

A close-up portrait of Jonathan Avery, MD, a man with a shaved head and a light beard, wearing a light blue dress shirt and a red patterned tie. He is looking directly at the camera with a neutral expression. The background is a solid, deep red color.

weillcornellmedicine

SPRING 2019

CHANGE FROM WITHIN

Jonathan Avery, MD,
is taking on healthcare's
bias against patients with
substance use disorders

W

S

A

Celebrating 10 years of Alumni-to-Student Knowledge

Alumni-to-Student Knowledge (ASK) sessions were launched in 2009 to connect medical students with alumni. ASK events feature alumni from particular specialties, who share their insights on educational, career and life matters in a Q&A format.

Since ASK's inception, WCM has linked nearly 700 medical students with 109 alumni speakers at 36 sessions, all offering mentorship and guidance to these future physicians.

On Monday, February 25, more than 165 students attended the ASK 10th Anniversary Celebration to network with 55 alumni, explore various specialties, and get educational and career advice.

Represented Specialties:

- Anesthesiology
- Cardiology
- Dermatology
- Emergency Medicine
- Hematology & Oncology
- Internal Medicine
- Neurology
- Non-Traditional Medical Careers
- Obstetrics & Gynecology
- Ophthalmology
- Orthopedics
- Pediatrics
- Psychiatry
- Surgery

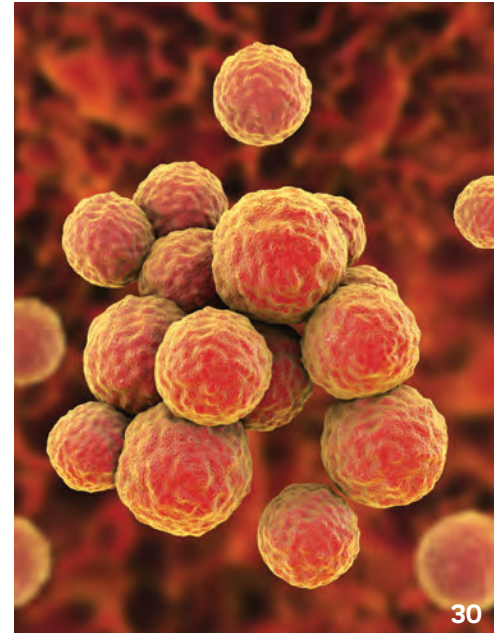


Dr. Natasha Leibel (MD '98), Weill Cornell Medical College Alumni Association President, right, with Dr. Paul Miskovitz (MD '75), longtime moderator of the ASK program and the evening's honoree

>> If you want to learn more about the ASK program or mentoring medical students, please contact the Office of Alumni Relations at alumni@med.cornell.edu or (646) 962-9560.



THE MAGAZINE OF
WEILL CORNELL MEDICINE
SPRING 2019



LETTERS TO THE EDITOR

Weill Cornell Medicine welcomes comments and correspondence from readers. Letters may be edited for length, clarity, and civility. We may not be able to publish all correspondence received, but we would like to hear from you. Please write to: wcm@med.cornell.edu.

Twitter: @WeillCornell
Facebook.com/
WeillCornellMedicine
Instagram.com/weillcornell
YouTube.com/WCMnews

For address changes and other subscription inquiries, please e-mail us at wcm@med.cornell.edu

COVER PHOTO BY JOHN ABBOTT

FEATURES

22 HEARTS & MINDS

HEATHER SALERNO

WCM's director of addiction psychiatry, Jonathan Avery, MD, is working to solve a pervasive problem that is slowly gaining attention: many clinicians—even psychiatrists and addiction specialists—hold negative attitudes toward patients with substance use disorders. That can not only increase patients' feelings of shame, but discourage them from seeking treatment and even limit the quality of care they do receive. "It turns out that doctors aren't different from anyone else," says Avery, an associate professor of clinical psychiatry at WCM and an attending psychiatrist at NewYork-Presbyterian/Weill Cornell. "Even after they learn the neurobiology of addiction and how it's a brain disease, doctors can still view it—much like the general population—as a moral failing, or people making bad choices that deserve more punishment than treatment."

30 FORMIDABLE FOES

BETH SAULNIER

For decades, antibiotics have been overprescribed and overused—from their widespread application in agriculture to the classic conundrum of a pediatrician faced with parents clamoring for a prescription for their sick toddler. That has spurred the rise of antibiotic-resistant bacteria, a threat with the potential to derail decades of medical advances. It's a pressing concern: according to the CDC, resistant infections cause 23,000 deaths and 2 million illnesses each year in the U.S. alone. Carl Nathan, MD, the R.A. Rees Pritchett Professor of Microbiology and Immunology and chairman of the department, has long been at the forefront of the movement to raise awareness about the issue and to promote policies that spur the development of new drugs. As he and colleagues warned in the *New England Journal of Medicine*: "A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the twenty-first century."

Published by the Office of External Affairs

WCM SENIOR ADMINISTRATORS

Augustine M.K. Choi, MD
Stephen and Suzanne Weiss Dean,
Weill Cornell Medicine;
Provost for Medical Affairs,
Cornell University

Mark Veich
Vice Provost for External Affairs

**ASSISTANT VICE PROVOST FOR
COMMUNICATIONS AND MARKETING**
Mason Essif

**WCM DIRECTOR OF
CREATIVE AND EDITORIAL SERVICES**
John Rodgers

WCM MANAGING EDITOR
Jordan Lite

*Weill Cornell Medicine is produced by
the staff of Cornell Alumni Magazine.*

PUBLISHER
Jenny Barnett

EDITOR
Beth Saulnier

CONTRIBUTING EDITORS
Alexandra Bond
Chris Furst
Adele Robinette

EDITORIAL ASSISTANT
Laura Britton

ART DIRECTOR
Jennifer Kloiber Infante

ASSISTANT ART DIRECTOR
Lisa Banlaki Frank

ACCOUNTING MANAGER
Barbara Bennett

EDITORIAL AND BUSINESS OFFICES
401 E. State St., Suite 301
Ithaca, NY 14850
(607) 272-8530; FAX (607) 272-8532



**Weill
Cornell
Medicine**

Printed by The Lane Press, Burlington, VT.
Copyright © 2019. Rights for republication
of all matter are reserved. Printed in U.S.A.



10



12



8

3 DEAN'S MESSAGE

Comments from Dean Augustine M.K. Choi, MD

4 HONORING OUR SCHOLARSHIP SUPPORTERS

6 SCOPE

Manuel Hidalgo, MD, PhD, to lead hematology-oncology. *Plus:* Carl Nathan, MD, receives Weill Award; Starr Foundation stem cell support reaches \$150 million; a record Match Day; Chelsea Clinton, PhD, speaks on campus; students visit Capitol Hill; future physician assistants don their white coats; diversity efforts honored; research funding shows dynamic growth; and an immunologist wins the Drukier Prize.

10 LIGHT BOX

At the NewYork-Presbyterian David H. Koch Center, pediatric surgery patients get a morale boost by cruising to the operating room in miniature cars.

12 TALK OF THE GOWN

Training med students how to break bad news to patients. *Plus:* Natalia De Marco García, PhD, studies whether disruptions in brain cell development give rise to autism; Juan Cubillos-Ruiz, PhD, aims to harness the immune system to fight ovarian cancer; and in the hope of preventing osteoporosis, pathologist Matthew Greenblatt, MD, PhD, is exploring the fundamentals of bone strength.

38 NOTEBOOK

News of alumni

47 IN MEMORIAM

Alumni remembered

48 POST DOC

Physician-magician Ricardo Rosenkranz, MD '90, uses magic as a teaching tool for med students at Northwestern.

Weill Cornell Medicine (ISSN 1551-4455) is produced four times a year by Cornell Alumni Magazine, 401 E. State St., Suite 301, Ithaca, NY 14850-4400 for Weill Cornell Medicine. Marketing Mail postage paid at New York, NY, and additional mailing offices. POSTMASTER: Send address changes to Office of External Affairs, 1300 York Ave., Box 123, New York, NY 10065.

Augustine M.K. Choi, MD
Dean of Weill Cornell Medicine

The Callings of Academic Medicine



Every year, thousands of patients seek treatment at Weill Cornell Medicine's more than forty clinical sites throughout New York City. We are dedicated to providing top-notch care for everyone who comes through our doors—but as an academic medical center, we also do much more.

Since our founding in 1898, Weill Cornell Medicine has had a three-part mission: to care, discover, and teach. This is what makes academic medical centers like ours so unique. We are a place where medical breakthroughs happen, where cutting-edge therapies are pursued, and where the next generation of physicians and scientists is trained to tackle the most complex problems in healthcare—all under a single umbrella. With

We are a place where medical breakthroughs happen, where cutting-edge therapies are pursued, and where the next generation of physicians and scientists is trained to tackle the most complex problems in healthcare—all under a single umbrella.

our powerful network of partners and collaborators, and our primary affiliate NewYork-Presbyterian, WCM is one of the largest and most comprehensive academic medical centers in the U.S., as well as a leader amongst our peers.

And according to the Association of American Medical Colleges, facilities like ours are critical to healthcare: although they represent only 5 percent of America's hospitals, they provide nearly 25 percent of all hospital care in the U.S. and deliver nearly 40 percent of the nation's charity care—achieving clinical excellence while meeting the needs of the country's most vulnerable patients.

Research, in particular, differentiates centers like ours from our counterparts outside the world of academic medicine.

WCM has made groundbreaking advances throughout its history, including the Nobel Prize-winning discovery of oxytocin by Vincent du Vigneaud, PhD, and the first documentation of HIV/AIDS in Haiti in the early Eighties by Jean William "Bill" Pape, MD '75, the Howard and Carol Holtzmann Professor in Clinical Medicine. Today, innovation continues to thrive here as our faculty members pursue solutions to formidable health challenges, from the rising danger of antibiotic-resistant infections to osteoporosis, brain diseases, and conditions that strike in childhood.

While our objective is for our research to lead to new therapies that can benefit as many patients as possible, we are also pushing hard to find specific treatments for each individual. This kind of precision approach is becoming an increasingly vital part of medical care—and it's at the very core of what we do. We're also committed to caring for populations that might otherwise be overlooked; our cover story focuses on the trailblazing work that psychiatrist and addiction specialist Jonathan Avery, MD, is doing to combat bias within the medical community against patients who are struggling with substance use disorders. Our faculty are forerunners in the classroom, instructing future doctors on how to treat patients with not only skill, but compassion and concern; another story in this issue illustrates how our medical students are taught the optimal ways to break bad news, which can affect not just a patient's wellbeing but also a physician's.

It is only at an academic medical center that education, research, and healthcare delivery combine in such complex, powerful synergy—and achieve more than the sum of their distinct parts. At Weill Cornell Medicine, we bring a unique combination of intellect and passion, embodied in our physician-scientists, that inspires the breakthroughs and the empathy that are shaping the future of healthcare.

Honoring Our Scholarship Supporters

For many medical students, scholarships are key to making their education possible, and Weill Cornell Medicine is grateful for our donors' gifts of scholarship, which ensure that these students can confidently pursue their aspirations.

Endowed Scholarship Campaigns

2001-2005

Advancing the Clinical Mission

Raised: \$13M for scholarship

2006-2013

Discoveries that Make a Difference

Raised: \$31M for scholarship

2014-2016

Campaign for Education

Raised: \$33M for scholarship



In 2018, graduates from private medical schools in the United States carried an average of \$186,000 in student-related debt. At Weill Cornell Medicine, by comparison, students carried a lower-than-average debt of approximately \$165,000. That savings can be attributed to donors' remarkable philanthropic scholarship support, including gifts from our alumni, for whom this is a dedicated cause.

Scholarship donors were honored in April at the 10th anniversary of Salute to Scholarship, an annual event that celebrates

scholarship donors and the exceptional Weill Cornell Medicine students who benefit from their philanthropy. The event offered the chance for students to meet the donors who helped them achieve their goals, and for donors to realize the impact of their gifts.

To support Weill Cornell Medicine, please contact:

Lucille Ferraro, Assistant Vice Provost for Development, at (646) 962-9491 or luf2003@med.cornell.edu.

In academic year 2017-2018:

\$6,427,414

Total amount awarded in scholarships

 **Weill Cornell Medicine**

Source: Office of Financial Aid Information for academic year 2017-2018



THANK YOU!

66%

of medical students received
financial aid

166

medical students received
scholarships

Manuel Hidalgo, MD, PhD, to Lead Hematology-Oncology



Manuel Hidalgo, MD, PhD

A physician-scientist who specializes in pancreatic cancer and drug development has been named chief of the Division of Hematology and Medical Oncology in the Weill Department of Medicine at Weill Cornell Medicine and NewYork-Presbyterian/Weill Cornell. **Manuel Hidalgo, MD, PhD**, who joins the faculty on June 1, will also serve on the leadership team at the Sandra and Edward Meyer Cancer Center at WCM. Recruited as the E. Hugh Luckey Distinguished Professor of Medicine,

Hidalgo aims to expand Weill Cornell Medicine's and NewYork-Presbyterian's cancer programs by recruiting outstanding new oncologists and hematologists; to enhance research and clinical collaborations; and to broaden access to cancer care and clinical trials for underserved populations. "He is a gifted clinician and a skilled leader and educator," says **Anthony Hollenberg,**

MD, the Weill Chairman of the Weill Department of Medicine at WCM and physician-in-chief at NewYork-Presbyterian/Weill Cornell, "and his innovative research in pancreatic cancer and drug development is unparalleled."

Hidalgo comes to WCM from Boston's Beth Israel Deaconess Medical Center, where he served as chief of the Division of Hematology and clinical director of the Rosenberg Clinical Cancer Center. He was also the Theodore W. and Evelyn G. Berenson Professor of Medicine at Harvard Medical School and deputy associate director for clinical sciences at Dana-Farber/Harvard Cancer Center. "The unified mission of Weill Cornell Medicine and NewYork-Presbyterian to offer the best, most cutting-edge cancer treatments, and the shared goal of curing this disease is very exciting to me," Hidalgo says. "There is a real opportunity for us to come together and build a team that will take our institutions to the next level in cancer care and innovation. We are looking for excellence—in training, research, and care—as we aim to have a lasting impact, offering hope to cancer patients across the city."



