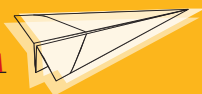


UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FALL 2021

PITTMED

LET THERE
BE SIGHT

VISION RESTORATION BREAKTHROUGH
INSPIRED BY NATURE



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- Best in Show: Ray Sprigle Memorial Award—Magazines

- Excellence in Written Journalism, Magazines—Medical/Health (G. Jenkins, “Oct. 27, 2018: Pittsburgh’s Darkest Day and the Mass Casualty Response”)

2020 Press Club of Western

Pennsylvania Golden Quill Award

- Excellence in Corporate, Marketing and Promotional Communications—Written, Medical/Health (G. Jenkins, “Surviving Survival”)

2020 Press Club of Western

Pennsylvania Golden Quill Award

- Excellence in Corporate, Marketing and Promotional Communications—Audio, Medical/Health (E. Vitone, J. Faust, M. Palko and E. Lloyd, Pitt Medcast: “Polio Pioneers”)

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Pitt alum **MICAELA CORN** [“App for Longhailer Mental Health” and other stories] was an intern for this magazine six years ago. She encourages Pitt Med readers to share stories that are likely to resonate with others who might benefit: “You never know what could grow out of it.” Corn is now a senior communications specialist in the Department of Strategic Communications, Health Sciences. When the pandemic first struck, she was recruited to Pitt’s COVID-19 Medical Response team to help inform the Pitt community about safety and prevention measures. “We got a lot of really kind feedback—that our updates were a helpful, clear and trusted source of important information—which felt good,” she says.

CHRISTINA LEE [“Is he vaccinated?” cartoon] read Sunday comics as a girl, then later, she discovered graphic novels; those media inspire her work today. Lee earned her Bachelor of Fine Arts in art and communication design at Carnegie Mellon University in 2014. Since then, she’s participated in various exhibitions and published her work in Refinery29, Teen Vogue, NPR and Rookie Magazine. Lee just moved from Pittsburgh to New York to attend the Fashion Institute of Technology, where she’s pursuing a Master of Fine Arts in illustration. She hopes to complete her own graphic novel during her time at FIT.



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UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, FALL 2021
VOL. 23, ISSUE 2



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Pittsburghers are leading efforts to restore vision. An experimental tool for the blind borrow's tricks from glowing algae. (Cover: Rugli/Getty Images © 2021.)



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PITTMED

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“The tree which moves
 some to tears of joy is
 in the eyes of others
 only a green thing
 that stands in the
 way. Some see nature all ridicule
 and deformity . . . and some scarce
 see nature at all. But . . . nature is
 imagination itself.”

—William Blake

Dear Pitt Med Reader,

I think most scientists and clinicians stand in awe of nature. And the better they get to know it, all the more so. Many useful inventions mimic what's found in the natural world, though typically the synthetic versions aren't as elegant. For instance, the idea for suction cups came from observing octopi, and SONAR was inspired by dolphins.

I'd like to tell you about an intriguing project here that's also inspired by nature—more sea life, in fact. The story starts more than 15 years ago, when scientists at Stanford realized they could take cues from glow-in-the-dark algae to probe fundamental questions about the brain. Bioluminescent algae showed them how to use light to turn cells on and off; and that turned out to be a great way to study neural circuits. You may recall stories about the promise of the algae-inspired tool, called optogenetics, in this magazine.

Optogenetics has illuminated neuroscience at a basic level. Now, in a study co-led by our own ophthalmology chair, José-Alain Sahel, with international collaborators, it has been put to therapeutic use. A blind man in Paris, afflicted with retinitis pigmentosa, was able to partially see again thanks to the approach. Trials are now under way in Pittsburgh and elsewhere to further test and develop this therapy. You can learn more about the study, and get the perspective of a trial participant, in our cover story. I'll be following the progress of Dr. Sahel's team with great interest.

As you read this issue, you'll see how easy it is for me to find inspiration in this very community: The ingenuity of our scientists. The dedication of our clinicians. The devotion of our staff. The idealism and energy of the upcoming generation. So yes, as William Blake notes, nature is a stirring muse. And, despite what we hear in world news reports, during these fractured and difficult times, we can also be uplifted and galvanized by *human* nature, if we're paying attention.

This August, many of our incoming health sciences students donned white coats (or “cloaks of compassion”) for the first time. For the School of Medicine's White Coat Ceremony, I asked our wonderful keynote speaker, Kurt Weiss (Res '08), associate professor of orthopaedic surgery, to share what energizes him.

First, a little background on Dr. Weiss, who directs Pitt's Musculoskeletal Oncology Laboratory. As a teenager, he was diagnosed with a bone cancer (osteosarcoma) that had metastasized. His parents were told he had a 25 percent chance of surviving. A team of doctors here and at MD Anderson Cancer Center saved his life, though he eventually had to have his leg amputated. Now Dr. Weiss is devoted to studying the same cancer that struck him.

“I am supposed to be passionate about this stuff—the research and treatment of sarcoma,” he said at the ceremony. “What gets me up in the morning and inspires me is the passion brought by my clinical and research partners who haven't been touched by sarcoma like I have, yet bring the same passion, resolve and relentless energy to the care of patients and the study of these diseases.”

This truly is an inspiring family that our first-year students are joining.

Anantha Shekhar, MD, PhD

Senior Vice Chancellor for the Health Sciences

John and Gertrude Petersen Dean, School of Medicine

AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH



Special COVID-19 Report

GETTY IMAGES



People who are immunocompromised fare better against COVID-19 when there are more coronavirus antibodies in their systems.

Path to a Pancoronavirus Vaccine?

University of Pittsburgh researchers have identified tiny molecules that show promise in preventing and treating COVID-19 and its variants. They seem to have uncovered clues to halting diseases caused by other coronaviruses, as well.

Pitt Med's Yi Shi, with other scientists, tested those microscopic molecules—called SARS-CoV-2 nanobodies—as an inhalable mist in hamsters and discovered how much potential they offer.

Last year, Shi, assistant professor of cell biology, and his fellow researchers extracted SARS-CoV-2 antibody fragments from a llama named Wally. Those fragments were later used to prevent and treat COVID-19 in the hamsters.

In the team's most recent research, Shi partnered with Pitt Med's Cheng Zhang, associate professor of pharmacology and chemical biology, James Conway, professor of structural biology, and colleagues at Case Western Reserve. They studied the nanobodies to better understand how they interact with SARS-CoV-2 to stop it from infecting cells and to probe how mutations found in variants might affect nanobody interactions. The team chose eight potent neutralizing nanobodies for further examination by first confirming that several work against alpha, delta and other SARS-CoV-2 variants. The team then classified the nanobodies into groups based on their interactions with spike proteins—which act as “keys” that grant the virus entry to human cells. The research revealed three classes of interest.

One of those classes of nanobodies binds to a region on the spike protein that has persisted through several permutations of coronaviruses. This means it may neutralize SARS-CoV-2 and its variants, as well as other coronaviruses.

Shi says this work “will not only help our team select and refine nanobodies to treat and prevent COVID-19, it also may lead to a universal vaccine, preventing not just COVID-19, but SARS, MERS and other diseases caused by coronaviruses.”

—Michael Aubele and Allison Hydzik

Big Questions for Immune-Vulnerable Populations

People who are immunocompromised are accustomed to frequent blood tests that plot their progress and guide their treatments. And lately, many of these patients have been clamoring for yet another screening—for coronavirus antibodies.

To date, the Centers for Disease Control and Prevention does not recommend routine antibody testing after vaccination. But Ghady Haidar's current project, dubbed CoVICS (for COVID-19 Vaccine in the Immunocompromised Study), involves antibody testing for research purposes on a monthly basis—and the results are available to patients.

This perk has presented Haidar and his colleagues with a very good problem: a tsunami of volunteers.

“We've been going through them as fast as we can to enroll them quickly,” said Haidar, in the throes of the signup phase this summer. Haidar is assistant professor of medicine and director of research, bone marrow transplant and

Sources for this special section include Pitt and UPMC reports.



Haidar

hematological malignancy infectious diseases at Pitt.

However, patients were interested in knowing what the results of the test mean for them and their care. Haidar's answer—hang tight while the science catches up—has been frustrating for all involved.

"We'll get there," Haidar said. "We're just not there yet."

With "getting there" in mind, CoVICS has enrolled more than 1,400 patients to date, studying how long antibodies last in immunocompromised individuals, as well as how they change over time, compared to controls.

In June, the team released an interim analysis in a preprint journal, reporting that the 489 immunocompromised patients had a wide range of antibody-response rates: 37% for solid organ transplant recipients, 54% for blood cancer patients, 83% for patients with autoimmune disorders and 94% for patients with well-controlled HIV.

Among solid-organ transplant recipients, vaccine efficacy varied widely, depending on which organ was transplanted—60% of liver transplant patients produced antibodies, while only 22% of lung transplant recipients did. The team also found that those who were a year or more out from transplant surgery fared better.

Several treatments were associated with decreased likelihood of producing antibodies: radiation therapy for cancer, certain monoclonal antibodies (known as anti-CD20) used by patients with autoimmune disorders and antimetabolites for transplant.

In a previous analysis focusing on patients with cancers of the blood and bone marrow, the team found that 46% did not produce detectable antibodies to the COVID-19 virus. Among those, 77% of patients with chronic lymphocytic leukemia did not produce antibodies.

The CoVICS study was among the first to answer a burning question about antibody testing in these patients: Do antibody levels actually reflect how well a body can neutralize a virus? In a subset of 26 immunocompromised patients and 30 healthy controls, the team pitted the virus against samples of individuals' blood sera in the lab, then compared the results of these mini cage matches to antibody levels.

The correlation was clear: The more antibodies present, the more likely that person was to neutralize the coronavirus—a relationship that was previously only speculative.

The team is now more confident in saying that people who do not produce antibodies truly are at greater risk of coronavirus infection, said John Mellors, Distinguished Professor of Medicine. However, antibodies are not the whole story. Other immune cells, including T-cells, may work to provide additional protection against the virus.

Haidar warned that a positive antibody test is not a free pass to throw caution to the wind.

"At this point, clinical advice does not change for immunocompromised people, whether an antibody test is positive or negative," he said. Thus vaccination, masking in public and social distancing remain vitally important for this population —*Elaine Vitone*



Adults hospitalized with COVID-19 are likely to develop neurological problems.

COVID-Hospitalized Hit Hard By Neuro Issues

In early 2020, after the United States had its first reported case of COVID-19, Sherry Chou and a group of her fellow neurointensivists—critical care clinicians who have neurological expertise—became concerned that the coronavirus would affect the nervous system. Chou recalls that history had taught them to be worried. The 1918 influenza, and other infectious diseases, affected multiple organ systems.

Chou, an associate professor of critical care medicine, neurology and neurosurgery at Pitt, created and leads the Global Consortium Study of Neurologic Dysfunction in COVID-19. The largest cohort study of neurological manifestations of the disease, it spans 133 adult and 109 pediatric study sites across six continents. Ericka Fink, associate professor of critical care medicine and pediatrics at Pitt, is the PI on the pediatric arm of the study.

In May, the consortium published first results in its adult population study in JAMA Network Open that show 8 out of 10 people hospitalized with COVID-19 develop neurological problems.

"We expected there'd be some, but that was a lot," says Chou, associate director of Stroke and Subarachnoid Hemorrhage at the Pitt Safar Center for Resuscitation Research.

It gets scarier: Hospitalized patients with clinically diagnosed neurological symptoms associated with COVID-19 are six times more likely to die than those without.

The study consisted of 3,744 adult patients; the results were broken down by symptoms self-reported by the patient and also syndromes captured by clinicians. Nearly 40% self-reported having headaches; about 30% said they had lost their sense of smell or taste.

Chou says that acute encephalopathy was the most common problem.

"These are people who are confused, who are delirious, who are not themselves," she says. "They have altered sensorium [including cognitive functioning], memory problems—and about every other person hospitalized with COVID-19 had that condition."

When the pandemic began, one of Chou's greatest fears was that the virus would directly attack the brain and cause meningitis and encephalitis (brain infection and inflammation). However, she says, that has been rare, occurring in less than 1% of hospitalized COVID-19 patients.

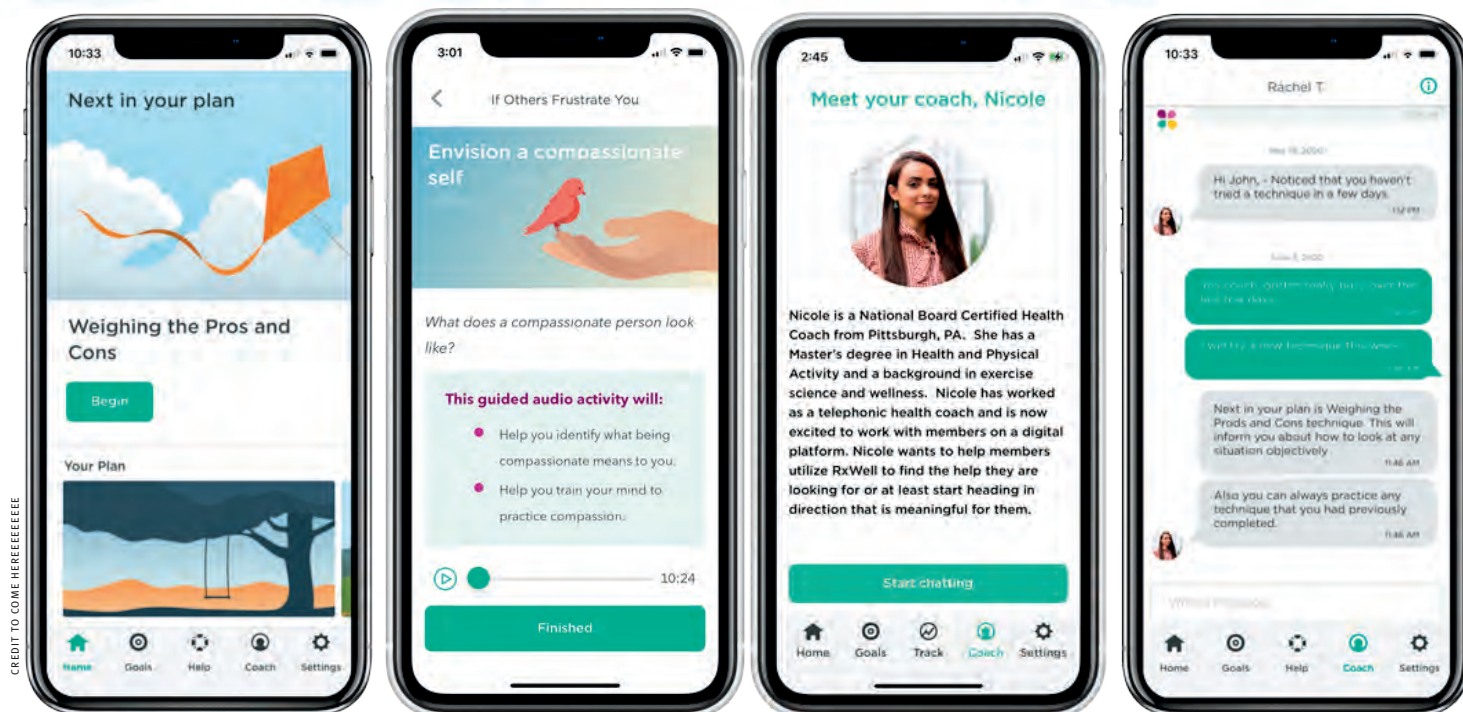
Patients who had been diagnosed with a neurological condition prior to the pandemic—from chronic migraines or dementia to spinal cord diseases—are more than twice as likely to develop a COVID-19-related neurological issue than those without this predictor, according to Chou. The JAMA Network Open paper reports on the first phase of the study. Chou hopes to answer more questions in the next phase, such as: How long do neurological symptoms last in COVID-19 patients? How does this impact the patient long-term? And the key question for her: How do we treat it? —*Gavin Jenkins*



Chou



Fink



App for Long-Hauler Mental Health

Long after someone with COVID-19 tests negative for the virus, physical symptoms can persist. So can behavioral ones, it turns out. Long-haul symptoms—those lasting longer than three months after a negative test—can range widely from person to person: persistent aches and pains, coughing, shortness of breath, brain fog, loss of taste and smell, sleep difficulty, the list goes on. Perhaps as many as one-third of these patients also continue to struggle with mental health issues—some for the first time in their lives. Since the beginning of the pandemic, studies have shown a high rate of new onset anxiety and depression in people who tested positive for COVID-19.

“A lot of people didn’t have very bad COVID, but continue to have a wide range of significant symptoms,” says Alison Morris, division chief of pulmonary, allergy and critical care medicine at the University of Pittsburgh.

“These symptoms are very stressful to people. They are suffering. We know this. However, with no tested therapies for these conditions, some patients may believe the symptoms are not real and are just ‘in their heads.’”

Morris directs UPMC’s Post-COVID Recovery Clinic, where an app is being used in clinical trials to help patients dealing with long-haul COVID through behavioral health interventions for more integrated care.

Developed by UPMC Health Plan’s Behavioral Unit for Digitally Delivered Interventions, the app, called RxWell (a trademarked name), is a cognitive behavioral therapy (CBT) tool that helps patients deal with the impact of stressors on daily life. The app uses empirically tested CBT and mindfulness techniques for stress, anxiety and depression to help manage symptoms and track progress over time. Patients can work directly with an integrated digital

health coach or on their own.

