

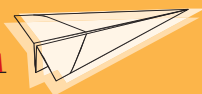
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FALL 2015

PITTMED

EVERY MORNING SHE HAD THAT NAGGING FEAR:
IF HER CLOTHES WEREN'T WRINKLE-FREE AND
PERFECT, SOMETHING *BAD* WOULD HAPPEN.



INSIDE THE WORLD OF OBSESSIVE
COMPULSIVE DISORDER



I, TWITTERATI

If you aren't following us on Twitter, you are missing out. Some heroes—i.e., Batman and Jim Withers (MD '84)—have made appearances. There's been lots of news from Hollywood—namely on *Code Black* (the documentary-turned-TV-series brainchild of alum Ryan McGarry, MD '09), the soon-to-be-released film *Concussion* (in which Will Smith stars as fellow alum Bennet Omalu, Fel '02), and Ken Burns's *Cancer: The Emperor of All Maladies* (which spotlights Pitt's esteemed Bernard Fisher, MD '43).

Some of the other feed topics: lactation in mammals (this has been a prolific baby-making season for some of our key contributors), inter-professionalism, intersexuality, and more on the interplay of science, medicine, and the rest of life.

Don't know how to get started on Twitter? Give Robyn Coggins's story "Tweet Talkin' Docs," on p. 32, a read.



Join us @PittMedMag

CLARIFICATIONS

Although this is the 60th year of graduating Pitt med students putting on a big show, Cyril Wecht (MD '56) points out that the play was not known as a "Scope and Scalpel" production until his class year, 1956. He and his mates were certainly inspired by the antics in the show from the Class of '55, *PMS IV*. (Flashback: The vaccine wars were a bit different then. Wecht recalls one 1956 scene parodying the competition between Jonas Salk and Albert Sabin.)

Radiology professor Ernest Sternglass's work on low-light imaging did in fact allow us to see those first close-ups of the moon. The system that grew out of his work at Westinghouse, however, did not result in the first photos, as we mistakenly reported—just the live video feeds.

CORRESPONDENCE

We gladly receive letters (which we may edit for length, style, and clarity).

Pitt Med

400 Craig Hall
University of Pittsburgh
Pittsburgh, PA 15260
Phone: 412-624-4152
Fax: 412-624-1021
E-mail: medmag@pitt.edu
pittmed.health.pitt.edu

For address corrections, or to change your print/online subscription preferences:

Pitt Med Address Correction

ATTN: Ashley Knoch
M-200K Scaife Hall
University of Pittsburgh
Pittsburgh, PA 15261
Phone: 412-648-9059
E-mail: medalum@medschool.pitt.edu

HEY, BUD.

Looking for something smart to download on your downtime? Check out **Pitt Medcast**, an award-winning series of leisure listens—plus a couple of audio slideshows—from these editorial offices.

We've got scintillating science stories, like: the neurobiology of itch, the molecular mechanisms of tinnitus, what makes genius happen—and, coming soon, the hunt for a cure for blindness, using stem cells from our own teeth! There's a cornea-copia of eye-opening research to tune into.

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PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, FALL 2015

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40 1/2

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As a content developer working in continuing medical education and pharmaceutical advertising, **KRISTIN BUNDY** ["We're Doing This for the Next Guy"] kept physicians in the know about the latest breakthroughs in medicine. When assigned her first feature story for *Pitt Med*, she was able to focus on a family affected by a disease, instead of the disease itself. Bundy moved to Pittsburgh five years ago after living in New York City for several years. She's happy to give up crowded sidewalks and subways but misses the colorful characters of the big city. Now, in Pittsburgh, she mellows out at BYS Yoga Studio and Shining Light Prenatal Education. Bundy is a yoga instructor who specializes in working with new and soon-to-be mothers. She is also a postpartum doula.

DUANE RIEDER ["We're Doing This for the Next Guy"] loves photography, baseball, and wine and has managed to combine all three into one eccentric 12,000-foot studio—Engine House No. 25, in Lawrenceville. Rieder has amassed the largest Roberto Clemente memorabilia collection in the world and runs the Clemente Museum out of the first floor of the engine house. His photography studio is on the second floor, and in the basement—a massive wine cellar where he makes his own vino. Rieder and Neil Alexander met in 2010, when Neil brought his son, Patrick, then 6, to the museum. Duane was hesitant to have such a young kid on an hour-and-a-half tour, but Neil insisted, saying to Rieder, "My kid will be teaching you a few things." And, Duane says, Neil was right.

COVER

Nine wardrobe changes, and she still can't decide what to wear. OCD can paralyze. (Cover: Cami Mesa © 2015.)



The Alexanders say, "Live Like Lou."

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A family inspired by Lou Gehrig wants to level the ALS playing field.

PHOTO ESSAY BY KRISTIN BUNDY AND DUANE RIEDER

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PUBLISHER

Arthur S. Levine, MD

EDITOR IN CHIEF

Erica Lloyd

ART DIRECTOR

Elena Gialamas Cerri

SENIOR EDITOR

Elaine Vitone

ASSOCIATE EDITOR

Robyn K. Coggins

CONTRIBUTING EDITORS

Kristin Bundy

Chuck Staresinic

INTERM

Brady Langmann

PRODUCTION MANAGER

Chuck Dinsmore

CIRCULATION MANAGER

Andre Burton

OBITUARIES CONTRIBUTOR

Macy Levine, MD '43

EDITORIAL ADVISORS

Jeremy Berg, PhD

Michelle Broido, PhD

Nancy Davidson, MD

Paula Davis, MA

Joan Harvey, MD

David Kupfer, MD

Joan Lakoski, PhD

David Lewis, MD

Margaret C. McDonald, PhD, MFA

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Steven Shapiro, MD

Peter Strick, PhD

Ann Thompson, MD

Bennett Van Houten, PhD

Simon Watkins, PhD

Marshall Webster, MD, Res '70

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Kenneth Service

Cindy Gill



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This past summer, I had the opportunity to travel to Uluru—a lone, bare, massive red sandstone formation in the outback of Australia's Northern Territory desert. It seems to rise out of nowhere. The aboriginal Anangu say it is a place forever connected to Dreamtime, the time before creation. My wife and I, camping at Uluru's base, viewed the rock at all hours of daylight; it was especially memorable to behold at twilight, as the rock glowed a brilliant crimson and the wind hummed along its fissures. And although I am not a follower of any structured religious beliefs, it became abundantly clear to me why the Anangu consider this monolith a sacred place: Uluru is an invitation to consider the unanswerable, the great mystery of our existence.

Often when scientists discover answers about our world's grand intellectual challenges, as Einstein imagined and theorized the continuum of space and time, the answers provoke further questions, adding another layer of wonder to it all. Not long after my return from Australia, I read about the DESI (Dark Energy Spectroscopic Instrument) project, in which 200 physicists and astronomers, including scientists from our University, will be probing the nature of dark matter and dark energy. They will start by mapping 30 million galaxies. *Thirty million galaxies*—that's just a handful of the number that's out there. If you place a grain of sand between your fingers and lift it toward the night sky, you'll cover about 10,000 galaxies with that grain. Astronomers estimate there are at least 100 billion galaxies. When I try to grasp this, I have the same profound feeling and awe that I had at Uluru.

Much as the findings of today's astrophysics seize my imagination and stir my thoughts, human biology seems even more extravagant to me. I have spent many of my years and days reflecting on the mysteries and enigmas of the molecular world: how you and I, and our cells and molecular events, came to be—and also the ways in which we will fade away. This improbable existence that we share, as the Anangu might say, is *wiru*, beautiful and grand.

So the scientists, including me at an albeit modest level, will go on plying away at how creation and destruction happen—in my case, how DNA is built, damaged, and repaired with fidelity or infidelity. But there are some larger things we each need to answer for ourselves. Namely, what to do with this gift of being? Or, as the poet Mary Oliver put it, *what is it you plan to do / with your one wild and precious life?* Oliver wrote further:

When it's over, I want to say: all my life

I was a bride married to amazement.

I was the bridegroom, taking the world into my arms.

Arthur S. Levine, MD

Senior Vice Chancellor for the Health Sciences

John and Gertrude Petersen Dean, School of Medicine



COURTESY A. LEVINE



*Devoted to noteworthy happenings
at the medical school*

The Nation Calls

It's the kind of morning most can only imagine: "I walked into the office one day," says Yuan Chang, "and learned the White House wanted me to return their call."

Chang, an MD Distinguished Professor of Pathology in the School of Medicine and researcher at the University of Pittsburgh Cancer Institute, is one of the Obama Administration's five new 2015 appointees to the National Cancer Advisory Board. In this role, Chang will work with the National Institutes of Health to further its cancer-fighting agenda, and she'll review cancer research grants to recommend project funding.

Chang's decades-long resumé of frontline pathology discoveries—including the landmark codiscovery of Kaposi's sarcoma-associated herpesvirus—has prepared her well to help locate and support the next generation of cancer researchers. "I spend a lot of time concentrating on the lab," she notes. "This is a great opportunity to help out the research community as a whole." —Rachel Mennies

JOSHUA FRANZOS



Chang

Preventing Suicide

It's not something parents want to pass down to their kids, but a study in a recent *JAMA Psychiatry* showed that parents who'd ever attempted suicide are more likely to have children who will try it themselves one day—their children are five times as likely to try, in fact. Yet there's good news, too.

"It's really a hopeful message," says David Brent, an MD who led the study, holds Pitt's endowed chair in suicide studies, and is a professor of psychiatry and pediatrics. "The study frames clear targets for intervention, which can guide the clinician to ways to prevent suicidal behavior from being passed from parent to child. Some of the targets we identified are impulsive aggression and mood disorders, both of which are treatable conditions."

—Robyn K. Coggins



KAREN ARTIS

FOOTNOTE

For second-year med student Gregg Robbins-Welty (above), nothing relieves stress like plucking "Oh, Shenandoah" on the banjo. Gregg's dad, Eric Welty, introduced him to the instrument while Gregg was still in the womb, but it wasn't until his teens that Gregg appreciated the art of twang. In 2013, father and son began playing against each other in state competitions; they tied for fourth place at Nationals. Last we heard, Gregg's new album, *Memoir*, was number 7 on AirPlay Direct's bluegrass charts.



CAMI MESA

Overheard

Abdesalam Soudi on Doctor/Patient/Computer Relations

Abdesalam Soudi grew up in a small village in Morocco, where his family didn't have access to a hospital or a pediatrician. As needs arose, his mother took care of him with herbal medicines. So he never imagined himself in the position he's in today: an expert in the sociolinguistic challenges that arise during a medical interview and how the computer in that setting influences doctor-patient relations. For three years, Soudi was a language coordinator for international patients at UPMC; he's now a PhD faculty member in linguistics at Pitt. He also codirects a master's-level course in cultural competence in medical education with the chair of family medicine, Jeannette South-Paul (MD '79), who is the UPMC Andrew W. Mathieson Professor of Family Medicine.

How did you get interested in electronic health records (EHRs)?

Initially I was interested in medical discourse in general—the language exchange between doctor and patient. But then, when I started transcribing the conversations, I couldn't ignore the sound of typing in the exam room. So that became the topic of my dissertation.

What are the issues?

The needs of the patient and the computer overlap and sometimes clash. So there is a tradeoff in attending to one or the other. . . . It's like texting and driving. If your texting is going well, your driving is suffering and vice versa. Another problem: There is a disconnect that exists between the patient and the computer. The patient doesn't have access to the computer, and the computer, of course, doesn't have access to the patient. They are blind to each other, which leads to problems in turn-taking and coherence. The responsibility to coordinate this three-way interaction mostly falls on the physician.

What might doctors want to keep in mind?

There are times when facing the computer is very good. But that first minute really shapes the rest of the encounter. Shake the patient's hand, *then* "greet the computer." Maybe first spend face-to-face quality time [with the patient] before logging in.

What would improve the situation?

Doctors are trained how to use the software and not how to use it in the patient care context. [Further, when designing systems], we should think about where and with whom the EHRs are going to be used: in the E.D., orthopaedics, etc. And the systems should be sensitive to fostering the doctor-patient relationship.

I don't see my work as a criticism of doctors. What I am critical of is the context in which they have to work. —Interview by Erica Lloyd

Next Generation

Oriana Hunter and Bradley End (MD '15) earned Honorable Mentions in the Gold–Hope Tang,

MD, 2015 Humanism in Medicine Essay Contest. The contest asked medical students to tell a story "about a time when learning a nonmedical piece of information about a patient led to an improved health care outcome." For instance, in her prize-winning essay, Hunter, a PhD and fourth-year medical student, describes caring for a nervous pediatric patient with an artificial heart. By decorating the boy's external heart equipment—which Hunter, a biomechanical engineer, also operated—to resemble Thomas the Tank Engine, Hunter empowered the youngster during a challenging time.

Busola Oluwole won a 2015 American Society of Hematology HONORS Award.

Pitt's Oluwole is a fourth-year medical student and a Clinical Scientist Training Program fellow. She and her mentor, assistant professor of medicine Enrico Novelli, an MD, are researching the connection between blood vessel changes and the development of cognitive deficits in sickle-cell populations.

Arpan Prabhu was awarded the 2015 Global Changemaker Legacy Award from the Foundation for Global Scholars.

Prabhu is in his second year of medical school. His research recently took him to Bolivia, where he investigated citizens' perspectives on the role of foreign medical workers in intercultural health care exchanges. In Pittsburgh, Prabhu is a volunteer for the Salud Para Niños (Health for the Children) clinic at Children's Hospital of Pittsburgh of UPMC.

—Rachel Mennies

Children Seen and Heard

What's one of the best things you remember about being a kid? For Camill it was a ritual: "My granddad picked me up from preschool, and every day he'd give me a lollipop." For Kailey it was freedom: "We would go to the woods and . . . make clubhouses out of . . . the junk we found." For Jashaun it was a reward: "I lost my tooth and got \$5!"

Recording the stories is the Mobile Giving Booth, which visited more than 20 locations around the city this summer. The booth serves as a reminder that kids need a chance to be kids.

Families are also using the booth to pay tribute to Children's Hospital of Pittsburgh of UPMC as it celebrates its 125th birthday. Denise, whose daughter was treated at the hospital, recalls how good it felt "to be somewhere where you could be comforted and know that your child is receiving the best of care."

You can see these Pittsburghers and others wax nostalgic about their youth at givetochildrens.org/125.

—Rachel Mangini

CATHERINE LAZURE



TOPCATS Roar

Wouldn't it be nice if med schools could hear directly from patients about how students performed? Soon, there'll be an app for that—developed by students themselves.

Four Pitt meders won the National Board of Medical Examiners (NBME) Centennial Prize for "innovation in the future assessment of health professionals" with an app called TOPCATS, short for Trainee-Oriented Patient Communication Assessment System.

"Patients' impressions of their hospital experience largely depend on the quality of their interactions with health care providers," says Myung Sun Choi, who conceived of the project. But those encounters can be hard to evaluate. Using smartphone-based TOPCATS, both docs-in-training and patients would assess their encounters. Data would then be analyzed, and reports and suggested resources would be sent to the student and her school for review.

The NBME will develop TOPCATS through the prototyping stage with the help of the Class of 2016's Choi and codeveloper Jennifer Hu, as well as second-year med students Devan Patel and Abby Koff. Patel says the experience has helped him "believe that medical students can play an active role in their own education."

—Rachel Mangini

CELEBRATE, CONNECT, CATALYZE

At an event this September dubbed A Toast to Diversity and Call to Action, Jeannette South-Paul, an MD, recounted a parable to the crowd: "When you see a turtle sitting on a fence, you know it didn't get there by itself."

South-Paul, cochair of the Physician Inclusion Council of UPMC/Pitt (PICUP) and the UPMC Andrew W. Mathieson Professor and chair of family medicine, added, "We know, no matter how smart you are, how good the pedigree of the institutions you come from, . . . you're successful because of the support and the mentoring of colleagues, friends, leaders in your field."

The dinner event at Heinz History Center aimed to connect and inspire physicians and researchers who identify as members of underrepresented groups within the health care field. Med students from all years, residents, fellows, and faculty were invited to sign up for action groups like the minority house staff council, which welcomes new minority staff to the hospital and brings in speakers like financial advisors to help young docs cope with stressors on the job.

Toward the end of the evening, Ann Thompson, an MD, vice dean of Pitt's School of Medicine, professor of critical care medicine and pediatrics, and member of PICUP, proposed a toast: "To each other—to toast the accomplishments and the potential in this room. The potential for new, creative ideas. The potential to mentor and support those who follow us. And the opportunities that we have to make a huge difference in the lives of each other and people in our community."

"Hear, hear!" the crowd responded, champagne flutes clinking, arms straining to reach new friends across the 20-some packed tables. —RKC

MIKE DRAZDZINSKI/CIDDE



Here's to achievement and potential!



AS WE SEE IT

Two stories below Terrace Street, on the mezzanine of Scaife Hall, there was a drab hallway outside the Office of Medical Education. Bland office doors divided a stretch of pale concrete—hardly a spot that represented med ed at Pitt. In 2011, John Mahoney, MD associate dean for medical education, decided to add a bit of life to those halls by collecting and displaying artwork by students, staff, and faculty. And so the Scaife Underground Gallery was born.