WELL-DESERVED HONOR (from left): Carl Nathan, MD, accepts the Weill Exemplary Achievement Award from Sanford and Joan Weill and Dean Augustine M.K. Choi, MD.

Nathan Honored with Weill Award

Carl Nathan, MD, who has chaired the Department of Microbiology and Immunology for two decades, has won WCM's Joan and Sanford I. Weill Exemplary Achievement Award. The R.A. Rees Pritchett Professor of Microbiology and Immunology and director of the Abby and Howard P. Milstein Program in Chemical Biology and Translational Medicine, Nathan is a leading authority on tuberculosis and an outspoken proponent of the need to develop new antibiotics. (For more on his efforts to raise awareness about the dangers of antibiotic resistance, see story on page 30.) His research findings have improved understanding of how the immune system works in infectious disease, cancer, and metabolism. WCM's senior associate dean for research from 1995 to 1997, Nathan most recently served as dean of the Weill Cornell Graduate School of Medical Sciences. Says **Augustine M.K. Choi, MD**, the Stephen and Suzanne Weiss Dean of WCM: "Carl has been one of Weill Cornell Medicine's most accomplished scientists for more than thirty years—a highly regarded leader who exemplifies our mission to care, discover, and teach." The award carries a \$50,000 cash prize, which Nathan gifted to WCM.

Starr Foundation Stem Cell Support at \$150 million

The Starr Foundation has continued its longstanding commitment to stem cell research with a \$50 million gift in support of the Tri-Institutional Stem Cell Initiative (Tri-SCI). A research collaboration between WCM, Memorial Sloan Kettering Cancer Center, and The Rockefeller University, Tri-SCI was established in 2005 through a \$50 million gift from the foundation, which renewed its support in 2012 with another \$50 million gift; the new gift brings its total support to \$150 million.

Tri-SCI laboratories investigate the properties of three kinds of stem cells: embryonic, which have the potential to differentiate into any cell type in the body; adult, which are found in various tissues and can give rise to specific cell types; and induced pluripotent, adult cells reprogrammed to an embryonic stem-cell-like state. The studies are opening new avenues for understanding a range of health conditions—including developmental disorders, neurodegenerative diseases, and cancer—and laying the groundwork for the design of regenerative therapies to replenish tissues lost to illness or injury. The Starr Foundation's previous gifts to the Tri-SCI have funded the research of eighty-six investigators at the three institutions who are tackling some of the world's most daunting health challenges—including Parkinson's disease, Lou Gehrig's disease, seizure disorders, peripheral nerve damage, diabetes, and stroke.

PHOTOS: HIDALGO, DANIELLE DUFFEY; WEILL AWARD, STUDIO BROOKE

A Record Match Day

On March 15, eighty-eight members of the Class of 2019 learned where they'll spend the next phase of their careers. The Match Day celebration featured champagne toasts and the opening of envelopes announcing internship and residency placements. This year's match was the largest on record, with graduating students competing for some 35,000 positions. Twenty-six students from WCM's Class of 2019 matched to NewYork-Presbyterian, and 100 percent of students seeking residencies in specialties such as dermatology, neurosurgery, ophthalmology, orthopaedic surgery, plastic surgery, general surgery, and urology earned positions. Half of the students will pursue primary care residencies in internal medicine, pediatrics, family medicine, and obstetrics and gynecology.



MOVING ON: Members of the Class of 2019 celebrate Match Day. For more photos of the festivities, see Notebook starting on page 38.

Chelsea Clinton, PhD, Speaks at WCM



HEALTH ADVOCATE:
Chelsea Clinton, PhD

Public health advocate, researcher, and educator **Chelsea Clinton, PhD**, spoke on campus in February as part of the Luminaries in Healthcare Leadership series, which brings experts to WCM to share their perspectives on cutting-edge issues related to healthcare. A member of WCM's Board of Overseers, Clinton—who holds a master's degree in public health and a doctorate in international relations—talked to students and faculty about her passion for children's health, among other topics. In a conversation with **Rainu Kaushal, MD**, chair of the Department of Healthcare Policy and Research, the Nanette Laitman Distinguished Professor of Healthcare Policy and Research, and an attending physician at NewYork-Presbyterian/Weill Cornell, she discussed the genesis of the Clinton Foundation—the nonprofit founded by her father, former U.S. President **Bill Clinton**, where she serves as vice chair—and its work in public health and advocacy, as well as the value of mentorship and the importance of work-life balance.



VITAL SUPPORT: Students from WCM and the Ithaca campus traveled to Capitol Hill in March to meet with members of Congress on Student Financial Aid Advocacy Day.

TIP OF THE CAP...

Wendy Béguelin, PhD, assistant professor of pharmacology in medicine, named a "NextGen Star" by the American Association for Cancer Research.

Maria Bustillo, MD, associate professor of clinical anesthesiology and of anesthesiology in clinical neurological surgery at WCM and an attending anesthesiologist at NewYork-Presbyterian/Weill Cornell, elected to the Association of University Anesthesiologists.

Joseph Fins, MD '86, the E. William Davis Jr., MD, Professor of Medical Ethics and chief of the division at WCM and an attending physician at NewYork-Presbyterian/Weill Cornell, winner of

the Nicholas E. Davies Memorial Scholar Award from the American College of Physicians.

Costantino Iadecola, MD, director of the Feil Family Brain and Mind Research Institute, the Anne Parrish Titzell Professor of Neurology, and a professor of neuroscience, named to the board of directors of the *American Journal of Hypertension*.

Sandip Kapur, MD '90, the Jeanette and Jeffrey Lasdon Director of Kidney and Pancreas Transplant Programs and professor of surgery (transplantation) at WCM and an attending surgeon at NewYork-Presbyterian/Weill Cornell, elected a fellow of the American Surgical Association.

Dolores Lamb, MD, PhD, recruited as a professor of molecular biology in urology, winner of the Outstanding Mentor Award from the Endocrine Society and the Christina Manthos Mentoring Award from the Society of Women in Urology.

Lisa Roth, MD, assistant professor of pediatrics and of pathology and laboratory medicine and the Charles, Lillian, and Betty Neuwirth Clinical Scholar in Pediatric Hematology/Oncology at WCM and an assistant attending pediatrician at NewYork-Presbyterian/Weill Cornell, winner of a Hartwell Individual Biomedical Research Award, which will support her research on childhood Hodgkin lymphoma.



IN UNIFORM: At the traditional ceremony in March, forty-two future physician assistants in the Class of 2021 donned their short white coats for the first time. The students are earning master's degrees in health sciences in the Weill Cornell Graduate School of Medical Sciences.

Faculty, Students Honored for Diversity Efforts

WCM held its second annual Diversity Week in April, with more than forty activities—from grand rounds to workshops to panel discussions—aimed at highlighting scholarship and projects designed to increase diversity and reduce disparities in healthcare. Among the week's highlights was an awards ceremony honoring seventeen faculty, trainees, students, and staff for outstanding service in promoting diversity at the institution. The honorees included:

Medical student **Joshua Adjei, MD '19**: the Ida Sophia Scudder, MD, Award for Excellence in Public Service.

Kevin Holcomb, MD, associate professor of clinical obstetrics and gynecology and an associate attending obstetrician and gynecologist at NewYork-Presbyterian/Weill Cornell, and **Nelson Sanchez, MD**, associate professor of clinical medicine: the Bruce Laine Ballard, MD, Award for Excellence in Mentorship.

Geraldine McGinty, MD, chief strategy officer of WCM's Physician Organization, an assistant professor of clinical radiology and of clinical healthcare policy and research, and an assistant attending radiologist at NewYork-Presbyterian/Weill Cornell: the Jessica M. and Natan Bibliowicz Award for Excellence in Mentoring Women Faculty.

Victor Wong, PhD, a postdoc at Burke Neurological Institute: the Louis Wade Sullivan, MD, Award for Excellence in Public Health Advocacy.

Research Funding Shows Dynamic Growth

In *U.S. News and World Report's* latest ranking of the nation's best medical schools for research, Weill Cornell Medicine rose to ninth—a distinction that reflects the dynamic growth the institution has seen in its research enterprise over the past five years. Since 2014, WCM's research support from the NIH has risen more than 40 percent. That increase coincides with the creation of the Belfer Research Building, which serves as a hub for translational research and has led to the recruitment of more than forty additional biomedical researchers. The state-of-the-art research facility houses numerous interdisciplinary centers and institutes that have been established in the past decade—including the Sandra and Edward Meyer Cancer Center, Caryl and Israel Englander Institute for Precision Medicine, Gale and Ira Drukier Institute for Children's Health, Helen and Robert Appel Institute for Alzheimer's Disease Research, Jill Roberts Institute for Research in Inflammatory Bowel Disease, and Feil Family Brain and Mind Research Institute—whose fundamental and translational research receives consistent grant support.



CARING FOR KIDS: Award winner Helen Su, MD, PhD (center), with Gale Drukier, EdD (left), and Ira Drukier, PhD, a WCM Overseer

Immunologist Wins Drukier Prize

A clinical immunologist who has made key discoveries about the genetic causes of rare immune system diseases in children has won the fourth annual Gale and Ira Drukier Prize in Children's Health Research. **Helen Su, MD, PhD**, is chief of the Human Immunological Diseases Section at the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH. Her research brings together clinical information with technological developments in genomics, biochemistry, and molecular biology—such as sequencing all the protein-coding regions of the human genome—to identify gene mutations associated with diseases that affect the immune system. The findings may lead to improved diagnoses and treatments.

Established in December 2014 as part of a \$25 million gift to WCM that also created the Gale and Ira Drukier Institute for Children's Health, the Drukier Prize honors an early-career pediatrician whose research has made important contributions toward improving the health of children and adolescents. "Dr. Su's research illustrates the value of understanding the basis of rare hereditary immune disorders," says pediatrician **Virginia Pascual, MD**, the Drukier Director of the Drukier Institute and the Ronay Menschel Professor of Pediatrics. "Not only has her work helped to guide treatment for children with these diseases, but she has also advanced the field of immunology through her fundamental insights into how the human body protects itself from infection. Her research has the potential to help children worldwide."

PHOTOS: WHITE COAT, JONES; DRUKIER, STEPHANIE DIANI

FROM THE BENCH

High-Fructose Corn Syrup Fuels Colon Tumors



MARCUS GONCALVES, MD, PHD

Observational studies have previously linked rising obesity rates with an increasing incidence of colon cancer. Now, a study in mice has demonstrated that one key factor in the obesity epidemic—consumption of high-fructose corn syrup—fuels the growth of colon tumors. As reported in *Science*, a research team led by **Lewis Cantley, PhD**, the Meyer Director of the Sandra and Edward Meyer Cancer Center at WCM and NewYork-Presbyterian, fed mice genetically engineered to develop colon tumors the equivalent amount of corn syrup to a human drinking one soda per day. After nine weeks, the mice had developed larger tumors than a control group. “If you are predisposed to getting polyps,” says lead author **Marcus Gonçalves, MD, PhD**, an assistant professor of medicine and of biochemistry and a member of the Sandra and Edward Meyer Cancer Center, “you should not be drinking any sugar-sweetened beverages.”

AI Optimizes Embryo Selection for IVF

Artificial intelligence could improve the success rate of in vitro fertilization procedures. In *NPJ Digital Medicine*, WCM researchers report the results of a study in which they examined 12,000 photos of human embryos taken 110 hours after fertilization (but prior to implantation) and designated each as “good,” “fair,” or “poor” based on their physical appearance and the known pregnancy outcome. That data was then used to teach an AI algorithm how to classify new images, which it can now do with 97 percent accuracy—potentially helping fertility specialists make better informed decisions about which embryos to implant for a successful pregnancy. The study was a collaboration between the Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine and the Englander Institute for Precision Medicine.

Gene Affects Breast Cancer in Black Women



MELISSA DAVIS, PHD

A genetic mutation that originated in Sub-Saharan Africa as a protection against malaria may explain why black women have poorer breast cancer outcomes than patients of other races. As senior author **Melissa Davis, PhD**, and colleagues report in *Cancer Epidemiology, Biomarkers & Prevention*, higher expression levels of an immune-related gene in breast tumors corresponds to longer survival times after diagnosis due to the gene’s regulation of proteins related to cancer growth. But that gene also corresponds to higher risk of malaria infection—so people of African ancestry evolved lower expression levels as a protective measure. “I think we are finally on track to characterize a specific tumor phenotype and tumor microenvironment differences that are driving race group disparities in cancer mortality that transcend the traditional social determinants of disparities,” says Davis, who was recruited as an associate professor of cell and developmental biology research in surgery.

Pathway Regulates Intestinal Health

A study in *Nature* may point the way to new treatments for chronic gut inflammation associated with inflammatory bowel disease or food allergies. The research is the first to identify innate lymphoid cells—immune cells that create and regulate interleukin-2 (IL-2), a protein essential to preventing gut inflammation—as a potential target. Senior author **Gregory Sonnenberg, PhD**, associate professor of microbiology and immunology in medicine, and his team analyzed the gastrointestinal tracts of mice and samples of human intestine. “In the future,” says Sonnenberg, a member of the Jill Roberts Institute for Research in Inflammatory Bowel Disease, “it may be possible to develop cocktails of microbes to stimulate the production of IL-2 from innate lymphoid cells and restore tolerance in the gastrointestinal tract of patients with these chronic diseases.”

Checklist Aids Triage of Anthrax Patients

A team led by **Nathaniel Hupert, MD**, associate professor of healthcare policy and research and of medicine, has developed a checklist for identifying patients who have anthrax, a rare but deadly disease that can be difficult to diagnose. “Since access to standard lab and radiology tests may be greatly outstripped by the number of people seeking care, and rapid treatment is vital for people with anthrax, we sought to give medical personnel an evidence-based way to make quick decisions about who should be sent to the hospital,” says Hupert, an associate attending physician at NewYork-Presbyterian/Weill Cornell and senior adviser to the CDC’s Division of Preparedness and Emerging Infections. After studying 408 confirmed anthrax cases—as well as 657 suspected cases that were later determined to be other diseases—researchers identified key symptoms that can be measured in minutes, diagnosing anthrax with 95 percent accuracy. The findings were published in *Annals of Internal Medicine*.