Since 2015, Eva Szigethy, a Pitt professor of psychiatry, medicine and pediatrics, who is the behavioral health director of UPMC’s Chief Medical Office, had been involved in testing RxWell within the UPMC health care system and beyond. Before the pandemic, the app’s usage was associated with reduction in anxiety and depression over three months, Szigethy says, “with an effect size consistent with any psychotherapy trial looking at short-term improvement for mild to moderate mental health issues.”

Since summer 2020, the Post-COVID Recovery Clinic has been enrolling people in Institutional Review Board–approved trials when they are first diagnosed with COVID-19, to gather data about persistent symptoms in conjunction with mood and behavioral health. COVID long-haulers showing initial anxiety or depression severity are offered RxWell as part of their treatment plan. Those patients with inadequate response to the app are then offered a structured psychiatric consultation to evaluate whether a psychotropic medication is the next-best step.

While there are no results yet, Morris says, anecdotal reports indicate that RxWell is helping people.

“Digital behavioral tools are a dime a dozen these days,” Szigethy says. “Many startups are creating these tools out in the world; [they are] mainly self guided, without the regulatory standards or ability to link to many other care coordination efforts to increase their reach and effectiveness.” RxWell, however, is embedded into the electronic medical records system, so it’s easy for clinicians to order it for UPMC Health Plan members and to track a patient’s progress.

“While scientists are still trying to figure out the underlying biology of long-haul COVID, how it manifests and can be treated differently in individuals, RxWell helps get patients to a higher level of behavioral intervention by taking full advantage of the medical system where we can provide stepped care,” Szigethy says. —Micaela Corn



In This Together, Apart

Whether during weekly Oakland safety walks, which had students, staff and administrators handing out face coverings, or during late-night study sessions buttressed by re-watching recorded lectures online, Pitt people forged ahead during 2020/21, a most unusual school year. A number of experts from the health sciences have helped guide the University during the pandemic to keep people learning and discovering. To watch a brief video featuring reflections from across campus, scan the code below. —MC

On Oakland safety walks: “We were genuinely concerned enough to put ourselves in their environment, to make a personal human connection, to get them to understand how we are all in this together— ‘We’re here where you live, and we want you to be safe. And it’s important enough for us to be in the community where you spend most of your time.’”

—Kenyon Bonner, Pitt Dean of Students

“Pitt really did do a god job of just trying to create the best experience possible, giving all the resources we need.”

—C’Enna Crosby (EDUC ’22G)



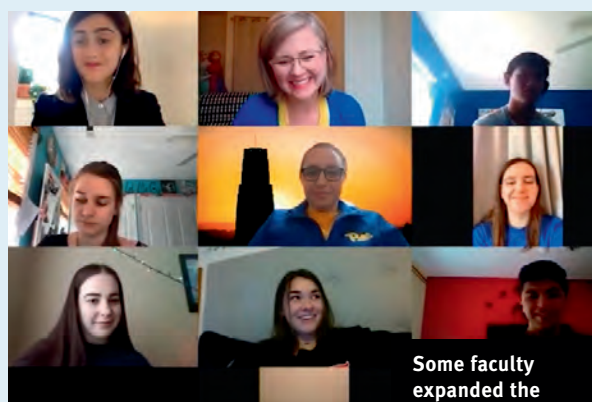
Pitt community members joined Dean Bonner (below) for his boots-on-the-ground effort to emphasize safety in Oakland.





“I’m so grateful for all the green space that we have on campus.”

—Sydney Dubose (A&S ’21)



Some faculty expanded the classroom, making the most out of the virtual setting.



“My professor was able to bring in guest speakers from across the state, from New York City, from so many different locations. We could connect, network with them and talk to them. I thought that was a great opportunity to reach out and meet some new people that I otherwise wouldn’t have been able to meet.”

—James Boston (CBA ’22)



Scan to see how Pitt reinvented life on campus.

Do You Need a Boost?

The current COVID-19 vaccines are highly protective against severe disease; as of August 2021, more than 98% of coronavirus patients who need hospitalization are unvaccinated. Yet, the White House recommends that adults who’ve received two jabs of Pfizer or Moderna mRNA vaccinations should receive a third shot as a booster. Pitt and other national experts answered our questions about this.

Why this recommendation for booster shots?

For tetanus and other inoculations, booster shots help the waning of immune memory.

The ability of the vaccines to keep your immune system protecting you may decrease over time, according to the FDA and the CDC. Another goal is “to try to reduce transmission of the highly contagious delta variant,” says John V. Williams, division chief of infectious diseases at the University of Pittsburgh and UPMC Children’s Hospital of Pittsburgh.

Who should get a booster?

Third doses of the Pfizer and Moderna vaccines have been approved for immunocompromised people (12 and older, at this printing) at least 28 days after the first two inoculations.

For individuals who are not immunocompromised, the White House suggests they receive a booster shot eight months after receiving their second dose of either the Moderna or Pfizer vaccine.

“The boosters are safe and will further reduce transmission,” Williams says. “Along with increasing vaccination rates and continued masking, these are the best ways to finally end this pandemic.”

When will boosters be available?

Booster shots are scheduled for availability in late September, after the FDA formally authorizes the expanded use.

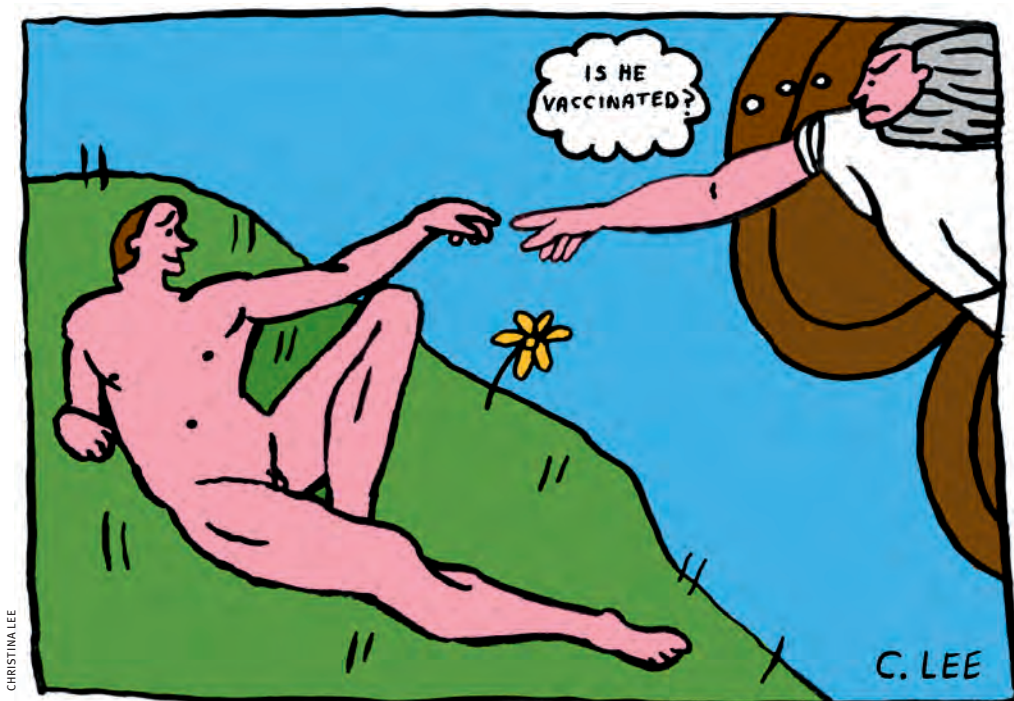
“As we plan for boosters, our main goal remains providing first and second doses to those who are still unvaccinated and providing third doses to immunocompromised people,” says Donald M. Yealy, an MD (Res ’88, Fel ’89) Pitt chair of emergency medicine, as well as senior vice president and chief medical officer of UPMC. “The average healthy individual is well-protected with their first two doses, and they do not need to rush to get a third shot at this time.” —G/

Vetting Boosters

Clinician researchers will continue to vet COVID-19 boosters here in Pittsburgh.

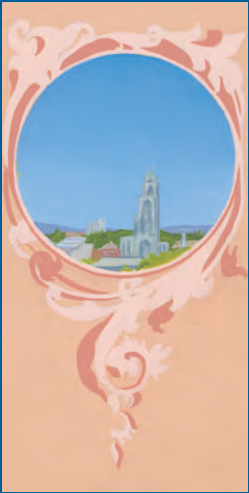
Led by Judy Martin, professor of pediatrics, the University of Pittsburgh Vaccine Trials Unit (PVTU) is participating in a national study of adult booster shots for the COVID-19 vaccine. It is one of 12 sites for this clinical trial series that assesses the safety, reactions and immune response of a delayed vaccine boost. The study is expected to run through May 2025.

“This is an adaptive study design,” Martin told WESA FM. “So we continue to bring in additional vaccines [including those targeting variants] over time to look at the combinations.” —G/



CHRISTINA LEE

*Devoted to noteworthy happenings
at the medical school*



Robert Gaunt works with study participant Nathan Copeland on sensory perception and feedback.

A LITTLE PICK-ME-UP GOES A LONG WAY

If you want to pick up a warm mug of coffee, and not have any of it end up in your lap, it helps to have full sensory and motor control over your arms and hands. When your neurological and musculoskeletal assets work together, you can feel the weight and temperature of the mug and adjust your grip accordingly.

Tasks like that become much more difficult when a person relies on a prosthetic arm or—granted there aren't many people doing this, but this is in our future—a robotic one.

University of Pittsburgh bioengineers from Pitt's Rehab Neural Engineering Labs have found that adding brain stimulation that evokes tactile sensations makes it easier for an operator to manipulate a brain-controlled robotic arm. Their results were published in *Science* in May. Pitt's Jennifer Collinger and Robert Gaunt were senior authors on the study. Both are associate professors of physical medicine and rehabilitation.

Nathan Copeland volunteered for the study. Copeland has limited use of his arms and legs after a car crash that also left him without feeling in his arms and hands.

After the researchers supplemented Copeland's vision with artificial tactile perception, he was able to cut the time spent grasping and transferring objects in half, from a median time of 20.9 to 10.2 seconds.

This paper is a step forward from a 2016 study on sensation for which Copeland also volunteered. That paper described how stimulating sensory regions of the brain with tiny electrical pulses evoked sensation in distinct regions of his hand.

In this new study, Gaunt and Collinger's team was able to offer sensory feedback to the robotic arm.

"Doing the task while receiving the stimulation just went together like PB&J," says Copeland.

Gaunt says: "We still have a long way to go in terms of making the sensations more realistic and bringing this technology to people's homes, but the closer we can get to recreating the normal inputs to the brain, the better off we will be." —Anastasia Gorelova



Overheard

The Flu and You: How viruses affect us differently

When researchers make predictions about how viruses spread, they often assume everyone in a population is equally likely to get sick. But, that's not the case, according to a study in *PLOS Pathogens* in February by **Seema Lakdawala**, associate professor in Pitt's Department of Microbiology and Molecular Genetics. Lakdawala and her team found that viruses like influenza generate varying immune system responses, and immunity to one virus can protect against other viral infections. They also discovered that a child's first influenza infection influences their immunity to future flu viruses. In the study, Lakdawala and her team used ferret models, which have a similar susceptibility and immune response to flu as humans.

Why are these findings important?

Different prior infections can shape susceptibility.

What are the implications for how we approach and treat infections?

We're starting to think more about personalized medicine. You could imagine a scenario where understanding the age and birth year of an individual and what they were first infected with in their immune history could shape what they're likely to be infected with. That impacts pandemic emergence. It's all related.

What can this study tell us about COVID-19 and future pandemics?

We think it will help inform studies looking at how pre-existing infections with human coronaviruses influence transmission or susceptibility to SARS-CoV-2. There was talk early [in the pandemic] that kids were less susceptible to COVID-19 because of their prior experience with human common-cold causing coronaviruses. I think there are a lot of parallels when we think about pandemics and respiratory viruses.

You are a flu expert, but can you tell us if you think that talk was right—that kids were less susceptible to COVID-19 because of their immune histories?

We've learned that kids can become infected with SARS-CoV-2 but, luckily, they don't develop severe disease. We've observed the rates of infections in children increasing and, with emerging variants of SARS-CoV-2, COVID-19 disease in kids could become worse. Whether the low disease burden in kids is due to prior immunity with [other] coronaviruses is still unclear, but it's something my lab is researching with our collaborators. —Interview by Prachi Patel

GETTY IMAGES



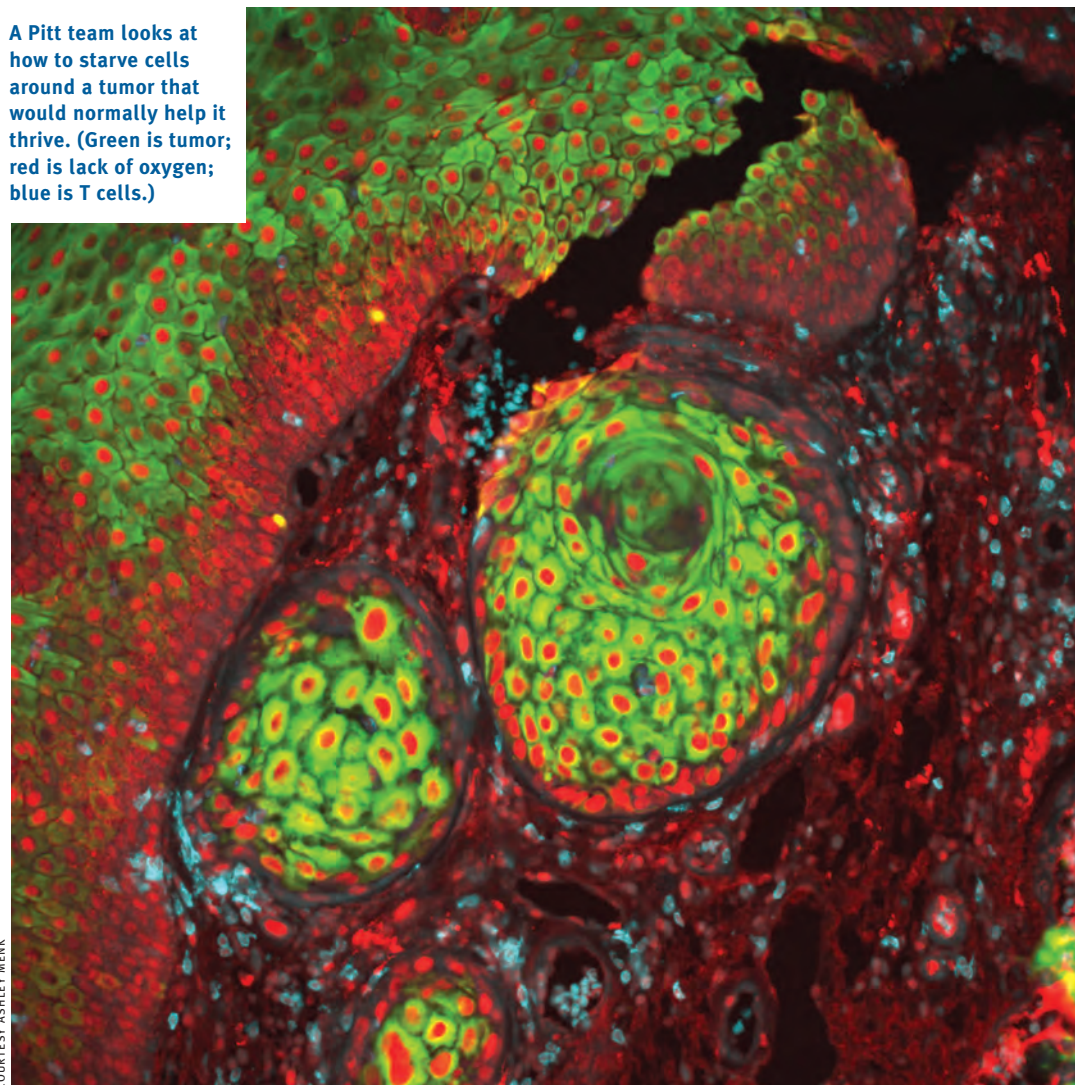
MAKING MEANING OUT OF WHAT WE SEE

When your eyes take in light, they see, but they don't perceive, according to **Avniel Ghuman**, associate professor of neurological surgery at Pitt. "A camera can take a picture, but it doesn't know what the picture is of. That's your brain's job," he says.

Ghuman's Cognitive Neurodynamics Lab studies the neural basis of the visual perception of objects, faces, words and social and affective visual images. And for the past nine years, in collaboration with neurosurgeon Jorge González-Martínez and the University of Pittsburgh Comprehensive Epilepsy Center, Ghuman and his team have been studying epilepsy patients who are undergoing brain surgery. As the patients recover in the hospital, the researchers examine neural activity to better understand how people perceive familiar faces and facial expressions. Their analysis indicates that a region of the visual processing stream—known as the fusiform face area—contributes to most stages of facial identity processing—that is, how you recognize someone. Ghuman and his team also found that the fusiform face area is involved in facial expression processing—like how you interpret someone's mood. However, many in the field thought the area was only involved in identity processing, says Ghuman.

Ghuman's research applies to the general population but may also be relevant for people with autism and schizophrenia: "There's a lot of perceptual deficits that go along with social perception." He says understanding the circuitry of how the brain actually recognizes those things can tell you something about how they work differently in those patients. —Christina Frank

A Pitt team looks at how to starve cells around a tumor that would normally help it thrive. (Green is tumor; red is lack of oxygen; blue is T cells.)



COURTESY ASHLEY MENK

Feed a Cold, Starve a T reg

Research on the immune response in cancer often focuses on the interaction between the individual types of cells involved. For example, scientists might look at how a T cell sees a tumor or how an immune cell sees a cancer cell.