“Suddenly it went from nothing to something,” says Mahoney. “And people liked it.” The hallway now displays artwork, including images of Pittsburgh and of sites around the world: a Viking drowning pool in Iceland, a boy surrounded by pigeons in Kuala Lumpur. Every few months, Mahoney swaps older pieces with new ones. “Whenever visitors come or students go, we say, ‘You’ve got to give us a picture!’” —Susan Wiedel

The batik shown here was created by Jane Phelps-Tschang (MD '14), now a UPMC child psychiatry resident.

Name Dropping

Pitt’s annual science and technology conference, Science 2015, celebrated its 15th year this October with a liberating theme—unleashed!

The Dickson Prize in Medicine lecturer, **Karl Deisseroth**, an MD/PhD, spoke at this same event three years ago as the Hofmann lecturer. His lab developed optogenetic technology, which uses light to precisely control activity in certain cell types in the brains of mammals. Later, in a 2013 *Nature* paper, he described a new method for revealing brain activity. Deisseroth’s new approach, called CLARITY, makes intact brain tissue transparent, allowing researchers to see the responses of large networks of neurons. Among other advances using CLARITY, Deisseroth has made anatomical discoveries and insights into the neural circuit control of increasingly complex behaviors.

Receiving the Dickson Prize is particularly meaningful says Deisseroth, because it supports undirected, basic, nontranslational research—something he believes should have more public support. Deisseroth is the D.H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences at Stanford University and a Howard Hughes Medical Institute (HHMI) Investigator.

James Collins, a PhD, HHMI Investigator, and Termeer Professor of Medical Engineering and Sciences at MIT, presented the

Provost Lecture. He discussed how his lab uses synthetic biology to try to combat and prevent infectious diseases. His lab has engineered *Lactobacillus lactis*—a probiotic yogurt bacterium—so that it will detect cholera bacteria in the intestine and produce antimicrobial peptides to kill them.

This year’s Mellon lecturer, **Pamela Björkman**, is a PhD and the Centennial Professor of Biology and Biological Engineering at the California Institute of Technology, where she established a lab in 1989 that has since solved the 3-D structure of more than 50 proteins and complexes of the immune system. Her research focuses on building antibody-like reagents for use in HIV treatment.

Andrew Feinberg, the Klaus Hofmann lecturer, is an MD/MPH, King Fahd Professor of Molecular Medicine, and director of the Center for Epigenetics at Johns Hopkins University. Feinberg received the 2011 NIH Director’s Pioneer Award, which continues to fund his novel research in understanding stochasticity in evolution, normal development, and cancer, as well as the discovery of nuclear structures that regulate epigenetic randomness and could predispose someone to developing cancer. —Kristin Bundy



NICU VIP

Twenty-nine-year-old Brittany O'Rourke's baby photos are all over the neonatal intensive care unit (NICU) at Magee-Womens Hospital of UPMC. They appear in the parent support book and hang on the unit's "Wall of Fame," an entryway display with hopeful stories for visitors. One photo shows a tiny O'Rourke clutching her own NICU discharge papers. "That's my golden ticket!" she says.

Her special recognition comes with being the NICU's most well-known "graduate": After spending her first 101 days in Magee's NICU, O'Rourke now works there as a registered nurse.

She was born prematurely, at 28 weeks, weighing just 2.8 pounds. Because of damage to her airway, she needed a tracheostomy at 15 weeks old and underwent extensive childhood surgeries.

O'Rourke jokes that she was always "a woman on a mission." Her vocational "training" began at age 3, when nurses would invite her to do small tasks with them at their stations while she was recovering in the hospital.

As a nursing student at Carlow University, O'Rourke began an internship at

Magee's NICU and stuck around. It was easy for her to connect with the place that saved her life as an infant—especially working alongside NICU nurses who'd cared for her as a newborn. She was also drawn to the unit's family spirit. Today, her favorite parts of nursing are making hats for the newborns she cares for and writing "notes" from them to their parents.

In her seven years working in the NICU, O'Rourke has also come to understand the power her presence holds for new parents.

"I knew my story of being a baby here would have some impact, but I never really knew just how much," O'Rourke says.

Once, she shared the details of her birth with the father of another infant born at 28 weeks; he told her afterward that he felt he could go home and sleep through the night.

"That made me feel like, *Okay, I'm where I need to be,*" O'Rourke says.

— Rachel Wilkinson

— Photograph by John Altdorfer

INVESTIGATIONS

Explorations and revelations taking place in the medical school



A percolation model of the brain, borrowed from mathematicians, may help scientists wake up to how anesthesia and other puzzles of consciousness and cognition work.

PERCOLATING BRAINS

CONSCIOUSNESS AND COGNITION

BECOME CLEARER | BY CHERYL ALKON

Some coffee drinkers claim they can't wake up or properly process information until they've downed their third cup of joe.

But how, exactly, does a noggin wake up? How is sensory information, like the heavy smell of a Colombian roast, transmitted across the brain and turned into an enticing thought? The mechanics of consciousness and cognition have been a puzzle for biologists and philosophers alike. Researchers at the University of Pittsburgh have come up with a new model explaining how the brain operates—and, well, it works like a coffeemaker.

With coffee production, water randomly flows through coffee grounds and a filter in a process called percolation. The liquid coffee eventually seeps into the bottom of the pot. Likewise, in the brain, information—in the form of external sensory stimulation such as images, sounds, or smells—gets processed as it travels through our neurons. This information moves from the thalamus, which acts like a relay station deep in the brain, to the cortex, where cognition and memory are formed and stored, explains Yan Xu, a PhD professor of anesthesiology, structural biology, and of pharmacology and chemical biology, and the vice chair for basic sciences in Pitt's Department of Anesthesiology.

This model is a way to grasp the complexity of the brain, Xu adds. "There are so many neurons in the brain. If you want to understand the general rules governing how the brain works, you will have to ignore some of the details," he says. "It's like the universe—you cannot study the details of every star. You have to abstract it out to understand the universe."

To abstract out brain workings, Xu and colleagues at Pitt and Carnegie Mellon University applied percolation theory from the field of mathematics. This approach illustrates the behavior of clusters that are connected directly or indirectly through other clusters and their connections.

Xu's team divided the brain into grids they called "nodes." ("Node" is a common term in neural network literature for groupings of cells or brain regions that are not anatomically defined.) Then the team calculated the probabilities that connections existed between

features clinically observed in recordings of brain activity when patients are transitioning from consciousness to unconsciousness under general anesthesia. In their model, changing a single variable that decides whether a connection is on or off can manipulate the system to replicate many of the changes that appear in brain waves when the mind is switched off under anesthesia.

"What is remarkable from a theoretical point of view is that a simple abstract model can recapitulate essentially all salient features in a system as complex as the human brain

"There are so many neurons in the brain. If you want to understand the general rules governing how the brain works, you will have to ignore some of the details."

the different nodes. Using a computer simulation, they found that the odds of a connection being present between nodes could be as low as 30 percent for the percolation of information to occur.

The team's work, "Percolation Model of Sensory Transmission and Loss of Consciousness Under General Anesthesia," appeared in the Sept. 4 issue of *Physical Review Letters*, the premier physics journal published by the American Physical Society.

Xu, who has studied anesthesia mechanisms for the past 23 years and has been continuously funded by the National Institutes of Health for the past decade, says there are still many questions about how anesthesia works at the molecular and cellular levels. The percolation theory offers one explanation.

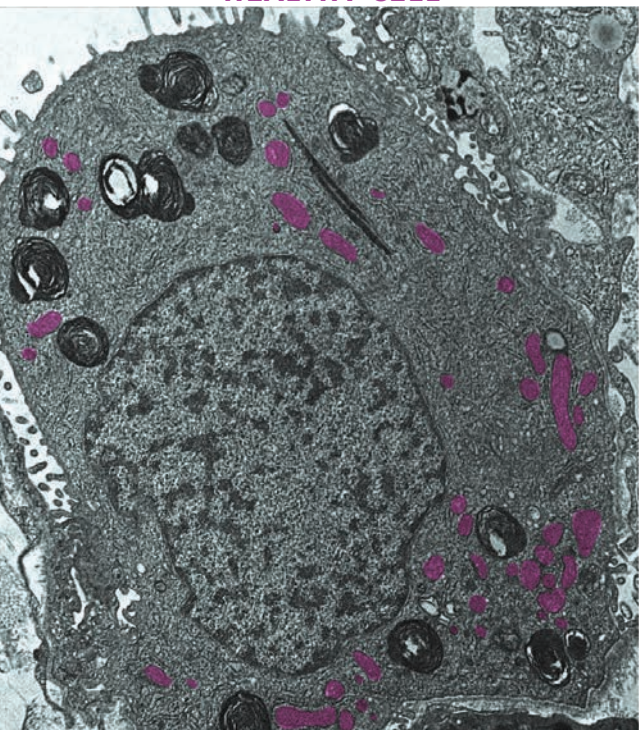
Xu's team validated their percolation model by showing that it reproduces key

when it transitions between conscious and unconscious states," Xu says.

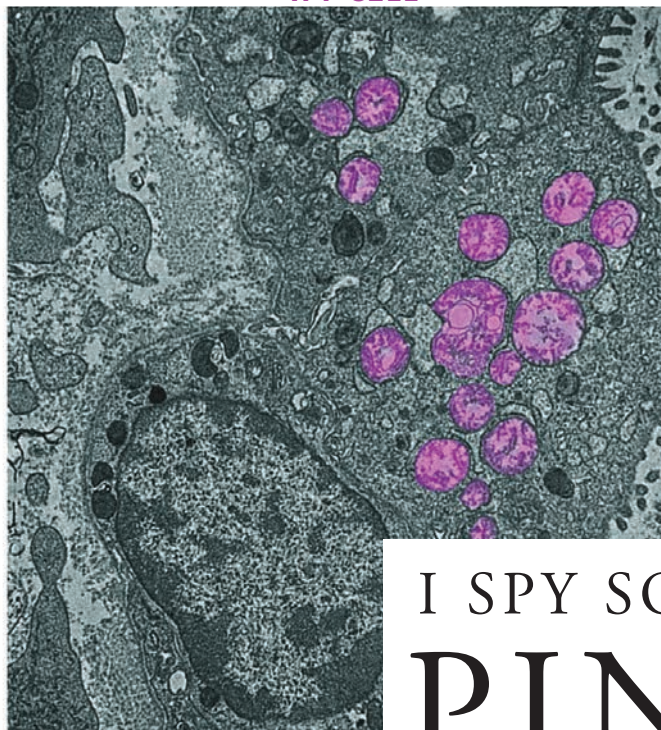
Returning to the metaphor of the coffeemaker, if a sheet of plastic is covering the coffee grounds to prevent water from running through them, the coffee will never reach the bottom of the pot. "The brain is the same way—you can use anesthetics to interfere with the information flowing from one end to the other to block cognition," says Xu. "The theory allows you to understand the fundamental rules that govern how our mind works—and how anesthesia works to turn it off."

Xu says scientists can use the model to examine questions like how and whether the brain learns in various states of consciousness (including under anesthesia), how memories are formed and retrieved, and why there is a surge in high brain-wave frequencies in the EEG of a near-death patient. **n**

HEALTHY CELL



IPF CELL



The shape of mitochondria (fuschia) changes from small sausages in a healthy lung to swollen circles in a lung with idiopathic pulmonary fibrosis.

ONE DISEASE
UNVEILS THE
MECHANISM
OF ANOTHER

BY KRISTIN BUNDY

I SPY SOMETHING PINK

COURTESY MARTA BUENO AND JUDITH BRANDS

Gray hair, wrinkles, perhaps a love of bath slippers—these are some of the universal signs of aging that we anticipate as we get older. Other age-related changes tend to be unique to each body. Some folks might not breathe as easily as they did during their racquetball days. Others might not remember what they did to pass the time yesterday. Although these ailments seem to be separate complications, there is new evidence that the underlying biology of some age-related diseases may not be so different after all.

One University of Pittsburgh team recently uncovered a connection between ailments of the lung and the central nervous system that tend to arise as we get older. Idiopathic pulmonary fibrosis (IPF), a progressive disease characterized by hardened connective tissue in the lung, might have ties to Parkinson's disease, which results from abnormal brain activity that first affects motor skills and can lead to dementia.

So how do the twain meet? The answer seems to lie in the mitochondria and how these sausage-shaped energy factories deal with aging and stress—a mechanism unknown in IPF until now.

Ana Mora, an MD and assistant professor of medicine in Pitt's Division of Pulmonary, Allergy, and Critical Care Medicine, and her team recently revealed the role mitochondria play in IPF. Those results were published in the February issue of *The Journal of Clinical Investigation*.

"Mitochondria was, for us, a natural target," Mora says. In IPF, the deposits of hardened connective tissue, or fibrosis, show up in the lung's alveolar epithelium; the epithelial cells contain the majority of the mitochondria in the lung, she says. "Any change in the mitochondria function probably makes [the cells] more vulnerable to injury and disease."

"And the second aspect that we thought was: [People investigating] age-related diseases have found that mitochondria also are an important factor for pathogenesis, especially [in] neurodegenerative diseases like Parkinson's."

Mora and her team began their investigation with IPF patient lung tissue samples they already had in the lab and confirmed that the epithelial mitochondria were indeed swollen, were less organized, and had accumulated in the cell, signifying insufficient mitophagy (the mitochondrion's inner quality control system).

Then they reviewed epithelial cells from lungs of healthy human donors of all ages and confirmed that mitochondria do become more dysmorphic and dysfunctional with age, but the effects are not as exaggerated as in patients with IPF. The team corroborated these results in mouse models.

"With age and stress, when we put [them] together, we can recapitulate the phenotype that we're seeing in the disease," says Mora. But age couldn't be the only factor that would lead to IPF; otherwise many more people would have the disease. So they began to think about the mechanism.

"We remembered that in Parkinson's dis-

ease, there has been a description of similar kinds of phenotypes, and they were associated with a mutation of a protein that is called PINK1," Mora explains.

So the team probed into the potential "pinkness" of IPF epithelial cells. They found that the cells are deficient in PINK1. Mora's team collaborated with Pitt's Charleen Chu, an MD/PhD, professor of pathology, and the A. Julio Martinez Professor of Neuropathology, to study PINK1-deficient mice that had been used to study mitochondrial pathobiology and Parkinson's.

Mora and colleagues analyzed the mitochondria in the epithelial cells of the alveoli without the presence of PINK1 in these mice, and sure enough, they were spontaneously swollen, and the lungs showed deposits of collagen. They then challenged the PINK1 knockout mice with two different types of stressors. Again, the epithelial cells were more prone to die, and the lungs were more likely to develop fibrosis.

The team concluded that if a cell doesn't express enough PINK1, the mitochondria's shape and function become abnormal, and cells begin to fail as they work harder to repair and proliferate during injury. In IPF, instead of mending, the cells try to close the wound in an exaggerated way, which turns into fibrosis.

Despite the PINK1 mutation connection, scientists don't know whether patients with Parkinson's are at any more risk of having IPF or vice versa.

Mora says their next code to crack is understanding "other hallmarks of aging that bring susceptibility to disease." **n**



GETTY IMAGES

KIDS TELL IT LIKE IT IS
BY JENNY BLAIR

LISTEN UP, DOCS

Imagine you're an HIV-positive teen leaving a clinic appointment, and you're miffed because the doctor only talked to your mom. Then you spot a poster for a medical study looking to sign up youth, but the description is so complex that you can't figure out what the study involves.

It's easy for health care professionals to fail spectacularly at connecting with young people. But in Pittsburgh, youth are speaking up, and providers and researchers are listening. In two groups associated with the Division of Adolescent and Young Adult Medicine in the Department of Pediatrics at the University of Pittsburgh, young people discuss and create lasting change in how they interact with health care. It's all part of the division's philosophy, which underlies the respectful way its faculty interact with youth. (See "You Don't Understand!" *Pitt Med*, Spring 2015.) Division chief Elizabeth Miller, an MD and PhD anthropologist, sums it up this way: "If you're actually going to do work with adolescents, it's really helpful to have them involved."

ADVISING RESEARCHERS

Studying youth can be ethically and culturally rocky, but Pitt researchers who want to get it right can check in with the Youth Research Advisory Board (YRAB, pronounced *why-rab*). Every month, this group of young people gets together to advise faculty who want to reach out and study the teen and young adult demographic. Trained in research ethics from Pitt's Institutional Review Board and the Clinical and Translational

Science Institute, YRAB members weigh in on questions like: Is this recruiting poster free of jargon? How can younger teens ethically participate if they'd rather their parents weren't involved?

"It's a really invaluable opportunity for investigators who are kind of in their heads and are only working with a research team on these things," says YRAB's supervisor, epidemiologist Heather McCauley, an ScD. "They can actually have youth as stakeholders in the development of their research projects."