Healthy Innate Immune System Mapped



LAUREL MONTICELLI, PHD

It’s long been known that dysfunction in the innate immune system breaks the first line of defense against pathogens, letting diseases flourish. Now, researchers are better equipped to help the body combat disease, thanks to the creation of the first anatomical “map” of a healthy innate immune system. As reported in *Immunity*, investigators characterized a specific type of immune cell in organs and other sites throughout the body. “Our goal is that this will be a universal resource tool for researchers investigating a wide range of inflammatory, infectious, or malignant diseases,” says **Laurel Monticelli, PhD**, instructor of immunology in medicine. “By allowing other scientists to compare their data against this baseline, we hope it will immediately provide greater insight to how a healthy innate immune system becomes dysfunctional.” Monticelli co-authored the paper with **David Artis, PhD**, the Michael Kors Professor of Immunology and director of the Jill Roberts Institute for Research in Inflammatory Bowel Disease.

Anemia Drug Promising Against Leukemia

A drug used to treat anemia could target cancer cells in acute myeloid leukemia (AML). In an article in *Nature Nanotechnology*, WCM researchers report that ferumoxytol—used to treat patients with low iron levels due to chronic kidney disease—successfully treated AML in mice. The drug, which consists of microscopic iron particles, essentially overloads cancer cells with iron. Healthy cells—which, unlike AML cells, are capable of exporting the extra iron—are unaffected. “Understanding the vulnerabilities of cancer cells, in this case their inability to export iron, results in an Achilles heel that can be targeted by delivering excess loads of iron,” says co-senior author **Monica Guzman, PhD**, an associate professor of pharmacology in medicine and a member of the Sandra and Edward Meyer Cancer Center.

Gene Deletion Promotes Prostate Cancer

A recent article in *Cancer Cell* describes how the deletion of a gene called CHD1 encourages the growth of prostate cancer. As senior author **Christopher Barbieri, MD, PhD**, and colleagues explain, in a healthy prostate, CHD1 regulates the positioning of balls of protein around which strands of DNA wrap; that determines how accessible the DNA is to molecules (called androgen receptors) involved in activating genes that keep prostate tissue functioning normally. But when CHD1 is absent—as is the case in about 15 percent of prostate tumors—androgen receptors instead trigger genes that promote cancer. “One of the big questions we have is whether the process is reversible,” says Barbieri, an associate professor of urology at WCM and an associate attending urologist at NewYork-Presbyterian/Weill Cornell. “Can we flip it back, so the androgen receptor may cause the cancer to slow down and stop growing?”

Hot Wheels

Undergoing surgery can be stressful for anyone, especially small children. A Weill Cornell Medicine pediatric otolaryngologist has been making the experience easier for patients, thanks to a pair of miniature cars that kids can play with as they await surgery—and can even drive to the operating room themselves. “It was a total game changer,” says Elena Silverman, whose four-year-old son, Jaime (both seen at right), came to the NewYork-Presbyterian David H. Koch Center in March for procedures to replace fluid-draining tubes in his ears and to reduce the size of his tonsils and adenoids. “Once he spotted those cars, it was like he was in a toy store rather than a hospital. It was a wonderful distraction.”

In addition to taking kids’ minds off of surgery, the program is designed to ease their anxiety and provide them with a sense of control of the hospital experience. The brainchild of Vikash Modi, MD, chief of pediatric otolaryngology, what started with one car donated by the family of a grateful patient proved so popular that Modi donated another. Now, for kids who are interested, NewYork-Presbyterian/Weill Cornell child-life specialists offer the choice between a red racer and a white Bentley, the latter of which can be remotely controlled by staff. That way, Modi says, children too young to operate it can still feel like they’re driving—and asserting themselves in a situation that can feel overwhelming. “Little things like this go a long way,” observes Modi, associate professor of otolaryngology in pediatrics and of otolaryngology–head and neck surgery at WCM and a pediatric otolaryngologist at NewYork-Presbyterian/Weill Cornell. “Parents just rave about it, and the kids love it. Afterward, they don’t remember the surgery. All they remember is getting in that car and driving around.”



PHOTO: JULIA XANTHOS LIDDY



CAREFUL CONVERSATION:

Medical student Matthew Harrell '20 (right) practices breaking bad news to a trained actor portraying a patient in the Margaret and Ian Smith Clinical Skills Center.



Tough Talks

Breaking bad news is one of the hardest parts of practicing medicine—and for the wellbeing of patients and even doctors, it's essential to do it right

Mohamud Verjee, MD, will never forget how he learned of his mother's death. In private practice at the time, he was in the midst of seeing a patient when the call came in to the front desk; after the patient left, Verjee's medical partner was tasked with giving him the awful news. "He knocked on the door and stood in the doorway—didn't even come in, just poked his face around—and said, 'There's no other way to tell you this: your mother's dead. You'd better go and see her,' and closed the door," recalls Verjee, an associate professor of family medicine and assistant dean for medical student affairs at Weill Cornell Medicine–Qatar. "It took seven seconds."

For the past decade, Verjee has been training medical students in the art and science of breaking bad news to patients and their families. And though the way he learned about his mother's passing wasn't a clinical encounter per se, he cites it to his students as a textbook example of breaking such news the wrong way. "It electrifies them," he says. "They all say, 'No—you can't do that!'"

It's an inevitable part of medical practice, a burden nearly every physician must bear: telling a patient and their loved ones the kind of news that no one wants to hear. It could be something relatively innocuous, like slightly abnormal results on a blood test that needs to be repeated. Or it could be devastating, such as a diagnosis of advanced cancer or the news that a family member has died of their injuries in a car accident. Practitioners have been having these difficult encounters for centuries—but in recent decades, the methods for doing so have become more codified, and today's medical students receive formal training on how to manage this element of their future practice. "I consider breaking bad news a high-level skill; it's a very complex discussion," says Yoon Kang, MD, acting senior associate dean for education, the Richard P. Cohen, MD, Associate Professor of Medical Education, and

director of the Margaret and Ian Smith Clinical Skills Center. "In many instances, it's a real challenge even for skilled and seasoned physicians to deliver bad news—not only to the patient, but often also to their family."

At Weill Cornell Medicine, students are introduced to the concept of breaking bad news as a distinct doctor-patient encounter early in their education. Their first year, in a session in the Health, Illness, and Disease course, students hear positive and negative examples and have the chance to role-play with each other. As part of the primary care clerkship, students participate in an assessment

'I consider breaking bad news a high-level skill,' says Yoon Kang, MD, acting senior associate dean for education. 'It's a very complex discussion.'

of real-world skills in which they interact with a trained actor—known as a standardized patient—that's centered around explaining worrisome test results. The topic of breaking bad news figures prominently in the Transition to Residency class, in which fourth-years are prepared for their lives as newly minted MDs. And in their clinical rotations, doctors-in-training not only have the opportunity to observe seasoned physicians break bad news, but participate in those conversations themselves. "I feel like the curriculum provides a professional extension to human empathy," says fourth-year MD-PhD student Kevin Boehm. "It emphasizes our shared humanity, that you really need to support the patient. These conversations always feel heavy, because you're giving someone news about the potential end of their life, or a major modification to it. There's a lot of sadness or even despair. Being able to practice how to stay steady and honest while also empathetic is so valuable."

And breaking bad news well isn't just a matter of supporting a patient emotionally; it can be a >

CONTINUING EDUCATION:

WCM-Q professors Mohamud Verjee, MD (below), and Liam Fernyhough, MD (opposite page), train practicing physicians in best practices for breaking bad news.

key part of a successful treatment plan. If the news is conveyed maladroitly, it can erode trust in the doctor-patient relationship—and if a patient leaves the encounter feeling hurt or even just confused, it can potentially discourage them from pursuing the appropriate care. “If you don’t break bad news in the right way, it can be difficult to get to that next clinical step,” Kang says. “The nuances are incredibly important, because the goal is to have the patient—in the best sense of the word—hear the news and to have a productive discussion.”

As medical ethicist Barrie Huberman, PhD, notes, when a patient receives a difficult diagnosis, it’s both an emotionally fraught moment and an intellectually demanding one. “There’s a lot for people to learn when they hear bad news for the first time,” says

Huberman, a new faculty member in the Division of Medical Ethics who addresses the topic in Transition to Residency, “and an emotional reaction doesn’t bode well for learning.” For example, a patient diagnosed with atrial fibrillation might find out that they can live with this type of heart arrhythmia well and safely if they take their medication properly—but that same medication can be very dangerous if it’s used incorrectly. “So—all within the course of a conversation or two—a person hears they have a heart arrhythmia and has to learn a lot of detail about the medication,” Huberman says. “There’s often a need to learn when you’re least prepared to.”

In both New York and Qatar, WCM students are schooled in best practices for breaking bad news—concrete ways to enhance patient care by ensuring that the encounter is as gentle and productive as possible within the context of an inherently stressful situation. “I find breaking bad news very emotionally difficult, but I don’t think that’s going to go away,” says Lynne Rosenberg, MD ’19, who matched to a combined residency in internal medicine and pediatrics at the University of Colorado. “I had a physician say to me early in my career, ‘It’s never the wrong thing to care. If it’s hard for you and it makes you feel sad, that’s normal and human.’ I think that any time you have to tell someone unfortunate news, it’s going to be scary. But I feel like I’ve been given the tools and the guidance to do it.” That guidance includes conducting the conversation in a private place without interruptions; constantly assessing the patient’s understanding of the situation as the encounter proceeds; and giving them the relevant information in layman’s terms, without medical jargon—for example, using “spread” instead of “metastasize.” “The idea is to establish rapport and keep the communication going; sometimes that means eye contact and appropriate body language,” Verjee adds. “A minute may pass where there’s nothing said. But the patient knows, ‘I’m engaged with you, and I’m giving you a chance to sort this out.’ ”

For a standardized patient encounter at WCM-Q, Merna Hussein ’19 was tasked with informing a woman that she’d been diagnosed with a form of leukemia. Afterward, the patient told Hussein that she’d done many things right, such as not interrupting—but also gave her some constructive criticism. “She didn’t feel like I gave her enough time or silence to take it all in, and I flooded her with more information than she had wanted,” Hussein recalls, marveling that “in real life, you’ll never get feedback like that.” Hussein, who is headed to an internal medicine residency at Johns Hopkins, sees breaking bad news as an essential part of her training; she



PHOTOS: JOHN SAMPLES

notes that during her first week on the wards, she was in the room when a physician gave a patient a diagnosis of colon cancer. In fact, she says, she would have welcomed a wider variety of simulated encounters on the topic. “Although you have a protocol in your head for how to do things systematically, not every patient is going to respond in the same manner,” she says. “One person may go silent, another may get angry. Another may use a defense mechanism of intellectualization, where they focus on the facts and ignore their emotional response.”

Last fall, Verjee and Liam Fernyhough, MD, an assistant professor of medicine at WCM-Q who specializes in hematology and oncology, held a breaking bad news training for practicing physicians in Doha; capped at twenty-four participants, it filled up quickly, and additional sessions are planned. “People perceive that hematology and oncology are fields where we break bad news, and that this is where we focus those skills. But in fact, every doctor is breaking bad news all the time; it could be someone who has had a stroke or has stage-four heart failure,” Fernyhough observes. “For most doctors, there’s a great deal of trial and error, and there’s a lot of personalization involved as well. What words are right to us? What personal space is comfortable?”

As Fernyhough and his colleagues point out, even what constitutes “bad” news can vary widely. One patient diagnosed with hypertension might shrug it off with the notion that it’s fairly common and contentedly take their meds. “Another person might have a family history with early death associated with high blood pressure, and it might be devastating,” Fernyhough says. “So we can’t always know what defines bad news for any given individual.” That notion comes into play in a simulated encounter that Kang developed, in which a student sees a patient who has received notice that there is a marked change in her annual mammogram compared to her results from previous years. “The context of this scenario is that all of the patient’s friends who’ve had abnormal mammograms have had breast cancer,” Kang says. “So in her mind, she already has cancer—that’s the framework she’s beginning with.”

Giving doctors the tools to break bad news well can benefit clinicians as well as patients. Breaking bad news is, after all, one of the toughest parts of practicing medicine, something that can contribute to job stress and burnout. Huberman, who’s trained in clinical psychology as well as in medical ethics, stresses the importance of having colleagues on a



‘I find breaking bad news very emotionally difficult, but I don’t think that’s going to go away,’ says Lynne Rosenberg, MD ‘19. ‘I had a physician say to me early in my career, “It’s never the wrong thing to care.” ’

case with whom physicians can process their feelings about particularly tough experiences. Having to break bad news, she says, can constitute a form of “moral injury”—the pain and frustration felt by a doctor who not only has to devastate a fellow human being with a potentially dire prognosis, but who might have no viable treatment options to offer. “One of the ways we can try to prevent that distress and injury is to give doctors good tools for helping, even when they can’t cure,” Huberman says. “Physicians get into this business because they hope to help people. If you learn how to connect to someone’s emotions and support them—to show them that you care, that they’re heard and understood—that’s a therapeutic intervention in itself. Even if you can’t save them, you have given them something.” ■

— Beth Saulnier

Failure to Communicate

Do early disruptions in brain cell development give rise to autism?