Rather than examining these cells in isolation, Greg Delgoffe, associate professor of immunology at Pitt, published a study in *Nature* earlier this year that focuses on the chemicals in the area surrounding a tumor, the tumor microenvironment.

“We have these regulatory T cells [called T-reg cells], and we noticed a few years ago that these cells thrive in tumor microenvironments,” says Delgoffe. “They proliferate, and they are very, very potent suppressors of the anti-tumor immune response. With cancer, this is not a good thing.”

Delgoffe and his team discovered that by essentially starving the T-reg cells of the nutrients in the microenvironment that are helping them thrive (one example is lactic acid), they were able to shrink tumors and increase sensitivity to immunotherapy drugs in mice.

“If we want to fully mobilize the immune system against cancer cells, we are going to have to figure out how to feed the right types of cells and starve the cells that may be working against that therapy.” —CF

Passing the Torch



Barger

Renae Barger was working as a reference librarian when her team at the Health Sciences Library System (HSLs) learned of a case unfolding in the UPMC Presbyterian emergency department. A woman’s arm was stuck in a meat grinder, and the doctors were considering the best way to safely extricate the arm without damaging it.

Barbara Epstein, director of HSLs, remembers Barger and co-workers searching the library and finding an article about the exact situation from years prior. “We pulled it off the shelf, and [Barger] had to go running into the surgical suite,” says Epstein. “That was pretty dramatic.”

This summer, Epstein will be passing the torch to Barger, who was named associate vice chancellor for the HSLs. Epstein has been with HSLs since 1995, and Barger joined her in 2002 as a reference librarian.

Epstein

Epstein’s legacy in HSLs is marked by large-scale moves from print to digital references, as well as the development of workshops to assist library users in accessing library resources and services.

Barger envisions a future HSLs that implements technology. She sees technological advances for HSLs to expand in areas of open science, online education and virtual reality and hopes to encourage more collaboration across all of Pitt. Barger says Epstein taught her to lead by example.

“She taught me everything I know about being an effective leader. We’re going to miss her terribly,” Barger says. —Evan Bowen-Gaddy

FOOTNOTE

Each year, applicants to the School of Medicine face tough competition for admission, but standing out this year was more challenging than usual. Pitt Med received a 20% increase in applications (8,600 people applied for 150 spots). Of those accepted to the Class of 2025, women outnumber men, making up 58% of the class, and Black students are the largest minority, at 14.56%. The average age is 24-years-old, and 65 of the new students are already residents of Pennsylvania. California, Florida, New York and Maryland are other states with 10 or more students accepted.



James and Ortiz head out with the MobileDerm team to a clinic on the North Side.

DERMATOLOGY ON WHEELS

The sun has begun to rise as Alaina James, assistant professor of dermatology, packs a black Suburban with medical equipment. James and the rest of the MobileDerm team—one resident, one medical student and sometimes an undergraduate—are preparing for a full day of seeing patients at rural community clinics. These areas are often more than an hour's drive from Pittsburgh, places where patients don't have regular access to a dermatologist. James sits behind the wheel on this cool, spring morning. Next to her, a student navigator mixes the directions to Coalport, Pa., in Clearfield County, with conversation about career goals, favorite restaurants and new movies to watch.

James created MobileDerm to offer dermatologic care to uninsured patients in the greater Pittsburgh area. After enlisting help from a couple medical students, she expanded MobileDerm's reach into rural areas in central Pennsylvania—counties she calls “dermatology deserts”—and partnered with community leaders to gain traction.

Camila Ortiz, a fourth-year med student, has accompanied James on

several visits to clinics in Clearfield and Butler counties, as well as one on Pittsburgh's North Side. Working with James has taught her how dermatologic conditions can “severely compromise people,” Ortiz says. “Something as apparent as your skin plays a role in your self-confidence, and how you operate, and how you act around others.”

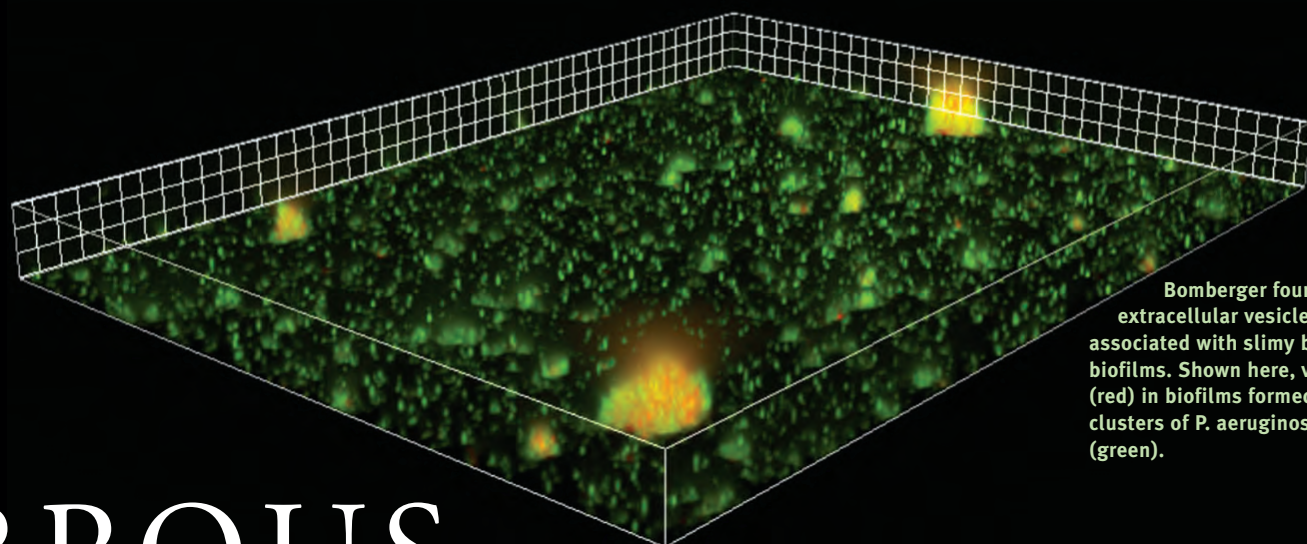
James says she encounters patients of all ages at the rural clinic; they have rashes, lesions, bumps and even melanomas. In the field, they're able to perform biopsies, whole-body skin exams and small procedures such as cryotherapy.

At about 4:30 p.m. in Coalport, the MobileDerm team packs up their equipment and loads it back into the Suburban. Today they treated about 25 patients.

“They're so thankful to have their care attended to,” Ortiz says. “And every time I leave the clinic, even if it's a long day, I'm on cloud nine.”

—Hope Reveche

—Photography by Aimee Obidzinski/University of Pittsburgh



Bomberger found that extracellular vesicles are associated with slimy bacterial biofilms. Shown here, vesicles (red) in biofilms formed by clusters of *P. aeruginosa* (green).

FERROUS, NEFARIOUS

IRON FLECKS FEED FEROCIOUS INFECTIONS | BY ALLA KATSNELSON

Viral infections in the respiratory system can have a nasty aftermath: On top of the illness they cause on their own, they are frequently followed by chronic bacterial infections—which are tough to stamp out and can even be deadly. Most people who died in the 1918 influenza pandemic actually succumbed to these secondary infections. Today, they are a scourge for people fighting off a variety of respiratory viruses, including influenza and even SARS-CoV-2.

Jennifer Bomberger, associate professor of microbiology and molecular genetics at Pitt, is beginning to unravel the biology at the root of this double whammy.

The new work stems from Bomberger's long-term research on cystic fibrosis (CF), a genetic disease of the lungs (and other organs). Chronic bacterial lung infections are very detrimental to CF's disease course, Bomberger says. "We don't know how chronic bacterial infections in cystic fibrosis are established, but there are clinical observations that patients frequently develop a chronic bacterial infection around the same time they've had an acute respiratory viral infection."

That observation led the team to ask the

question: Does an acute viral infection change the environment of the respiratory tract to allow chronic bacterial infections to develop? That question has driven her lab's research for a decade.

In 2016, they discovered a piece of the puzzle: For a bacterial infection to turn chronic, the bacteria must form what's known as a biofilm, configuring themselves in a protective slime that is highly resistant to antibiotics. Working with human airway cells grown in a dish with the bacterium *Pseudomonas aeruginosa*, Bomberger and her colleagues found that several types of viral infections trigger biofilm formation in airway bacteria.

In the new work, published in *Cell Reports* in January, the researchers investigated how that might be happening.

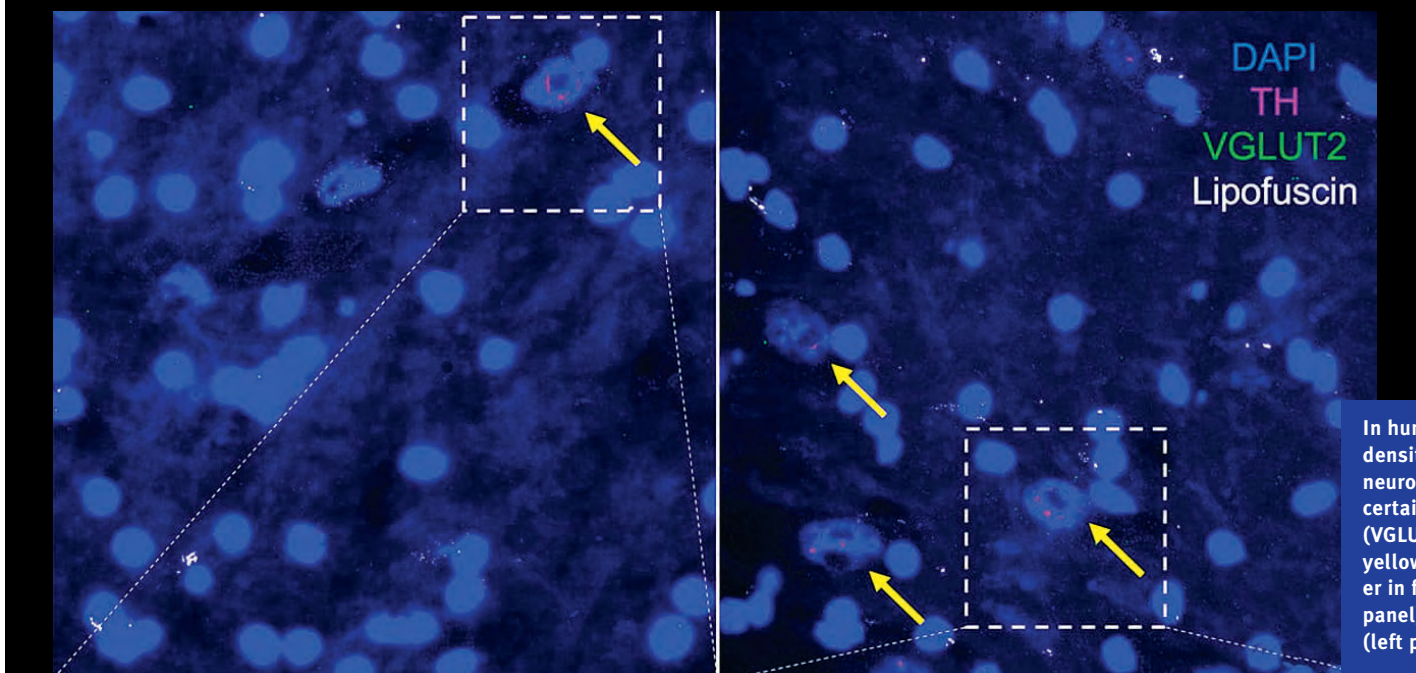
They found that the bacteria are somehow obtaining iron, a nutrient that host cells typically sequester. A closer look revealed that the iron lies on the surface of tiny sacs, called extracellular vesicles, which host cells secrete—and that these sacs become more abundant when the cells are invaded by viruses.

"We discovered that these extracellular

vesicles are released in higher numbers during an acute viral infection," Bomberger says. "The bacteria are able to interact with these vesicles and acquire iron from them—and we think that's actually what's inducing biofilm growth."

What these vesicles do normally, in the absence of infection, is still not fully understood. Current studies in Bomberger's lab are trying to pin down what else they contain—but it's undoubtedly not just iron, she says. For example, they may be carrying immune molecules meant to help fight the viral infection. Regardless, it appears that the bacteria may have somehow co-opted the host cells' communication and delivery systems for their own voracious needs.

"The host antiviral response is really good at controlling the viral infection," she says. "But it's probably leaving an Achilles heel that the bacteria are exploiting," which suggests some intriguing treatment implications. For example: combining antibiotics with iron chelation therapy could slough off the bacteria's food supply. Potentially, that could help stave off such secondary infections—by turning feast to famine. ■



In humans, the relative density of dopamine neurons carrying a certain kind of protein (VGLUT, shown by the yellow arrows) is greater in females (right panel) than in males (left panel).

A POTENTIAL NEW TARGET FOR PARKINSON'S

GAME-CHANGER FOR AGING IS LINKED TO SEX

BY ADAM REGER

One of the enduring mysteries of Parkinson's disease is why it disproportionately affects men. The debilitating neurodegenerative disorder is observed far more often in men than in women—perhaps twice as often—and generally begins at an earlier age in men.

Recent findings from Pitt scientists suggest a potential explanation, opening new possibilities for understanding and treating Parkinson's and other aging-related brain disorders.

In a paper published in *Aging Cell*, Zachary Freyberg, assistant professor of psychiatry and cell biology, and Silas Buck, PhD candidate in Pitt's Center for Neuroscience, examine the role that vesicular glutamate transporters (VGLUT) play in neurodegeneration.

VGLUT is a protein that helps move glutamate, a chemical that plays a vital role in maintaining normal brain function.

The team found VGLUT in greater abundance in females. To explore a possible link between VGLUT and females' greater resilience to aging-related neurodegeneration, researchers used genetic tools to remove VGLUT from female *Drosophila* flies. With just a 60- to 90-day lifespan, the flies are handy for observing the effects of aging.

Monitoring the male and female flies

as they aged, researchers found something incredible.

"Females ordinarily were protected" from losing dopamine neurons and locomotion, says Freyberg. But with VGLUT removed, these measures deteriorated in the females at the same rate they did in males, an outcome he describes as "shocking."

The research offers hope, Freyberg says, that VGLUT could be an important target for future therapies treating Parkinson's and other aging-related brain disorders. More broadly, the findings contribute to an ongoing effort in the scientific community to factor sex differences into understanding the human body and the diseases that challenge it.

"By understanding what makes men and women different biologically, we can find the factors that provide women greater survival benefits and apply them to more vulnerable men and women," says Buck. "And everyone benefits."

Freyberg described his investigations in flies to a colleague, Thomas Hnasko of the University of California, San Diego (a coauthor on the *Aging Cell* paper), and was surprised to learn that Hnasko had observed the same phenomenon in work with rodents.

To determine whether VGLUT was at work in humans, as well, the team worked

with Pitt's NIH-sponsored NeuroBioBank and David Lewis, Jill Glausier and Kenneth Fish. Examining postmortem brains, they found that VGLUT was, indeed, in greater abundance in females than it was in males.

Though encouraged by the findings, the team says there is still much work to be done in deepening our understanding of VGLUT.

"It's still possible that it's not VGLUT driving these differences, that it's just a marker of something else," says Buck.

Freyberg adds, "The next step is to understand what controls VGLUT expression itself. What is it about VGLUT that increases survival?"

Buck will focus on the protein over the remainder of his PhD studies, trying to unlock the mechanism of how VGLUT offers protection against aging-related degeneration.

What makes Parkinson's disease so devastating, Freyberg says, is that existing therapies address only its symptoms.

"But nothing stops the pathology," he says. "So if you can prevent the cells from dying in the first place, you can slow the progression or even stop it. That's something that's absolutely new and important, and that will help everyone. And then that becomes a game-changer." ■



An international team of researchers has taken cues from bioluminescent algae to create a new therapy to help restore partial vision in blind people.

RUGLIG/GETTY IMAGES

LET THERE BE SIGHT

PITTSBURGHERS HELP OTHERS SEE ANEW

BY ELAINE VITONE

Growing up in rural Ohio in the '50s, Roger St. John learned to feel the rain before the thunder and clouds rolled in. He could tell by the way the air shifted and tugged at him, swelling with that distinct, almost electric scent—sensations likely due to barometric pressure and ozone, the voracious reader would later learn. This keenness never left him.

St. John and his kid brother, Will (we've changed their names), knew trouble could be heading for them. A heritable condition robbed many of the men in their family of their sight. They had an uncle, a great uncle and several cousins with this disease, known as retinitis pigmentosa (RP). It's typically diagnosed in young adulthood. In Will's late teens, he started noticing symptoms. RP is not a halfway thing, Roger St. John says. "You *will* become blind. That's almost certain." St. John himself was well into his 20s by then and doing fine. "I thought I'd dodged a bullet."

But some years later, he began to notice that driving at night was getting harder. An ophthalmologist confirmed the storm was coming for him, too.

St. John's night blindness steadily worsened—walking into dimly lit restaurants became impossible without holding onto a friend's elbow—and bit by bit, darkness blotted out his periphery. His field of vision gradually narrowed to a smaller and smaller pinhole. Ten years after the first onset of symptoms, he was totally blind.

But as St. John, 73, explains this now over the phone, there's not even a hint of sadness in his voice. Sure, when he learned his diagnosis in his early 30s, he did a kind of bucket list, traveling to China and boarding a bus tour across North America, "all the usual tourist traps, the Grand Canyon and that kind of stuff," he says.

But as he gradually lost function in the ensuing years, he didn't so much stop doing things as just learn how to do things differently.

"I volunteer to drive for my wife, but she doesn't take me up on it."