When assistant professor of pediatrics Ana Radovic, an MD, was designing a confidential social media website for adolescents with depression, for instance, YRAB members warned her that an option to "like" content could discourage young people whose posts receive few likes.

"The group was very thoughtful about the specific needs of depressed adolescents and helped guide our design to be more patient centered," Radovic says.

ADVISING OTHER PATIENTS

Smoothing the transition from pediatric to adult health care is the *raison d'être* of the Children's Hospital Advisory Network for Guidance and Empowerment, or CHANGE. This group of young people discusses ways to make the transition easier, especially for youth who face barriers to care. Most CHANGE members are experts on these barriers, having coped for years with disabilities, chronic

illnesses, and logistical hurdles like living in a rural area. So they're in a good position to support one another and advise parents and health professionals.

CHANGE and YRAB member Megan Marmol is a 20-year-old Carlow University student who lives with a chronic illness. She points out how fraught even a simple medical visit can be for a young person, like when a provider talks to parents instead of the patient herself.

"That causes tension between the parent and the young person," she says. Recognizing this, Pitt providers now make a point of seeing young people alone for the first few minutes of an appointment. CHANGE members have also suggested that potentially intimidating objects like speculums be stored out of sight, and they've reviewed the clinic's welcome letter to make it more patient friendly.

Marmol praises CHANGE for an inclusiveness that many youth might not often experience. After all, the very kids who often feel shunted aside in daily life—the one in a wheelchair, the one who is excluded from the general ed classroom—are often best acquainted with the complexities of obtaining health care. As they talk to one another and give presentations to those who attend CHANGE meetings, Marmol says they are learning to navigate the system with confidence.

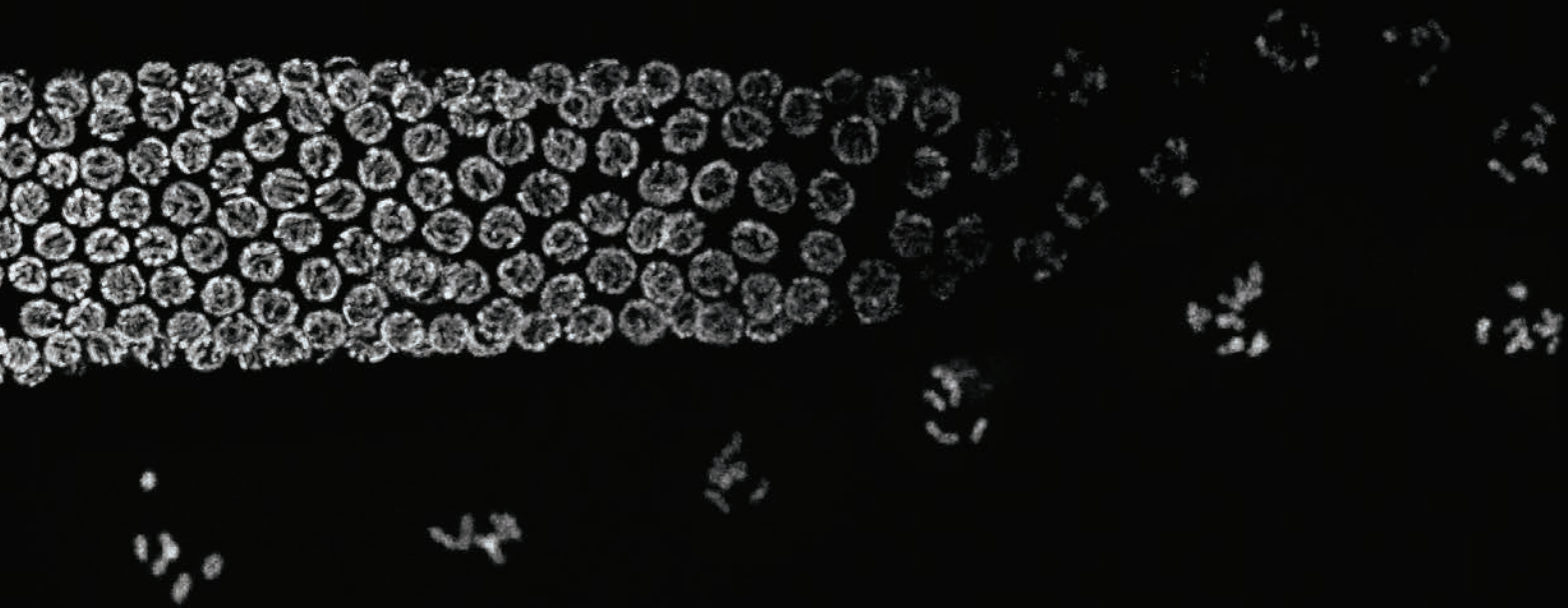
"Their voice matters," Marmol says. "The more you can help people develop these leadership skills, their self-advocating skills, their voice—that changes everything." **n**



EMPTY NESTS

When a woman is pregnant with a baby girl, the pair is at an incredible, understudied biological juncture: Mom, baby, and potential grandbabies are all in one vessel—flourishing on or suffering from the same nourishments, reacting to one another, interacting with the world around them. Past, present, and future nestled into one body; somehow three beings at once.

Perhaps your grandma had a set of those Russian nesting dolls—a round, squat woman who houses another squat woman, who contains yet another decorative matryoshka doll, and so on, until you reach a teeny version of all the women before her on the inside. When made in their traditional way, these dolls—also called babushka, or grandmother, dolls—are hand carved and decorated with a unifying theme. Each doll shell is made from the same block of wood so that they whittle similarly and warp together over time.



THE BIOLOGY BEHIND INFERTILITY

BY ROBYN K. COGGINS

Primitive worm, preliminary model. The gonad of *C. elegans* is orderly, visible, and relatively simple compared to humans' undercover reproductive tracts. Meiosis—the strictly regulated process by which a cell divides to become a gamete—may hold secrets to causes of infertility, and worms are helping Pitt researchers expose the genetic generation of generations.

All images courtesy Judith Yanowitz

Likewise, ovaries—and the eggs, or oocytes, inside them—are influenced by the body they're in, the body they've been in.

"The ovaries themselves are affected by the environment," explains Aleksandar Rajkovic, who's an MD/PhD professor of obstetrics, gynecology, and reproductive sciences and the Marcus Allen Hogge Professor in Reproductive Sciences at the University of Pittsburgh studying the genetic markers of ovarian aging and dysfunction. However, he says, "It's difficult to study the connection between the ovary environment and the overall health of an individual, since ovaries are not easily accessible in a woman to actually study." Most studies before the genomic revolution relied on animal models or postmortem dissection and didn't give a complete picture of living ovarian function.

Another method of assessing ovarian and reproductive health is looking at families. Some of Rajkovic's research focuses on large cohorts of women and their female relatives to spot trends. The problem, however, is that by definition, families with fertility issues are small.

Consider the condition known as primary ovarian insufficiency, or POI. An irreversible spectrum disorder of the ovaries, POI causes subfertility or infertility. Sometimes its root is genetic; in other cases, POI is triggered by autoimmune disorders like lupus or by chemotherapy damage to the organ. Of the 1 to 4 percent of American women who have POI, only about 10 percent of cases have a known cause, usually a mutation in the FMR1 gene, which is also linked to fragile X syndrome.

When ovarian function dwindles, hot flashes, mood swings, low libido, vaginal dryness, missed periods, and many of the other symptoms associated with low estrogen and menopause flare. Half of the women who spontaneously present with these symptoms see at least three doctors before any lab work is done or diagnosis is made. POI is often missed and is a greatly misunderstood condition.

But POI is not simply early menopause. Imagine being told that your ovaries are failures. POI used to be called premature ovarian failure, evoking some kind of personal biological bankruptcy. Imagine being 27 years old—the average age of onset—and getting the news that you'll likely never have a family without reproductive assistance. Maybe you didn't want children in the first place, but that quick snip of fate's thread can still seem cruel. Yes, you will probably hit menopause early. While your friends are having children, you'll look at their swelling bellies and wonder why your body won't mindlessly jumpstart its opaque reproductive machinery.

And, until very recently, women were often given the news of this diagnosis over the phone, or even by e-mail.

"It's not uncommon for them to be at work," says alum Lawrence Nelson (MD '73), who's a commissioned officer in the U.S. Public Health Service and studies the genetic origins of POI in mouse models and in humans. "Then they have to find a place to cry."

In his private practice, Nelson saw his first case of POI in the '80s—"I'd never heard of it before," he says. He looked for more information in the medical literature, but not much was written on POI, which meant he had very little to offer his patients as they sought to understand their condition.

Not surprisingly, one of Nelson's more recent studies on the psychosocial effects of POI found that the top three words women used to describe how they felt after diagnosis

were "devastated," "shocked," and "confused." Physicians like Nelson and Rajkovic are out to change that upsetting experience. But, first, they need to know more about the condition.

In 1990, when Nelson got a chance to do research at the National Institutes of Health, he pounced on the opportunity to dig into POI's origins. His basic science approach led to the discovery of Mater—a gene, which, when knocked out in mice, stops embryonic development in the oocytes and causes sterility. He's now translating that to clinical research, examining the exomes of women with POI to find more causes.

Nelson suspects the cause will be more complicated than just finding a gene that leads to POI. The condition is often unpredictable—ovarian function may wax and wane, which allows some 5 to 10 percent of women with the diagnosis to conceive. As of yet, there's no reliable way to tell whether that will happen in a particular woman.

He speculates that POI's cause will be more like congenital deafness and other conditions with multiple genetic origins and biologic interactions. That's why researchers are turning to large-scale sequencing of the genome and the exome (just the protein-coding genes).

Furthermore, POI can affect more than just fertility, Rajkovic explains.

"Women who have premature menopause or ovarian failure—which usually means when they stop menstruating prior to age 40—they are at risk for osteoporosis, for cardiovascular mortality and morbidity, and overall mortality is actually increased in these women. And it's not been well understood what causes this increase. . . . Ovaries are so essential to women's health."

Although hormone replacement therapy delivered through a skin patch can mitigate some POI symptoms, its effects on this population aren't well studied, and HRT doesn't address infertility at all.

As Pitt's director of reproductive genetics, Rajkovic, with his nine-person lab team, is trying to fill in some of the knowledge gaps surrounding ovarian development and dysfunction. Recently, the crew sequenced genetic samples from families with strong evidence of genetic causes for ovarian dysfunction. "This is an international effort. We've collaborated with individuals in Saudi Arabia and in Turkey to actually recruit families that had genetic forms of ovarian failure. And we then used the new genetic sequencing

approaches to . . . identify causes."

Funded by a \$2.5 million R01 grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rajkovic and his team discovered two genes that had never been previously implicated in POI: MCM8 and MCM9.

"In the first three families that we actually sequenced, we found that in one family there was a mutation in MCM8, and in two families there was a mutation in MCM9—MCM9 is MCM8's partner." In women with MCM8 and MCM9 mutations, their ovaries do not develop typically, and inside are very few or even no germ cells; plus, chromosome breaks abound. Using their findings on this pair, Rajkovic's lab members hope to model more genes implicated in infertility.

In total, they are sequencing nearly 100 POI cases and 300 typical menopause controls. In animal models, they've found more than 300 genes implicated in ovarian insufficiency, which they've termed the "ovariome."

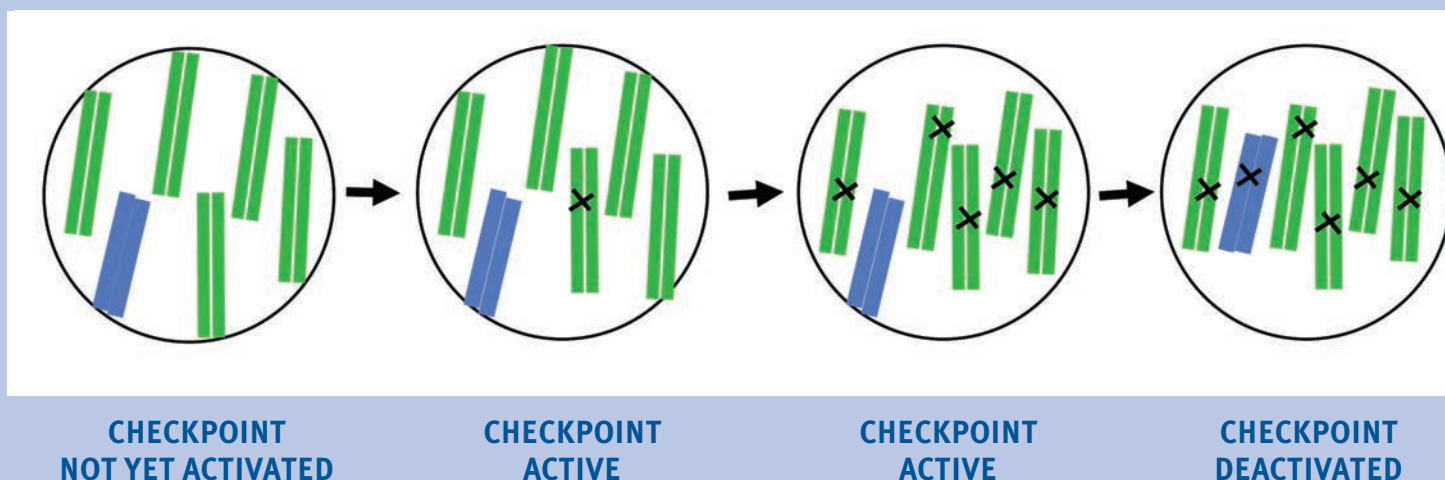
Rajkovic, along with postdoctoral fellow Michelle Wood-Trageser (PhD '09) and colleagues from pathology, chemistry, and human genetics at Pitt, has continued investigating 10 of these ovariome genes, and the scientists are currently recruiting patients for further studies.

In addition to the ovary, his lab also studies uterine fibroid tumors, testicular failure, and problems in spermatogonia (undifferentiated germ cells that eventually become sperm).

Others at Pitt, including Rajkovic's Magee-Womens Research Institute colleague Alexander Yatsenko, an MD/PhD, are looking at genetic mutations on the X chromosome that cause male infertility. (Recall that men have XY sex chromosomes, whereas women have the more redundant, and sometimes protective, XX.) Yatsenko, an assistant professor of obstetrics, gynecology, and reproductive sciences, and collaborators in Poland found that the TEX11 gene, inherited from a man's mother, interferes with meiosis, producing genetic errors in the cell and, ultimately, causing male infertility. Those results were corroborated by colleagues in Germany, and their findings were published in *The New England Journal of Medicine* this spring.

In both men and women, elevated levels of follicle-stimulating hormone (FSH)—a substance that kick-starts production of sperm in men and initiates follicular growth, and thereby ovulation, in women, among other biological duties—can signal fertility issues, as well. Doctors sometimes use FSH levels as an indicator for ovarian

As mom's and dad's DNA begins to mingle, the cell needs to monitor the swap, kind of like a border agent. Yanowitz has developed a theoretical framework, pictured here, of these crossover "checkpoints" during meiosis—points where the cell checks its papers to make sure everything's in order as the two genetic bits become one. Once the first crossover (x) is made, a checkpoint is activated.



reserves: too much, and you're in premature menopause; too little, and you might have polycystic ovarian syndrome (another possible cause of infertility). Abnormal hormone levels plus a few missed periods usually prompt doctors to look for POI, but that alone is too imprecise to yield a definitive diagnosis. Furthermore, researchers suspect that problems with the follicles themselves, either through dysfunction or depletion, might contribute to POI, but no one is sure yet.

An April paper by Rajkovic and colleagues on FSH receptors in two Indian sisters with POI showed some incredibly specific causes of the syndrome—an inherited recessive trait that resulted in a novel variation of FSH receptors, which affected protein signals in the women's bodies, triggering POI.

Siblings from consanguineous parents, as in the Indian case, are much more common elsewhere—more than 10 percent of marriages are between first cousins in some parts of Asia and the Middle East. These close ties are ideal for studying POI because genetic mutations are easier to detect. But, according to Rajkovic, "For us to really understand ovarian function, we need to understand development." In other words, he wants to know what goes on in early germ cells. And he wants to understand what precise genetic roots rob many women of their dreams of having families.

"Part of who we are is to reproduce," Rajkovic says. "People don't understand the anguish and depression and effect on relationships and marriages. It's profound."

According to him, ovaries and their function are a window to future generations, or a lack thereof.

And "oogenesis, the formation of the fully

competent egg, begins in the ovary!" he adds. "If eggs have abnormal chromosomes, we try to understand the mechanisms," Rajkovic says. So to study ovaries, you'll want to know about eggs; and to study the eggs, you'll want to know their ovarian origin's origin—meiosis.

Aristotle also wondered about conception and development. That mighty philosopher used an observational technique still replicated in contemporary high school biology; he would ever so gently chip a small hole in a chick's shell, careful not to penetrate the membrane underneath. He hoped to watch the development of the creature inside—to see how it went from yolky mass to chirping chick. How did the heart form? When did the beak appear? And can the inner life of a chicken's egg give hints about human development?

Today, reproductive researchers go primitive—seeking answers from a wriggling, transparent creature known as *Caenorhabditis elegans*.