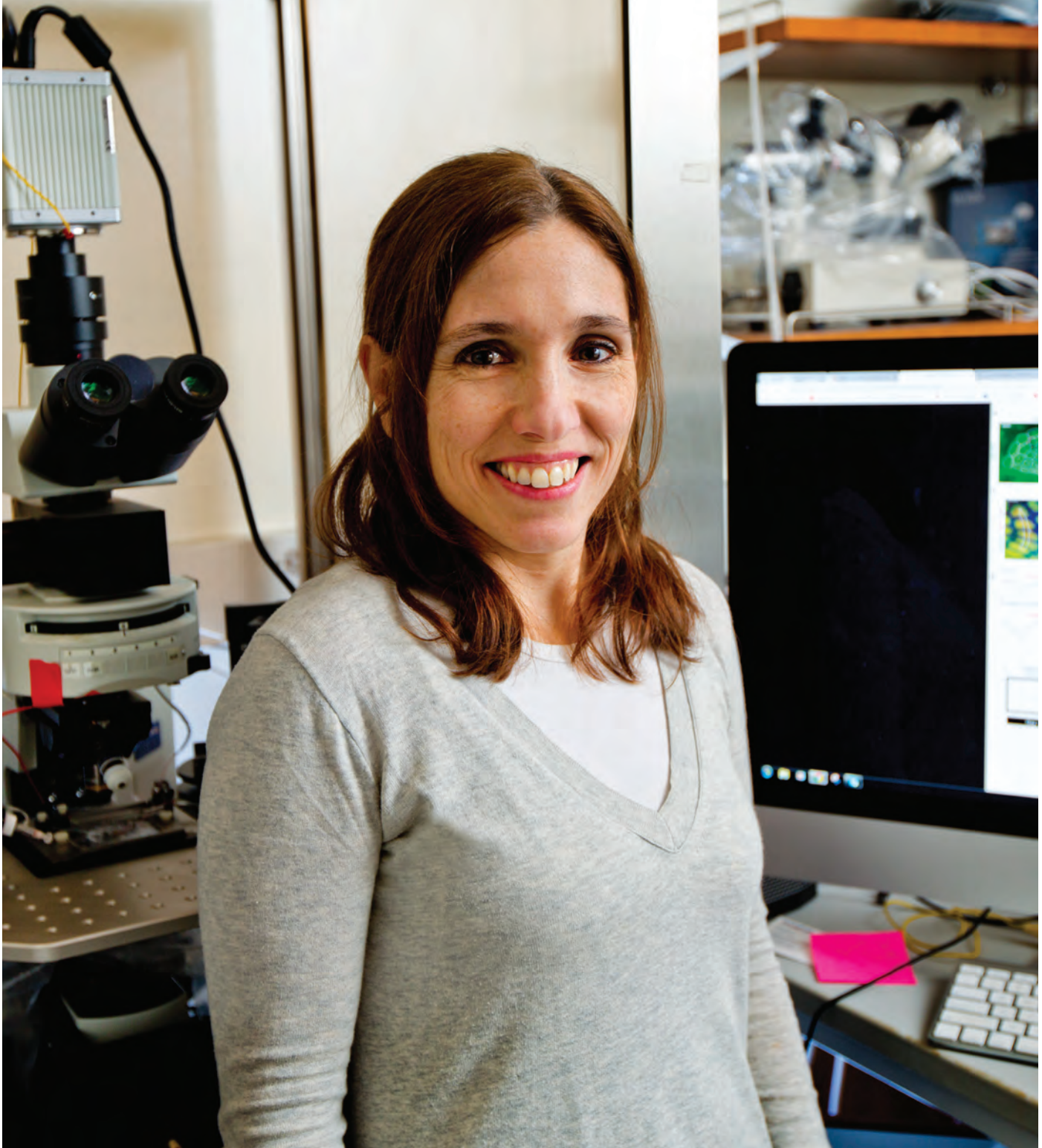


PHOTO: ABBOTT

Natalia De Marco García, PhD

Despite decades of research, it's still not clear what causes autism, which now affects one in fifty-nine children in the U.S. While genetic factors are involved, they don't fully explain how the disorder arises in the brain. This lack of certainty contributes to the dearth of universal treatments for the condition, whose prevalence has more than doubled since the turn of the millennium. Natalia De Marco García, PhD, an assistant professor of neuroscience and a member of the Feil Family Brain & Mind Research Institute at Weill Cornell Medicine, is parsing the intricate neural underpinnings of autism in search of more definitive answers.

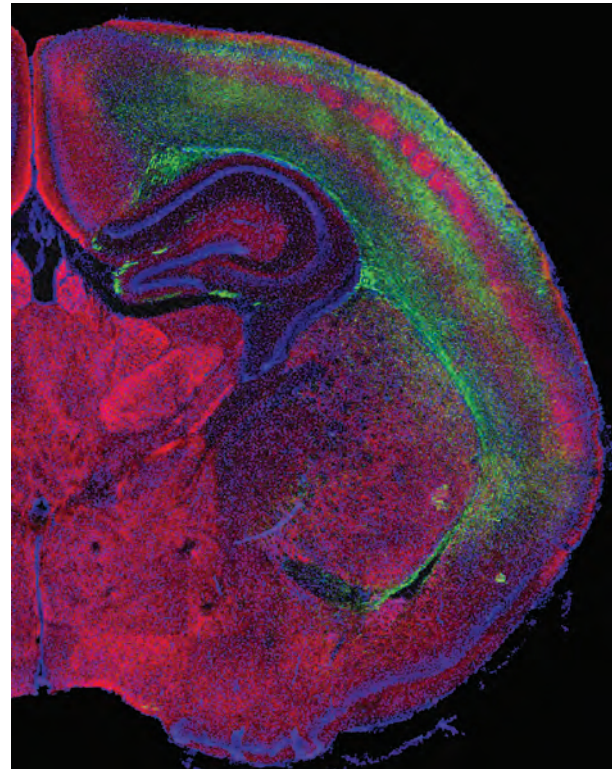
On the WCM faculty since 2014, De Marco García studies how developing neural cells communicate with one another to form a healthy nervous system; disruptions of intercellular communication within the system are thought to play a role in the emergence of autism. Some of De Marco García's keenest interests lie in interneurons—specialized nerve cells that facilitate these neural chats. The human body contains some 20 billion of these tiny, skilled intermediaries. Scientists are learning that interneuronal diversity is also immense. “We keep getting information that there are many more subtypes than we could ever imagine,” De Marco García says.

Interneurons that inhabit the brain's cortex often malfunction in individuals with autism, previous research has shown. In fact, some scientists have pointed to this impairment as a potential cause of the disorder—a hypothesis supported by evidence that many genes linked to autism are strongly expressed in developing cortical interneurons. Researchers also suspect that deficits in interneuron function may give rise to sensory impairments—a common symptom of autism that can manifest itself through abnormal reactions to touch or certain sounds. While this theory remains to be confirmed, De Marco García's recent research strengthened its foundation.

In a study published online in *Neuron* in June 2018, De Marco García's team looked at how quickly cortical interneurons develop in young mice, finding that the nerve cells become functional just six days after birth. To mimic the dysfunction that may befall human interneurons, the researchers artificially disrupted the cells' activity in other young mice a few days after birth—a period critical for interneuronal development. When the rodents grew up, they were able to receive sensory stimuli from the environment, but failed to process them correctly; for example, they couldn't differentiate textures by touch.

These findings suggest that, at least in mice, disrupted interneuron function early in life may indeed lead to sensory problems. But De Marco García's ultimate goal is to understand how they occur in people—to study the development of human interneurons and to figure out how to intervene if dysfunction arises. Her ultimate dream is to find a non-invasive way to repair interneuron function in individuals with autism. “If you could restore the way in which the neurons talk to each other,” she says, “then you might be able to repair behavior.”

De Marco García's passion for deciphering neuroscientific mysteries dates back to when she was nearing the end of her undergraduate studies in biology in her native Argentina. She took three



WITH FEELING: The cerebral cortex's receptive areas for the sense of touch (depicted in red) are seen surrounded by neural cell projections (green).

neuroscience courses and became smitten with the many secrets lurking in the human brain. “It's a very complex organ,” says De Marco García, who holds a doctorate in neuroscience from Columbia. “We know very little about it, and it's a defining feature for humans.” One long-neglected structure that has captured De Marco García's interest is the insula—a small but industrious region of the cortex whose dysfunction has been implicated in depression, bipolar disorder, and autism. Among the area's many roles is integrating, interpreting, and responding to various sensory stimuli—tactile feedback, images, sounds, and flavors—that the brain receives from the outside world.

In a key function that is often disturbed in people with autism, the insula also allows people to read their internal bodily signals

‘If you could restore the way in which the neurons talk to each other,’ De Marco García says, ‘then you might be able to repair behavior.’

such as hunger, thirst, heartbeat, and body temperature. De Marco García and her team are now mapping the complex communication pathways spanning the primary somatosensory cortex—the brain's major receptive area for the sense of touch—the insula, and other regions responsible for cognition. Through this research, De Marco García aims to see how the brain selects the relevant sensory information from the plethora of environmental stimuli. The findings, she hopes, will pave the way to a more thorough understanding of how sensory impairments arise. “It's a constant challenge,” De Marco García says of her work, “but it's very rewarding.” ■

—Agata Boxe

'A Beacon of Hope'

By harnessing the immune system to fight ovarian cancer, Juan Cubillos-Ruiz, PhD, aims to improve survival rates for the first time in decades

Juan Cubillos-Ruiz, PhD, got his first look at ovarian cancer early in his doctoral research, which focused on understanding how the microenvironment of a tumor affects a patient's immune system. "It was one of my first experiments," recalls Cubillos-Ruiz, now an assistant professor of microbiology and immunology in obstetrics and gynecology at Weill Cornell Medicine, where he is also a member of the Sandra and Edward Meyer Cancer Center. "I got a specimen from a patient to analyze, and I was absolutely shocked by what an ovarian tumor looks like. It's a monster."

As Cubillos-Ruiz explains, ovarian tumors tend to grow especially large, both because the cancer grows quickly and because diagnosis is often delayed. Early symptoms—such as fatigue,

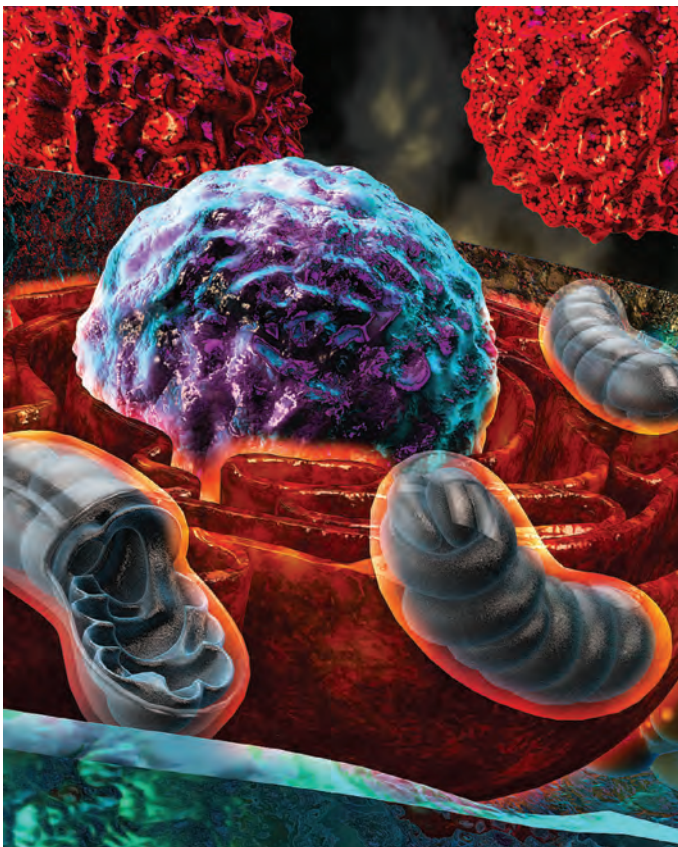
bloating, and irregular menstrual periods—can be vague enough to go unnoticed. In the vast majority of patients, the cancer has already metastasized by the time it's identified, so traditional treatments like chemotherapy are much less effective. Despite recent advances against many other cancers, the five-year survival rate for metastatic ovarian cancer still hovers around 27 percent, and has for decades.

It's a grim figure—but recent work by Cubillos-Ruiz and his team at WCM is deepening scientists' understanding of the complex interaction between the immune system and this highly aggressive malignancy. Their work with mouse models of disease and analyses of human ovarian tumors, including a recent study published in *Nature*, is already informing the development of new treatments that are currently being tested pre-clinically. "Right now, if a woman is diagnosed with late-stage ovarian cancer, she has a very bad prognosis," says Cubillos-Ruiz. "But this brings a beacon of hope."

One reason why ovarian cancer has remained so frustrating is that it resists one of oncology's most promising new tools. Immunotherapy essentially takes the brakes off a patient's immune system, allowing it to hunt down and destroy cancer cells. In various cancers, including melanoma and lung cancer, immunotherapy has saved the lives of patients who just a few years ago might have been considered terminal. It's often much more effective than standard treatments like chemotherapy—and if it could be made to work in ovarian cancer, it could save thousands of women's lives. "Immunotherapy is an incredible breakthrough," Cubillos-Ruiz says. "But ovarian cancer has evolved multiple strategies to inhibit the protective function of immune cells."

For more than a decade—first through his PhD work at the Geisel School of Medicine at Dartmouth, then during postdocs at Harvard and WCM, and finally in his own lab, which he started in 2015—Cubillos-Ruiz has sought to understand why ovarian cancer is so different and immune-suppressive. The answer, it seems, has to do with its microenvironment—the mix of cells, the presence or absence of different compounds, and other conditions inside a tumor—and its effect on an intracellular structure called the endoplasmic reticulum, or ER. "The endoplasmic reticulum is tremendously important," Cubillos-Ruiz explains, "because it's involved in the synthesis of all the proteins that will be located on the surface or secreted out of the cell."

One crucial job of the ER is the folding of proteins, which can't function correctly if their three-dimensional configuration is altered. Improperly folded proteins accumulate in the ER, like broken widgets jamming the works of a factory. This induces a state known as "ER stress," which prevents the cell from fulfilling its role in the body. Cubillos-Ruiz and his team have shown that in ovarian cancer, the lack of nutrients inside the tumor alters the



STRESSFUL SITUATION: A scientific illustration shows how T-cells that are exposed to harsh conditions inside a tumor experience endoplasmic reticulum (ER) stress, depicted by "burning" ER (orange) surrounding the nucleus (purple and turquoise). Mitochondria are seen in bluish gray, with cancer cells in red.

IMAGE, LEFT: ELLA MARU STUDIO. PHOTO, RIGHT: RENÉ PEREZ



Juan Cubillos-Ruiz, PhD

protein-folding ability of the ER within T-cells, the immune cells that destroy invaders. “Immune cells need nutrients to properly form and fold proteins in the ER,” Cubillos-Ruiz explains. “If, for example, cancer cells are stealing glucose from immune cells, that will immediately trigger ER stress because there’s an accumulation of those misfolded proteins. We discovered these adverse conditions inside the tumor are constantly triggering ER stress in the T-cell, which acts as a brake that blocks their protective anti-cancer activity.”