St. John relies on smell, texture and timing when he cooks—which he does often, and with pleasure. (He used to teach a Chinese cooking class.) When he's out and about, his golden retriever helps him navigate, but St. John gets around fine without his four-legged guide when they're at home. When they go out to the backyard, subtle shifts in the ground orient St. John. When it's time to head back inside, the sounds bouncing off the brick and wood along the back of the house tell him exactly where the door is.

If someone walks past him on the street, he knows it. If he goes someplace new, he can tell that there's, say, a bank of cabinets in the room and point to them. He shrugs all of this off: Blind folk don't hear better—they just pay more attention, he says.

St. John is a gadget guy. For a time, product testing of assistive technology devices was part of his job. He followed the evolution of screen readers in the 90s as their robotic voices became increasingly more intelligible. Now, in his retirement, St. John uses the text-to-speech function on his Mac every morning to catch up with emails and take in the news as well as pleasure reading. His favorite subject is anthropology—and anything sciencey, really.

Several months ago, when a University of

Pittsburgh/UPMC research team called St. John to invite him to participate in a new study, he gladly signed up. He then read about the clinical trial in *The New York Times*. In that trial, an international team of researchers, led by Pitt's José-Alain Sahel, chair of ophthalmology, partially restored vision to a blind man in Paris. St. John then read other articles about where his next adventure would take him: into an emerging field called optogenetics, which the researchers used therapeutically to restore vision. These optogenetic tools are inspired by nature—using engineered proteins that glow like those in bioluminescent algae. (See "Out of the Dark" for more on this technology and the first breakthrough therapeutic case.)

St. John's adventure started with a shot in the eye, he says—but no worries. There was a very effective numbing agent involved. He chuckles. "They asked my wife if she wanted to come and observe, and she declined."

As we chat on the phone two weeks after the injection, he gives me his short version of this very complex technology, more than a decade in development and now in use with its first handful of study participants, including St. John and other Pittsburgh volunteers:

In RP, the photoreceptor cells (called rods and cones) are completely destroyed. So this injection uses a harmless virus to deliver specially engineered genetic material right to the ganglions, a smaller group of cells that are still alive and kicking and attached to the optic nerve. And in turn, he says, "that genetic material prompts the ganglion cells to start producing a protein that is light sensitive. ... Then, [the ganglions] can respond to patterns that appear on the retina."

The effects are subtle, though, which is where the gadget part comes in. A special set of glasses equipped with both a camera and a projection system amplify light for these repurposed ganglion cells. In this early phase of product development, St. John's glasses are 2-and-a-half inches thick, maybe 3 inches high and span the entire width of his face.

It takes a couple of weeks for the virus to attach to the cells, and several weeks longer for the protein-production to get up and running, he explains.

And then over a period of months, the

brain must learn to see anew with this wildly innovative workaround.

"Training-wise," he says, "I will do all kinds of things: walking around, looking for doors and marks on the floor, looking for patterns on a screen." He was doing plenty of the latter already when we spoke in July—hours-long sessions of baseline measures—while waiting for the injection to kick in. There's lots of prompting: *Where is the square? Which direction is the letter C facing?*

"I call it making me lie. All my responses are total guesses."

St. John is optimistic that in time, he won't just be "lying" anymore, and he'll be able to see certain things as the patient in Paris did. But he's also a realist. Using these genetically modified stand-ins for his former photoreceptors, things are going to look pretty low-res.

But that's okay.

"I'm doing it," he says, "because I'm hoping this might make a contribution to future developments that will work even better."

"And I want to know what's going on with this whole thing."

"I'm very curious scientifically."

St. John's favorite subfield of anthropology is cultural anthropology, the study of how various peoples adapt to their physical environments and devise their own cuisine, kinship systems, ideologies and technologies. I point out that, in this moment, he's a case study of the latter, and he laughs. "I'd never considered it!"

Cultures around the world treat blindness differently. Musicianship is often a big part of it—the blind bard Homer was thought to have sung the *Iliad* and the *Odyssey*. And in some places, blindness is considered a sort of tradeoff for clairvoyance, St. John notes; so I have to ask if he has any experience with that.

"Sure," he says, "That's a very nice outfit you have on." I laugh into the phone, slouching in pandemic athleisure.

There is a big-picture sense, though, a long view that rallies St. John as he donates hours upon hours of his time, his effort and his blood, urine and tear samples in the name of science.

"I'm not doing it because there's some deficiency in my life experience," he says. "I'm doing it because I want to help." ■



Using a protein found in algae, a new technology partially restored the sight of a completely blind man. In an experiment (shown here), he was able to identify the position of two cups. Leading the research is Pitt's José-Alain Sahel in collaboration with Botond Roska in Basel, Switzerland.

OUT OF THE DARK

BREAKTHROUGH THERAPY HELPS PATIENT SEE

BY ANASTASIA GORELOVA

An idea borrowed from nature is the basis for a breakthrough therapy that partially restored vision to a blind man. The therapy uses light-sensing proteins found in bioluminescent algae.

In a paper published in May in *Nature Medicine*, an international team of scientists reported on this first case of partial vision recovery employing tools of a technology called optogenetics. The study marks the first time a patient has achieved functional recovery in any neurodegenerative disease with optogenetics.

Optogenetics, or manipulating proteins and cells with light, was developed in the early 2000s and drove major discoveries about the inner workings of our brains. Yet, while actively researched in experimental animals, functional improvement using this method was never reported in humans—until now.

“I hope it will be a major breakthrough,” says first author, José-Alain Sahel, chair of ophthalmology at the University of Pittsburgh, director of the UPMC Eye Center and professor at Sorbonne University in France. “This paper is a culmination of more than 12 years of work. I am very pleased to have contributed to this effort with Botond Roska in Basel [Switzerland] and all

my colleagues at Institut de la Vision in Paris.”

The paper describes the progress of a patient in Paris who 40 years ago was diagnosed with retinitis pigmentosa—a progressive neurodegenerative disease that destroys light-sensitive cells in the retina and leads to complete blindness. Retinitis pigmentosa is caused by mutations in more than 71 different genes.

“The eye is a complex system that allows our vision to adapt to different levels of light,” says Sahel. “But complex systems are very fragile—so when vision disappears, there are few treatments left aside from using prosthetics or reactivating remaining cells in the retina.”

So, the researchers decided to activate the nerve cells directly.

Researchers injected the worse-seeing eye of a patient with a benign virus that carried genetic information encoding a light-sensing protein (channelrhodopsin protein ChrimsonR). These proteins, found in glowing algae, respond to light by changing their shape and allowing the flow of ions in and out of the cells. The flow of ions activates the cells and, in the case of neurons experimentally engineered to express the proteins, causes them to fire and transmit the signal through nerve endings to the brain.

For this study, researchers chose ChrimsonR protein because of its preference for activation by amber-colored light, which is safer and causes less pupil constriction than blue-spectrum light, like that from computer screens. The construct targeted ganglion cells of the retina—neurons that collect signals from cones and rods and transfer them through the optic nerve to the brain, where that information is processed ultimately as a visible image.

The scientists figured out how to transform the light that bounces off objects in the environment to a single wavelength in the amber spectrum. To do that, researchers used special goggles equipped with a camera that detects changes in light intensity pixel by pixel as distinct events. The transformed image from the camera is then projected as discrete light pulses onto the retina in real time, like a movie projector onto a theater screen.

The results were remarkable. After a period of adjusting and learning how to use the technology, the patient was able to locate, identify and count objects using the treated eye while wearing the goggles. The patient could not visually detect any objects before the injection or without the goggles after the injection.

“Adjusting to using the glasses takes time,” says Sahel. “Initially, the patient didn’t find the glasses very useful; but after a few months, he started to see the white stripes on a crosswalk and after several training sessions was able to recognize other objects, big and small.”

The researchers are testing the technology in more people in Paris, London and Pittsburgh as COVID-19 restrictions are lifted. See “Let There Be Sight” (p. 15) to learn about the experience from a local trial participant’s perspective. ■



THE GIFT OF
TIME



LOST IN LOSS

STUDENTS FIND THEIR WAY
BACK FROM GRIEF

Kortni Ferguson (MD '21, MPH '21) was only days into her second year of medical school when her mother died unexpectedly of unknown natural causes. At the same time, Ferguson's classmate Priya Roy (MD '19) was struggling with the devastating news of her father's esophageal cancer diagnosis. Roy's father died a year-and-a-half later.

Grieving the loss of a parent while taking on the daily challenges of coursework and rounds was overwhelming. Ferguson and Roy found support in one another, yet they never found any scientific research or support groups relating to their particular circumstances as bereaved medical students.

“There’s a lot of resources on how to cope with medical school. There are a lot of resources on how to cope with grief,” says Ferguson, who is now a psychiatry resident at Stanford. “But there’s really nothing that addresses the intersectionality of being a young bereaved person and a medical trainee who’s constantly exposed to morbidity and mortality.”

In 2019, Ferguson and Roy cofounded a nonprofit called BereaveMed to help medical students address their experiences with death and grief—whether the experience is the loss of a family member, a patient or a way of life (as has happened with the COVID-19 pandemic). BereaveMed has expanded to include volunteer staff members from medical schools beyond Pitt, and the team hopes to one day partner with national medical organizations. Their website includes links to research studies about grief, a blog with expert interviews and personal stories.

“One of the most cathartic experiences I had was writing my story for the website,” says Roy, who is now an internal medicine resident at the University of Wisconsin-Madison. “For a long time I was kind of struggling silently, as many medical students do through experiences like this. And it wasn’t until I put proverbial pen to paper that I realized what I was going through.

“There’s something really cathartic about just sharing your story,” Roy adds. “That’s what I’ve heard from other students who have read our site as well and started writing their own stories for us to publish. You really get this space to be completely open and honest about what you’ve been going through.”

The essays that follow are excerpted with permission from [BereaveMed.com](https://www.bereavemed.com).

—Cara Masset

THE GIFT OF TIME

BY PRIYA ROY

It was the summer after my first year of medical school when I got the call.

“I have some bad news,” my sister started.

Our dad had been having some difficulty swallowing lately and had unintentionally lost about 20 pounds in the past eight weeks. That afternoon, he had gone to the hospital for an upper GI endoscopy, and they found a 5-centimeter mass in his distal esophagus. Listening to her describe it, I couldn’t help but think back to the previous fall, when our anatomy instructor summoned the class around a cadaver in the anatomy lab to examine a particularly impressive example of esophageal cancer. The spidery black tumor was plastered across what was left of the cadaver’s posterior chest wall. It was like looking at a Jackson Pollock painting. My

conversation with my sister was punctuated by silence, neither of us knowing quite what to say. Finally, after a particularly long pause, I told her that I loved her, hung the phone up and broke into tears.

The next few days were a blur. I sent a frantic email to my mentor to inform him that I had to suspend my summer research. Little did I know, I wouldn’t come back to it for another year and a half. I booked a one-way ticket home for later that week and spent the next few days just trying to distract myself. At 3 a.m., the morning of my flight, I sat in bed weeping while I drafted an email to my friends, explaining the situation. It had been five days since I had gotten the news, and I was still shell-shocked. I hadn’t been able to work up the courage to tell them in person, knowing that I would dissolve into a blubbing mess

if I tried to answer the question “How are you?” honestly. Typing it out for the first time was excruciating. This may sound cliché, but putting my dad’s diagnosis into words for the first time really did make it all feel so much more real.

In the coming weeks, we would learn his official diagnosis: stage 3 esophageal adenocarcinoma of the GE junction. My sister and mother are both doctors, so like the diligent, evidence-based medical providers that we are, the first thing that the three of us did was perform a literature search on PubMed.

Weird, I know.

So, no one showed up at my door one day to warn me about how hard it was going to be. How exhausting it would be to lie every day, pretending for my patients and classmates and attendings like nothing was wrong. No one prepared me for the confusion I would feel when I slowly began to hate all of my friends—how I wanted to scream at them when they couldn’t seem to understand why I might be having a bad day. I even started to resent my classmates for their accomplishments, though rationally I knew that they deserved their success. They don’t know how lucky they are, I would think to myself. How unfair is it that they have the luxury of focusing all of their energy on school while I’m trying to juggle a dying parent and a family that’s falling apart. And now residency programs expect me to compete with my classmates? Seriously?

I began to hate how angry and self-centered I had become.

Through trial and error, I slowly found little ways to fight back. I tried my best to compartmentalize and forgave myself for the days when I couldn’t. I learned that I can (and should) push back when I need help but am told “no.” I made conscious efforts to shift my perspective, and each day I would force myself to write down one thing I was proud of accomplishing or one thing I’d witnessed that had brought me joy. Most importantly, I stopped bottling everything up inside of me and started talking to the people I loved about what I was going through.

So if you happen to be a student who is struggling, know that you are not alone. That



Priya's father,
Pravin Roy.

may sound obvious from the outside looking in, but when you're in the trenches and fighting for your life, it can be hard to look beyond the obstacles in front of you to recognize that there are others by your side. It's okay to lean on them. In 2017, 1 in 4 medical students reported being depressed. So that feeling of loneliness? Like no one can relate? It's an illusion. A lie. Complete and total bullshit.

But here's the kicker: Only 16% of students will ever seek professional help. That number seems to surprise the deans of medical schools across the country, but it really shouldn't. After all, it takes courage to admit that you're struggling. And it takes energy and strength that you don't always have to ask for help. Like me, you may also feel conflicted when you realize that we can also become our own biggest obstacles. There's pressure to outperform each other (and ourselves): to have the highest board score, to get honors, to showcase our dedication by being the first to arrive in the morning and the last to leave. But there's not much talk about how that mindset can really harm us in the long run. For example, I didn't seek help for my depression until nearly a year after I recognized that something was wrong. I remember knowing that I needed to talk to a psychiatrist but not being able to fathom how I could even fit a doctor's appointment into my schedule. As a third-year medical student, I wondered, Can I just leave rounds? Is that allowed? What if my resident thinks I'm being lazy? Or what if that's my only day on service with a particular attending? How will they be able to grade me if I'm not there? I put so much pressure on myself to be "the

perfect student" on paper that I had also put off the task of working through the one thing that was holding me back. As it turned out, I did have the time to see a therapist. Really. I had the time to start taking an antidepressant. I had the time and the power to delay a shelf exam or request an extra study month. I had the time to get help. I only wish I had learned that lesson sooner.

Six months ago, my dad was diagnosed with metastatic disease. He's on a palliative chemotherapy regimen that, on average, maintains efficacy for about five months; in the back of my mind, I'm just waiting for the other shoe to drop. For his CEA levels to rise. For his ascites to return. After two years, I've grown used to the uncertainty of it all. For now, he'll keep getting his biweekly infusions. Eventually those drugs will stop working; so we'll move on to the next one and then the one after that, until we run out of options.

I'll take next year off school and join a research program [so I can be near him]. I don't mean for that to sound bleak. It's just the truth. It's the reality of trying to be a full-time daughter within the pillared constraints of medical education. We'll manage his side effects for now and brace ourselves for what's to come. We'll continue to live each day. We'll watch. We'll wait.

So it goes.



Figure 1. Happy Father's Day

NOTES ON THE ARTWORK:

PAGE 17 DIAGRAM: The diagram is meant to be a tongue-in-cheek representation of the "gift" of the remaining time that I had with my dad and points out the unique cruelty of anticipatory loss. On the one hand, I wanted to spend as much time as I could with my dad before he died. And even looking back now, I feel lucky to have been able to step away from medical school to be able to do that. On the other hand, I recognized the inevitability of my dad's death and the tumultuous nature of his illness, which made his progressive decline even more difficult to bear witness to.

"FIGURE 1" ABOVE: Marigolds were his favorite flower. —Priya Roy



Kortni Ferguson
and her mom,
Marcia Ferguson.

THE PATH TO RESILIENCE

BY KORTNI FERGUSON

“H ey Kortni! Your mom just sent you a text message,” Michael, my fiancé (now husband) told me.

I walked into the living room to check the message:

HELP ME

DYING

I responded with, “what’s up?” not fully understanding the gravity of her message. Letting her text message sink a little further in, I called her immediately. I asked her what was happening.

“Can’t breathe,” she said.

“Can’t breathe.”

I told her that I was going to hang up and call an ambulance. She managed an “OK,” and we hung up. I don’t remember if I told her I loved her, but I hope that I did. I couldn’t just call 911 from Pittsburgh. I started looking for the emergency contact information for Sacramento, California. It. Took. Forever.

I was forwarded again and again. When I finally got in touch with someone who could help, they dispatched an ambulance to her location. I then texted her to let her know that the ambulance was on the way.

The last time we’d corresponded was two days prior. I’d told her that I loved her, and that I would call her soon. I didn’t call. I still feel guilty about that.

I waited one hour to call, because I didn’t want to interfere with the process. I didn’t want to interrupt my mother’s phoneline if they were trying to contact her. I paced my apartment for the full hour. Michael was trying to make light of the situation, telling me that my mom was probably just having a panic attack. I wasn’t convinced. After exactly an hour, I called the fire department back, and they referred me to the hospital they took her to.

I was connected to the emergency department and asked about her status. It turned

out that she was brought in as a “Jane Doe.” I eventually got connected to a woman who told me that I needed to “come in” to discuss the status. That didn’t sound good.

I explained to her that I was in Pennsylvania. She said something along the lines of, “Oh dear,” and put me on hold. Having worked as a scribe in the ED before medical school, I knew that they always asked survivors of loved ones to come in to discuss deaths. I said nothing—not fully committed to her death, but not at all optimistic either. I was then connected to a physician.

He started with, “We did all that we could. We gave her some medicines—”

I cut him off. “Did she die?”

She had.