Pitt's Judith Yanowitz is a PhD assistant professor of obstetrics, gynecology, and reproductive sciences. She studies meiosis in *C. elegans*—tiny nematodes that are an ideal subject for genetic tinkering and studies on fertility, as they're simple in structure and relatively straightforward in development. The worms have just six pairs of chromosomes and 100 million base pairs (compared to 23 and 3 billion, respectively, in humans), which made them an attractive subject during early whole genome sequencing. (Theirs was the first whole genome to be sequenced.) *C. elegans*'s reproductive tracts, especially, are orderly: From end to end, the gonad's germ

cells and developing embryos form a progressive timeline of conception to birth.

Yanowitz explains this as she swaps dishes of *C. elegans* under a microscope—she's looking for just the right squirming millimeter to illustrate her work. She and the half-dozen or so colleagues in her Magee-Womens Research Institute lab have been engineering mutant *C. elegans*, which are typically self-fertile hermaphrodites with XX sex chromosomes, for genetic variations and processes related to reproduction. A portion of their research focuses on the rare males, who have only one sex chromosome, represented as "X0," and thus further remove a genetic variable. Broadly speaking, Yanowitz wants to figure out where errors in cell division begin. That means wending her way back to meiosis—one of the earliest events of life for any sexually reproducing creature.

Yanowitz has dark curly hair, a standing desk, and the most enthusiastic attitude toward worms you've ever seen. In her guest editor's introduction to a special issue of *Methods* last year, Yanowitz suggested that *C. elegans* isn't just a toolbox—it's a toolshed, and one that needs expanding.

"They're cool!" Yanowitz says of the worms. "Let's go look at them."

Under the microscope, she can see the *C. elegans* wriggle in their dishes, glowing green and pink according to their mutations. Their eggs, little time capsules, line up inside the slippery sine wave of a body. Her lab techs have fixed the worms at various stages of reproduction, allowing observation through the entire process. Each batch of worms has a different genotype, crafted by the crew, to play out controlled iterations of chromosomal exchange.

Several times, Yanowitz exclaims, “I’m in love with chromosomes!”—how they copy, how they express in different regions, how DNA gets repaired, how it all coordinates. “There are many questions about the underlying biology that just knowing the genes doesn’t reveal.”

One of the key events during meiosis is a genetic swap: “The maternal and the paternal copies of every chromosome in our cells actually exchange DNA; that’s a process known as crossing over, or recombination,” Yanowitz explains. In diagrams, recombination looks somewhat like 46 people playing a game of Twister—legs and arms wrap around each other and tangle together. But this game of Twister is twisted: The arms and legs, hands and feet, actually swap between partners, resulting in genetic diversity in the offspring’s DNA. Some places are more prone to swapping than others, and these are called hotspots. “One of the projects in the lab is trying to understand what makes a hotspot hot, what calls up this particular region, what makes it more prone for this double-strand break,” Yanowitz says.

Yanowitz’s lab studies mutations that affect double-strand breaks and how they’re made. That is, why some chromosomes get breaks and others do not.

Sometimes things go awry. “If you fail to get a crossover, or if it happens in what we call ‘unfavorable’ places on the chromosome—we don’t really understand what that means—the chromosomes mis-segregate during cell division.” That can mean offspring with extra or missing chromosomes. Or it can mean a failure for the chromosomes to ever create offspring—to cross the next “checkpoint” of meiosis.

The concept of checkpoints is new, and even a little controversial, in biology and genetics. During the two-part process of meiosis, Yanowitz and others theorize, the burgeoning cell checks up on its own development, much like a passport check at an international border—somebody has to make sure everything is in order. If not, the journey’s over.

One gene they’ve identified is *xnd-1*, which regulates chromosome crossover and segregation. Experiments conducted by postdoctoral fellow Mainpal Rana, a PhD, have shown that its absence can cause sterility in *C. elegans*. So, too, can genes *nos-1* and *nos-2*. Ninety-eight percent of worms missing *xnd-1*, *nos-1*, and *nos-2* are infertile, and 92 percent have no germ cells. Their findings on *xnd-1* were pub-

lished in *Nature* in 2010.

Similarly, through studies of *C. elegans*, Yanowitz’s team found that mutations in *him-5* reduce the frequency of crossover on the X chromosome and change crossover distribution.

More recent studies have provided further evidence for this genetic border patrol: “We have evidence that there actually is a true crossover checkpoint that monitors each chromosome pair, each maternal-paternal homolog pair, to make sure that they’ve created this crossover,” Yanowitz says. Those results were submitted for publication this fall.

But let’s back up. Meiosis occurs early in fetal development, and its result is a package of gametes—the eggs or sperm needed for future reproduction. After DNA replicates, meiosis begins, then the twisted chromosomes swap bits of themselves at hotspots and line up along the poles of a cell. Spindle fibers draw pairs from mom and dad to each other, at which point they scuttle over to either end of the cell. Finally, a cleavage forms to clip off both sides into their own haploid cell, called daughter cells. Each daughter cell has a nucleus and a single set of unpaired chromosomes called chromatids.

At this stage in female development, meiosis pauses for about 7 million oocytes (immature egg cells). In female humans, hormones like FSH won’t shoot the starter pistol for the million or so oocytes remaining at birth to trigger what’s known as meiosis II until puberty.

For males, meiosis I and II begin in puberty and run on autopilot, ready for reproductive action—though sperm, too, need to cross checkpoints through meiosis on their way to maturity. In mouse models, Rajkovic’s lab has discovered another gene pair, *SOHLH1* and *SOHLH2*, that, when knocked out of the genome, stop sperm from maturing.

Supposing a gamete does mature, in meiosis II, a very similar process to meiosis I occurs, though chromosomes don’t replicate again. The chromatids split, align, and dance across the cell to opposite ends. Then chromatids become full-blown chromosomes and break into a total of four new cells. In males, all four become sperm; in females, two or three become “polar bodies,” which often die or assist in other bodily processes, and the lucky one begins the journey to mature ovum.

The oocyte begins its maturation pilgrimage to the follicles and eventually to ovulation. In all, only a few hundred eggs will make

this trip before menopause. (That voyage, too, is incredibly complex and ongoing. Many eggs are maturing at once, competing for the right to attempt fertilization—and that maturation process takes over a year for each. And that’s before the thing has even met sperm—which, as we know, bring their own genetic baggage to the relationship. It’s a wonder any of us are even born, when you think about it.) And, like any odyssey, a flat tire or wrong turn of the caravan can delay arrival at one’s final destination.

“Aleks and I talk quite a bit about [how] *Wouldn’t it be great if we could detect bad oocytes?*” Yanowitz says. “That’s the million-dollar question: Is there something fundamentally different or some signal that an oocyte that has not correctly undergone meiosis is sending out?”

“Chromosomal abnormalities play an important role in an egg’s demise, but some [eggs] that survive will give rise to offspring with unbalanced chromosomes,” Rajkovic adds. So a discovery at one stage will probably help elucidate problems at another developmental stage.

How might genetic knots and splinters warp future generations? The answers to that question go beyond just infertility and into the realm of aging and DNA repair. Eggs, and to a lesser extent sperm, carry proteins, a mess of mitochondria, and other essential building blocks of life.

By whittling away at the causes of POI and other variations in the reproductive system, researchers could eventually identify infertility before it happens. Rajkovic dreams of a future where artificial ovaries stave off early menopause and help women conceive without an egg donor.

For now, scientists will have to settle for returning to the beginning, again and again.

As Rajkovic identifies mutations for POI, Yanowitz would like to generate homologous mutations in *C. elegans*. Then, she’ll evaluate the functional significance of those variations to see whether they cause fertility or meiosis defects in the worms.

“This will allow for a rapid screen of putative pathogenic variants that we identify in our sequencing of patients,” Rajkovic says.

When Rajkovic’s team published the papers on *MCM8* and *MCM9*, Yanowitz says, “One of the first things Aleks said was, ‘You should study it in worms!’ I immediately looked it up online and said, ‘Unfortunately, of that whole complex, those are the two proteins that are not conserved in worms and flies.’”

So, they’re back to the beginning, brainstorming potential collaborations, ready to start anew. ■



ONE LAST TIME!

BY EM DEMARCO



WHEN WE LAST LEFT THE CLASS OF 2015, THE STUDENTS HAD JUST A FEW WEEKS TO GET EVERYTHING IN ORDER BEFORE **SCOPE AND SCALPEL'S** OPENING NIGHT. DURING THE FINAL COUNTDOWN, TENSIONS RAN HIGH. THE ORCHESTRA COULDN'T MAKE THE LAST FEW REHEARSALS BECAUSE OF A **MAJOR EXAM**. SOME OF THE BLOCKING ON STAGE STILL NEEDED TO BE **FINESSED** ... AND NOW, IN **LESS THAN AN HOUR**, THE CURTAIN WILL RISE ON THE 60TH **SCOPE AND SCALPEL** PERFORMANCE.

THIS YEAR'S STORY PARODIES **MODERN FAMILY**, A TV COMEDY THAT USES A DOCUMENTARY STYLE (THE CHARACTERS OFTEN SPEAK DIRECTLY TO THE CAMERA). THE HEART OF THE STUDENT SHOW **EXPLORES LOVE, SCHOOL, AND PRESSURES** FROM PARTNERS AND PARENTS. ONE CHARACTER IS GAY, WITH A NEW BABY; ANOTHER IS A HIGH-ACHIEVER WHO MAY HAVE FOUND TWO PASSIONS AMID HER METICULOUSLY ORGANIZED LIFE. BOTH ARE MED STUDENTS AND CHILDREN OF DOCTORS; THEY ARE STRUGGLING TO FIND THEIR OWN PATHS.

OUR STORY BEGINS BENEATH THE STAGE. ABOVE US ARE THE SOUNDS OF FEET SCUFFLING AS THE ORCHESTRA TWEAKS ITS CUES. HERE IN THE PREP ROOM, IT'S A FRENZY OF ACTIVITY AS PROPS ARE POSITIONED FOR DEPLOYMENT, WIGS ARE DONNED, MAKEUP IS APPLIED ...



ADAM COHEN, A HEAD WRITER, CAST, ETC. (CHILDREN'S NATIONAL MEDICAL CENTER, GEORGE WASHINGTON UNIVERSITY, PEDIATRICS)

* ADAM'S SPECIALLY MADE SCRUBS HAVE SWAPS ALONG THE EDGES, SO HE CAN DO A SPEEDY ON-STAGE COSTUME REVEAL OF A RED SPANDEX OUTFIT.

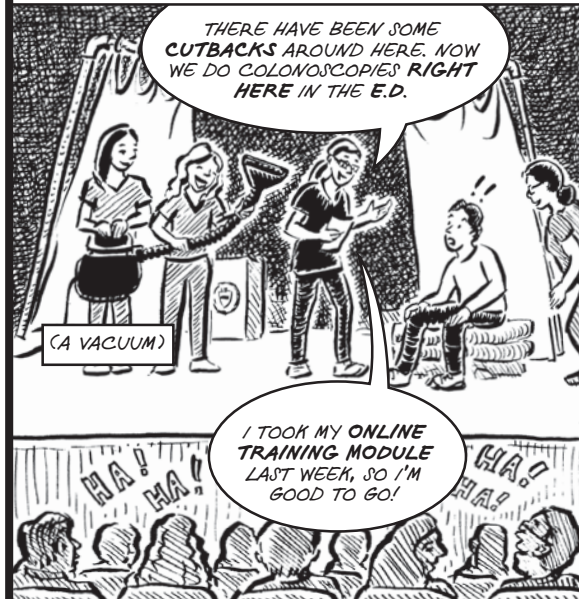


JORDAN KNOX, DIRECTOR, CAST, ETC. (UNIVERSITY OF UTAH AFFILIATED HOSPITALS, FAMILY MEDICINE)

AND WITH THAT, THE 60TH PRODUCTION OF SCOPE AND SCALPEL IS UNDER WAY.

DURING A SCENE ABOUT PREPPING FOR AN ANATOMY EXAM, STUDENTS PLAY A DRINKING GAME IN FRONT OF A PAINTED BACKDROP OF THE ANATOMY LAB -- FEATURING BODIES UNDER SHEETS AND A SKULL ON ONE OF THE TABLES ...

BACKSTAGE, STUDENTS RUN FROM THE WINGS TO CHANGE COSTUMES.



(A VACUUM)

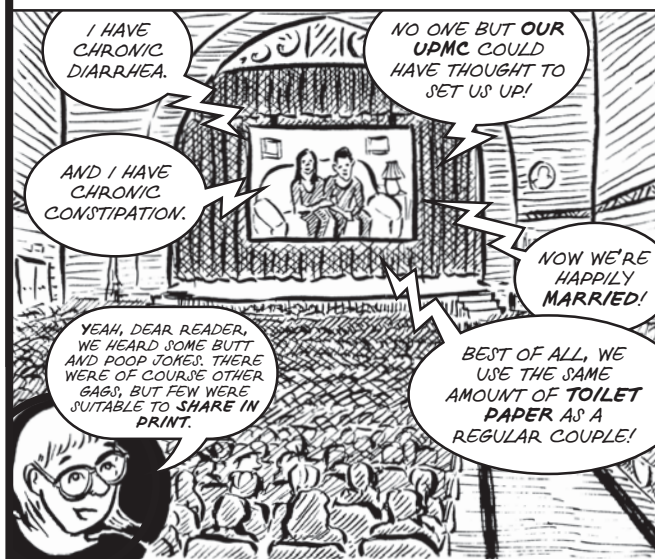


SARAH COHEN, ART. DIRECTOR, WRITING COMMITTEE, ETC. (DUKE UNIVERSITY MEDICAL CENTER, INTERNAL MEDICINE - PEDIATRICS)

BEFORE INTERMISSION, ONE OF THE "COMMERCIALS" ON THE SCREEN OVERHEAD IS A JOKE ABOUT HOW THE DATA COLLECTED BY THE MEDICAL CENTER FOR PERSONALIZED MEDICINE INSTEAD ARE USED TO CREATE AN ONLINE DATING AND MATCHMAKER SERVICE CALLED OUR UPMC.

THEN A "REAL, LIVE" OUR UPMC USER TAKES THE STAGE, REGALING THE AUDIENCE WITH HOW HE FOUND LOVE USING THIS MATCHING SERVICE.

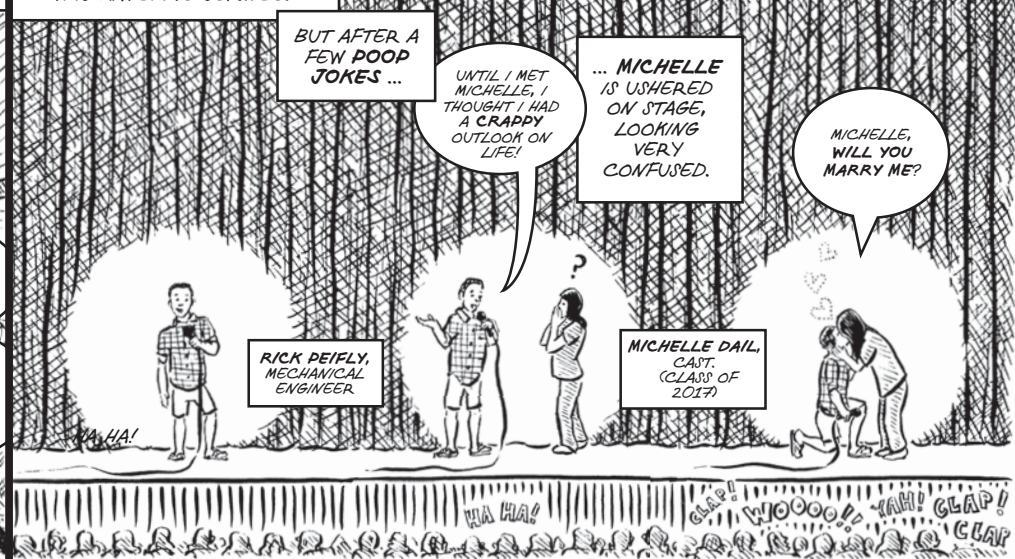
USUALLY THE FIRST ACT ENDS WITH A BIG NUMBER, NOT AN ACTUAL MARRIAGE PROPOSAL.



AND I HAVE CHRONIC CONSTIPATION.

YEAH, DEAR READER, WE HEARD SOME BUTT AND POOP JOKES. THERE WERE OF COURSE OTHER GAGS, BUT FEW WERE SUITABLE TO SHARE IN PRINT.

BEST OF ALL, WE USE THE SAME AMOUNT OF TOILET PAPER AS A REGULAR COUPLE!



RICK PEIFFLY, MECHANICAL ENGINEER

MICHELLE DAIL, CAST. (CLASS OF 2017)

MICHELLE, WILL YOU MARRY ME?

THE SECOND ACT IS PEPPERED WITH CROWD FAVORITES -- AN ELABORATE **BOLLYWOOD DANCE**, A TODDLER IN SCRUBS (A GOOD-NATURED JAB AT ONE OF THE INSTRUCTORS), AND A SCOPE AND SCALPEL TRADITION ...