This new understanding of how ovarian cancer affects the immune system could point the way to treatments that prevent or control the ER stress response within T-cells, which could in turn unleash a patient’s immune system to fight the tumor. This could involve genetic tools that silence the expression of ER stress sensors within T-cells, or new drugs that could bind to and block those

‘Immunotherapy is an incredible breakthrough,’ Cubillos-Ruiz says. ‘But ovarian cancer has evolved multiple strategies to inhibit the protective function of immune cells.’

sensors. Cubillos-Ruiz is a co-founder of and scientific adviser to a start-up biotech company, Quentis Therapeutics, which was established around core technology arising from his research, under agreements generated and negotiated by both Cornell’s Center for Technology Licensing at WCM and WCM’s Office of BioPharma Alliances & Research Collaborations. Quentis is already working to develop drugs that target a cellular pathway Cubillos-Ruiz and his team have identified. “Developing these new forms of immunotherapy will be challenging,” he says, “but we’re very excited.” ■

— Amy Crawford

Skeleton Keys

Studying the fundamentals of bone strength, pathologist Matthew Greenblatt, MD, PhD, aims to protect people from osteoporosis



Matthew Greenblatt, MD, PhD

Heat disease, high blood pressure, and diabetes are known as “silent killers,” so named because they often have subtle symptoms that go undetected. While osteoporosis may seem an unlikely addition to that list, Matthew Greenblatt, MD, PhD, says the common bone-thinning disease can be just as quiet, debilitating—and deadly. “For older people who fall and fracture their hip, there is a very low chance they’ll ever walk again,” he says. “And there’s a surprisingly high chance they’ll die due to complications.”

But Greenblatt, an assistant professor of pathology and laboratory medicine at Weill Cornell Medicine, is doing his best to change that. Over the past few years, he’s made groundbreaking discoveries that may lead to life-changing therapies for osteoporosis and other skeletal disorders. The National Osteoporosis Foundation estimates that some 10 million people in this country have the disease—which causes bones to weaken as we get older—and another 44 million

Americans are at a heightened risk because of low bone density. Experts calculate that osteoporosis-related bone breaks cost the U.S. healthcare system \$19 billion a year, with that figure projected to rise to more than \$25 billion by 2025.

About half of all women, and up to a quarter of men, will break a bone in their lifetimes due to osteoporosis. And though the fracture itself is usually not fatal, potentially deadly complications such as pneumonia, blood clots, and post-operative infection are common—meaning that, shockingly, these fractures ultimately kill as many women each year as breast cancer. New treatments, says Greenblatt, are “extremely important not only to the health of individual patients, but for public health as well.”

As Greenblatt notes, the majority of existing osteoporosis medications don’t help patients build new bone; instead, they stop the bone that is already affected from deteriorating further. So he and

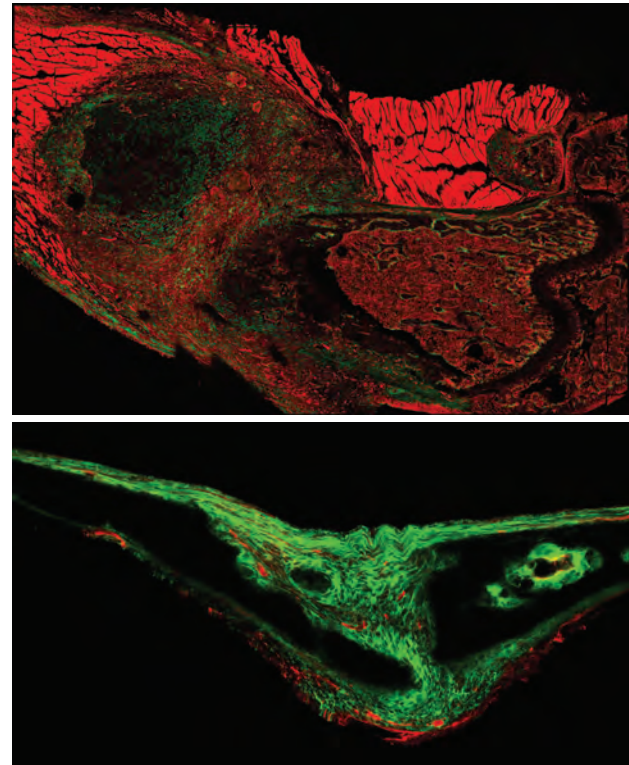
colleagues decided to look at a new approach involving special types of blood vessels inside of bones. They performed experiments on mice that were genetically altered to lack a protein—called SLIT3—that promotes the growth of these blood vessels and learned that the rodents without this protein exhibited low bone mass.

The team then wondered if SLIT3 could be used as a form of treatment, and tried it in a mouse model of postmenopausal osteoporosis. The strategy worked: not only was the osteoporosis reversed, fractures healed more quickly. Their results were published in *Nature Medicine* in May 2018. “We compared it head-to-head with the established drug used in this space,” says Greenblatt, the study’s co-senior author, “and it performed at least as well in helping to build bone in these mouse models.” He notes that the established drug currently used has limitations, since it can only be used for two years because there are concerns that it may increase the risk of developing bone cancer. Greenblatt’s project has so much promise, he recently received an award from the Daedalus Fund for Innovation, a WCM program designed to accelerate and build value around early-stage research projects with significant commercial potential. He will receive up to \$300,000 over two years to advance this research and, in close collaboration with the Office of BioPharma Alliances and Research Collaborations, is searching for an industry partner to help develop these findings into a new medicine.

Greenblatt also spearheaded another key study on bone pathology, in which he identified a type of stem cell that plays an essential role in growing and healing the bone’s hard outer surface. As a *Nature* article described in September, he and his collaborators are the first scientists to discover these cells—called periosteal stem cells—along with evidence that bone contains multiple kinds of stem cells that each have distinct functions and are found in different places throughout the bone. This suggests another potential avenue for treating bone disorders, since Greenblatt theorizes that targeting periosteal stem cells directly could lead to the development of more effective drugs—noting that “this is probably the most important cell in the body for resisting fractures.”

A Missouri native, Greenblatt’s interest in science was sparked by his childhood asthma, a condition that improved as he got older. The experience inspired him to read medical textbooks, and by high school he was spending summers doing research at nearby medical schools. That curiosity continued through his graduate years at Harvard, where he entered a combined MD-PhD program and began his doctoral dissertation by looking at problems facing patients taking immunosuppressants. But after talking to colleagues who were doing bone research, he decided to shift focus. “I was in the field of immunology where we know a tremendous amount of detail about all the cells involved,” he says. “With bone, we know much less about the molecular pathways involved, and even less about the cells that are present. So I felt there were opportunities to do very important work in bone biology.”

Greenblatt came to WCM in 2014 as a third-year resident in clinical pathology after two years at Brigham and Women’s Hospital in



BONE DEEP: A microscopy image taken six days after a fracture (top) shows an expansion of periosteal stem cells (shown in green). Above: That same type of cell as seen in the skull of a fifteen-day-old mouse.

Boston. The following year, he won both the NIH Director’s Early Independence Award and the Burroughs Wellcome Fund Career Award for Medical Scientists—which, he says, allowed him to transition directly to running an independent research lab without the traditional step of a postdoctoral fellowship. “The most

The majority of existing osteoporosis medications don’t help patients build new bone; instead, they stop the bone that is already affected from deteriorating further.

valuable thing you have in life is time,” says Greenblatt, who joined the faculty in 2015. “Taking that path shaved several years off my trajectory and let me get into doing work I was enthusiastic about right away.”

Moving forward, he hopes his research can help in areas beyond osteoporosis. For example, he aims to study whether periosteal stem cells might aid patients undergoing orthopaedic procedures; he’s also investigating whether malfunctions in these cells could be a cause of bone cancer, as well as a number of birth defects affecting bones in the skull. “Our ultimate goal is to understand what steps these cells take toward becoming bone-forming cells,” he says. “We think that is the foundation to understanding how bones work, how diseases of the bone develop, and how we can treat them.” ■

— Heather Salerno

Hearts & Minds

Jonathan Avery, MD, is working to combat stigma within the medical community against patients who struggle with substance use disorders

By Heather Salerno

Photos by John Abbott

Robin Kellner's daughter, Zoe, was the kind of child that would make any mother proud. She was bright and beautiful, creative and curious. But by the time Zoe was a sophomore at a college in Florida, she was struggling with drug misuse—once accidentally overdosing while Kellner was visiting in fall 2003. Kellner rushed to the ER to find Zoe on a gurney, incoherent and her mouth black from the charcoal doctors had used to try to absorb the Xanax in her stomach. But during the thirty-six hours that her daughter spent in the hospital, Kellner says the two were treated with disdain; Kellner was even told to sit down and be quiet when she tried to ask questions. No one offered much guidance on how to support Zoe once she was discharged, Kellner says, or informed them that Zoe was at a significantly higher risk of overdosing again in the future. As Kellner recalls: "I was >



A MOTHER'S MISSION:

Ever since her daughter, Zoe (seen in a black-and-white photo in the family home), died of an accidental overdose, Robin Kellner has advocated for awareness that drug addiction is a disease that deserves compassionate treatment.



Jonathan Avery, MD

left trying to figure out, 'How did this happen? What do we do now?'"

After Zoe returned home to New York City, Kellner reached out to doctor after doctor, desperate for advice. She says their responses were often unsympathetic and unhelpful—with one prominent physician recommending that she have her daughter arrested to scare her into sobriety. "There were so many moments when Zoe interacted with doctors that I think were missed opportunities, that could have really turned things around," Kellner recalled in January during a seminar for first-year internal medicine residents at NewYork-Presbyterian/Weill Cornell Medical Center who were learning about substance use disorder. "But instead of looking at Zoe as someone who had mental health issues that were pushing her in this direction, she was looked at as a spoiled kid who was indulging in bad behavior. No one was saying, 'This is a sick child, and this is what her treatment should be.' " Zoe eventually started going to therapy, resumed her studies in the city, and seemed to get better; then one day, Kellner came home from work and Zoe was high again. Finally, someone told Kellner about an addiction specialist who might be able to help. Zoe agreed to meet with him, but in April 2007— just days before her appointment—she died in her bedroom of another accidental overdose. She was only twenty-two. "Stigma is a killer," Kellner told the six residents. "It keeps people from getting the help they need."

Capturing the raw and sometimes harsh experience that patients like Zoe can endure is integral to the mission of Jonathan Avery, MD, director of addiction psychiatry and an associate professor of clinical psychiatry at Weill Cornell Medicine and an attending psychiatrist at NewYork-Presbyterian/Weill Cornell. His goal is to reform a pervasive problem that is slowly gaining attention: many clinicians—even psychiatrists and addiction specialists—hold negative attitudes toward patients with substance use disorders, which can increase these patients' feelings of shame, discourage them from seeking treatment, and limit the quality of care they do receive. He is studying the stigma these patients face and—in part with philanthropic funding from Kellner and her husband, John Sicher—is developing interventions at the educational and practice levels that are aimed at shifting doctors' mindsets, with the goal of improving the likelihood that people with substance use disorder will overcome their dependence on alcohol or drugs. "It turns out that doctors aren't different from anyone else," Avery says. "Even after they learn the neurobiology of addiction and how it's a brain disease, doctors can still view it—much like the general population—as a moral failing, or people making bad choices that

deserve more punishment than treatment."

Avery's advocacy around the judgment that people with substance use disorder encounter coincides with a broader societal reckoning with inequities rooted in racism, sexism, and other forms of discrimination. The soul searching extends to medicine, where practitioners are reflecting on their own entrenched biases and wondering how they can provide more equitable

'Even after they learn the neurobiology of addiction and how it's a brain disease,' Avery says, 'doctors can still view it—much like the general population—as a moral failing, or people making bad choices that deserve more punishment than treatment.'

and appropriate care. Avery believes his work is tied to these important movements, since individuals with substance use disorders face prejudice on many fronts—and he isn't the only one trying to reduce addiction-related stigma. Doctors from institutions such as Massachusetts General Hospital and Johns Hopkins University are addressing the problem, and the New York City-based nonprofit Center on Addiction has made eliminating stigma part of its mission. "Hopefully," says Avery, "the current environment of advocacy and sharing difficult life experiences will help."

His work is also critical given the country's current opioid epidemic, which the U.S. government has officially declared a public health emergency. According to the Centers for Disease Control and Prevention, drug-related deaths have more than tripled since 1999, with more than 70,000 lives lost in 2017 alone. In New York City, more people die of drug overdoses than homicides, suicides, and motor vehicle crashes combined, with opioids involved in more than 80 percent of all overdose deaths. Despite this crisis, Avery says, many clinicians avoid working with patients who have addictions. Just 10 percent of patients with addictions to substances other than nicotine receive treatment, according to a 2012 report from the Center on Addiction. Discrete courses on addiction are rare in medical schools, and required addiction-related >

content on board exams is “minimal,” according to the report. What’s more, it found that of the 985,375 actively practicing doctors in the United States, just 1,200 are addiction specialists, with 355 self-identified as addiction psychiatrists. With most medical training based in hospitals—where substance use disorder patients tend to be in crisis, and with little exposure there to positive outcomes—many physicians are disillusioned and feel disempowered by the

‘Starting with medical school, I started having these really positive experiences with people with substance use disorders,’ says Avery. ‘They’re at rock bottom, and before you know it they have a family and a career and their life is back on track.’

time they complete their training, Avery says. But he says that possessing the skills and comfort to treat affected patients is essential—not only as a matter of social justice, but of practicality, since such patients present throughout the healthcare system. “There needs to be this culture shift where all doctors are addiction doctors,” Avery says, “where we’re happy to see these patients and can help them.”

Avery is working to bring fellow psychiatrists and physicians from other specialties—from emergency medicine to internal medicine to ob/gyn—into the fold by teaching them the best strategies to engage with and treat those who misuse drugs or alcohol. He directs seminars for medical students, interns, and residents that are partly intended to inspire empathy for people with substance use disorders—a feeling he hopes will stay with these doctors throughout their careers and motivate them to take a more active interest in helping such patients get better. Avery gives similar talks nationwide, including at meetings of medical organizations like the American Psychiatric Association, and has created a series of videos highlighting patients in recovery, which have been viewed by more than 10,000 doctors nationwide. Avery also co-authored *The Stigma of Addiction: An Essential Guide*, one of the few books on the subject; published in January by Springer, it discusses ways in which professionals and laypeople can avoid stereotyping

addiction and improve negative attitudes, with the aim of achieving better outcomes. “Jon isn’t just working in our local community, he’s working in a way that others can be educated on a broader scale,” says Francis Lee, MD, chairman of psychiatry at Weill Cornell Medicine and psychiatrist-in-chief at NewYork-Presbyterian/Weill Cornell. “I think what he’s doing to target doctors in other fields is also brilliant, because most of the physician workforce is going to encounter these patients—not just psychiatrists, who mainly see them when their condition is very bad. They typically present in the general ED or in primary care settings. And ultimately, we all need to be aware that if clinical care providers have negative attitudes toward these patients, they will likely not get better.”