My role model, cheerleader and inspiration to live a life of service was gone.

D r. Samson (not her real name) was acting as our attending for two weeks. She noticed how long I was taking to write, and rewrite, patient notes in the team room. The first time I met her, she was sweet, but she asked a question that I recommend no one ask an adult:

“Where do your parents live?”

I was caught off guard; no one had asked me that kind of question since my mother had died. I paused, then my eyes started to well up with tears, so she walked me outside of the team room. I told her a brief story of how I struggled through second year, having lost my mom at the beginning. This turned out to be a big mistake.

For two weeks, she was patient with me. She sugar-coated everything and rarely gave feedback; but at the end of the rotation, she revealed what she really thought. She told me about a friend of hers who had a similar situation to mine and explained her understanding of that experience. She’d interpreted my stating that I’d struggled in second year as meaning that I was a terrible student that year.

“In order to be a good student in third year, you have to be a good student in second year,” she said.

Not to mention how long it took me to finish my patient notes! Honors students don’t spend hours on notes.

Then she said, “Of all the students I’ve

worked with, I would want you to be my physician one day. You're not an honors student or a high pass student, but we can get you there."

I claimed that my issue was my anxiety, but she refused to accept it. She knew my experience better than I did. In that moment, I felt powerless to a situation completely out of my control. I regretted ever sharing a piece of my life. I regretted showing any weakness. I regretted trusting her. I began to cry.

It was the first time in my life in which I'd cried after receiving feedback.

My mother raised me with the perspective that we are forever students in life, that change should be embraced and that self-growth is important. That meant that I should be honest with myself about what my strengths and weaknesses are and be receptive to constructive feedback.

Dr. Samson looked at me and said, "It's a good thing that I don't cry when other people cry, or else I would be crying right now."

Was I that pathetic?

That moment changed everything for me.

I asked my doctor to prescribe me propranolol for my performance anxiety. I started every day practicing power stances in the bathroom. I shared no details about my life with my teams. And I became a shell of a person. Months rolled on. I became less and less myself. I would be enthusiastic at work because I really did care about the wellness of my patients, but when I went home, I stared at a wall. I was exhausted. Wearing a mask for 12-plus hours a day took everything out of me.

Near the end of third year, I had my psychiatry rotation. When talking with my patients, I found out that many of them were suicidal after losing important people in their lives. I had never attempted suicide myself, but I'd had my own moments of hopelessness, loneliness and self-loathing.

It was the first time I'd talked to a counselor about grief. Not my grief, of course—our patients' grief.

I couldn't process it all. I started experiencing flashbacks of my mother's death and how alone I'd felt. I was starting to remember my mother's voice and her demeanor. I didn't even realize that I'd forced myself to forget her until the memories came back. The fact that I'd pushed her away contributed to the pain. How could I push away my best friend? The intensity of my feelings turned ugly, and I started to feel suicidal ideation again.

After counseling patients, our team would go into a room and discuss the treatment plan. I felt

like I did not belong there. I didn't belong with the physicians. I was more like a patient. I felt like an imposter. So, I just stopped going. Eventually, the course director called me in and told me to find a therapist. I did.

That therapist was exactly who I needed. It took years of work, but I'm now on the other side of my "complicated grief."

I finally took a break. I visited Michael's family and thought about what had happened to me throughout the past two years. I was living a lie. I was forcing myself to believe that I was fine, and that I was done grieving. Yet, after the shock had passed, I never truly allowed myself to grieve. During those years, I told myself over and over that "medicine doesn't wait." I wanted to be the high-functioning Kortni again. The AMSA president. The interview coordinator. The SNMA volunteer coordinator. The otolaryngology tinnitus lab rat. The [insert ambition here]. I wanted to go back to who I used to be, and I constantly punished myself for not being able to. I was in denial for so long that I had no idea what normal looked or felt like anymore. The truth was that I couldn't go back. My life was forever changed. Accepting that allowed me to consider moving forward instead.

After starting my break, I began considering a research year. When looking into a possible focus on intimate partner violence and behavioral interventions, I realized I wasn't experienced enough in the field. This led me to look into pursuing an MPH. A few phone calls and one application later, I matriculated into the Pitt Public Health Behavioral and Community Health Sciences master's program. It was one of the best decisions I've ever made. I gained a wealth of knowledge for my research, learned what resilience really looks like and determined that behavioral change is extremely difficult.

I found myself thinking, "Why was I willing to be patient with individuals who'd experienced trauma from intimate partner violence but not with myself? Wasn't losing my mother, the only relative I really had, traumatizing? Hadn't I been living in defense for multiple years?"

These were the things I started to consider, and for the first time, I started to forgive

myself for all my actions, all my mistakes, all my negative self-talk. This is what my therapist was trying to show me.

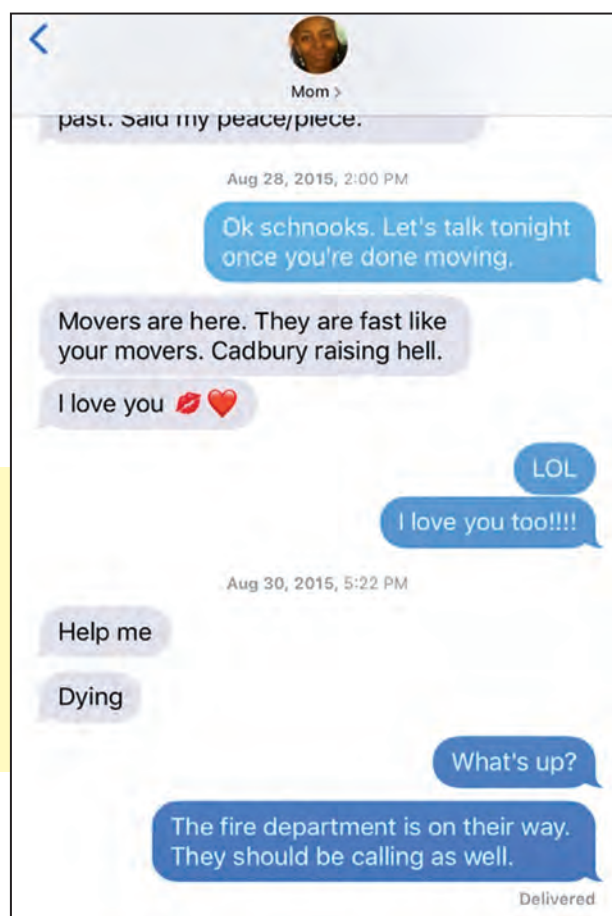
The behavior change was not easy. It took a lot of self-help audiobooks, a lot of conversations and a lot of journaling. I started applying behavioral intervention theories to my own life. All this time, I'd been focusing on a deficit-based approach, rather than identifying my assets.

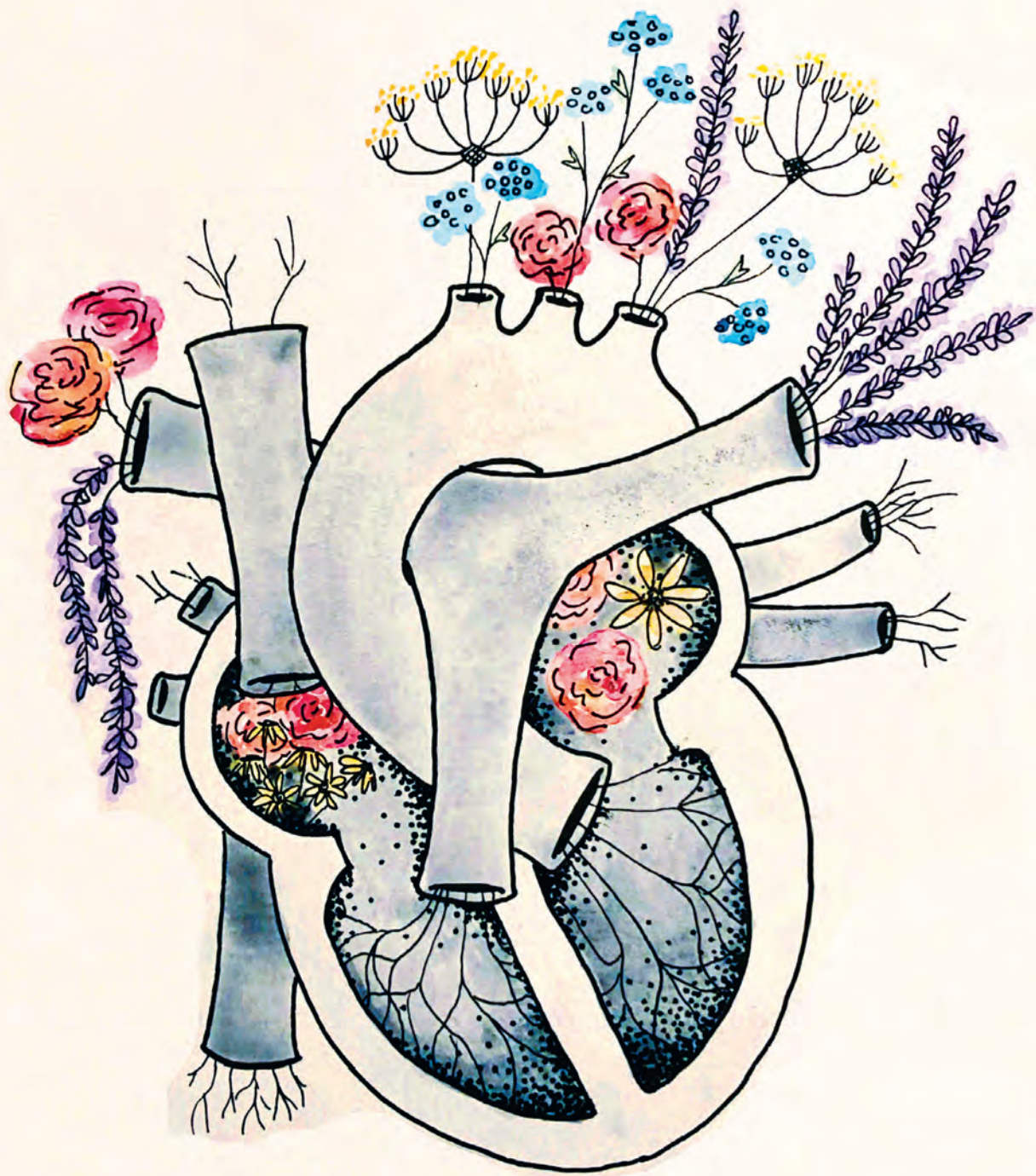
I began celebrating my mother's life through what she had taught me. I now strive to make strangers smile the way my mom did. (She welcomed and loved everyone, even the people some would argue were hard to love. And she somehow befriended the unlikeliest of strangers.)

I try to do something nice for people any chance I get, with nothing expected in return. Most importantly, I've learned to establish boundaries. My mom was an altruistic person; she gave what she could not afford to give. I'm inclined to believe that years of stress from past traumas and financial hardship led to her early death.

Now, I practice self love and give what I'm able to. That was a skill I had to learn on my own. But now, I have the energy to do much more than I ever did before—even before my mother's death.

Healing is a process, and the happy ending is not the only thing that matters. ■





WHEN GRIEF DOESN'T ABATE

BY CARA MASSET

ILLUSTRATION BY PRIYA ROY

Every Monday when the psychiatry team reviewed patient logs, the sociologist in the room listened with curiosity. It was the mid '90s, and Holly Prigerson was a new postdoc working with University of Pittsburgh psychiatry professors Ellen Frank and Charles F. Reynolds III. Prigerson had recently defended a sociology doctoral dissertation at Stanford on end-of-life care, and while the subject of mood disorders was unfamiliar to her, data analysis was not.

The psychiatrists were tracking bereaved patients dealing with what they thought was depression. Week after week, the patients' grief scores remained high, but their response to depression treatments remained flat.

The psychiatrists initially thought the grief scores were benign, since grief wasn't characterized as a mental illness. "You don't know that the depressive symptoms are any more—or less—lethal, toxic or benign than the grief symptoms," Prigerson pointed out. They invited her to explore that assumption.

After culling through the team's data sets, Prigerson unearthed a distinct symptom cluster. She realized that while a mental illness like depression can be triggered by the trauma of losing a loved one, these bereaved patients weren't experiencing depression (only some overlapping symptoms), and therefore they weren't responding to treatments for it. Plus, they were experiencing something different from normative grief (typically, the most intense reactions of shock and disbelief dissipate over time). Their grief was prolonged, and their symptoms included constant yearning for the deceased, avoiding reminders of the death, reduced capacity for self-care and rumination about the future.

Most alarming were the results of a predictive model that Prigerson and the team put together to analyze what they considered "complicated grief." It showed the cluster of symptoms was significantly associated with poor health outcomes like hospitalizations, sleep problems, cancer and suicidality. The idea of pathological grief existed, but it was not well understood or treated, says Reynolds: "Systematic clinical assessment had not been well worked out or established."

In 1995, Prigerson was the first author of the Pitt team's Inventory for Complicated Grief. The validated instrument underpins the tools for diagnosing prolonged grief today. Prolonged grief disorder is now the syndrome's official name, coined in a 2009 paper by Prigerson and colleagues at Cornell University, where she is the Irving Sherwood Wright Professor of Geriatrics and codirector of the Center for Research on End-of-Life Care with her spouse, Pitt alumnus Paul Maciejewski (MA '96). The disorder is gaining visibility, particularly after being accepted in November 2020 for inclusion in the forthcoming edition of the American Psychiatric Association's tome, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR).



Nadine Melhem has found an astounding number of bereaved people who lost loved ones because of COVID-19 experience a troubling syndrome known as "prolonged grief." She's building on work on the disorder done at Pitt for decades.

After identifying the disorder, the Pitt team reached out to their departmental comrade, Katherine Shear, an MD with expertise in anxiety disorders, to ask for help with designing treatments. Prolonged grief encompasses hallmarks of anxiety, namely avoidance and rumination; so Shear tailored common anxiety treatments such as exposure therapy for overcoming avoidance. She led a pilot study and the first randomized controlled trial to evaluate the treatments' effectiveness. The good news: Many patients improved. Shear went on to direct several multi-institutional trials and now heads a center focused on the disorder at Columbia University, where she is the Marion E. Kenworthy Professor of Psychiatry.

In 2019, Prigerson and Shear were among the leaders with a Pitt connection who presented at an American Psychiatric Association workgroup meeting to evaluate the literature on prolonged grief over the previous quarter century and establish official criteria for the disorder's addition to the DSM-5-TR. Although there have been concerns about pathologizing the natural, if unwanted, human experience of grief, the body of literature has shown that patients with prolonged grief disorder only respond to targeted treatments.

Shear praises Pitt's psychiatry department as a "generative department" that fosters an environment where disorders can be clarified and treated. "It was . . . a natural outgrowth, I would say, of a department that had such strength in both mood and anxiety disorders for so long."

Pitt researchers have studied prolonged grief in children and adolescents as well.

Nadine Melhem, associate professor of psychiatry, and David Brent, professor of psychiatry, were the first to characterize the course of grief reactions and identify the phenomenology of prolonged grief in bereaved children and adolescents. Melhem adapted a version of Prigerson's inventory for those populations. She also coauthored several papers with Shear on prolonged grief in adolescents and adults.

Melhem conducted one of the first mental health surveys during the pandemic. Her initial data from about 400 adolescent and adult respondents who lost a loved one to COVID-19 show 55% are experiencing symptoms associated with increased risk for developing prolonged grief. That's concerning, says Melhem. The typical rate among bereaved people for developing the disorder is around 10%.

Raising awareness of the disorder and its treatments is essential, says Shear, particularly among professionals who may be misdiagnosing patients. Shear notes that for every life lost to COVID-19, about nine close contacts are grieving, according to a multiplier calculated by sociologists last year. Other studies suggest the rate of bereaved family and friends is even higher in this multifarious pandemic.

"We don't stop having a relationship with someone who we are not physically with," says Shear. Grief is a process that never completes, she says, but people can make peace with their loss and find ways to re-engage with life while continuing to honor their loved one. ■

TAKEAWAY: Patients with intense grief symptoms lasting longer than a year may need to seek diagnosis and treatment.

Collaborative Healing

BY CARA MASSET

When Cassie and Jim Grassmyer brought their terminally ill son home for hospice care, a friend offered to take photographs. She captured every beautiful detail of 8-year-old Jack—hair, nose, fingers, toes. After he died, those photographs were a source of solace for Jack's parents. Cassie Grassmyer says she appreciated the gesture of photography because she wouldn't have thought to do it herself in those final days when she was preparing her son, her spouse, her parents and—finally, herself—to say goodbye.

It's not easy to provide meaningful support for families grieving the loss of a child, says Leslie Scheunemann, University of Pittsburgh assistant professor of medicine. "There's so little research into parental bereavement" to provide guidance, she says. Partly, it's out of sensitivity. Yet the lack of knowledge may contribute to parents feeling isolated and misunderstood in their grief, she adds.

Scheunemann is part of a first-of-its-kind project at Pitt combining filmmaking, art therapy and health research to better understand

pediatric end-of-life care and family bereavement. Using a method invented by researchers in Pitt Public Health called "collaborative filmmaking," study participants will be trained in videography and invited to create short films to tell their stories. Then the researchers and filmmakers will analyze the films together to identify common themes and important findings among the grief and coping experiences.

By reviewing films created by the participants, researchers hope to capture nuances and emotional context beyond your average survey or qualitative interview.

"There are arts-based approaches to health research, but the number that use film is relatively limited," says principal investigator Jessica Burke, interim vice dean for Public Health and professor of behavioral and community health sciences.

