, Brown University, Gift Cashier, Box 1877, Providence, RI 02912; and Butler Hospital, Foundation Office, 345 Blackstone Blvd., Providence, RI 02906.

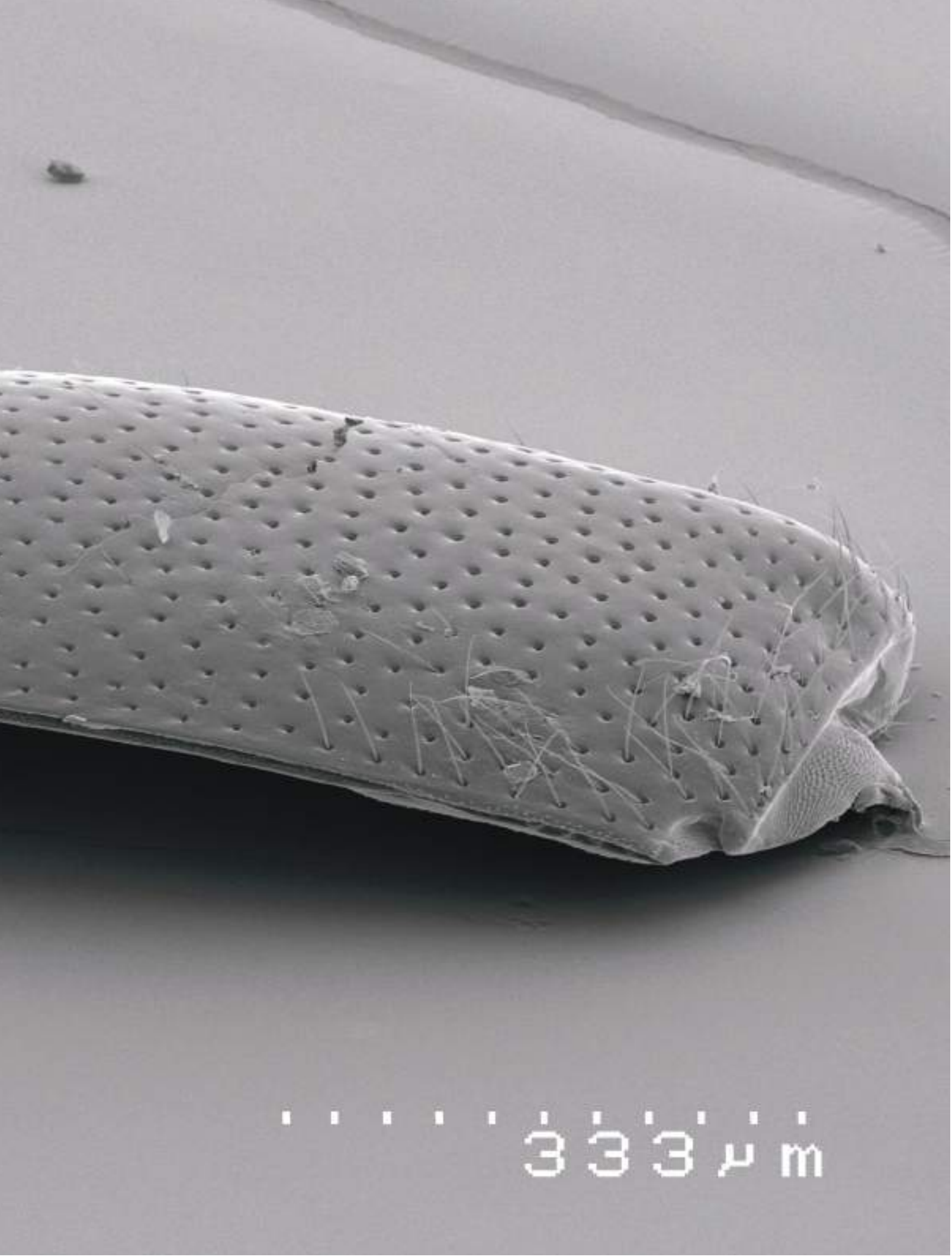
RUTH E. TRIEDMAN, MD

Ruth E. Triedman, 83, died August 15 in Providence after a brave battle with pancreatic cancer. A graduate of Wellesley College, she was one of just a few women in her class when she earned her medical degree from Columbia University College of Physicians and Surgeons. After completing her dermatology residency at Harvard, Dr. Triedman spent more than 30 years in private practice in Providence, served on the staff of The Miriam Hospital, and was a clinical assistant professor of dermatology of Brown University School of Medicine. She was a long-time member of the board of the Miriam Hospital Women's Association and the first physician to serve as president. She received the group's lifetime achievement award at their annual luncheon on June 1. "She was quite a trailblazer among women of that era who paved the way … for those of us following in their footsteps," says Marlene Cutitar '83 MD'86 RES'92, a breast surgeon and clinical assistant professor of surgery at Alpert Medical School. "We are indebted to the determination and success of such leaders." Dr. Triedman was predeceased by her husband, M. Howard Triedman, MD, and is survived by three children and six grandchildren. Donations in her memory may be made to The Miriam Hospital or your favorite charity.

More Than Meets the Eye

Microscopist and photographer Geoff Williams, MS, finds artistic opportunity in unusual places. His daughter's eye, for example. Five years ago, when she was 6, a beetle collided with her face while she was playing soccer, lodging a chitinous forewing under her eyelid. "She had to go to Hasbro [Children's Hospital] and be sedated because the pediatric ophthalmologist couldn't get close enough with forceps to pluck it off without her flinching," Williams says. "The shape was really cool," so he took the 1 mm-long wing back to Brown's Leduc Bioimaging Facility, coated it with a film of pure gold, and put it in a scanning electron microscope. At nearly 350x magnification, it's even cooler: you can see her corneal cells stuck to the wing. When Williams displays his work, he doesn't always identify the object. "The point is trying to get people to first visually, aesthetically react, and then maybe want to figure out what they're looking at," he says. ***—Phoebe Hall***

See the prepared beetle wing specimen, and read more about Williams, on page 10.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"Growing up in Brazil, we only went to the doctor as a last resort. Experiencing how a lack of access to health care impacts lives inspired me to become a physician. I moved to the US 10 years ago and am pursuing my dream at Alpert Medical School. My journey here has only been possible with the help of generous donors to the Brown Medical Annual Fund." —CHARLES FAGUNDES MD'18

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