SHIFTING OUTLOOKS

Avery’s own studies reinforce the need for such change. One of his latest investigations, published earlier this year in the *Primary Care Companion for CNS Disorders*, found that resident physicians’ attitudes toward people misusing substances was more negative than those toward people with schizophrenia or major depressive disorders—and that those attitudes tend to get worse over time. Plus, he found that emergency medicine residents held a poorer view of these patients than did residents in internal medicine and ob/gyn. Why? Avery believes it’s because doctors who work in acute care settings like emergency departments more frequently encounter the most severely ill substance-using patients, who can be challenging when they’re intoxicated or in withdrawal.

At the same time, he says, most doctors and healthcare workers are rarely exposed to individuals who have overcome their addictions—even though the latest figures show there are 23.5 million Americans in recovery, a bigger population than the estimated 21.5 million who currently suffer from a substance use disorder. “If your active experience is with those who are using or misusing substances,” says Avery, “you tend to forget about the people who get better or are likely to get better in the future.” Michael Sideris, a third-year medical student who is assisting Avery with research in this area, witnessed the problem firsthand when he worked as an EMT in Boston after graduating from college. He was shocked by comments his colleagues sometimes made when they got repeated calls to help the same overdosing patients—things like, “We should just let them die. Why are we even going?” “That experience had a profound effect on me,” Sideris says. “If patients can’t even get their foot



THE BASICS: Avery (center) gives medical students an introductory lesson on issues surrounding drug misuse.

in the door without feeling stigmatized or mistreated, then providers are doing them a disservice in the long run. They deserve better.”

Avery counts himself fortunate to have witnessed good outcomes early in his training, which informed his understanding of the issue. As a resident, he followed one patient who used alcohol excessively and was hospitalized for depression, but ultimately went on to stop drinking, get married, and have a child. “Starting with medical school, I started having these really positive experiences with people with substance use disorders,” says Avery. “They’re at rock bottom, and before you know it they have a family and a career and their life is back on track.” He notes that there are many paths to recovery. Addiction can be treated in numerous settings—from long- and short-term residential treatment to individualized and group counseling—using a variety of behavioral and pharmacological approaches. According to the National Institute on Drug Abuse, there are currently 14,500

specialized drug treatment facilities in the U.S. that provide services to patients with substance use disorders. Though relapse is common, with rates between 40 and 60 percent, experts point out that these rates are similar to those for other chronic diseases like hypertension or Type I diabetes. Research, too, backs up the idea that treatment can work. Data from the Partnership for Drug-Free Kids and the New York State Office of Alcoholism and Substance Abuse Services indicates that 10 percent of all American adults have overcome a problem with alcohol or drugs.

To encourage a more optimistic view among his colleagues, Avery includes real patients in recovery in his training seminars and videos. They include Liam (who asked that his real name be withheld to protect his privacy), who has been giving in-person presentations to Avery’s students and others at NewYork-Presbyterian/Weill Cornell for the past three years. Liam has been sober since 2012, after more than a decade of misusing >



Zhanna Livshits, MD

alcohol, marijuana, and other drugs. “Alcoholics and addicts are not necessarily bad people turning good,” he said, speaking at the same session as Kellner. “We’re sick people getting well.” Liam noted that he was hospitalized thirteen times before finding a psychiatrist who properly adjusted his medications for a mood disorder, a major factor in his drug use. He added that having physicians who listened to him without judgment was also critical in his recovery. “I know doctors don’t always have time for that,” he said, “but even ten minutes can make a big difference.”

That ability to meet patients where they are is another strategy Avery addresses with medical students and residents, and he explains how to shift from scolding a patient about substance misuse—what he calls “finger wagging”—to discussing the problem in a respectful, open-minded way in a technique called motivational interviewing. Word choice can be a subtle but course-shifting tactic: He points out that terms like “addict,” “junkie,” and “abuse” demean patients who have a real disease, and can turn

patients off from continuing to work with a doctor. Instead, he suggests that physicians ask patients if they can share their concerns about the effects of addiction (for example, “Would it be all right if I share some thoughts on why I’m worried about your marijuana use?”), rather than simply providing information, since most patients already know that their behavior is unhealthy. He argues that motivational interviewing is not just better for patients—it also relieves pressure on doctors who may feel they need to “save” them on the spot. “The idea is that there’s a part of everyone that doesn’t want to change and a part of everyone that wants to change, and so through patience and questioning you align yourself with the part of the person that wants to change,” Avery says. “It’s really just about rolling with resistance and being patient in knowing that the likelihood is that people will get into recovery and that motivation will come.”

REACHING OUT

Avery also urges clinicians to talk about addiction with patients, even if they’re coming in about a separate medical problem. That made an impact on Chou Chou, MD, a first-year resident in internal medicine who attended the January seminar. “As internists we’re on the front lines, and sometimes it’s easy to just roll with things when you’re in the hospital with a lot of sick patients,” says Chou. “Someone may come in with the flu or a heart issue, and we take a look at old providers’ notes and see ‘alcohol abuse,’ but it’s something that hasn’t really been addressed during the hospital visit because other things are going on. This was a nice reminder not to miss an opportunity.” Chou also appreciated that while Avery talked about the benefits of behavioral therapy and counseling, he emphasized that there are effective, FDA-approved medicines like naltrexone—which blocks the effects of narcotics—that physicians can prescribe to help manage alcohol and drug use disorders. “I never offered those medications before because I felt so uneducated about them,” says Chou. “It makes you feel like there’s something active you can do for those patients.”

Avery is finding that even short interventions with physicians can influence their attitudes. For a study published in February in the *Hospital for Special Surgery Journal*, he sent a questionnaire about individuals with alcohol and opioid use disorders to internal medicine and psychiatry residents, then had them view an eight-minute online training video about addiction stigma; when he followed up with the same questionnaire six months later, he found that the residents’ views of people with substance use

disorders had improved significantly. While Avery acknowledges that the study had its limitations—for example, the clinicians’ attitudes might have been improved by factors other than the training video—he sees it as an encouraging sign, since those views tend to become more negative during residency training. “It’s about giving them tools that allow them to be open and non-judgmental,” he says, “and letting them feel that they have the ability to offer patients options—and hope.”

Another initiative that could make a marked difference is the medical center’s program for distributing naloxone, a drug that can reverse an overdose. If a doctor or nurse suspects that a patient in the ED is misusing opioids, he or she can ask if that patient or a family member would like to take home a kit containing two nasal spray doses; the patient is also given a list of local pharmacies that will dispense naloxone without a prescription. That program was supported by a gift from Kellner and Sicher, who also funded a separate effort through NewYork-Presbyterian/Weill Cornell that distributes naloxone kits in the city. Programs like these are associated with a reduction in deaths from opioid overdose; they also give healthcare professionals an opening for a larger conversation about possible treatment. “We plant the seed that we’re here for patients if they ever want any resources,” says Zhanna Livshits, MD, an assistant professor of clinical emergency medicine and clinical director of WCM’s Opioid Overdose Prevention Program. Livshits is also helping Avery examine whether the naloxone distribution program is affecting how equipped ED physicians feel to help patients with substance use disorder. “Every life is important,” she says. “People are allowed to have second, third, fourth, fifth, and sixth chances.”

Arnab Ghosh, MD, an assistant professor of medicine at WCM and an assistant attending internist at NewYork-Presbyterian/Weill Cornell, is also collaborating with Avery to encourage more clinicians to treat addiction. Since federal law requires that doctors take an eight-hour training course before they can prescribe buprenorphine, a drug that reduces opioid cravings and withdrawal symptoms, much of his work involves making it easier for physicians to meet those requirements and encouraging them to pursue the training. Ghosh is part of a task force that is working on building an opioid education segment into training for nurses, social workers, and patient care managers at the medical center, so they can better identify high-risk patients and direct them to appropriate outpatient facilities that provide specialized care. Ghosh also helps distribute information about those facilities to doctors who prescribe buprenorphine, so

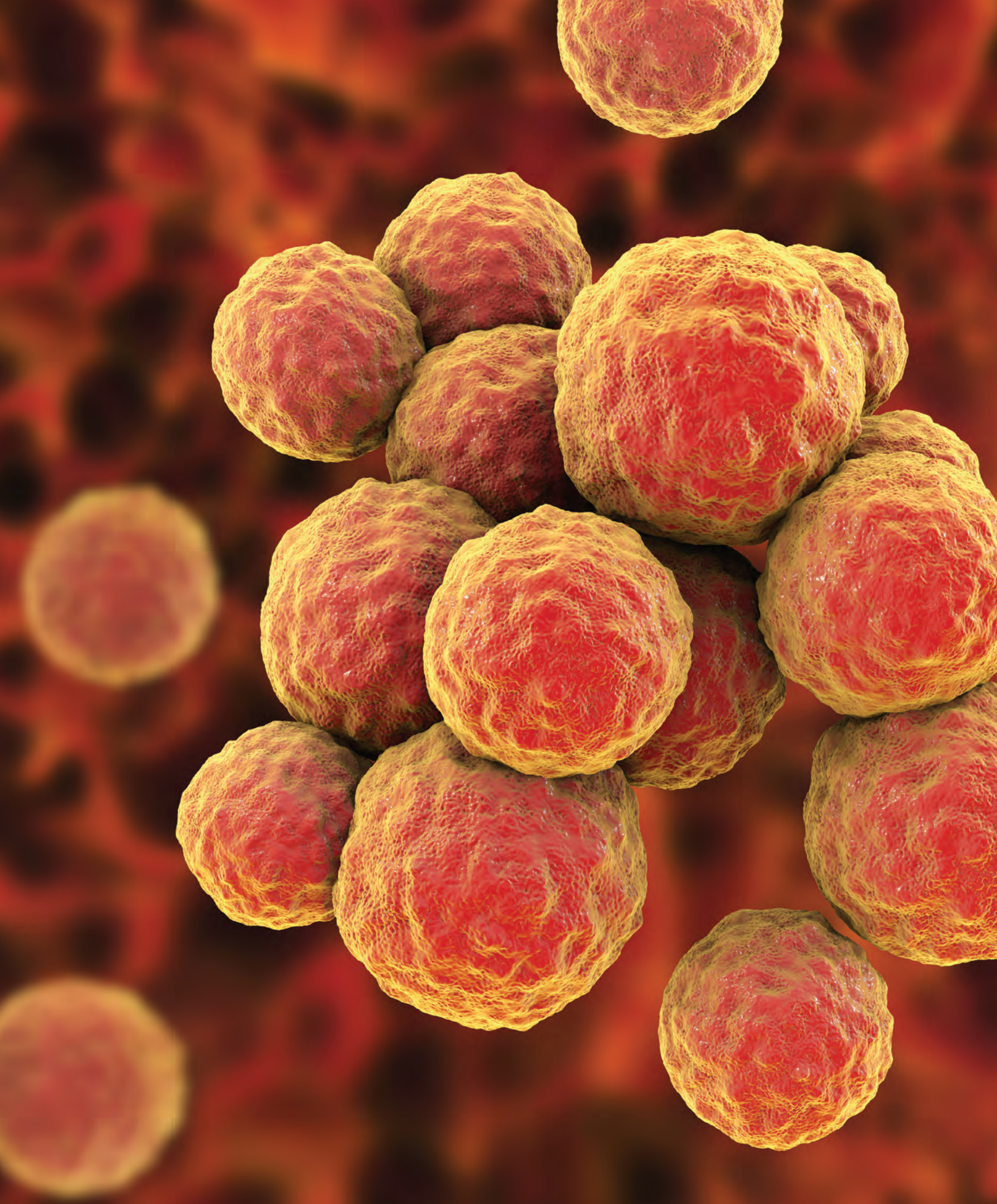
‘We plant the seed that we’re here for patients if they ever want any resources,’ says Zhanna Livshits, MD. ‘Every life is important. People are allowed to have second, third, fourth, fifth, and sixth chances.’

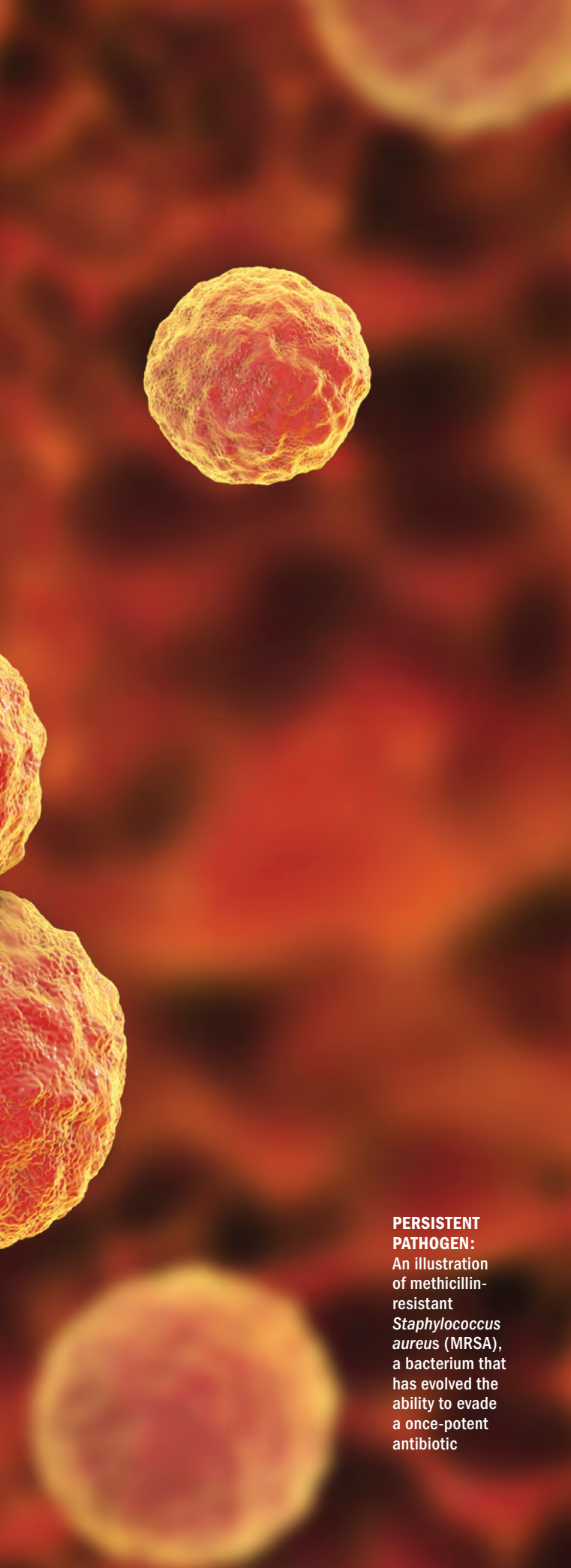
they know where to send patients who have an opioid use disorder. “We know that someone in New York City dies of an overdose every six hours,” he says. “There is an urgency to this.”