... UTERUS COSTUMES!

THE SONG, "I-U-D," PARODIES "I WILL WAIT" BY MUMFORD & SONS, AND FEATURES COSTUMED STUDENTS WEARING IUD, SPERM, AND UTERUS OUTFITS.

THIS YEAR'S HANDMADE "LEFT SHARK" COSTUME POKES FUN AT POP STAR KATY PERRY'S NOTORIOUSLY OUT-OF-STEP BACKUP DANCER DURING THE 2015 SUPERBOWL.

SUNDAY'S PERFORMANCE GOES JUST AS WELL AS THE FIRST NIGHT'S.

EARLIER, A '55 ALUM SAID,

IT'S SOMETHING THAT I'VE LOOKED FORWARD TO SINCE MY FIRST YEAR ... HOPEFULLY, AT THE 100TH ANNIVERSARY I CAN COME BACK AND WATCH.

"WE HAD NO IDEA THERE WAS GOING TO BE A 1956 [PRODUCTION], LET ALONE A 60TH ANNIVERSARY."

THE WHIRLWIND WEEKEND OF WIGS, MAKEUP, AND ADRENALINE ENDS. TOMORROW THE STUDENTS GRADUATE -- STEPPING ONTO A STAGE TOGETHER FOR ONE LAST TIME, TO GET THEIR M.D.s.

* MY MIND IS SET, AND THIS I VOW THAT NO ONE IN THIS TOWN OF STEEL CAN TELL ME WHAT TO DO OR FEEL AND NO ONE'S GONNA BRING MEEEEEE DOWNWWN!

*"DEFYING FAMILY" SUNG TO "DEFYING GRAVITY" FROM THE MUSICAL WICKED.

GURNEY RISING

THE END!

KATHLENE BABALOLA, CAST: ALBERT EINSTEIN MEDICAL CENTER, EMERGENCY MEDICINE



WARDROBE CHANGE NUMBER 9

BY CARA MASSET

INSIDE THE WORLD OF OCD

The alarm went off at 6 a.m. Instantly, the question pushed into Hilary Zurbuch's head: *What am I going to wear?* She slipped out of bed in precisely the same manner that she did every morning, getting out on the right side. Then she approached her closet, the question still pounding: *What am I going to wear?*

Zurbuch, a 30-something woman, picked out an ensemble, then pressed it under a hot iron. Something wasn't right. Although the khakis and plaid shirt were fine last week, today they just didn't *feel* right. No, she couldn't wear this to her job. Zurbuch picked out another pair of slacks and a collared shirt. Ironed those. *Would this make me look like I'm 12?* she wondered. Scratch that. Zurbuch decided on another outfit. Ironed it. Would she look perfect in this? She wanted to look perfect. Plus, she felt that nagging fear she's had since childhood that if her outfit wasn't just right, something *bad* would happen that day.

It was the same wicked dread that led Zurbuch to quit crayons and coloring books for good as a preschooler because she thought she might fail to color perfectly. The fear that she'd been *bad*, and that it would be her fault if *bad things* happened to her parents or siblings. The fear that if she didn't turn around 16 or 32 times before getting into bed, things would go bump in the night.

A woman with obsessive compulsive disorder shares the story of how she was paralyzed by the decision of what to wear each morning, among other concerns. Intensive exposure therapy helped her get out of the OCD trap. But that therapy is difficult to pursue. Pitt's Susanne Ahmari is revealing the brain workings of this painful condition in hopes of finding other effective therapies.

PHOTOGRAPHY | CAMI MESA



ABOVE: Compulsions often manifest as rituals, like excessive ironing. OPPOSITE PAGE: Zurbuch got out of bed in precisely the same manner every day. As a child, she believed that if she didn't turn around at least 16 times before getting under the covers, something terrible would happen.

Nearly two hours have passed, and Zurbuch is still in her apartment, selecting clothes, ironing, and starting over again. *What am I going to wear?* She has to be at work in an hour, and she's still not dressed for the job. She hasn't eaten breakfast.

The kitchen. She hasn't gone into the kitchen. Not the kitchen. Not today. She can't handle the fear that *something awful* will happen if she enters the kitchen. Sometimes the fear leads her to skip meals. She won't tell a soul about the distressing thoughts invading her brain. But maybe someone could help her get through the morning.

She calls a friend. *Can you help me get breakfast?*

Zurbuch is a young professional who holds a master's degree, golfs regularly, takes annual pilgrimages to the beach with friends, volunteers in her community, and laughs a lot. She's also a person living with obsessive compulsive disorder (OCD).

The disorder is characterized by a tug-of-war between obsessions and compulsions. In OCD, obsessions are intrusive, often fearful thoughts, like Zurbuch's fear that she'll have a bad day if she doesn't choose the right outfit in the morning. Compulsions are repetitive behaviors or rituals that people with OCD often engage in to try to control their obsessions. Initially the rituals may provide

temporary relief from the fixations, but as they become more frequent, the actions can disrupt daily living and become embarrassing and exhausting. Even though many people with OCD may recognize that their compulsions are senseless, they engage in them for hours at a time.

What happens in the brain to lock people with OCD into their rituals is still not known. A team of researchers at the University of Pittsburgh is using clinical observations and new neuroscience tools to extricate a deeper understanding of the disorder. Led by Susanne Ahmari, an MD/PhD and assistant professor of psychiatry in the School of Medicine, the team is striving to help patients like Zurbuch who have, at different periods in their lives, become consumed by OCD. The disorder has been cited by the World Health Organization as one of the 10 most handicapping conditions because of decreased quality of life and loss of income. The Burroughs Wellcome Fund and other organizations have recognized Ahmari's approach to studying the mysteries of obsessions and compulsions.

In its investigations, Ahmari's team is primarily using mouse models. It is among the first in the world to equip the mice with a tool that's blowing the neuroscience field away: a mini-microscope that can record activity in real time from hundreds of neurons. "What this allows us to do is, basically, to have streaming video from the brain of a mouse,"

Ahmari says in awe. "I never could've imagined this technology in grad school." (That was in the late '90s and early '00s.)

The mini-microscopes were, in fact, developed at the institution where she attended grad school—Stanford University—but they were only dreamed up in the years after Ahmari had moved on to a residency and faculty position at Columbia University. When she was at Stanford, using electrodes to obtain signals from single neurons was cutting edge.

Ahmari's excitement over the newest tech developments in her lab may come from growing up in a family of engineers. "My first rebellion was to become a biologist," she says, joking. The family engineers wonder how she can work with messy, living things rather than clean, logical devices like microchips. *How can you stand it?* they tease.

Ahmari stands it just fine. In fact, she revels in it. She pursued her bachelor's degree in biochemistry and biology close to her home, Chicago, at the University of Illinois at Urbana-Champaign, where as a freshman she won a Howard Hughes fellowship. As she perused the faculty laboratory list, she was immediately intrigued by a research lab studying learning and memory in the brain.

The lab was headed by the late William Greenough, who was among the first psychologists to demonstrate that the brain is a flexible organ that can change with exercise and other enriching experiences. He was, she recalls, a fabulous mentor who encouraged her to follow a career in research. She worked in his laboratory at Illinois throughout her undergraduate career, planning all along to continue on to graduate school and earn a PhD.

Then, Ahmari learned about MD/PhD programs, and began to consider a wider path that would make the family engineers proud, but a little squeamish, too. "I always knew the reason I wanted to do research was to help people," she says, adding that she was concerned that, by solely earning a PhD and working in a laboratory environment, she would never meet any of the people who might be helped by her research. So she decided to get an MD, as well.

During the research portion of the MD/PhD program at Stanford, Ahmari studied synapse formation at the molecular and cellular levels in the hippocampus brain region. Although it was valuable and exciting work from a basic neuroscience perspective, she says

it made her realize that she would prefer to apply her lab skills to examining poorly understood illnesses. Many of her neuroscience MD/PhD peers elected to pursue neurology residencies; she chose the more unusual direction of specializing in psychiatry.

The outfit was horrendous. A mashup nightmare. The sort of getup that only a 4-year-old could pick out and unabashedly wear in public: purple paisley boots, Captain America socks, plaid pajama pants, a Superman T-shirt, and a knit toboggan cap. The cringe-inducing combination of garments upped Zurbuch's anxiety. Not only was the color combo hideous, but the clothes hadn't been ironed. And now she was being dared to walk. In front of others. Wearing *that!*

Zurbuch's therapist gently coaxed her to go out in the unironed, absurd outfit. On one level, Zurbuch knew that she could walk out of the room in her ridiculous garb and everything would be fine, just like she knew that wearing two shades of violet to work probably didn't mean she was a bad person. On another level, she felt paralyzed. It felt physically impossible to step outside in the hideous outfit. Like when she tried to tell herself that

with a range of mental illnesses. While treating patients with OCD, she was surprised and humbled by how severe and debilitating the disorder was. For instance, at one point in her life, Zurbuch was in the grip of obsessions or compulsions nearly constantly.

Ahmari learned that the treatment options available for OCD are limited. The family of drugs most commonly used to treat mental health conditions—selective serotonin reuptake inhibitors (SSRIs)—only provide remission in approximately 10 percent of OCD patients and mild-to-moderate improvement in 30 to 50 percent, she says. There's also exposure therapy, which makes patients confront their fears—as Zurbuch did when behavioral therapy coaches sent her out in public in a mismatched outfit. “Patients who are able to complete the treatment can have great results

that I've worked with is that they're very interested in the research. They're very motivated to understand what is happening in their own brains. Why can't they stop themselves from performing these compulsions?”

In the lab at Columbia, Ahmari conducted a study on OCD circuitry that yielded surprising results and landed publication in



On one level, Zurbuch knew that she could walk out of the room in her ridiculous garb and everything would be fine, just like she knew that wearing two shades of violet to work probably didn't mean she was a bad person. On another level, she felt paralyzed.

it would be okay to go to the grocery store or enter her kitchen, but the wicked dread stood in the way of even hunger and won.

Then, finally, Zurbuch put one purple paisley boot in front of the other and walked out the therapy center door. She made it down the hallway before her anxiety stopped her from going farther. Another day, she wore the outfit outside the therapy center. Later, she and her therapist walked farther from the building, where strangers were passing by. Finally, after a month, Zurbuch went grocery shopping with her therapist. Wearing that. And her anxiety level, well, it had gone down to about a 2 out of 10. Everything, Zurbuch recalls, was okay.

During her psychiatry residency and subsequent fellowship at Columbia, Ahmari was exposed to patients

from this, but it's incredibly difficult for patients to do,” Ahmari says. And qualified therapists with enough time in their schedules to offer exposure therapy are not always available. Although there are good services in Pittsburgh, Zurbuch traveled to Boston, staying three months, because she required intensive and lengthy therapy.

So Ahmari began hunting for other solutions. In her work as an assistant professor of clinical psychiatry at Columbia, Ahmari began focusing more on treating patients with OCD; she also dove into neuroscience research on the disorder. “I've found clinical care incredibly rewarding,” says Ahmari. “Independent of [my] research's impact on people's lives, I get the reward of helping people to use the tools at their disposal—medications, therapy, their own inner resources. Even more so, what I really love about the patients

Science. The 2013 paper described her team's use of a mouse model to test whether hyperstimulating circuits in the brain's orbitofrontal cortex (involved in decision-making) and ventromedial striatum (involved in selecting particular actions and responding to rewards) would lead to increases in OCD behavior. The team chose to examine those parts of the brain because prior imaging studies had shown homologous areas to be hyperstimulated in patients with OCD. However, no one was quite sure whether the hyperstimulation actually led to OCD symptoms or was a compensation for the symptoms. (Maybe that was just the brain's attempt to fight off the domineering thoughts.)

For the study, Ahmari applied a method known as optogenetics. (That technology was brought to you by Pitt's 2015 Dickson Prize in Medicine winner, Karl Deisseroth; see p.

6.) It worked like this in Ahmari's lab: Her team used a virus that's darn good at getting inside cells—an adenovirus, which typically causes ailments like the common cold. The virus's genetic code had been engineered to include a pigment called channelrhodopsin that's sensitive to light.

Ahmari's team injected the virus into the orbitofrontal cortex of the mice. The virus wriggled its way into the neurons—including through long projections to the ventromedial striatum; and because the virus was carrying the light-sensitive channelrhodopsin with it, the entire neuron became sensitive to light.

Step two of the process was to surgically implant tiny fiber-optic probes into the mouse brains. The probes allowed the research team to shine light into the brains to activate the light-sensitive neurons in the regions associated with OCD.

Ahmari and her colleagues expected that when they hyperstimulated the orbitofrontal

her breath. Rituals emerged for brushing her teeth, using mouthwash, and popping breath mints.

Obsessions can be very selective. Zurbuch would stress for hours over her outfit, for example, but hardly think about her hair. During behavioral therapy, her therapists actually encouraged her to get a haircut and pay more attention to her blond locks.

The same year that the *Science* paper was published, Ahmari was recruited to Pitt by David Lewis, chair of the Department of Psychiatry, the Thomas Detre Professor of Academic Psychiatry, and director of the Translational Neuroscience Program.

"She's developed a research program that begins with observations made clinically about the nature of obsessive compulsive disorder and then converted those observations into hypotheses about the nature of the

all those things. She's a magnet for mentees."

One of Ahmari's first mentees is James Hyde, a postdoctoral associate who holds a PhD in neurobiology and developmental science. "She's an incredible mentor. She has a psychiatry background and brings that to bear when it comes to training her students. It helps with figuring out how to approach a behavioral problem," he says. "She's also a very precise, very exacting researcher. And she has a very large research network. If there's something I don't know, she knows someone who does."

Hyde has been tasked with the coolest job in the lab: running experiments with the mini-microscopes and mouse models. The microscopes build upon the optogenetics technique that Ahmari used in her *Science* paper. With the microscopy technique, rather than injecting a virus engineered with channelrhodopsin into the mouse brains, Hyde injects a virus engineered to encode a molecule called GCaMP6. This protein creates a burst of light

For people with OCD, triggers can range from monumental incidents, like the death of a parent, to everyday slights, like a friend teasing about a bad hair day.

cortex and ventromedial striatum circuits, they would immediately see more OCD behavior—in this case, excessive grooming by the mouse. But nothing happened. At least not initially. They did eventually see compulsive grooming behavior, but only if they stimulated the circuits for a few minutes daily for several days.

This unexpected finding, Ahmari says, provides some insight into her own clinical observation and the observations of other psychiatrists that OCD symptoms may gradually emerge over time. It seems that relevant brain regions are first repeatedly activated by triggers in the environment. The paper's findings may reveal more of the wiring of OCD, creating a map to ultimately help pharmaceutical researchers find better drug treatments.

For people with OCD, triggers can range from monumental incidents, like the death of a parent, to everyday slights, like a friend teasing about a bad hair day. In an hour-long BBC program on OCD that aired in September and featured a segment on Ahmari's research, one patient who was interviewed described the trauma of having a friend in middle school casually mention that she had sour breath. The shame replayed itself in her mind, and she became obsessed with

underlying brain disturbances, which she has been testing in elegant experimental models and animals," Lewis, an MD, says.

Ahmari calls her peers in the Translational Neuroscience Program a "wonderful group" of supportive, idea-bouncing colleagues and says that she has been impressed by the rich collaborative environment of the Pittsburgh neuroscience community. "It's not the case everywhere," she says. "It was extremely attractive to go to a department that had a shared vision and a goal of using the newest, most powerful technologies for attacking this really important [mental health] problem," she says.

Since arriving at Pitt, Ahmari has devoted her time to setting up her laboratory in the Bridgeside Point II building along the Monongahela River in South Oakland. She has begun hiring and training postdoctoral fellows and graduate students—another area where she excels. "She's not only really good in training individuals in the conduct of science but also in how to think as a scientist," Lewis says. "It's not just about learning how to do something at the bench but about how to think and also about how to behave and interact with other scientists. A lot of people want to come and work with her because she has

(fluoresces) in the presence of calcium. Because calcium is one of the primary molecules that neurons take up when they send and receive signals, neurons treated with the GCaMP6 protein will flash every time they fire.

Hyde then surgically implants tiny base plates into the mouse skulls. During experiments, Hyde connects miniature microscopes weighing only 1.9 grams to the base plates. The microscopes are lightweight, so the mice can run around as they normally would; that's a big advancement over other technologies that require animal models to be fixed in one spot. The microscopes contain cameras like the ones in smartphones, so Hyde can record the flashing neurons.

"What's astounding is the combination of things in these tiny microscopes," Ahmari explains. "Now we're not looking at one neuron at a time. We can look at up to 200 neurons at a time, and we can look at them over the course of weeks or months. The microscope can peer inside the brain . . . and we can see what language or code they're using when engaging in behaviors related to OCD." The technology is so advanced, she says, that her research team can watch communication between groups of neurons or individual neurons. It's like having the ability to listen to an

entire orchestra—then choosing to listen to one section of violins or cellos—and homing in even further to hear every single player on a solo level.