Burke codeveloped the concept of collaborative filmmaking (now registered as an invention with Pitt's innovation office) along with Sara Baumann, Pitt assistant professor in the school of public health. Burke and Baumann have used the method to partner with young women in Nepal to study men-

strual practices. They've also partnered with adolescents in Pittsburgh to study mental health.

Their projects include public screenings of participant films to raise awareness and start discussions on public health interventions.

Last year, Scheunemann read a Pittwire article about collaborative filmmaking. She immediately thought it could apply to her research on clinician-family communication in the ICU and her experiences with end-of-life care. (See her May 2019 report in *JAMA Internal Medicine*.) Meanwhile, Burke and Baumann were talking about their new research method with colleagues who suggested filmmaking could bring end-of-life care and bereavement issues to light.

The researchers connected, and, in July, the team received a grant from the McElhattan Foundation for the project. They are partnering with the Pediatric Palliative Care Coalition to work with parents who are at least 6 months to a year beyond the death of a child.

"There's no pill for grief," says Scheunemann. ■



WHEN CANCER

GETS POOPED

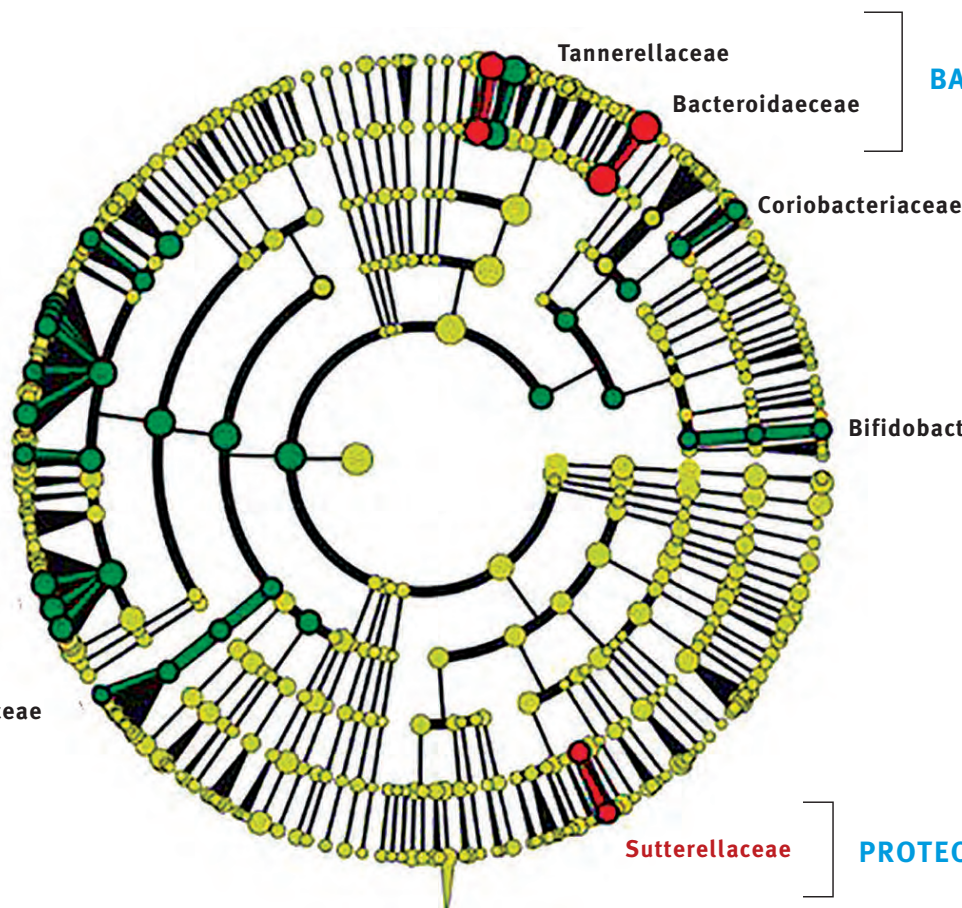
DAYS POST
TRANSPLANT

FIRMICUTES

Lachnospiraceae

Ruminococcaceae

Erysipelotrichaceae



BACTEROIDES

ACTINOBACTERIA

Bifidobacteriaceae

Sutterellaceae

PROTEOBACTERIA

• Increased after transplant in long-term responders

• Decreased after transplant in long-term responders

A transplant of fecal matter helps some patients with melanoma respond to immunotherapy. ABOVE: Pitt physician-scientists are tracking how gut bacteria changed in responding patients after fecal matter transplants. (Each ring represents a day past transplant.) Bacteria are arranged by phylum (blue print) and family (black and red print). Pitt researchers are also exploring paths to more targeted therapies.

CHANGING THE MICROBIOME HELPS SOME MELANOMA PATIENTS BY ALLA KATSNELSON

Jamie Reitinger, a father of three in Tipp, Ohio, was living in the shadow of a deadly cancer when he ran out of treatment options in the fall of 2018. Three years before he had what initially looked like a wart under his thumb-nail—it turned out to be melanoma.



Reittinger was referred to UPMC Hillman Cancer Center where a multidisciplinary team of doctors recommended an amputation of half his thumb. Despite the radical surgery, the cancer resurfaced three years later—this time, it had spread to his lungs.

Melanoma is the deadliest form of skin cancer. Although timely treatment and surgery is curative in most cases, sometimes patients develop advanced melanoma.

In the past decade, a new wave of immunotherapies has changed cancer care. These monoclonal antibodies have transformed many cancers, including melanoma. Yet only about 40% of melanoma patients respond, and Reittinger fell into a vexing majority of patients whose cancers fail to respond to these treatments.

“Cancer immunologists are really trying to improve upon current immunotherapies,” says Hassane Zarour, professor of medicine, immunology and dermatology at the University of Pittsburgh, who coleads the UPMC Hillman Cancer Center Melanoma Program. “We need to find ways for people with advanced cancers to respond to these treatments.”

Yet this is not a story of personal loss and tragedy. So far, for Reittinger and a few others in similarly dire straits, things have turned out well—remarkably so. What turned the tide for them is an unusual treatment involving other peoples’ poop—and researchers are barely past the starting line of a long race to figure out how and why it helped.

In the fall of 2018, Diwakar Davar, a hematologist/oncologist and assistant professor of medicine, and Zarour, along with colleagues at the National Institutes of Health, were launching a clinical trial that aimed to do that.

Mounting evidence in animal and human studies suggested links between the lineup of species in the brigade of bacteria that live in the gut—the “gut microbiome”—and responses to certain immunotherapies, in particular, therapies targeting the inhibitory immune checkpoint known as programmed death-1 (PD-1). So Zarour, Davar and their colleagues set out to test whether modifying the microbiome

could make immunotherapy work. Their study, supported by the National Cancer Institute and Merck, involved transferring fecal matter from patients whose melanoma responded to immunotherapy into patients like Reittinger, whose cancers had not.

Therapeutically transferring poop—a procedure called fecal microbial transplantation, or FMT—isn’t as outlandish as it may sound. Chinese practitioners used this treatment more than 1,500 years ago. Infectious disease specialists have recognized FMT as the most effective treatment for severe diarrhea and colitis (an inflammation of the colon) caused by *Clostridioides difficile*. *C. diff*. colitis causes half a million infections in the United States each year, and in some older patients, it is a significant cause of death. FMT is widely used for the treatment of this colitis; although following reports of multiple cases of life-threatening infections, the U.S. Food and Drug Administration recently issued a caution regarding its use. Hence, in their trial, Davar and Zarour tested both donors and recipients extensively for potentially transmissible organisms.

Based on the promising data generated by Davar and Zarour, Reittinger’s physician, John Kirkwood, Distinguished Professor of Medicine at Pitt and coleader of the UPMC Melanoma Program, recommended that Reittinger enroll in the clinical trial. Reittinger says he didn’t need much convincing to sign on as the study’s first subject. It certainly sounded bizarre, he says, but Davar’s explanation of FMT—and the absence of other treatment alternatives—reassured him. “I told them, ‘OK, sounds cool—as long as you think it’s going to work,’” he recalls.

“Hey, I’m game for anything.”

He admits, however, that the reality of the situation was a bit jarring. A gastroenterologist at UPMC Shadyside Hospital performed the transfer using a colonoscope—a flexible tube



Diwakar Davar (left) and Hassan Zarour (right).

inserted through the rectum. Reittinger was put under conscious sedation, but the drugs had minimal effects on him. And the room was full of clinicians observing the first-ever use of FMT to treat cancer in the United States.

“When I saw the big tube they were going to stick up my butt, and I had an audience of 20 people watching, I thought, ‘What the hell did I get myself into!’” he recalls.

As the researchers reported in the journal *Science* in February, the study was a remarkable success. Six out of 15 participants for whom immunotherapy previously didn’t work benefited from it after receiving FMT. In three of those participants, the cancer went into remission, and in another three it stabilized and stopped growing. Reittinger was in the first group. He received his last immunotherapy treatment in June 2020, and though his cancer might not be completely gone—“there’s still what they call nonmeasurable nodules in my lungs,” he explains—now so small that they are undetectable by routine scans. “I can’t complain,” he says.

Davar was not surprised that the intervention worked, but he was amazed that FMT alone, with no other interventions, would be so effective. “We always believed the signal was there,” he says. “But we did not think that a single FMT transfer would have produced such durable responses—especially given that we did not alter anything else.”

The trial provides intriguing data, says Davar, but it included few patients and the findings raise many questions. He and Zarour have already obtained funding to continue



testing FMT in larger trials in patients with advanced melanoma and lung cancer. What's still unknown, though, is how exactly the microbiome exerts its influence. Scientists know that the area surrounding the tumor—the “tumor microenvironment”—produces molecules that help cancer cells hide from the immune system.

But recent work shows that some factors may act more distantly: “And that may be how the gut microbiome comes into play here,” says Zarour. They suspect that certain key bacteria in the gut set up a signaling cascade that can dampen the ability of certain immunotherapy drugs like PD-1 inhibitors.

“When you don't have these adverse bugs—or you get rid of these bugs—you remove the barrier that prevents PD-1 inhibitors from working,” says Davar. Through more studies

tumors that form there.

Why choose *H. hepaticus*? It causes inflammation in mice that are prone to inflammatory bowel disease, so Hand assumed the microbe would worsen colorectal tumors.

“It turns out we were 100% wrong about that,” he says.

Instead, tumors in those mice shrunk and the mice lived much longer. “It was like a protective therapy, caused by the transfer of just one bug.” In a paper under review, he and his colleagues report that the bacteria appear to be powering up helpful immune cells called T cells, which then promote the formation of cellular clusters called tertiary lymphoid structures, which, finally, in turn spur a strong anti-tumor immune response.

Timothy Hand (below) and Tullia Bruno.



the moonshot,” Hand says, adding that narrowing a particular

clinical effect to distinct microbes and homing in on the mechanism would help anchor the field. The move from mouse to human isn't straightforward, because the microbial species that inhabit the bodies of these two animals are different. But the work strongly hints

“We always believed the signal was there. But I don't think we would have thought that a single fecal matter transplant would have produced such durable responses—especially given that we didn't alter anything else.”

in humans and animals, Davar and Zarour hope to further elucidate this mechanism in melanoma and other cancers and to pinpoint exactly which bacteria are beneficial so that more targeted forms of bacteria than FMT can be developed and tested in cancer patients

MICROBIAL MOONSHOTS

The hints they have now, however, are the tip of the iceberg in a vast new field that scientists are just beginning to explore. Timothy Hand, assistant professor of pediatrics at Pitt, is taking a different approach to studying how the microbiome might affect the immune system's response to cancer. He studies not the fecal microbiome but the microbes that live in the mucus lining the intestine. Because they rub up right against the lining, “those are the bacteria your immune system deals with directly and the ones that induce immune responses,” he says. They took the mucosal bacterium *Helicobacter hepaticus* and set out to see how its presence in the lining affects colorectal

This mechanism might provide a fairly direct model for understanding the microbiome's role in cancer, Hand says.

“You're using a specific component of the microbiome to supercharge immunotherapy of the colon. And by identifying the bacteria that does this in humans, we could design a widely usable microbiome that helps anti-tumor immunotherapy and use it like a pill,” he says.

He is collaborating with Tullia Bruno, assistant professor of immunology, to see how *H. hepaticus* correlates with colorectal cancer outcomes and with the formation of those lymphoid structures within tumors. These structures are similar to the normal lymphoid organs in your body, like tonsils and lymph nodes, where immune cells are educated, but in tumors they form slightly differently than normal. “These structures really do correlate with better prognosis and better response to immunotherapy,” Bruno says.

If their presence aligns with the bacterium, that might suggest that *H. hepaticus* can help people with colorectal cancer. “That would be

that researchers may have to look beyond the fecal microbiome, even though it's the easiest to sample. The mucosal microbiome offers a better bet for success, according to Hand, yet it's much tougher to access because doing so requires a biopsy that's generally taken during a colonoscopy.

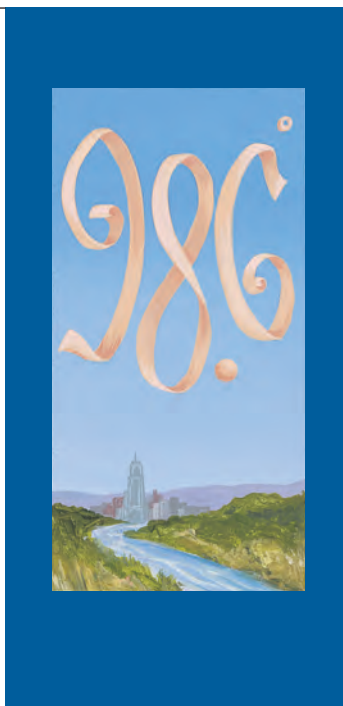
Hand and Bruno aren't entirely sure how the improvements that Davar and Zarour saw in their study relate to what they see. Perhaps there is enough *H. hepaticus* in the fecal microbiome to exert an effect, even at a distance from tumors; or perhaps something entirely different is going on. They hope that mouse studies, in which cancer progression and microbiome composition can be monitored over time, might reveal some clues.

Reitinger has no doubt that scientists will eventually zero in on just how the microbiome plays a role.

“The world of cancer is changing,” he says. “From the time I initially started treatment five years ago to today, they aren't even using the same drugs anymore.” He knows that people will benefit from that progress. ■



*People and programs
that keep the school
healthy and vibrant*



STUDENT FUND HONORS HOFKOSH

For students in the LGBTQ+ community, the intensity and financial strain of medical education in these uncertain times can come with an additional heavy load, explained Elyse Marks, student coordinator for Pitt's Medical Student Pride Alliance (MSPA).

Some may not yet be "out," she explains. Some may not have support from their families. "Knowing that at any given time, there may be med students grappling with their gender and sexuality in their personal lives, it's important to create an environment where students feel safe to be themselves."

To this end, the Pride Alliance and the School of Medicine created a new fund, a first-of-its-kind endeavor at Pitt to support LGBTQ+ medical students. Awards will be chosen based on students' financial need, service to diverse communities and contributions to the diversity of the School of Medicine.

The fund's namesake: Dena Hofkosh, an MD and MEd, is a beloved faculty member of nearly 40 years who has long championed this underserved population. Hofkosh retired in April.

"I'm very happy to have my name associated with this fund, because it's really all about supporting the students," Hofkosh says. "I absolutely feel very honored."

A professor of pediatrics and vice chair

writing a more inclusive curriculum.

Hofkosh has long held dear the importance of nurturing physician well-being. After coming out in her 40s, Hofkosh explained in a recent interview with [Physician Thrive?, a UPMC wellness program], she felt a duty to use her voice.

"I realized I was in a very privileged position to be able to speak out . . . to show people, to set an example, to be a model for the struggling medical students and the struggling residents in this domain," Hofkosh says.

She began working with her colleagues to create a support network, leading to what is now UPMC's PRIDE Health, an affinity group for LGBTQ+ faculty, staff, students, residents, fellows and providers.

"LGBTQ+ students in any field—not just medicine—can feel quite marginalized," Hofkosh says.

"These folks are people who have a set of needs that may distinguish them from others, and to provide some funding is a way of providing support for things that they might not otherwise be able to do," Hofkosh says. For her, it's a way of saying: "We recognize your particular talent and want to help you move forward."

The Dena Hofkosh, MD, MSPA Support Fund will officially launch during A PrideFULL Celebration fundraising event being held at the Mattress Factory on Oct. 1 from 6–10 p.m. The kick-off event in Hofkosh's honor will feature guest speakers, live music and light refreshments.

—Sierra Smith

To register for A PrideFULL Celebration or to make a gift to the Dena Hofkosh, MD, MSPA Support Fund, visit pi.tt/pride-fullcelebration.



Hofkosh

LUNG RESEARCH CATCHES AIR

Think about the difference between healthy- and unhealthy-looking lungs. Typically, diseased lungs are dark and scarred, while fit ones are pink. Melanie Königshoff, an MD/PhD and visiting professor of medicine at Pitt, wants to understand how diseased lungs transform so drastically.

For Königshoff's work on human translational pulmonary fibrosis (PF) models, Pitt's School of Medicine received a \$1.7 million award from the Three Lakes Foundation to develop and refine a new model to better understand the progression of PF and to identify possible therapies.

PF is a chronic, degenerative lung disease that causes lung tissue to become damaged and scarred, making it difficult for oxygen to enter the bloodstream. Each year, 40,000 Americans die from PF, yet little is known about the mechanisms of the disease.

With this award, Pitt joins Yale as one of two centers included in the Three Lakes Consortium for Pulmonary Fibrosis, which aims to change how the disease is diagnosed and treated. Königshoff serves as the lead investigator of one of the consortium's three working groups. That group will develop models to help expedite the discovery and validation of drugs to treat PF.