As for Avery, his next steps include creating an online interactive module that physicians and other healthcare providers could use to get immediate feedback on how their own attitudes about people who misuse substances compare with those of other clinicians. He also aims to develop a virtual reality program that would allow providers to better understand what addiction feels like from a patient perspective. In these, as in all of his training and intervention efforts, Avery wants to convey his belief that treating such patients can be incredibly rewarding. “All of medicine is about battling chronic diseases,” he says. “But I personally feel like you get more change with these folks than with any other patients. These are people who—if they can get their substance use under control—can live very different lives.” ■

LIFE SAVER: A medical student examines a sample of Narcan (a brand of naloxone), which can reverse the effects of an overdose.







PERSISTENT PATHOGEN:
An illustration of methicillin-resistant *Staphylococcus aureus* (MRSA), a bacterium that has evolved the ability to evade a once-potent antibiotic

PHOTO: KATERYNA KON/SHUTTERSTOCK

Formidable Foes

Physicians, researchers, and policymakers around the globe are grappling with the rise of antibiotic-resistant bacteria—a threat with the potential to derail decades of medical advances

BY BETH SAULNIER

In an earlier era, Carl Nathan, MD, might not have lived to see his first birthday. Born in 1946, Nathan contracted bacterial pneumonia as an infant. His life was saved by penicillin—a “miracle” drug that had prevented untold numbers of military casualties in World War II and had only recently been released to the civilian population. Flash forward to today: while medical science has advanced remarkably in many ways, that particular drug has lost its power against pneumonia—because, as is the case for myriad antibiotics, the bacteria that cause the disease have evolved the ability to resist it. “Within the lifespan of a single, not yet terribly old person—in effect, the blink of an eye—we’ve come to benefit enormously from these life-saving drugs, which are the single most useful class of medicines,” observes Nathan, the R.A.▶



Carl Nathan, MD

Rees Pritchett Professor of Microbiology and Immunology and chairman of the department, “and to face losing them, because of our profligate approach to how we use them.”

An expert on tuberculosis, Nathan has long been sounding the alarm about the perils of antibiotic resistance. Over the past fifteen years, he has repeatedly addressed the issue in academic journals, the mainstream media, and forums with national and international policymakers. It’s a pressing concern: according to the CDC, resistant infections cause 23,000 deaths and 2 million illnesses each year in the U.S. alone. As one CDC official—Arjun Srinivasan, MD, associate director of Healthcare Associated Infection Prevention Programs—warned in a May 2017 keynote address at a symposium on antibiotic resistance co-sponsored by Weill Cornell Medicine and the Ithaca

campus, the danger has risen so high that resistance should be counted among the problems that “can threaten the very security of the nation or the world.”

The reasons for the current predicament are no mystery. For decades, antibiotics have been overprescribed and overused—from their widespread application in agriculture (where they’re routinely given to animals because they make them gain weight faster) to the classic conundrum of a pediatrician faced with parents clamoring for a prescription for their sick toddler, even though the illness could well be viral and the drug of no use. According to a 2017 CDC report, some 30 percent of antibiotics prescribed in doctor’s offices, emergency departments, and hospital clinics are not needed—for a whopping 47 million unnecessary prescriptions written annually. And the more antibiotics there are out in the world, the

PHOTO: ABBOTT

faster organisms evolve resistance to them, and the sooner the drugs become useless. “What we’re seeing now, looking back, is that microorganisms can outwit almost everything we have,” says Roy Gulick, MD, chief of the Division of Infectious Diseases and a professor of medicine at WCM and an internist and infectious disease specialist at NewYork-Presbyterian/Weill Cornell. “And it’s become a real crisis, particularly in recent years—to the point that we now have bacteria that are resistant to all available drugs. That is a real concern. When you try to explain to family members that their loved one has an infection that we don’t have a treatment for, people are shocked and skeptical. They wonder, ‘Why don’t you?’—and that’s a valid question.”

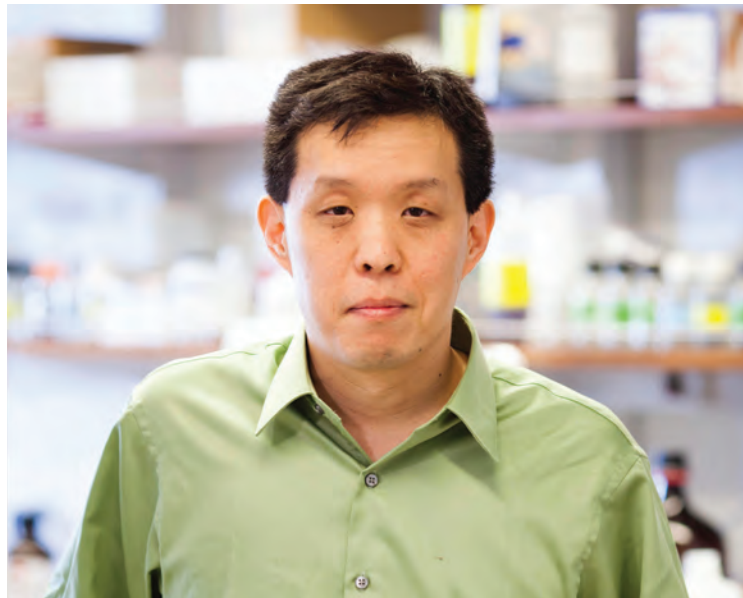
That conundrum underscores the other side of the equation: the dearth of new drugs to replenish the antimicrobial arsenal. Why hasn’t drug development kept pace with resistance? Experts say the reasons are more economic than scientific. Given the resistance issue—plus the fact that these drugs are generally needed only occasionally and taken for just days or weeks—pharmaceutical companies have gravitated away from them; far more profitable are the medications, like those for high blood pressure or cholesterol, that people take every day for decades. “The pharmaceutical industry left anti-infectives research because the economics of it didn’t work out,” says Kyu Rhee, MD, PhD, associate professor of medicine and of microbiology and immunology. “It was difficult to rationalize investing the money, time, and effort to make a product that will have a limited duration of use and limited shelf life before it risks becoming nonfunctional due to resistance. The business model for the return on investment just wasn’t there.”

In February 2015, the FDA approved ceftazidime-avibactam, one of the first drugs able to combat the rising threat of carbapenem-resistant gram-negative bacteria—a group of organisms against which a typically highly effective class of drugs (called carbapenems) is ineffective. But as Michael Satlin, MD, MS ’12, points out: “Within a year of coming to market, reports of resistance popped up from many places around the country.”

According to Satlin, the William Randolph Hearst Foundation Clinical Scholar in Microbiology and Infectious Diseases and an assistant professor of medicine at WCM, that’s a prime example of bacteria’s status as a formidable enemy. “They’ve been around for over a billion years,” says Satlin, also an internist and infectious disease specialist at NewYork-Presbyterian/Weill Cornell. “Their ability to adapt is pretty incredible.”

Satlin was an infectious disease fellow at WCM and NewYork-Presbyterian/Weill Cornell a decade ago when he was struck by the number of patients who were battling resistant bacteria; at that time, he says, carbapenem-resistant gram-negative bacteria were proliferating in New York City, and clinicians had few appealing options for how to treat these infections. “We were actually forced to use polymyxin B, which

‘The pharmaceutical industry left anti-infectives research because the economics of it didn’t work out,’ says Kyu Rhee, MD, PhD. ‘The business model for the return on investment just wasn’t there.’



Kyu Rhee, MD, PhD

is an antibiotic that came out in the Fifties and was abandoned in the late Sixties and early Seventies because of toxicity,” Satlin recalls. “But that was the only antibiotic that the organism was susceptible to.” The experience prompted Satlin to devote his research to the topic of drug resistance in a particular patient population: those who are neutropenic (having low levels of a type of white blood cell, and therefore a severely weakened immune system) due to chemotherapy during cancer treatment.▶



Michael Satlin, MD, MS '12

'Antibiotic resistance could prevent us from doing lifesaving procedures,' says Michael Satlin, MD, MS '12, 'like bone marrow transplants, organ transplants, or giving intensive chemotherapy to cure cancer.'

Under a \$500,000 grant from the CDC, he's been working with a biomedical engineer on the Ithaca campus to study antibiotic-resistance genes in the gut bacteria of neutropenic patients, with the aim of understanding how those genes spread and how antibiotics affect their proliferation. (The gut is a common source of infection in cancer patients, he explains, because chemo can damage the intestinal lining—hence the common symptoms of nausea and vomiting—and make it easier for gut bacteria to get into the bloodstream.) His ultimate aim is to provide personalized treatments by identifying which drugs are likely to be successful in preventing infections in particular patients, based on which antibiotic resistance genes are carried by their gut bacteria.

Satlin's work highlights one of the serious concerns about the antibiotic resistance crisis: not only does it put patients at risk of the infections themselves, but it can have dire consequences for many aspects of healthcare. "Antibiotic resistance could prevent us from doing lifesaving procedures like bone marrow transplants, organ transplants, or giving intensive chemotherapy to cure cancer," he stresses. "A lot of our advances in modern medicine are being threatened by these resistant bacteria."

Incremental Progress

Curbing antibiotic resistance remains an uphill battle—and repeated outcry from physicians, scientists, and other concerned parties over the years has yielded little in the way of concrete results. But some progress has arguably been made in the effort to stem antibiotic overuse and spur the development of new drugs. In 2015, the Obama Administration hosted a White House summit on antibiotic resistance; the U.N. General Assembly devoted a September 2016 meeting to it; in June 2017, the European Union adopted an action plan on the issue, which included strategies to boost drug research; and the WHO declared a World Antibiotic Awareness Week in November 2018. "I'm not confident—but I'm hopeful," says Rhee. "The fact that it has flagged the attention of the international community and has finally begun

to manifest in concrete commitments at the level of governments in trying to restimulate antibiotic development—that actually is different."

Like Nathan, Rhee focuses his research on TB—a disease in which drug resistance has long been a major stumbling block to treatment. His lab at WCM uses a type of mass spectrometry to gain insights into precisely how drugs enter living cells and destroy them, potentially pointing the way to better therapies that can overcome bacterial defenses. "People often think about TB from the standpoint of global health as the leading cause of death from infectious disease worldwide—but it's also the leading cause of death due to antibiotic resistance," Rhee says. "In many ways, TB is a model for highlighting the major barriers to solving this problem. If we can figure out ways of solving antibiotic resistance in TB, many of those approaches will have applications to other bacteria."

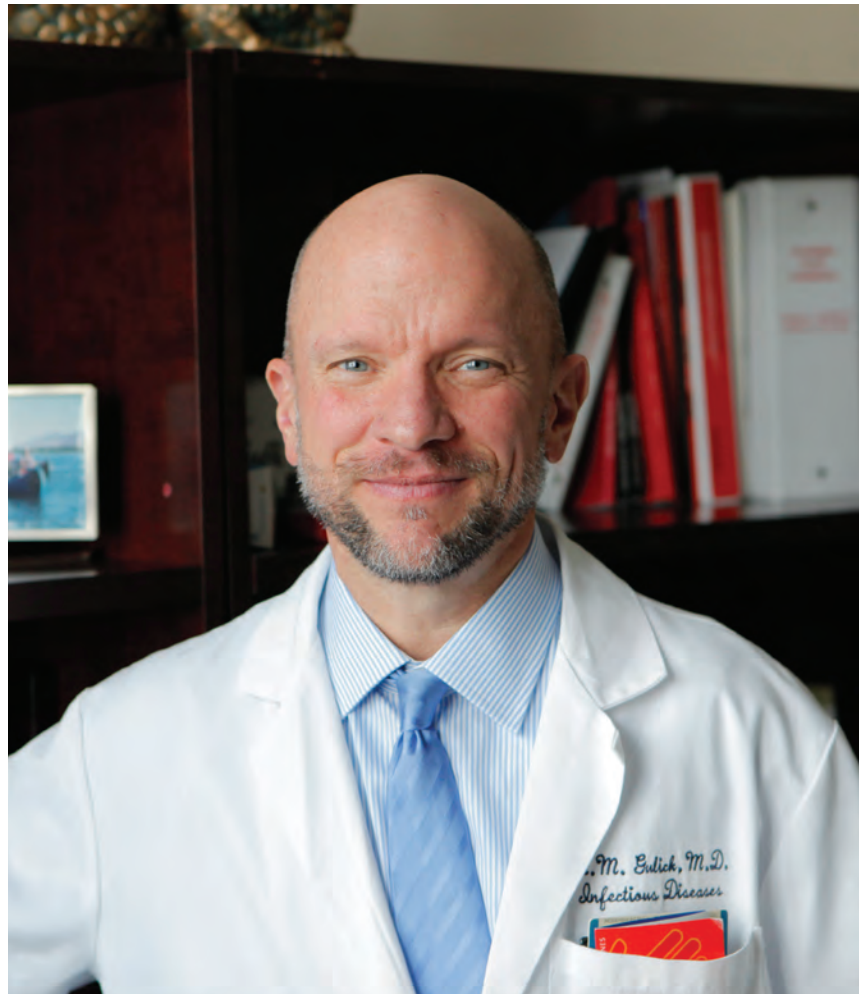
As Nathan points out, while antibiotics are life-saving drugs, they have potentially serious side effects—making it doubly important to avoid prescribing them when they're not needed. By killing off the gut's "good" bacteria, for example, antibiotics can clear the way for *Clostridium difficile*, a potentially fatal gastrointestinal infection (which, as the CDC notes, is seven to ten times more common in people who are on antibiotics or have taken them in the previous month). A key method that Nathan suggests for eliminating unnecessary antibiotic use is the development of rapid point-of-care techniques for diagnosing whether a patient has a bacterial infection in the first place—and if so, what type. That could allow a pediatrician, for instance, to confidently explain to parents that an antibiotic wouldn't help their child. "The problem now is that the practitioner is stuck," Nathan says. "They don't have the tools to tell you, 'It really is a virus.' "

Nathan compares antibiotic resistance to another looming crisis: climate change. In both situations, humans have been profligate in their use of a resource—fossil fuels on the one hand, antibiotics on the other—with potentially calamitous results. But the antibiotic crisis has occurred on a much faster timeline, he says, in part because

it involves a devilishly clever adversary. “Bacteria are intelligent,” says Nathan, a former dean of the Weill Cornell Graduate School of Medical Sciences who also serves as director of the Abby and Howard P. Milstein Program in Chemical Biology and Translational Medicine. “They don’t have brains or a nervous system, but the fact that they can evolve rapidly in response to pressure has the same effect that intelligence has in an individual—that is, the ability to adapt to change and respond accordingly. They can accelerate mutation by exchanging genetic information within and across species; sometimes whole blocks of resistance genes can be exchanged at one time. Remarkably enough, there’s cooperative evolution. So it’s not just like an intelligent being; in effect, it’s like an intelligent society that cooperates in a way that sometimes our own does not seem able to do.”