“The other real innovation comes in the acquisition of data,” she adds. One recent morning, Hyde recorded brain activity in two mice for 30 minutes. The recordings yielded 100 gigabytes of data. He offloaded the data sets onto the lab’s workstations to process them during the next 24 hours. The next day, Hyde sent the data to a statistics team at Carnegie Mellon University that has been building algorithms and suggesting ways to fully comprehend all the information.

The Carnegie Mellon team, headed by statistics professor Robert Kass, is part of the Center for the Neural Basis of Cognition, a joint venture between Pitt and CMU. Kass and Ahmari began collaborating this year.

Kass says the new mini-microscope approach is among the more exciting recording technologies coming online for neuroscience. And it’s generating more information than ever before. “It’s in the realm of what we call Big Data these days,” he says.

Yet it can be difficult to assess all of the information. That’s where he can help. “It’s easy to find patterns in data that seem to give you an explanation of something, when actually what you’re looking at is random stuff. If you’re not careful, you can’t tell the difference. The challenge in statistics is to say, how much do we know from this data?”

“The collaboration has been so critical for us,” says Ahmari.

So far, Ahmari’s team has just preliminary results from the mini-microscopes. The research will be funded during the next three years through a \$75,000 McKnight Scholar Award from the McKnight Endowment Fund for Neuroscience. Only six scholars nationwide were selected for the 2015 award, which is reserved for young scientists who are establishing their labs. Ahmari is looking forward to attending a meeting for McKnight awardees next summer, along with fellow 2015 McKnight awardee Marlene Cohen, a Pitt PhD assistant professor of neuroscience who studies how visual attention guides behavior.

Next year, Ahmari also hopes to be able to set up a clinical practice and start seeing OCD patients again.

Patients have raised important research questions for Ahmari. She notes that one patient told her “the experience of having anxiety relief from performing a compulsion was extremely

rewarding even though having the obsessions and compulsions was not rewarding at all.” That got Ahmari thinking about the neural pathways involved in reward. What are those pathways like in a brain dealing with OCD?

In recent months, Elizabeth Manning, a postdoctoral associate in Ahmari’s laboratory, has been conducting some experiments related to reward. Clinical observations have shown that OCD patients often struggle to adapt to new situations, Manning says. Even when rewards are involved, it’s difficult to change behavior. Manning has shown this through a test in optogenetic mouse models.

Manning trained mice to push one of two levers. If they pressed the correct one, they would receive a chocolate pellet. Initially, the left lever produced the chocolate, so the mice learned to push that one. Later, the right lever became the magic button for chocolate. The mice displaying typical behavior would learn to push only the right lever within a day or two. The mice displaying OCD-like behavior, however, were unable to adjust their behavior for as long as a week to get the chocolate prize.

Manning wonders, were the reward circuits underactive or overridden by hyperactivity in other areas? And they’ll be exploring which neural circuits were involved.

On a golf course, Zurbuch concentrates on the ball near her feet. She swings and pops the ball into an arched trajectory toward the green. She watches it land, then carries her bag toward it. Hitting the ball, watching it land, inching closer to the hole—these are the only things she thinks about while on the course. There are no added rituals. There are no obsessive thoughts. She is only thinking about the here and now. Golf.

Zurbuch’s grandmother taught her to golf in the backyard when she was 8 years old, and she took up the sport more regularly in college. She now tries to get out for at least a nine-hole round every day. Zurbuch says that golf relaxes her and has helped her to become healthy; it creates a space for her to practice the art of mindfulness, of living in the moment.

In the winter, when golf courses are dormant under snow, Zurbuch has found that she’s able to practice mindfulness through cooking. As a result of her hard work in intensive exposure therapy sessions, she’s no longer afraid of the kitchen. And she can get dressed



Zurbuch plays nine holes every day; it helps her live in the moment. Her grandmother, who made her this children’s golf bag, started teaching her how to golf when she was 8.

without panicking or changing 10 times. Some of her obsessions still show up, but they’ve faded into the background, like when you become desensitized to the sound of a ticking clock. When the obsessions become louder, she is confident that she doesn’t need to pay attention to them.

This year, Zurbuch, now a licensed behavioral therapist, opened a private practice. After years of studying, training, and improving her own health, she specializes in helping children as young as 3 overcome OCD, anxiety, and phobias through evidence-based treatments. “I love being a therapist,” she says. “It’s the best job I could possibly have in the world. To understand the depths of OCD and the pain . . . and then to help people . . . is very rewarding [and] unbelievable to me from where I was at.”

On her desk, she keeps a box of her grandmother’s golf balls. It’s a reminder of what Zurbuch calls the beauty of the game: If you swing and miss or send the ball into a bunker, it’s okay.

All you have to do is adjust your grip and swing again. ■



LOU GEHRIG'S GRATITUDE INSPIRES A FAMILY
TEXT BY KRISTIN BUNDY
PHOTOS COURTESY DUANE RIEDER
AND SUZANNE ALEXANDER

"WE'RE DOING THIS FOR THE NEXT GUY"

Suzanne Alexander is no stranger to telling the story of how her husband, Neil Alexander, was diagnosed with amyotrophic lateral sclerosis (ALS) or how his body deteriorated over time. She has recounted it dozens if not hundreds of times on her blog and to family, friends, and journalists. But on this sunny late-August morning, the element of surprise still lingers in her voice as she recalls her husband's death just five months prior.

His absence was especially palpable at breakfast that morning, when Suzanne continued a tradition Neil had started with their two children, Abby, 13, and Patrick, 11.

"The first day of school, last day of school, and birthdays, he always made chocolate chip pancakes. So I made that for them this morning," Suzanne explains. "Even when he couldn't use his hands—I made them, of course—but it was always him."

This was the first back-to-school morning Neil wasn't with them—one of many such firsts the family would experience. "These little milestones," Suzanne says. "I was just thinking, *God, I just got through this without him. I can't believe it. I can't believe it.*"

Neil Alexander, diagnosed with ALS in 2011, wanted the world to see how his body changed over time. For nearly four years, Pittsburgh photographer Duane Rieder and Neil met periodically for photo shoots. This photo was taken in February 2015.





Neil spent many years going in and out of doctors' offices for what seemed to be unassociated ailments. But in 2011, a pulmonologist noticed muscle atrophy in Neil's left hand and suggested he see a neurologist.

That June, Neil visited David Lacomis, an MD, professor of neurology and pathology, and chief of the Division of Neuromuscular Diseases at the University of Pittsburgh, expecting a routine visit. Instead, Lacomis told him he had a motor neuron disease, progressive muscle atrophy.

After a series of tests at Pitt and a corroborative second opinion at the Cleveland Clinic, Neil was diagnosed with ALS. This disease is characterized by the degeneration and death of motor neurons. As neurons die, the muscles weaken, twitch, and atrophy. Eventually, people with ALS can expect to lose the ability to stand, eat, speak, move, and breathe. (More rarely, it results in dementia.) Life expectancy is, on average, three to five years after diagnosis.

The Alexanders described the time right after the diagnosis as "crushing." For weeks, they dealt with anger, resentment, and sadness.

Then, reaching for some hope, Neil looked for inspiration from others with the disease; he could find only one.

Lou Gehrig, baseball great from the 1920s and '30s, became the namesake for ALS, mainly because few people have gone public with their diagnosis. In 1939, Gehrig gave a farewell speech at Yankee Stadium, during which he expressed gratitude to those around him. He closed by saying, "I might have been given a bad break, but I've got an awful lot to live for."

It was Gehrig's expression of appreciation that changed Neil and Suzanne's perspective. They shifted their focus from what had gone wrong to what had gone right in their lives.

The family celebrated Neil's relatively good health that first year by making memories together. They traveled all over the United States and spent time in St. Lucia and Ireland. The Alexanders were together so often that, "The kids were hardly in school," says Suzanne.

Neil and Suzanne also began to raise awareness for ALS, with the help of others in their lives. Hefren-Tillotson, the financial firm Neil worked for, immediately signed up for the 2011 Walk to Defeat ALS in Pittsburgh after his diagnosis, raising \$45,000. Friends and family joined similar walks around

For the photo series, Neil wore T-shirts that represented the people who made extraordinary contributions to his life. As the series progresses, changes in his body become more noticeable. His wife, Suzanne Alexander, recounts that his symptoms started with atrophy in the left, then the right, arm and then atrophy and edema in the legs. **OPPOSITE PAGE LEFT:** A teacher at Columbus Academy, where Neil went to high school, was instrumental in directing Neil to Fordham. Taken December 2011. **OPPOSITE PAGE RIGHT:** Neil was a young kid who “had no money and came from a broken home,” as Suzanne describes, but Fordham gave him a chance for an undergraduate education. Taken July 2012. **RIGHT:** After Fordham, Neil moved to LA where he served as a police officer for the LAPD for five years. He met Suzanne on Manhattan Beach on July 4, 1989. Taken February 2013. **BELOW:** The family poses for a Christmas card. Neil and Suzanne are shown with their children, Abby and Patrick, and their dog Libby. Taken November 2011.



February 2013

the country, contributing an additional \$13,000. These walks led to more homegrown philanthropic events that continue today, including bike rides, golf tournaments, Swim-A-Thons, lemonade stands, and Donut Dashes.

As their community rallied around them, the Alexanders worked with the Pittsburgh Foundation to develop a fund called Live Like Lou. This organization would become their new life's work.

Neil also used Live Like Lou to put a face on the disease. This was two years before the viral ALS Ice Bucket Challenge, and few people with ALS were talking about their experiences. Neil contacted Pittsburgh photographer Duane Rieder and asked him to document the changes in his body over time. The two met periodically at Rieder's studio, which happens to be above the Roberto Clemente Museum (also run by Rieder) in Lawrenceville. For each shoot, Neil would don a cut-off T-shirt and compression shorts for the camera.

This photo series, which began in late 2011, became what Neil called “A Journey of Strength—The Progression of ALS Over Time.” The photos not only showed the course of his disease, they also represented the people behind the organizations who touched Neil's life from his teen years forward.





March 2014



June 2014

"He said the greatest display of his gratitude would be to wear these T-shirts and to wear them as his body declines," Suzanne notes. "And the thinking is, as his body gets weaker, he wants to wrap himself up in the images that gave him strength."

As Rieder turned his lens on Neil, Neil turned his focus to the science behind ALS. He was struck by how little the medical research community knew about the disease, despite the fact that ALS was discovered nearly 150 years ago. Today, there are no long-term, effective treatments.

Neil began to talk to his friend and neighbor Mark Gladwin, an MD, the Jack D. Myers Professor of Internal Medicine, and chair of the Department of Medicine at Pitt, about using the money they had raised through Live Like Lou for research.

"We discussed the idea of creating a research center," says Gladwin, "where we could actually recruit talented people to Pittsburgh to do research in ALS, encourage the brilliant people that we have here at the University of Pittsburgh [who] are already experts in neuroscience to get involved, and to engage them in his mission of finding a cure and

treatments for ALS."

Gladwin introduced the Alexanders to the scientific director of the Pitt Brain Institute, Peter Strick, a PhD, Distinguished Professor, Thomas Detre Professor, and chair of neurobiology. Strick was enthusiastic about bringing this type of research to Pitt and was inspired by the Alexanders' dedication. "Neither Neil nor Suzanne are scientists or medically oriented people, but they are people who get things done," says Strick. He described the Alexanders as "indefatigable" in trying to understand what was needed and how they could make a difference.

In February 2015, Neil and his daughter, Abby, presented a check to Pitt from the Pittsburgh Foundation for \$500,000 to help create the Live Like Lou Center for ALS Research at Pitt's Brain Institute.

"We're doing this for the next guy," said Neil at the event. "For the next father, the next husband who looks down at his left arm and realizes the muscles in his arm have been twitching uncontrollably. . . . We're doing it for when the doctor walks into the examining room



February 2015

As the years and the disease progressed, it became harder for Neil to stay coiffed and clean-shaven, so they buzzed his hair and kept a goatee. Suzanne liked the goatee because it was his “vacation look.” Starting in 2013, Neil moved quickly from walker, to scooter, to wheelchair as his ALS advanced. In October 2013, Neil had a diaphragm pacing system implanted to assist with his breathing. In 2014, he sat down in his “big wheelchair,” as Suzanne calls it, and he never stood unassisted again. **OPPOSITE PAGE LEFT:** Neil applied to nine law schools while still in LA. Pitt accepted him within two weeks of him submitting his application. Neil and Suzanne took that as a sign and moved here in 1994. Taken March 2014. **OPPOSITE PAGE RIGHT:** Neil’s grandparents lived in Pittsburgh and took him to Pirates games as a boy. He was an avid fan through adulthood. Taken June 2014. **THIS PAGE LEFT:** Neil began working for the financial planning firm Hefren-Tillotson after law school and stayed for 14 years. Suzanne says that the company was instrumental in supporting the family after Neil’s diagnosis. “They immediately rallied . . . they were fearless and determined to lift us up.” Taken February 2015. **ABOVE RIGHT:** We can see atrophy in Neil’s left hand. Taken January 2013. **RIGHT:** Neil liked this picture because he and Suzanne are holding each other. That’s something they did more and more as his body became weaker. Taken March 2014.



and says, ‘I’m really sorry, but we think you have ALS.’ And when that father and husband says, ‘Okay. What do we do now?’ We’re doing it so that doctor actually has something to say.”

This August, Chris Donnelly, a PhD, joined the Live Like Lou Center for ALS Research. The new assistant professor of neurobiology will continue his studies into the cellular changes that occur with ALS and pursue possible treatment approaches.

Donnelly was recruited from Johns Hopkins University where he had been working with Jeff Rothstein, a clinician scientist who aided the FDA approval of the first and only drug currently available for ALS, riluzole. In a recent *Nature* article, Donnelly’s lab described how proteins end up in a traffic jam heading in and out of the nucleus of motor neurons. Using stem cells derived from ALS patient skin biopsies that were then “tricked” into becoming motor neurons, they’ve identified ways to get that traffic moving again.

In his search for a faculty job, Donnelly was especially drawn to Pitt’s commitment to ALS and the community that supports it.

“This is a dream of mine, this type of work that we’re doing. Not

just the science but also the ability to work with patients, work with David Lacomis, to help him with his clinical research, to help fund-raise for the cause. So it’s not just, for me, coming in and working in a lab every day and doing an experiment. . . . It’s more about the big picture. . . . It’s more human than just being a research scientist in ALS.”

Neil had hoped to live long enough to meet the person who would join the center and conduct the basic research so badly needed for this disease. But he died on March 24, the day before Chris Donnelly would arrive in Pittsburgh for his second interview.

When asked what he would say to Neil if he were here today, Donnelly replies, “First I would thank him for really getting this thing off the ground and getting this center set up. The second—I would say that they are putting a lot of trust in me, and there’s no way I will let him down.” ■

The Live Like Lou fund has pledged to raise \$2.5 million in five years for Pitt’s ALS research center; the University has agreed to match that and is hoping to raise \$10 million. For more information: livelikelou.org.

AmarKohli(@akohliMD), ProjectTycho(@ProjectTycho), Center for Women's Health Research and Innovation(@CWHRI), Pitt Emergency Medicine Residency(@upmcm), Pitt Health Sciences(@PittHealthSci), Internal Medicine training program(@PittIMChiefs), Pitt Plastic Surgery(@PittPlasticSurg), Jeremy Berg(@jeremymberg), Paula Davis(@PKDavis), Amesh Adalja(@AmeshAA), Michael Morowitz(@morowitzmj), Brian Zuckerbraun(@zuckerbraun), Benjamin Davies(@daviesbj), Walid Gellad(@walidgellad), Pitt Med Magazine(@PittMedMag)

TWEET TALKIN' DOCS

HOW PITT PHYSICIANS
AND SCIENTISTS ARE
USING TWITTER

BY ROBYN K. COGGINS

Peggy Hasley (MD '85, Res '88, Fel '91) needed a better way to connect her 16 generalist track residents who work in a number of hospitals—UPMC Shadyside, Montefiore, and Presbyterian and the VA Pittsburgh Healthcare System. Plans were falling through, and information was getting lost between the busy, spread out doctors. Hasley's daughter, a med student, suggested they bridge the gap with Twitter.

As associate program director for ambulatory medicine, director of the generalist track in internal medicine, and associate professor of medicine at the University of Pittsburgh, Hasley's interest was piqued. She's especially interested in curricular innovations for resident medical training; so in 2012 she tasked then-resident Amar Kohli (Res '13, Fel '15) with researching the site.

Kohli, now an MD assistant professor of medicine at Pitt, was a casual Facebook user, but he'd never even heard of Twitter: "I was like, *Okay, I need to learn about this, I guess,*" he remembers dubiously saying to himself.

Twitter. Faster than a carrier pigeon, shorter than a newsletter—it's a collection of telegraph-like messages that's attracting doctors and researchers to the great digital human conversation. As of July 2015, the site had 316 million active monthly visitors. After setting up a profile just last year and fiddling around with the site's features, Kohli started to see its professional potential.