Königshoff notes that pandemic has increased the need for a deeper understanding of—and more effective therapies for—chronic lung conditions generally. As more people recover from COVID-19, more people are living with the long-term effects of chronic lung disease. —Micaela Corn



SOLSTOCK/GETTY IMAGES

In terms of health risk, flying solo is right up there with obesity or lack of exercise.

TABLE FOR ONE

HOW CAN WE COMBAT THE HEALTH EFFECTS OF ISOLATION AND LONELINESS?

BY ELAINE VITONE

For decades, public health experts have been sounding the alarm about a health hazard that's underappreciated by the public as well as health care professionals, a killer that's taken on even more significance since the pandemic hit.

But it's not one of those usual-suspect diseases, bound in bodily organs and blood vessels. It's rooted in our emotional well-being.

Social isolation—the objective state of a lack of social connections—affects nearly a quarter of Americans over 65. And loneliness—the subjective feeling of being isolated (regardless of the degree of contact with others)—affects more than one-third of Americans 45 and older. Both social isolation and loneliness are associated with a range of adverse health outcomes, including heart disease, stroke, dementia, depression and anxiety.

And that's what we knew before COVID-19.

In a poll conducted by the University of Michigan in March through June of 2020, loneliness in older adults had doubled compared to two years before. Among younger adults in those early days of lockdown, a survey from the University of Miami found increased feelings of loneliness in some 65% of respondents.

In terms of health risk, flying solo is right up there with obesity or a lack of exercise, increasing the likelihood of death from all causes. In fact, evidence suggests that social isolation and loneliness can be every bit as dangerous as smoking 15 cigarettes a day.

Last year, the National Academies of Sciences, Engineering and Medicine released a report recommending increased focus on research into the biological mechanisms of these health effects, as well as effective strategies to combat them. Both of these areas are still in their infancy.

“The health care systems,” the authors wrote, remain “an underused partner in preventing, identifying and intervening for social isolation and loneliness among adults over age 50.”

A number of groups are especially vulnerable: older adults; individuals with chronic illness, hearing or vision impairment, or mobility issues; individuals who live alone; immigrants, who may lack support networks and language skills; and sexual- and gender-minority individuals, who may face stigma, discrimination and barriers to care.

Countries around the world are beginning to take notice of the societal impacts of social isolation and loneliness. The U.K. and Japan have each appointed a minister of loneliness in recent years. (In Japan, death by loneliness has a name, *kodokushi*.)

Recently, Pitt Med sat down with two experts on the topic—Pitt's unofficial ministers of loneliness—to talk about this all-too-common phenomenon and how providers can intervene.

Thuy Bui is associate professor of medicine, director of the social medicine fellows program and also director of the Homewood Produce to People home-visit initiative at the School of Medicine. Her clinical focus is care for high-need, complex and disenfranchised individuals, including those who are homeless, recent immigrants, refugees and uninsured individuals.

David Nace is associate professor of medicine, director of long-term care and clinical chief of geriatric medicine. He is also chief medical officer of UPMC Senior Communities, which provides long-term care services to more than 3,000 older adults in central and western Pennsylvania.

How can providers help people facing social isolation and loneliness?

TB: There's still not a lot of awareness in the public about the danger of social isolation. We need to screen more often. And we need to do more to reduce the stigma around this issue.

In our practice here in Oakland, we ask patients things like, 'How many times do you talk on the phone with family, friends or neighbors? How often do you get together with them? How often do you attend church or religious services? Do you belong to any clubs or organizations?'

Most do not answer those questions! I think that is because we ask them to fill out a lot [of paperwork]. [Laughs.] But I think there's some hesitancy in answering that, as well. I have patients ask, "Why are you guys interested in knowing about these things?" Which is great, because then we can have a conversation.

DN: It's one of the things that I always look at as I'm seeing patients. What is their support network like? How do they spend their time?

I find that often, when you screen for depression, somebody will say, "No, I don't really feel bad." [But if you ask], "Do you feel lonely?" it's "Yeah, I do." I've been amazed at how often they're direct with me when it's part of looking at their mood.

TB: Many primary care physicians ask these questions about social support in annual wellness visits, but then we're not sure what to do with that.

What kinds of interventions do you find helpful?

TB: Volunteering 15 hours a week has been shown to improve cognitive function and delay the development of any kind of cognitive impairment in seniors. They're happier, more physically active. There's Experience Corps, a

program matching seniors with students from kindergarten to grade five. I just love that intergenerational connection. [For more on this tutoring program and other resources, see sidebar.]

DN: In our long-term care facilities we have had all kinds of programs where we connect residents with elementary school and high school students. It is really something that the residents look forward to. We have people that come in and play music for our residents. We have art classes. The goal is to enrich the environment. Studies have shown that [people in] environments that are more stimulating have better physical outcomes, have less cognitive decline, less progression to dementia.

For individuals who might still be at home, and have had a loss of a spouse, connecting them with a pet is actually quite helpful. We find that that's one of the protective factors against that sense of loneliness. There is also a lot of interest right now in artificial pets—robots as pets, essentially. In some preliminary studies that seems to have a positive effect, as well. It's kind of unusual, maybe, for many of us, but that will probably change. Being able to pick up a phone and talk to somebody without it being connected to the wall was unimaginable 50 years ago. Having a robot that you connect with and have conversations with in the future might be much more common than we think.

What tools and strategies have you begun using since the COVID-19 pandemic?

TB: We did a lot of porch visits, which was fun. Now we're back into the home again. I can see the happiness in my patient's faces with things slowly turning back to normal again.

DN: During the past year we had a lot of students sending postcards and letters. It was neat to see a younger generation learn about postcards! And also how well received that was by the older adults.

Remote platforms have been extremely helpful for most of the residents in long-term care. People could connect and FaceTime or Zoom with a family member. It was a good stand-in. We did have very positive responses with it.

It's a tool. It doesn't replace human contact. We found hearing impairment or visual

impairment or cognitive impairment all affected the ability of the person to really get the full value from the platform or device. We also know that it's not quite the same as having them in person with you where you can hug each other and read each other's expressions a little bit easier.

Even coming out of COVID, I think we learned that this is something that could be used moving forward in the future.

A lot of the museums started offering virtual tours, and that's been helpful in getting people thinking and engage outside of the walls of where they were.

TB: Many of our patients don't have access to broadband internet and the devices. From a tech equity digital divide, I think we could do better.

There are programs through Housing and Urban Development (HUD) called ConnectHome that bring internet services to senior high rises in the area.

The Jewish Healthcare Foundation launched programs called Senior Connections, and they also introduced the virtual Senior Academy, which is this free interactive platform that offers classes through video conferencing. That's a way to kind of bring people together.

In addition to the adverse health effects, how do social isolation and loneliness affect the health care system as a whole?

TB: We know that those who identify as being lonely or socially isolated tend to use more health care, and increased costs go with that. There's been some study out of the U.K., as well as in this country, looking at this issue. The question is why. And I think for many people, especially our elderly patients, contact with the health care system might be their main social contact in their daily activities. And with the higher rates of anxiety, depression and so on, that go with social isolation, they then look to health care providers as a form of social support, as well as trying to



Thuy Bui



David Nace

explain some of the symptoms they're having from day to day.

It's interesting that social isolation—even when it doesn't go along with a feeling of loneliness—is bad for our health. How do you approach someone who's not particularly concerned about loneliness but is really isolated?

TB: I've done home visits in Homewood and Wilksburg now for over 10 years. And I have recently focused on elderly individuals—men, specifically—who live alone and sometimes are estranged from families and friends for various reasons. They're usually quite attached to their home, even when the home conditions are not conducive to healthy living. Some do not trust outsiders and often don't want anyone to come. They don't pick up

the staff. He would give them advice, whether they wanted it or not. [Laughs.] He took art classes—I had never seen my father take art classes! He just really blossomed. Wonderful, meaningful relationships. And he even connected with old family friends [in the facility].

What's on your wish list from a broader, societal perspective?

TB: I think we need to reimagine community spaces, transportation and housing that promote connectedness. Design the built environment to decrease loneliness. And I'm not sure if architects and city planning groups take this into account.

DN: With the development of highways, the suburbs and the distancing that goes on, we're seeing these effects. But we're starting to see a little bit of planning around making sure

that our communities are adaptable throughout the lifespan to encourage physical activity as well as connectedness to other individuals.

It's a critically important thing to do. And the hotel industry realized this years ago. Now, they'll have a buffet, common areas where people can accidentally bump into one another.

TB: Our society is becoming less community-engaged all the time. But once in a while, when I do see involved neighbors, it just makes me so happy and hopeful. I had one patient in the hospital, and he did say that he didn't have electricity or running water in his home, and so I kind of pushed my way in, like, 'Let me come visit you.' And it turned out that he was very attached to his home, but during the winter he was sleeping in his car, with the car running. This had been going on for a while. So when I came to visit him, a neighbor across the street invited us in and said how concerned he was, and was there anything he could do to help? And it was just really nice to see. ■

"I think we really need to reimagine community spaces, transportation and housing that promote connectedness."

their phone that often, and they don't always have a smartphone or any other devices.

From my standpoint, it takes a little bit of pushiness and a lot of persistence to engage these individuals. I'm always so thrilled and grateful that some of them allow me and the medical students that I work with to be part of their lives.

DN: There are certain individuals that are going to be happy being socially isolated, because that's where they're comfortable, and they may not have the loneliness. But those are the exceptions rather than the rule. Most of us are used to being around other individuals much more commonly. So when you start to see that loss of the spouse or family members, that becomes very worrisome.

I think back to my own parents. My mother died in 2003 and my father lived through 2010. For him, staying in that home was so important, but he was not able to maintain it. His friends weren't coming around, because most had passed away. And that environment started to get smaller and smaller.

Then he was placed for the last six months of his life in a nursing facility because of some health issues. And that actually ended up being a fantastic experience for him. He got to know

GET WISE

To find out more about how to help older adults who are experiencing social isolation and loneliness, visit:

Area Agencies on Aging (AAA): A network of hundreds of organizations providing information and assistance with nutrition and meals, caregiver support and more. www.n4a.org

AARP: Helpful information to help improve older adults' quality of life, including access to its Community Connections resource. www.aarp.org

Eldercare Locator: Resources ranging from financial support to caregiving services to transportation. The site also includes a brochure on how volunteering can help keep individuals socially connected. www.eldercare.acl.gov

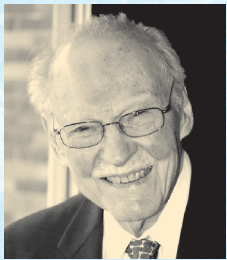
National Council on Aging: A partnership of nonprofits, government agencies and businesses providing community programs and services that support healthy aging, healthy eating habits, social connectedness and financial security. www.ncoa.org

Social Isolation and Loneliness Outreach Toolkit: A National Institute on Aging collection of educational and awareness-raising materials for older adults, caregivers and health care providers. The materials include a flyer, video and social-media animations and graphics. www.nia.nih.gov/ctctoolkit



CLASS NOTES

'50s **Lester Bolanovich** (MD '51), a psychiatrist, still sees patients twice a week at his Pittsburgh practice. Last year, he published the book "Reflections on Life, Marriage, and Anger," based on case studies and insights drawn from his 60-year career. "I was interested," he says, "in why people



Bolanovich

are attracted to others from a psychological standpoint." From this initial spark, Bolanovich studied how innate psychological traits can contribute to anger and interpersonal conflicts within romantic relationships. Postpublication, the book's research subjects have become some of its biggest fans: "I have gotten good feedback from my patients," he says.

'60s **Christine Williams** (MD '67) and **Gary Williams** (MD '67) met as Pitt Med students and were married the winter before graduation. After a storied career in pathology, Gary Miller is professor emeritus of pathology, microbiology and immunology at New York Medical College. Christine Miller, whose career in pediatric medicine and public health



Gary and Christine Williams

spanned 40 years, retired in 2007, and the pair now reside in Florida. "Gary and I are fortunate," Christine recalls, "that our careers complemented each other in so many ways. Many times, he would help me solve a medical mystery, or I would have a good idea for his work."

'70s

Pierce Scranton

(Orthopaedic Resident '77) has a namesake award with the American Orthopaedic Foot & Ankle Foundation. Their new Pierce E. Scranton Humanitarian Service Award recognizes those who have followed his example. Scranton, a former foundation president, established its outreach and education program. He and fellow surgeons have treated more than 1,500 landmine-harmed patients in Vietnam through one of the program's most successful projects. "That they've named this award for me, I'm very honored and humbled," says Scranton, whose career highlights include practicing at Swedish Medical Center in Seattle and serving as a physician for professional footballers, figure skaters and ballet dancers.



Scranton

'80s

Laura E. Riley (MD '85, Obstetrics/Gynecology Resident '89) chairs the Department of Obstetrics and Gynecology at Weill Cornell Medicine and is obstetrician and gynecologist-in-



Riley

chief at New York-Presbyterian/Weill Cornell Medical Center. By developing her expertise in infectious disease and high-risk pregnancy during HIV/AIDS and H1N1 outbreaks, Riley "gained a perspective," she says, "on the need for clinical research into the efficacy and safety of drugs and vaccines during pregnancy." She currently serves on a COVID-related task force with the American College of Obstetricians and Gynecologists and the CDC to write guidelines for treating COVID-19 in pregnancy and talking to patients about vaccines.

'00s **John Dubinion** (PhD '06),

who grew up next door to Pitt Med in Pittsburgh's Hill District, is a pharmacologist for the FDA's division of pharmacology/toxicology in infectious diseases. In that role, he says, "I analyze animal- and cell-based studies that support the safety of antiviral drugs." He also provides recommendations on which drugs should advance to clinical trials and ensures that a drug's product information insert, once on the market, describes all known risks. Dubinion was part of the review team for the approval of the first COVID-19 therapeutic drug, remdesivir, which works to stop replication of SARS-CoV-2.



Dubinion

'10s **Adebola Giwa**

(MD '13) says he wears "just a few hats." He's a clinician at the Kennedy Krieger Institute in Baltimore. He's a research investigator in pediatric endocrinology at Johns Hopkins, where he and his colleagues in the Hamad Laboratory discovered an immune cell that may trigger type 1 diabetes. (See their 2019 report in Cell.) And he is associate medical director for Ascendis, a company developing a drug for achondroplasia, a form of dwarfism. Giwa also wears community service hats. He received Hopkins's Martin Luther King Jr. Award for Community Service for fundraising for school supplies at a Baltimore school.



Giwa

Samantha Slight-Webb

(PhD '13) is an immunology consultant for



Slight-Webb

the Oklahoma Medical Research Foundation. She studies lupus as part of a team in the James and Guthridge laboratories, specifically investigating which immune features result in higher lupus rates in African Americans. One in every 250 African American women will develop lupus in their lifetime, says Slight-Webb, and “once they do develop the disease,” she notes, “it’s likely to be more severe.” Her lab is researching lupus’s preclinical autoimmune features; she hopes that work might one day allow providers to target lupus earlier and determine more personalized treatments.

—Rachel Mennies

SPOTLIGHT

DAVID LYTER ON MEETING LGBTQ+ NEEDS

David Lyter was a Pitt Med student in the early 1980s when he “barhopped” for research on a dangerous new virus that was spreading. Lyter (MD ’84, MPH ’88, Res ’91, Fel ’94) spent his nights and weekends traveling to gay bars throughout western Pennsylvania, eastern Ohio and West Virginia in search of gay men willing to have their blood drawn, frozen and later tested.

Lyter was recruiting participants for a pilot study for which he would later serve as medical director. That pilot grew into the current Pitt Men’s Study, the country’s longest-running HIV/AIDS research investigation with more than 1,700 participants. The study’s principal investigator, Charles Rinaldo, Pitt professor of pathology and of infectious diseases and microbiology, credits Lyter with playing an essential role in the landmark study’s success.

“Recruiting was a lot of fun for me,” Lyter remembers. “And in some of the small outlying towns, there was no one else [participants] could talk to or ask questions.”

Four decades later, the most urgent health care need facing LGBTQ+ people, Lyter says, remains finding “a physician knowledgeable and sensitive to their issues.” Lyter has provided this lifeline throughout his career. After Pitt Med, he worked as an



Lyter founded the Diversity Health Center of Tampa.

AIDS oncologist in Chicago, then moved to Tampa, where he opened the Diversity Health Center in 2018.

The center is a primary care practice for patients across the LGBTQ+ spectrum, as well as a broader catchment of Tampa residents. In addition to

addressing primary care concerns, Lyter offers specialized care, such as hormone therapy for trans patients.

“For a lot of [my] transgender clients,” he says, “I’m the first physician that they’ve come out to, [so I’ve] been able to discuss their history and their excitement to get started on their transition with hormones and eventual surgeries.”

Lyter continues to offer AIDS/HIV-related care. “I do a lot of PrEP work,” he notes. PrEP, which stands for pre-exposure prophylaxis, is a drug that people at risk for HIV can take to prevent contracting the disease. His time at Pitt Med “taught me how to diagnose and treat HIV from the early days of AZT until today,” he says. —Rachel Mennies

MAA SAYS, BE OUR GUEST

Shane Ellis (MD ’12) still appreciates the kindness of the medical students at the University of Pittsburgh who drove him to Alan Magee Scaife Hall for his entrance interview. Now, he’s volunteering to help Pitt’s fourth-year med students navigate the intense process of finding their residency.