If a resident can't make it to a conference with the ambulatory staff, for instance, she could search her colleagues' tweets (short posts about the event) afterward "and basically find six, eight, 10 key pieces of information from the lecture. So they don't feel like they missed out, and they're a little bit on board with their colleagues," says Kohli.

It wasn't long before Kohli was tweeting about School of Medicine events and other conferences, as well as daily bits of interesting medical information. Then he started teaching others how to tweet, too—he now leads a biannual noon lecture series on how Pitt trainees and doctors can use Twitter themselves. Senior faculty to second-year med students have attended, and he's planning more meetings this year.

This June, Kohli tweeted a version of his lecture series and got quite a bit of online attention when the Association of American Medical Colleges collected and shared his 12 tips on their student feed, @AAMCMedStudent. (Don't know what any of that means? Check out the Twitter Terminology cheat sheet on this page.)

Truthfully, though, the in-person lectures have been hit and miss. Lest you think it's the silver-haired crowd resisting social media, Kohli says his generation, the supposed natives of the digital world, are the largest chunk of attendees who walk away unimpressed. *It's one more thing to learn, they might say. I don't have the time. I'm too busy. It's hard to integrate it into my everyday life.* But Kohli offers a different way to look at social media.

"I need to be up-to-date with what *JAMA* says about the new anticoagulation drug or something anyway. And so it just pops up [on my Twitter feed] because a lot of people found that interesting, as well. It just makes my life a little easier doing it this way." In other words, once you get past the hump of setting up your feed, and once you fit it into your daily schedule, social media could actually make professional responsibilities more streamlined.

Kohli summarizes Twitter's benefits and best practices into four categories: teach, advocate, learn, and connect. We've excerpted some of his AAMC-approved tweets below:

Teach. "It's hard to be succinct in 140 characters," writes Kohli, "but learning to be clear and concise is an excellent practice in #MedEd." Talk about a public health crisis; link to important treatment updates. Plus, this is a chance to reach patient populations—for instance, alum Deborah Gilboa (MD '00), AKA @AskDocG, tweets primarily about parenting and family health issues.

Advocate. "~900M people use Twitter," writes Kohli, "I'm guessing that's more ppl than in your email contacts. #SaveGME#SaveStudentAid#DocShortage." Encourage the use of vaccines; share a handwashing sign with colleagues and professional groups.

Learn. "Can't keep up with new articles?" asks Kohli. "Twitter will do the work for you! Every major journal posts key articles, @NEJM @JAMA_current @BMJ_latest." (That's *The New England Journal of Medicine*, *Journal of the American Medical Association*, and what was formerly called the *British Medical Journal*, in case you didn't decipher those handles.)

Connect. Perhaps best of all is visibility and access. A researcher with a question for National Institutes of Health director Francis Collins (@NIHDirector) has a direct line to him. On a smaller scale, Kohli can contact someone like Eric Holmboe (@boedudley)—a renowned medical education researcher and internist at Yale whom he's never met in person but follows on Twitter—for a quick question about a new study. "I would probably never meet [Holmboe] outside of maybe a national conference. . . . But he's following me on Twitter," says Kohli. "And so I could say something or comment on something he has said, and it's like immediate face time."

Kohli adds, "My division chief—everybody—always tells you, *it's important for you to be visible—that's how you get opportunities*. People want to do a large multisite study? *Hey that guy over there in Pittsburgh is doing this.*

"Embrace it and just start fiddling for a couple minutes a week." Kohli suggests. He says it's really very little extra work. "A small effort on my part perpetuates itself." n

TWITTER TERMINOLOGY

Tweet: A 140-character message that you write and publish publicly on your feed, which is a live update of tweets. To see other people's tweets, you probably want to **follow** them, which is much like subscribing to a magazine.

Handle: A person's username, starts with @. Think of it like a user's public journal, a collection of that person's words and ideas all under one name.

Retweet (RT): If you really like what you see and think others should see it too, you can RT someone else's tweet, meaning it'll go to all of the people who follow you. Kind of like a recommendation—the way you might hand off the latest *NEJM* to your colleague or share a link on Facebook.

Hashtag: Similar to an index, starts with #. It makes the ocean of tweets much more searchable. You might see Pitt meders tweeting about **#FOAMed** (free, open-access medical education), **#BigData**, or **#hcsn** (health care social media). And alums unite with **#PittMedAlum!**

Like: An acknowledgment that you've enjoyed someone's tweet.

Direct message (DM): A private note to another user, like passing a note in class. Use this feature if you don't want to broadcast the message to all of your followers. —RKC

TWITTER DOC DO'S AND DON'TS

DO interact with colleagues around the world. Congratulate them on publications, ask them follow-up questions, commiserate after a tough day, retweet them. You may be surprised how big a community you can build.

DON'T share any confidential or patient information or offer detailed medical advice. But you knew that already, right?

DO be selective about who you follow. Rather than haphazardly following accounts, be choosy—remember, you're curating a personal magazine, so load it with content you actually want to see.

DON'T say anything you wouldn't in a public setting. Some follow the Grandma Rule. (If Oma wouldn't approve, skip it.) Some follow the Boss Rule. (If the bigwigs wouldn't like it, don't post it.) And some follow the If You Don't Have Anything Nice to Say Rule. (There's enough negativity in the world already, isn't there?) After you've thought about how you want to portray yourself, follow your own rules.

DO let colleagues know if they cross a line. We're all figuring this out together, and missteps are part of the process. The American Medical Association suggests, "When physicians see content posted by colleagues that appears unprofessional, they have a responsibility to bring that content to the attention of the individual." Kindly do so.

DON'T be afraid to jump in! "Comment on one tweet. Follow one person," suggests Kohli.

For more on professional Twitter conduct, see the American Medical Association's suggestions: bit.ly/AMASNS and Kohli's AAMC-lauded tip list, bit.ly/KohliTwitter.

And while you're out there, look us up:
[@PittMedMag](https://twitter.com/PittMedMag)

—RKC




ABOVE: Kids get their hearts pumping with music at Heart Camp. Shaking their groove thing after every meal is a tradition.
RIGHT: This year Bill Neches Heart Camp for Kids celebrates its 25th birthday.



SCALED A WALL, ESCAPED A RHINO

IT'S JUST HEART CAMP

BY RACHEL WILKINSON



On Day 2 of the Dr. Bill Neches Heart Camp for Kids, the morning is full. There's a climbing wall to scale, archery, and crafting. Then it's time for the 124 campers to gather in the dining hall and ask each other "silly questions."

Is it fun to look at your X-rays? Yes.

What was your favorite part about heart surgery? Bubble gum-flavored anesthetic.

What stories have you made up about your scar? Animal attacks, including: gored by a rhinoceros, bitten by a cow, and fought off a shark.

The four-day sleepaway camp held annually at YMCA Camp Kon-O-Kwee Spencer in Fombell, Pa., is the nation's first camp designed for children living with a heart condition. This year, the campers range in age from 8 to 15. During the popular "Ask the Counselor" session, the kids have the chance to ask their camp counselors—all former Heart Camp attendees themselves—questions only others coping with heart disease can answer. At the mention of shark bite stories, the entire room laughs in recognition.

Bill Neches hoped to create this kind of kinship when he founded Heart Camp in 1991.

"Our vision of Heart Camp was that [it] would be an opportunity for children with heart disease to get to know a group of other children just like themselves," Neches wrote in a booklet celebrating the camp's 25th anniversary this year. (The camp is one of several medical specialty camps organized by the Children's Hospital of Pittsburgh of UPMC staff, including Camp STAR, for young amputees; Camp Chihopi, for pediatric liver and intestine transplant recipients; and Camp INSPIRE, for children with tracheostomies, ventilators, or BiPAP machines.)

Heart Camp arose from Neches's 33-year career as a pediatric cardiologist at Children's. He noticed that although approximately 1 percent of U.S. children are born with heart disease, there were few ways for affected families to connect. A believer in treating "the entire patient," Neches collaborated with UPMC social workers to found Heart-to-Heart, a parent support group; they followed that up with an annual family picnic.

Despite the success of these efforts, he felt a peer-to-peer connection was still missing. Neches consulted social workers again to discuss the possibility of a camp for cardiology patients. It would

be a challenge because, according to Neches, most children with heart disease are not allowed to participate in school athletics and often lead "very sheltered lives." In addition, the camp would need a full staff of doctors and nurses on-site. Eventually, Neches secured the piney, 500-acre Camp Kon-O-Kwee, busing in an inaugural group of 32 campers.

"We didn't know what to expect," Neches recalls. Neches is a former director of pediatric cardiology at Children's and a Pitt emeritus professor of pediatrics. Fearful of overexerting the campers, staff initially denied their pleas to play baseball. But when they finally relented, the campers played for two and a half hours. All 32 of them.

"We said, 'My goodness, these are normal kids!'" Neches says. "It completely changed the way we looked at kids with heart disease."

This adventurous spirit still pervades Heart Camp today. Trey Romian, a high school senior from West Middlesex, Pa., didn't expect that he'd be able to do much at Heart Camp when he first attended four years ago. To his surprise, he was allowed to play tackle football. Romian was born without a pulmonary valve—a rare congenital heart defect called pulmonary atresia—which required three operations and a pulmonary valve replacement when he was 15. Although Romian is a baseball player, he's not normally permitted to play more vigorous school sports. But at Heart Camp, where he can be carefully supervised, his favorite activity is gaga ball, a more contact-heavy version of dodgeball.

"It's amazing," Romian says. "We've got swimming pools, basketball, football—anything you can think of." Like most of his peers, Romian now returns to the camp every year; he is training as a junior counselor.

Though Heart Camp is full of fun and games, it also realizes Neches's vision of creating emotional support among children with heart disease.

Toward the end of the counselor Q&A, a young girl camper says through tears, "I'm getting a heart transplant soon. Do you have any tips for someone who's scared?"

"Embrace the fear," a counselor and heart transplant recipient reassures her. "It's okay to be scared—most definitely."

Romian says humbling moments like these happen often. Ultimately, he loves being in an environment where he and his peers can be themselves, in moments bitter and sweet.

"I wish it would be more than once a year," he says. n

SCOTT GOLDSMITH





CLASS NOTES

'70s

Although **Graham Johnstone** (MD '70, Orthopaedics Resident '77) loves retirement ("Don't tell all the people who are working"), he has not retired his love of orthopaedics or of teaching. Since 2002, Johnstone has visited several African countries,

where he performs orthopaedic surgery and teaches residents from the Pan African Academy of Christian Surgeons. This fall, Johnstone and his wife, Marilyn, are returning to SIM Galmi Hospital in Niger for six weeks, bringing along as many medical supplies as they legally can. "It's always exciting to see all the supply cartons arrive at the airport at the same time, knowing we'll be able to

use them. . . . I'm in clinic the day I arrive, and I operate the next day." While he's there, he works 12–14 hour days, five days a week. In addition to his international volunteer work, Johnstone is on the board of Brother's Brother Foundation, a Pittsburgh-based nonprofit that sends medical supplies all over the world. Before retiring in 2014, Johnstone, who was clinical associate professor of orthopaedic surgery at Pitt, had the opportunity to train his second son, **Stephen Johnstone** (Orthopaedic Surgery Resident '15), who's now a fellow at Columbia University.

'80s

Paul Worley (MD '80) is a neurologist-cum-basic neuroscientist who studies protein synthesis in excitatory synapses that are involved in learning and memory. A professor of neuroscience and neurology

at Johns Hopkins University, Worley researches several brain disorders, including schizophrenia, autism, Parkinson's, binge drinking, drug addiction, and Alzheimer's—all of which are related to alterations in the way information is stored in the brain. Worley published a paper earlier this year in *Neuron* on a gene that is thought to have derived from a virus that integrated into the genomes of primitive organisms eons ago and may be a cause of and target for schizophrenia. His work with patients early in his career remains top of mind in the lab. "It is front and center in our thinking that the work should be translatable [to treatment]," says Worley. "I'm a basic scientist, but I'm a pragmatist, as well."

William Simmons (Pediatric Critical Care Resident '86, Pediatric Anesthesiology Fellow '87) is leading a program to get more young African American men interested in science—an effort that just received national recognition. Simmons is president of the Gateway Medical Society, which earned the National Medical Association Large Society of the Year Award for its "Journey to Medicine" program. This program is geared toward 6th- through 12th-grade boys from Pittsburgh Public Schools who show a particular interest in science and mathematics. Participants are given hands-on learning experiences led by physician, resident, and medical student mentors. The organizers strive to build confidence in the boys' current academics and teach them about future medical occupations. In general, the young men who participate have higher GPAs and better attendance at school. "It is the mentorship that actually makes the difference in our program," says Simmons.

Steven Fisher (Internal Medicine Resident '89), professor of medicine and physiology at the University of Maryland, traces his interest in muscle and the way it adapts under disease conditions back to his residency days. "I saw patients who had suffered from heart disease for long periods and whose cardiovascular systems had adapted before symptoms presented, and I got interested in taking a closer look at what was going on."

Today, Fisher primarily studies that question with respect to molecular physiology—in particular, he's interested in how gene expression affects blood flow. In one of his most recent studies, Fisher examined how different signal pathways converge in a disease model to cause muscle relaxation and increase blood flow. He says that sepsis is a particularly interesting disease in this regard; he and colleagues discovered a novel explanation for the massive dilation of the blood vessels, which suggests therapeutic targets.

'90s

An associate professor of psychiatry, anesthesiology, and clinical and translational science at Pitt, medical director of psychiatry at UPMC Pain Medicine at Centre Commons, and director of the geriatric psychiatry fellowship, **Jordan Karp** (MD '98, Geriatric Psychiatry Fellow '03) runs clinical trials for older adults with comorbid depression and chronic pain conditions. "Pain makes depression worse, and depression makes pain worse. They have a shared biology and shared psychology," says Karp. The geriatric population presents differently with depression than do younger populations. "Older adults can have feelings of hopelessness and fear about the future. They worry about falling, becoming dependent upon others, losing functioning. They have a fear of being alone. We need to be age- and culturally sensitive." Karp hopes to find ways to break the cycle of physical deconditioning from inactivity and pain that feeds into low self-esteem and depression by testing novel interventions and studying the shared psychobiology of these linked conditions.

Pittsburgh is abuzz about the opening of the new Three Rivers Mothers' Milk Bank. As NICU medical director at Magee-Womens Hospital of UPMC and a member of the board of the Three Rivers Mothers' Milk Bank, **Jennifer Kloesz** (Pediatric Resident '98, Neonatal-Perinatal Medicine Fellow '01) is dedicated to helping more premature babies have access to their own mother's milk as well as donor milk. Breast milk is important for preemies, she reminds, because it significantly decreases the risk of necrotizing enterocolitis, shortens the length of hospital stays, and decreases allergies and ear infections. "We are moving toward using donor milk for all of our very low birth weight babies if their mother's milk is not available." Breastfeeding advocacy is a part of life in Kloesz's household. Kloesz is married to **Albert Wolf** (MD '97), CFO of the National Breastfeeding Center in Pittsburgh. The couple met while Kloesz was an intern and Wolf was a Pitt med student.

'00s

Nima Sharifi (MD '01) has devoted more than a decade of research to the field of prostate cancer. He published his most recent findings in *Nature* last June. Sharifi and his research team at Cleveland Clinic found that D4A—a metabolite of a drug for metastatic prostate cancer—could eliminate cancer cells more effectively than the drug, called abiraterone, itself. If D4A is given directly to patients, the study suggests, the metabolite could prolong their lives by blocking androgen production. Sharifi won the American Association for Cancer Research Award for Outstanding Achievement in Cancer Research in 2014. He's



Stephen and Graham Johnstone



Sharifi

the codirector of Cleveland Clinic's Prostate Cancer Research Center of Excellence and holds its Kendrick Family Endowed Chair for Prostate Cancer Research.

As a freshman at Yale, **Seth Hawkins** (Emergency Medicine Resident '03) figured he'd go into anthropology or archaeology, but after taking a wilderness EMT class, he got hooked on the idea of providing physician-level services in the great outdoors. He's interested in translating formal EMS systems into a wilderness environment—emphasizing a more effective system of prevention and diagnosis, along with the treatment of injuries and medical conditions in the wild. An emergency physician at Blue Ridge HealthCare hospitals, he moonlights as a wilderness medicine educator. In 2007, he founded the nonprofit

Appalachian Center for Wilderness Medicine.

Following stints as a postdoctoral fellow and research associate at Stanford University, **Payal Watchmaker** (PhD '07) joined Achelois Pharmaceuticals as a research scientist in June. At the San Francisco-based company, she'll work with a team of researchers to develop a more effective cancer immunotherapy drug. Watchmaker also hopes to continue her Stanford research in the new position, particularly to build on the findings of her 2013 *Nature Immunology* paper on the role of intestinal dendritic cells in immunity. Although she's

been on the West Coast for almost seven years, Watchmaker says she's constantly reminded of Pitt with the abundance of Steelers fans in the Bay Area. —*Kristin Bundy, Lori Ferguson, Brady Langmann, and Susan Wiedel*



Watchmaker

JOY RUFF

FROM IRAQ WITH LOVE

“When you're in a situation where you're being told to leave, you don't think about what to pack,” says Joy Ruff (MD '12). “You just run.”