In the new Help Our Students Travel (HOST) program, Pitt’s Medical Alumni Association (MAA) will match students, interviewing around the country for residency programs, with interested alumni based on location, institution and program. HOST volunteers are Pitt Med alumni (including former fellows and residents) who are willing to offer meaningful conversations about specialties, career paths and opportunities. Help can range from a phone call or video meeting for advice to an in-person dinner for mentorship to an overnight accommodation for students traveling on their search.

Ellis is available to help Pitt students interested in a residency in the Twin Cities. He works in internal medicine at St. Francis Regional Medical Center in Shakopee, Minnesota, a suburb of the Twin Cities.

“The residency interview process is simultaneously stressful and fun. The thrill of traveling to new cities, meeting interesting people and living out of a suitcase for a few weeks was certainly a unique experience,” he says. “Hopefully through the HOST program, I can be a resource for prospective Pitt applicants to learn more about where they may be living for the next several years.” —Bentley Boyd



Ellis

To volunteer for the program or to get more information, contact Michael Downs at medalum@medschool.pitt.edu or 412-648-9059.

CHARLES V. BENDER

NOV 20, 1949—MAY 24, 2021



Bender

Charles Bender made the NICU feel more like home. During his 25-year tenure as clinical director of the NICU at Magee-Womens Hospital, he spearheaded a ward design with private rooms.

“At the time, it was not necessarily felt to be the best approach to care and certainly presented new challenges to the staff, but he always put the babies and the families first in the decision-making,” says Jon Watchko, Pitt professor of pediatrics. Magee became the first NICU to provide private rooms for all their patients, with this standard being adopted across the country.

Born in Detroit, Bender earned his medical degree from Ohio State and served as assistant professor at the University of Cincinnati and Wright State in Dayton, Ohio, before coming to Pitt’s pediatrics department in 1990.

He’s remembered by colleagues not only as a compassionate neonatologist, but a good friend who donned his Santa suit for patients. “He was a very good listener. You could go to him and talk to him about different things, whether it was something at a personal level, something happening in your life, your family or something related to the NICU,” recalls Burhan Mahmood, medical director of the neonatal ECMO (extra-corporeal membrane oxygenation) program.

As a teacher, Bender was known to be patient with his students. “He’d ask you something, and if you didn’t know it, he’d just tell you to look it up, and he’d discuss it with you the next day. He would never make you feel bad about not knowing something,” says Jennifer Kloesz, Pitt pediatrics professor and current medical director of Magee’s NICU. She says Bender was responsible for many of his residents and interns solidifying their paths in neonatology. —*Hope Reveche*

GERALD S. LEVEY

JAN 9, 1937—JUNE 25, 2021



Levey

When Gerald Levey chaired Pitt’s Department of Medicine, he hosted annual

picnics for new interns and residents, taking his station behind the grill flipping burgers and rotating hot dogs until everyone ate. He took a keen interest in learning about these young doctors—like he did for faculty and staff.

“He had a way of making you feel alive,” says Linda Marts, who worked as an administrator with Levey for 10 years at Pitt. “He remembered

everyone’s name and even details about their families.”

Born in New Jersey, Levey earned his MD at Seton Hall and trained at Harvard, Massachusetts General and the National Institutes of Health. In 1979, he came to Pitt as chair of medicine along with his wife, Barbara Levey, who was appointed associate dean and director of admissions.

During a conversation with the late Thomas Detre, then senior vice chancellor for the health sciences, Gerald Levey expressed his aspiration to lead a major medical school. Detre advised him to hone his business management skills. In 1991, he took a job at Merck & Co. Three years later, UCLA recruited him.

Levey served as vice chancellor of medical sciences and dean of the David Geffen School of Medicine at UCLA from 1994 to 2010. His crowning achievements were the construction of the Ronald Reagan UCLA Medical Center and the sealing of a \$200 million gift to the school from film executive David Geffen. “It’s not possible to say in a short time what Jerry Levey means to UCLA,” says UCLA Chancellor Gene Block. “He left us with a state-of-the-art hospital, an endowed medical school, five new research buildings and 100 endowed chairs. Many generations will reap the benefit of his vision, leadership and dedication.”

Alan Robinson, former vice chair of Pitt’s Department of Medicine, worked with Levey for about 40 years, including at UCLA. “I have so many memories, but I can tell you that when I had to make a decision, I knew it would be the decision Jerry would make,” he says of Levey’s influence on him.

—*Michael Aubele*

NANCY H. TANNERY

JAN 26, 1955—MAY 14, 2021

Nancy Tannery, whose 40-year Pitt career took her from researcher to senior leadership in the Health Sciences Library System to assistant provost, died in May. “She was just a consummate professional and added value to everything she got involved with,” recalled David DeJong, Pitt senior vice chancellor for business and operations.

Following a two-decade career in medical technology and research, at both Pitt and local hospitals, Tannery earned a master of library science degree from Pitt in 1995. She then joined the Health Sciences Library

System (HSL) as a faculty librarian and rose through several management positions. As senior associate director, she helped shape the programs and future direction of HSL while supervising more than 20 librarians and staff members. She also was coinvestigator of the HealthCAS project, a year-long, online post-master’s degree Certificate of Advanced Study in Health Sciences Librarianship.

In addition, she held a secondary Pitt appointment as affiliated faculty in the Department of Biomedical Informatics in the School of Medicine. She served on the Provost’s Advisory Committee on Women’s Concerns and the School of Medicine’s Curriculum Committee.

Through the years, she authored or coauthored numerous peer-reviewed articles, abstracts and presentations on the development of clinical information tools for the electronic health record, clinicians’ use of knowledge-based information resources, the design of library-based information services in molecular biology and other topics. In 2011, she was awarded the Medical Library Association’s Estelle Brodman Award for the Academic Medical Librarian of the Year.

Tannery served on the National Institutes of Health’s Literature Selection and Technical Review Committee from 2012 to 2016 and chaired from 2015 to 2016.

“She was a caring, empathetic person,” DeJong says, “with a great sense of humor—just brightened any room she walked into and left a positive impression with absolutely everybody she interacted with.” —*Marty Levine*

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Tannery

IN MEMORIAM

'40s

JOHN R. ORIE
MD '47
JUNE 25, 2021

'50s

RONALD F. KETTERING
MD '58
APRIL 7, 2021

THOMAS E. PIEMME
MD '58, RES '60, '64
APRIL 17, 2021

DAVID S.
RAUSCHENBERGER
MD '58
MAY 25, 2021

'60s

HARVEY M.
ROSENBAUM
MD '61
JUNE 1, 2021

GARRY S. BRODY
RES '64
APRIL 29, 2021

JAMES T. BROWN JR.
RES '63
APRIL 24, 2021

DAVID RYAN COOK
MD '66
JUNE 20, 2021

G. DAVID GARDNER
MD '67
MAY 28, 2021

CONCENTRATE, OXYGENATE MTONGA INVENTS SOLUTIONS

BY SHARON TREGASKIS

“Eighty percent of medical equipment in developing countries is donated,” says Timothy Mtonga (PhD ’20), “and only 10–30% of it is ever operationalized.” Shortages of skilled technicians and spare parts are only part of the story—many devices are already broken when they’re donated.



Mtonga

Growing up in Malawi, where his mother and sister are nurses, Mtonga had seen firsthand the piles of dusty, abandoned machines. As the pandemic made medical oxygen scarce, Mtonga took another look at those devices to engineer new ways to help people breathe. His OpenO2 project launched in August 2020 to resurrect oxygen concentrators across Malawi. The concentrators are portable electrical units that purify oxygen from the atmosphere and deliver it through a nasal cannula or face mask.

Compared to compressed oxygen cylinders,

says Mtonga, “Concentrators provide an infinite and more sustainable oxygen supply.” They also cost less. A cylinder might last eight hours before it has to be refilled by a technician at a cost of \$82; a concentrator can run indefinitely on just \$2/day in electricity.

Trained as a software engineer, Mtonga now develops affordable information technology interventions to improve health care delivery in low-resource settings. As a Pitt Med master’s student, Mtonga worked with Gerry Douglas (PhD ’09), Pitt assistant professor of biomedical informatics and of health policy and management, and Arielle Fisher (PhD ’17) to build RxMAGIC, a pharmaceutical inventory management system at Pittsburgh’s Birmingham Free Clinic.

For his dissertation, Mtonga returned home to develop and pilot a computer on wheels (COW) at Kamuzu Central Hospital in Lilongwe. Clinicians use the COW to update electronic health records, order lab tests and review results from a patient’s bedside. This is a first-world health care approach, says Douglas, who was Mtonga’s PhD advisor and directs Pitt’s Center for Health Informatics for the Underserved. “There’s no other hospital in Africa that has what he has implemented.”

Mtonga defended his dissertation by videoconference in April 2020. In May, he was hired to direct the Global Health Informatics Institute (GHII) in Lilongwe, founded in 2015 by Douglas and his spouse, Thuy Bui, Pitt associate professor of medicine and director of the Internal Medicine Track in Global Health and

Underserved Medicine. OpenO2 is a center within GHII.

Mtonga initially envisioned OpenO2 as tech support: Identify the makes and models of concentrators, aggregate the product manuals, write repair guides and post it all online for free (www.openo2.org). That approach extended a project Mtonga oversaw in 2019, when he mentored an engineering intern at GHII who was developing a generic control board, the most common (and expensive) source of failure among oxygen concentrators, which are also used to treat pneumonia, emphysema and COPD.

When a second COVID-19 wave was cresting in Malawi in February 2021, the OpenO2 team—five technicians and four interns with bachelor’s degrees in engineering—began site visits to hospitals around the country. They hit the road in a donated bus retrofitted as a mobile workshop. At each hospital, they analyze and certify every concentrator, repair what they can and scavenge parts. At this writing, they’ve visited 35 hospitals and repaired 310 concentrators. “Enough to support 1,800 adult patients or 9,000 pediatric patients with a continuous flow of oxygen for one week,” says Mtonga.

In Lilongwe, the team tests fixes for common problems they see in the field. They developed a hand-held analyzer for clinicians to spot-check unit performance. They also devised a way to pair concentrators to meet the high-flow needs of severe COVID-19 patients.

This spring, Mtonga fielded inquiries from people in Nigeria and Ghana hoping to replicate OpenO2. “We’re not just helping our people,” he says. “We’re sharing and helping to solve a global problem.” ■

COURTESY OF TIMOTHY MTONGA



Mtonga’s OpenO2 team revives concentrators to help patients breathe.

ROBERT R. COPE JR.
MD ’69
APRIL 15, 2021

’70s
PHILIP J. LE FEVRE
RES ’70
FEB 8, 2021

LEE W. GOULD
MD ’76
APRIL 17, 2021

STANLEY D. MACMURDO
MD ’76
JUNE 10, 2021

WILLIAM P. AULL
MD ’77
JULY 28, 2020

LARRY R. MASTRINE
MD ’79
JAN. 2, 2021

’80s
MICHAEL J. DALY
RES ’86
MAY 29, 2021

DEAN J. ROTONDO
RES ’86
APRIL 28, 2021

’90s
LEON L. HALEY JR.
MD ’90
JULY 24, 2021

’10s
TARA COOK
MD ’18
MAY 31, 2021

FACULTY
JOSEPH J. COTTRELL JR.
FEL ’14
OCT. 29, 2020



Fontenot with her cat, Potato.

Potato to the Rescue

For more than a year, Amber Fontenot's office was in her family's dining room. Light shone through the house's front windows and the sliding glass patio doors in the rear as Fontenot, Pitt Med's registrar, helped students schedule courses and meet academic requirements.

Often unsung heroes, office employees like Fontenot have been guiding Pitt Med through the pandemic. In the 2020/21 academic year, many worked from their home offices, scheduling video conferences for administrators and connecting students with faculty—some while also caring for children.

"I think working remotely was an interesting opportunity for the staff, but I don't think everyone welcomed making their home visible in the same way," says Ann Thompson, vice dean of Pitt Med.

Fontenot, who won the Best Staff Member award from the Class of 2021 at Scope and Scalpel last spring, didn't shy away from letting people see into her home life. She found it helpful. When talking to third- and fourth-year medical students who felt anxious after a rotation was cancelled or rescheduled, she related to them on a personal level. Sometimes, she had no choice. Her 6-year-old daughter made regular appearances in video conference calls.

"Life was going on around us. So I made that part of my work life," Fontenot says.

During moments when she didn't have answers for students, she turned

to her cat, Potato, for help. "I'd say, 'Sorry I don't know right now but tell me where you want to go for residency; and here's a picture of Potato.'"

Emily Mosher, a fourth-year student who faced scheduling issues last year, says that receiving pictures of Potato always brightened her day.

"It was funny to see him pose, looking like a human," Mosher says. "That personal touch after a bad day was really great."

From 2000 to 2007, Fontenot worked in Pitt Med's admissions and financial aid office. She left the medical school to start a family, and then in 2016, after giving birth to three children, she returned to Pitt Med to work in student affairs. She eventually was promoted to registrar; that job started at the beginning of this year.

With more than a decade of experience at Pitt Med, Fontenot knew that being registrar during the pandemic would be a seven-day-a-week job. She allowed students to call her in the evenings and on the weekends:

"I'd send out an email that said I'd be 'working between these hours on Saturday if you want to reach me, but after that I have to feed my kids.'"

Fontenot says she bonded with several students during the pandemic. "Normally, I would not have made these wonderful relationships," she says.

—Gavin Jenkins

—Photo by Aimee Obidzinski

CALENDAR

FOR ALUMNI & FRIENDS

Unless otherwise noted, for information: Michael Downs at 412-648-9059 or mld139@pitt.edu

MEDICAL ALUMNI WEEKEND SEPTEMBER 17–18

Reunion Classes:

1970, 1971, 1995, 1996 (In-person);
1960, 1961, 1965, 1966, 1975, 1976,
1980, 1981, 1985, 1986, 1990, 1991,
2000, 2001, 2005, 2006, 2010,
2011 (Virtual)

PITT HOMECOMING SEPTEMBER 22–26

<https://homecoming.pitt.edu>

HOST A STUDENT! FALL–WINTER

Help Our Students Travel (HOST) is MAA's new program to support fourth-year Pitt Med students through interviews for residency. We'll match students with interested alumni based on location, institution and program. The program will help determine the safest ways to connect during the pandemic. To register: <http://pi.tt/HOST>

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

GROWL

Belly bellows.

FOR REAL! TWEEN SCIENCE



Grrrrrowl. You've just gotten home from school and need to find something to stop the gut grumbles. After scouring the fridge for an afternoon snack, you munch on a slice of pizza and finish it off with a glass of water. *Grrrrrowl.* You wonder, "Why is my stomach still making noises?"

The sound of your belly grumbling, also known as borborygmi (bor-ber-ig-me), comes from gas or food moving through your gastrointestinal (G.I.) tract; that route starts with your mouth and typically ends with a trip to the bathroom. Not to worry, though! This process is normal and is usually not painful. And we all experience it.

Imagine you're squeezing toothpaste to the top of the tube. The process in which your body moves food through your G.I. tract is similar. This squeezing is known as peristalsis; your organs are involuntarily contracting and relaxing, slowly moving contents further and further through your system. And the grumbling is just the result of this movement.

Think of your stomach as a tank for a second. If your tank is empty, any sounds that occur in the chamber may be louder or echoed. Also, cruciferous vegetables like broccoli and cauliflower tend to cause more gas buildup because of all of the nutrients found in them. Those veggies can really get the rumbles rolling.

Conditions such as lactose intolerance and Celiac disease make it harder to process certain foods, and that makes the grumbling all the more aggressive.

So how do you get rid of borborygmi? Well, if you're feeling hungry, just eat! And if you think you need to pass gas, find a bathroom—and quick! —*Hope Reveche*

Thanks to the Department of Medicine's Naudia Jonassaint—medical director, hepatology, and vice chair for diversity and inclusion—for helping us get to the bottom of this.



Art and Greta Rooney donated to concussion research to help athletes at all levels. Shown here: quarterback Ben Roethlisberger, dropping back to pass.

Inspired Performance

With a generous donation from **Art and Greta Rooney** and the Pittsburgh Steelers, University of Pittsburgh physicians and scientists will expand clinical trials of treatments for concussion. Under Director Michael (“Micky”) Collins, professor of orthopaedic surgery, the UPMC Sports Medicine Concussion Program has identified phenotypes of concussion, and the donation will help support research on therapies for these distinct clinical profiles.

Collins says that support from the Rooney family has directly led to

groundbreaking advances in diagnosis, treatment and rehabilitation.

“We are learning more and more about risk factors that make people more susceptible to the effects of concussion, like migraine history and motion sensitivity,” Collins says.

Collins’ research team at the UPMC Sports Medicine Concussion Program includes full-time staff, as well as numerous Pitt graduate and med students. Thanks to this gift, Collins says they will also be able to hire the first Ambassador Dan Rooney Research Fellow. Named for the late Ambassador Rooney, the fellow will help direct research efforts for the UPMC Concussion Network in Ireland, where there are seven clinics throughout the country.

The UPMC Concussion Program is the largest clinical and research concussion program in the world. Elite athletes from around the country travel to Pittsburgh for care.

“The support we have received over the past two decades from the Rooney family and Steelers,” says Collins, “has allowed our program to thrive.”

“Greta and I, as well as everyone connected with the Steelers, recognize the value of having some of the world’s most prominent, well-respected and knowledgeable concussion experts in our city,” Art Rooney says. “The medical research that is being conducted by the team of medical professionals at UPMC is very important to our community, not just for those who actively participate in sports, but everyone in our Western Pennsylvania region who might suffer an unfortunate head injury.”



Steelers owner Art Rooney II

To make a gift, contact Jen Gabler: 412-802-8317, jag188@pitt.edu, Giveto.pitt.edu