Ruff recently returned from a 10-day trip to Northern Iraq where she and other physicians treated refugees fleeing the Islamic State-controlled areas of Syria. The doctors set up makeshift care facilities in abandoned warehouses and treated upwards of 100 patients a day. In many cases, the refugees they met had to evacuate their homes within minutes, meaning they arrived in Iraq with no possessions—including vital medicines.

Although Ruff is a family practice physician, she says much of what she did in Iraq was triage—administering stitches, checking vitals, and supplying prescriptions. But according to Ruff, the most important thing she did was listen.

“Just sitting down and talking to these people, hearing their stories, hearing their frustration—it was heartbreaking,” says Ruff. “Most of the time I felt like what they needed was someone to give them an ear, someone to help them process the grief and trauma.”

Ruff's trip was part of a holistic family medical residency program called In His Image, which is based in Tulsa, Okla., at St. John Medical Center. Disaster relief is part of its outreach curriculum.



Ruff tries on a Kurdish style hat at a market in Iraq.

As the mother of three children—Nathan (7), Zach (5), and Grace (1)—Ruff said it was difficult to hear stories of families being forced out of their homes. She cared for engineers, pharmacists, and bakers—normal people living normal lives until the moment ISIS started firing bullets at them.

She thinks the time she spent in Iraq will make her a better family doctor down the line.

“When you see people suffering on a large scale like that, it keeps you soft and reminds you why you're doing it,” says Ruff, who is a fellow at the University of Alabama.

“It gets you away from the bureaucracy and paperwork and other issues we sometimes have to deal with. Just seeing those people and feeling their need, offering your skills and your care and your love.

“That's actually the heart of medicine.” —*Jason Bittel*

MAA SAYS—MAKEOVER EDITION

Maybe you saw her at this year's Medical Alumni Association homecoming tailgate. Or perhaps you shook hands at October's health sciences alumni reception in San Diego. **Jennifer Gabler** has gotten to know many Pitt med alumni through her previous positions in development for the school. As the new executive director of a streamlined medical development and alumni relations team, she plans to give the Medical Alumni Association a facelift. Gabler will be working closely with MAA staff members to reach out to a more diverse pool of alumni and prospective Pitt meders and to further engage alumni with the school.

Gabler's team will work with MAA President **Jan Madison** (MD '85) and the executive committee to revamp reunions (details to come) and to hold more frequent local events for alumni in the 'Burgh. Expect to gather with former MAA President **Brian Klatt** (MD '97, Res '02) and President-elect **David Metro** (MD '94, Res '98) at the upcoming shindigs.

“We want alumni to be able to reach out to their classmates,” Gabler says, “to connect them with former faculty members and to have a good time when they do come back to Pittsburgh.”

Whereas the development team, which makes more than 600 alumni visits around the country each year, used to go about their work independently from MAA, now the two organizations' efforts will be more closely aligned. They hope to engage young alumni—those hard-to-reach residents in particular—and use their now tripled staff to keep everyone in the loop. “We'll be able to offer more to our alumni,” Gabler says. —*Robyn K. Coggins*



Gabler



Madison

MEDICAL ALUMNI ASSOCIATION WWW.MAA.PITT.EDU

KLAUS BRON

FEB. 7, 1929 – JULY 23, 2015

Klaus Bron, a professor of radiology, had a tradition. The last Friday of every month, he took residents out to lunch at the end of their rotations. While everyone else stayed in their scrubs, Bron would change into a suit and tie when he joined his colleagues and residents to eat and talk politics, religion, and current events.

"You take your time eating with Dr. Bron," says Philip Orons, a DO, professor of radiology at Pitt, and former fellow under Bron. He describes him as a Renaissance man.

Bron, who in addition to his faculty position at the University of Pittsburgh served as the medical director of UPMC Presbyterian's radiology department from 1985-89, died in July.

Bron and his family moved to the United States from Germany in 1936 to escape the Nazi regime; he later earned his undergraduate degree from Columbia University and his MD at NYU. Following internship and residency training at Philadelphia General Hospital, two years stationed in Turkey as a U.S. Air Force captain, and a teaching position at Stanford University, he joined Pitt in 1964. There, Bron helped lead the shift from diagnostic



Bron

to interventional angiography in the early '80s, which used X-ray imaging and dye to view blocked or narrow blood vessels.

Alongside Thomas Starzl, an MD/PhD and Distinguished Service Professor of Surgery, Bron made significant contributions to Presbyterian's liver transplantation program. In 1985, he collaborated on a study that evaluated the use of angiographic procedures to increase the survival rate of liver transplantation patients.

Like Orons, Carl Fuhrman, an MD and professor of radiology at Pitt, remembers Bron as "a gentleman in the European-type tradition," who drove a Volvo sports car and started each morning with coffee and *The New York Times*. Regarding Bron's medical work, Fuhrman says he was "truly a perfectionist in his angiography career," keeping hundreds of handwritten books on his cases.

That's why Orons, when training with Bron in 1990, was horrified when he mistakenly pulled out a wire during a several-hour-long biliary drainage. Bron simply responded: "Let's get it back in."

"He always expected top level performance from the people who worked for him, and he had the same demands on himself. His first priority was the patient under his care," Fuhrman says. "He was always very respectful, very courteous to people."

—Brady Langmann

VERYL MAE RILEY

AUG. 12, 1926 – AUG. 1, 2015

Although she wouldn't admit it, Veryl Mae Riley (MD '49) was always ahead of her peers. Riley skipped grades in elementary school and continued doing so all the way through her undergraduate studies at Pitt in the 1940s—when she graduated in two and a half years. At the School of Medicine, she earned her degree after three years and was one of only five women in the graduating class of 68 students.

"[Those women] were ahead of their time, without a doubt," says her daughter, Gail Riley-Wright. "[Riley] was just a standout, in her own way—not that she was trying to be anything different."

Riley died in August. She was one of two obstetricians in Warren County, Pa.—an area covering more than 40,000 residents—for 50-plus years.

Riley was known as "the mother of Warren County," making house calls in the middle of winter, delivering thousands of babies, and always answering phone calls when someone needed medical help. After her husband, George—a general practitioner with whom she opened a dual practice—died, she helped care for his patients.

Riley practiced until she couldn't get out of bed. On her last day of work, she performed three surgical assists and woke up the next morning with a pinched nerve that left her unable to walk. She was 83 then. —BL



Riley

IN MEMORIAM

'40s

WILLIAM M. REILLY JR.
MD '43
JULY 20, 2015

ALLAN K. BRINEY
MD '45
JUNE 15, 2015

PETER JOHN WARGO
MD '46
AUG. 12, 2015

JOHN USYK
MD '48
AUG. 18, 2015

'50s

ALBERT MEDWID
MD '51
MAY 22, 2015

CHARLES W. MASON JR.
MD '53
JULY 14, 2015

ROBERT CARL BLOCK
MD '58
AUG. 22, 2015

GROVER T. DAVIS III
MD '58
AUG. 28, 2015

'60s

DOUGLAS A. MACDONALD
MD '67, RES '74
AUG. 15, 2015

TED K. ENCKE
RES '69
JULY 27, 2015

'70s

JOCYLINE L. MEDINA
RES '70
JUNE 27, 2015

JOHN B. MARTIN JR.
MD '72
AUG. 20, 2015

RICHARD PAN PURSUES COMMUNITY IMMUNITY

BY SHARON TREGASKIS

In the past three years, the Golden State has done an about-face. Back in 2010, California claimed some of the most lax childhood vaccination requirements in the nation; today, it has some of the toughest.

Credit the state's senator from Sacramento, Richard Pan (MD '91). Signed into law by Governor Jerry Brown in July, Pan's SB 277 legislation eliminates California's personal belief and religious exemptions. Beginning in July 2016, only children up-to-date on all state-mandated vaccinations—or those with a note from a physician noting that immunization is not safe for them—will be allowed to enroll in public or private schools. "This is the first time that a state has rolled back all of [its] exemptions," says Pan. "I'm hoping others will follow our lead."

Pan coauthored the bill with state Senator Ben Allen as last winter's measles outbreak—originating at California's Disneyland—turned local vaccination rates into a national story. "Looking at the data, those of us in the public health realm had recognized we were vulnerable," says Pan. "That became a real-life danger as measles spread across the state."

And yet, the legislative move has been far from universally popular. After a series of threats against Pan, capitol security guards began accompanying him to hearings and votes on the bill. Within days of the governor's signature, activists launched recall efforts aimed

both at the senator's seat and the legislation itself. (They failed to get enough signatures.)

SB 277 was Pan's second foray into the world of vaccine legislation. As a state assemblyman—the first MD elected to California's Democratic Caucus and the first pediatrician elected to the state's legislature—he authored AB 2109, mandating a health care provider's signature on exemption forms. "That law reduced the personal belief exemption [use] by 20 percent," says the senator. "Once they had to go to the doctor to get the exemption, many just got the vaccination instead."

Pan, who turned 50 this fall, was born two years after the measles vaccine was released. Vaccinations for pertussis and polio—the latter developed, of course, by a team led by Jonas Salk, an MD, during his tenure as director of Pitt's Virus Research Laboratory—were already commonplace. By the time Pan started kindergarten, vaccines were also available for mumps and rubella. When the aspiring physician arrived at Pitt in the 1980s, vaccines were so broadly deployed, faculty couldn't imagine a resurgence of preventable childhood illnesses. In his microbiology course, recalls Pan, the textbook featured photos of a measles rash, but the professor—Julius Youngner, an ScD virologist instrumental in developing the polio vaccines, who's

now Distinguished Service Professor Emeritus in Pitt's Department of Microbiology and Molecular Genetics—assured his students that, like polio, measles had been all but eradicated. "We were taught that unless we went on a mission outside the country," Pan says, "we weren't going to see some of these diseases."

And yet in his fourth year of medical school, as a trainee with the U.S. Public Health Service, Pan came face-to-face with measles. It was January 1991, and Philadelphia was in the grips of an epidemic that originated in two religious communities whose members refused both vaccines and medical care. Throughout the course of six months, more than 1,000 people were infected and nine children died.

"It was horrible," says Pan.

To make his case with fellow legislators this summer, Pan used FRED (Framework for Reconstructing Epidemiological Dynamics), a computational modeling tool from Pitt's Graduate School of Public Health that simulates disease outbreaks and allows users to compare the potential severity of an outbreak depending on whether a city has an 80 percent vaccination rate versus a 95 percent vaccination rate. "I'd pull up a colleague's city and say, *Here's what will happen in your city, in your county. Watch the dots,*" says Pan.

"It was a great way to illustrate at a very direct level what would happen if we didn't get our immunization rates up."

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Pan speaks at a hearing of the California Senate Health Committee for his legislation SB 277, which has toughened vaccination requirements for California schoolchildren.



LORIE SHELLEY

A FRIEND INDEED

Got the scoop on a fellow alum who's doing something great? We're all ears at medmag@pitt.edu.



Elsie Hillman, 1925–2015

CONFLUENCE BUILDER

Everything needs a real doer . . . somebody who is willing to do anything for the thing that they are passionate about. —Elsie Hillman

Elsie Hillman was generous with her voice and her resources and her energy. She seemed to have a knack for bringing people together, for bridging divides.

For instance, Hillman, a strong Republican Party advocate, defended a woman's right to reproductive freedom.

As press reports noted after her August 4 death, Hillman was as comfortable rubbing elbows with parking attendants as she was with U.S. presidents. She regarded them equally for the human behind the job. (And was likely to call them all "Dearie.")

The wife of a billionaire, Henry Hillman, she could have kept to cloistered circles. Instead she brought dinner to people with AIDS in the '80s when few offered compassion to that population.

She wore costume jewelry rather than the real thing because, as she once told a friend, "I have more important things to do with my money." We noticed.

She and her husband gave a second chance to some of the region's sickest children through the Children's Hospital of Pittsburgh of UPMC's Hillman Center for Pediatric Transplantation.

And they lent their family name to two endowed professorships at Pitt: One supports the understudied field of women's health. (It's held by Yoel Sadovsky, scientific director of the Magee-Womens Research Institute.) The other is in oncology. (That one is held by Nancy Davidson, director of the University of Pittsburgh Cancer Institute and UPMC CancerCenter.)

Elsie and Henry Hillman brought a spirit of connection to the construction of the Hillman Cancer Center, which opened in 2002; by design, it links scientific and clinical efforts. They gave millions to fund innovative studies of nearly 100 Pitt faculty members there. Perhaps not so surprising was another priority for Elsie Hillman: She was devoted to making patients as comfortable as possible during their treatments.

—Kristin Bundy and Erica Lloyd

CALENDAR

FOR ALUMNI & FRIENDS

**MEDICAL ALUMNI ASSOCIATION
EXECUTIVE COMMITTEE BOARD MEETING**
NOVEMBER 18
6 p.m.

For information:
Jen Gabler at 412-647-3792
jag188@pitt.edu

**C.F. REYNOLDS MEDICAL HISTORY
SOCIETY LECTURES**

JANUARY 26, 2016

6 p.m.
Scaife Hall, Lecture Room 5
Speaker: Andrew Herlich, DMD, MD
"The Development of Anesthesiology
in Pittsburgh: Contributions from the
Dental and Medical Professions"

FEBRUARY 23, 2016

6 p.m.
Scaife Hall, Lecture Room 5
Speaker: Clyde Partin Jr., MD
Jonathon Erlen History of Medicine
Lecture: "The Holmes Heart, Alligators,
and Maude Abbott"

For information:
Jonathon Erlen at 412-648-8927
erlen@pitt.edu

WINTER ACADEMY

FEBRUARY 17, 2016

Mar-a-Lago Club, Palm Beach, Fla.

FEBRUARY 19, 2016

Ritz-Carlton, Naples, Fla.

For information:
Jen Gabler at 412-647-3792
jag188@pitt.edu

To find out what else is happening at the
medical school, visit www.health.pitt.edu
and maa.pitt.edu.

How we grow up. Literally.



GETTY IMAGES



FOR REAL! TWEEN SCIENCE

Hey kids, did you just jump up a shoe size? If so, watch out. Soon, you might have to replace those pants you're wearing, too. Why? During puberty, our hands and feet grow faster than the long bones in our arms and legs. So, if you've outgrown your favorite shoes, then you're likely about to get a heck of a lot taller, and quick—something called, you've probably heard of it, a growth spurt.

Young men and women go through growth spurts at different times. Girls grow taller sooner, starting around age 9 or 10 and accelerating around 11 or 12. Boys' growth spurts start around 11, with their fastest growth around 13.

Interesting tidbit: Your body goes through its fastest growth during your first two years of life and during puberty. And a related bit: Your spine actually doubles in size from birth to age 2; then it doubles again by the time you reach your full height.

Doctors can predict about how tall you're going to be as an adult by doubling how tall you were at 18 months old (for girls) and 2 years old (for boys).

You can also figure out how tall you will be if you know your mother's and father's heights. If you're a girl, add your parents' heights, subtract 5 inches, and divide that number by 2. If you're a boy, add your parents' heights, add 5 inches, and divide the result by 2. Pretty darn cool.

Your parents' heights are the biggest influence on yours, but lifestyle and environment also play roles. If you eat right, sleep well, and exercise, you're more likely to wind up at a higher altitude. So . . . another serving of those veggies?

—Kristin Bundy

Thanks to Pitt and Children's Hospital surgeon Patrick Bosch for helping us bone up on height. For more science for kids, see howscienceworks.pitt.edu.



THE OWL, 1973

WHERE THE THEATER USED TO BE

If you’ve ever gotten directions along the lines of *Turn left at the joint that’s not there anymore*, you might be a Pittsburgher, or at least a Pitt alum.

And if you remember this street corner, you’re old enough to benefit from a [charitable gift annuity \(CGA\)](#). It’s a way to provide yourself and/or a loved one with a guaranteed income for life, and receive a tax deduction, while building a stronger future for Pitt. You can even designate a specific area that your gift will benefit, like the medical device researchers at the McGowan Institute for Regenerative Medicine—they’ve got spiffy green-design labs down on the Mon now, where LTV Steel used to be. Or the up-and-coming docs at the new Children’s Hospital of Pittsburgh of UPMC in Lawrenceville—you know, where St. Francis Hospital used to be.

The examples below are based on a minimum gift of \$10,000.

AGE	RATE	YEARLY INCOME	ESTIMATED DEDUCTION
55	4.0	\$400	\$2,327
60	4.4	\$440	\$2,638
65	4.7	\$470	\$3,282
70	5.1	\$510	\$3,946
75	5.8	\$580	\$4,468
80	6.8	\$680	\$4,946
85	7.8	\$780	\$5,615
90	9.0	\$900	\$6,271

To learn more, contact:

Lisa J. Sciuolo
Forbes Tower, Suite 8084
3600 Forbes Ave.
Pittsburgh, PA 15213
412-647-0515
slisa@pmhsf.org
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Because of varying restrictions, Pitt is not able to offer gift annuities in some states.