And, he says, it’s precisely that kind of collaborative effort, on a global scale, that will be required to combat resistance. As he and a co-author explained in an October 2014 article in the *New England Journal of Medicine*—one of Nathan’s numerous publications on the subject—he’s calling for a multi-pronged strategy, including public-private partnerships for drug discovery akin to the Gates Foundation’s TB Drug Accelerator program. (That program, to which Nathan and Rhee were founding signatories, brings together pharmaceutical companies, research institutes, and universities—Cornell included—to develop improved treatments for the disease.) He also advocates worldwide restrictions on antibiotic use in agriculture, as well as the establishment of an international fund that would reward drugmakers not on sales but on quality-adjusted life years saved (a standard way to measure the value of a treatment or the burden of a disease, based on both quality and quantity of time a patient gains or loses). In outlining the stakes, the article quoted a sobering prediction that the WHO had made that spring: “A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the twenty-first century.”

One promising strategy that has already been adopted in the fight against resistance



Roy Gulick, MD

is the establishment of antibiotic stewardship programs, an element of a U.S. national action plan formulated after the 2015 White House summit. In January 2017, the Joint Commission implemented a new medication management standard for hospitals and nursing homes that includes tracking antibiotic use, educating staff and the public about appropriate use of the drugs, and tapping in-house experts who can guide individual doctors’ decisions about what to prescribe. “I like the word ‘stewardship,’ because we’re trying to help clinicians be the most effective when they use antibiotics,” says Gulick. “For example, we have antibiotics that are highly potent against multiple bacteria, but

you don’t need that for a common infection. Sometimes people want the ‘strongest’ drug, so they’ll use something that’s really not necessary. We’re trying to change that culture. Using the right antibiotic for the right amount of time will help us save these drugs for people who really need them.” ■

Nathan is a paid and unpaid scientific advisory board member to various non-profits. He is also a paid scientific advisory board member of the Pfizer Centers for Therapeutic Innovation, which supports early-stage drug discovery at many academic institutions in collaboration with Pfizer, Inc. Satlin is a paid consultant to Shionogi & Co. on matters related to new antimicrobial agents.

Call to Arms

A physician-author sounds the alarm about drug-resistant bacteria—and shares his own experiences on the front lines of treatment



Matt McCarthy, MD

“This was the moment everything changed,” Matt McCarthy, MD, writes of his decision to collaborate on a clinical trial for a promising new antibiotic, “when I went from a passive observer of drug resistance to an active participant in the race to stop the expanding threat of superbugs.” In his latest book, McCarthy—an assistant professor of medicine at WCM and an internist at NewYork-Presbyterian/Weill Cornell—chronicles his efforts to conduct the trial, as well as to treat hospitalized patients who have potentially life-threatening infections. Published in May by an imprint of Penguin Random House, *Superbugs: The Race to Stop an Epidemic* is aimed at a general audience. “It’s for anyone who has ever seen a doctor and wondered how they make decisions,” McCarthy says, “who is interested in the future of medicine and drug development, or who just wonders what life is like inside the halls of a major hospital.”

The book includes a historical tour of infection research and treatment, from the battlefields of World War I to the halls of the NIH. McCarthy contemplates ethical issues in drug testing over the past century, describes the systems that have been put in place to protect patients—such as the

‘I spend most of my waking hours thinking about this issue,’ McCarthy admits, noting that ‘things that were easily treatable with an oral antibiotic a few years ago are now requiring an intravenous antibiotic and hospitalization.’

institutional review boards that oversee research involving human subjects—and offers an impassioned warning about the escalating threat of superbugs that are rapidly outstripping medicine’s ability to combat them. “I spend most of my waking hours thinking about this issue,” McCarthy admits, noting that “things that were easily treatable with an oral antibiotic a few years ago are now requiring an intravenous antibiotic and hospitalization.”

Superbugs is McCarthy’s third book; he has also published *The Real Doctor Will See You Shortly*, a memoir of his intern year. In addition to his nearly fifty peer-reviewed articles in academic journals, he has written for such mainstream publications as *Sports Illustrated*, *The Atlantic*, and *Slate*, and regularly contributes book reviews to *USA Today*. “For me, writing is a tremendous outlet that helps me stave off burn-out,” McCarthy says. “It’s a way to cope with the stresses of the job. It helps me get through the really tough days.”

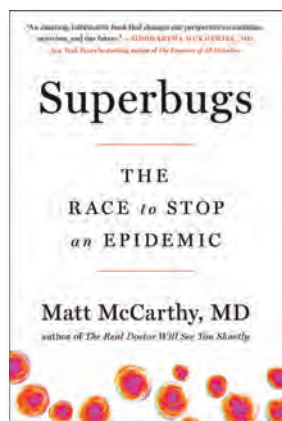
In addition to chronicling the effects of drug-resistant microbes on patients in *Superbugs*, McCarthy describes the rigorous IRB review process that he and his mentor and collaborator—infectious disease expert Thomas Walsh, MD, a professor of medicine in microbiology and immunology and in pediatrics at WCM and an internist at NewYork-Presbyterian/Weill Cornell—underwent before conducting their 2017–18 clinical trial.

The study assessed the efficacy of dalbavancin, an antibiotic developed by the pharmaceutical company Allergan that is aimed at treating infections resistant to other drugs. (McCarthy can’t yet comment on the outcome, other than to say

that he and Walsh were “delighted by the results,” which they’ll present at a major conference this summer.)

The dalbavancin study was the first clinical trial McCarthy had ever led. He found one aspect of the process particularly affecting: the task of recruiting participants. “I suddenly found myself at the bedside of vulnerable patients, asking something of them that they had not anticipated when they walked into the hospital,” he recalls. “I took that responsibility very seriously. Some people would ask me, ‘Would you give this drug to your own mother?’—and that’s a very powerful question.”

PHOTOS: THIS PAGE, NINA SUBIN; OPPOSITE PAGE, SMITHSONIAN INSTITUTION ARCHIVES



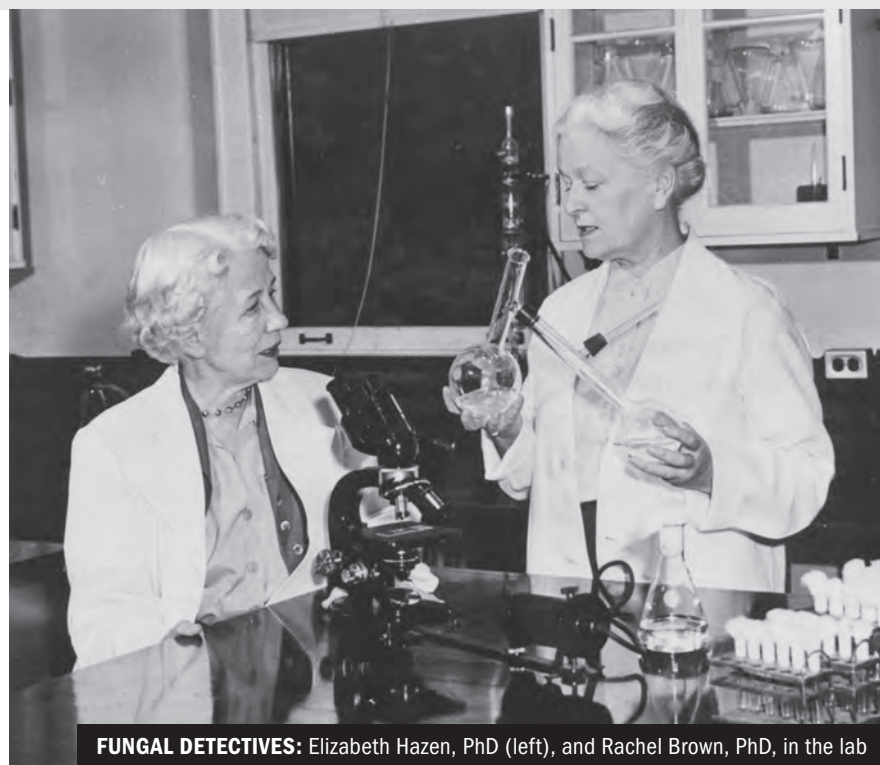
Unsung Heroines

In an excerpt from *Superbugs*, McCarthy recalls two forgotten pioneers of drug discovery

Alexander Fleming's chance discovery of the first antibiotic is enough to spark the imagination of any child with a budding interest in science, but the discovery of the first antifungal drug is equally compelling. It's a story about two brilliant women that has been omitted from most science books, and it's unknown to most of today's young physicians.

Elizabeth Hazen was orphaned when she was just three. She spent the majority of her childhood bouncing around rural Mississippi at the turn of the twentieth century, living first with her grandmother and then with her uncle. After high school, she attended what is now known as the Mississippi University for Women and then moved to New York to study bacteriology at Columbia University. Her studies were interrupted by World War I, during which she served in the Army, but she eventually obtained a doctorate before moving to New York City's Division of Laboratories and Research in 1931.

A dozen years later, during World War II, physicians noticed that penicillin was protecting soldiers from bacterial infections, but many were contracting fungal diseases. There was no cure, and some suspected that Fleming's discovery was actually predisposing the men to the fatal infections. Elizabeth Hazen was tasked with finding a way to treat



FUNGAL DETECTIVES: Elizabeth Hazen, PhD (left), and Rachel Brown, PhD, in the lab

them. In her laboratory, she went about the painstaking project of isolating organisms found in soil samples and testing them against two fungi that were known to infect humans, *Candida albicans* and *Cryptococcus neoformans*. When Hazen had a potential hit, she mailed her samples in a mason jar to a chemist in Albany, New York, named Rachel Brown.

Upstate, Dr. Brown would purify the samples and send the drugs back to Hazen for testing in animals. Their work progressed at a blistering pace, and was made possible by the remarkable efficiency of the U.S. Postal Service. In just a few years, they reviewed thousands of molecules, but almost all the drugs that killed fungi in test tubes turned out to be highly toxic in animals. Finally, after years of searching, one worked. The compound destroyed fungi without harming animals or humans, and, of all places, it had been found in the garden of Hazen's friend, Jessie Nourse. A bacterium in the soil was producing the antifungal drug; Hazen named it after her friend, *Streptomyces noursei*.

The two researchers announced their results at the New York meeting of the National Academy of Sciences in 1950 and immediately attracted interest from Big Pharma, which was entering its golden age. Hazen and Brown

were suddenly rich and, briefly, famous. They invested their millions in a nonprofit that funded more research. They named their fungal drug nystatin, after the New York State Department of Health, and continued to collaborate throughout their lives, discovering two more antibiotics together.

Nystatin has saved countless lives—I prescribe it all the time—and it's even used occasionally to restore damaged artwork. (After a flood in Florence, Italy, curators at Boboli Gardens sprayed nystatin on more than 200 paintings to protect them from mold.) Its effect has been staggering: it is on the World Health Organization's list of essential medicines and is one of the cheapest and most effective products on the market today. But the nystatin story isn't taught to fledgling scientists, medical students, or residents. Forgetting this piece of history speaks to our failure as educators. Everyone knows about Alexander Fleming, but no one knows about Elizabeth Hazen and Rachel Brown.

.....
Reprinted from *SUPERBUGS: THE RACE TO STOP AN EPIDEMIC* by arrangement with Avery, a member of Penguin Group (USA) LLC, A Penguin Random House Company. Copyright © 2019, Matt McCarthy, MD.

NEWS OF MEDICAL
COLLEGE AND GRADUATE
SCHOOL ALUMNI



Dear Alumni,

For the past four years, I have participated in a program at Cornell University that matches physicians with undergraduate students who are considering entering the field of medicine. Twice a year, we sit down with these young adults and speak with them frankly about what we find to be the most rewarding and the most difficult aspects of our careers. Recently, I've been struck by the number of questions the students ask me about how I find work-life balance in such a demanding profession. This is a question that is on so many of our minds these days, as we become more acutely aware of the importance of self-care in a notoriously demanding field. And it's a question that many of us physicians, myself included, don't always know how to answer.

Early in my career, I wasn't sure if I'd ever be able to find work-life balance. I was just starting to practice endocrinology, and my husband was a surgeon working long hours; we had two young kids, and we were exhausted. I remember wondering how we were going to get through it. Thankfully, I was fortunate to have an incredible support system—I had my family and friends, colleagues who were also struggling, and mentors who had been through this earlier in their careers—and survived. I am so grateful for that network of people who encouraged me and helped me to put one foot in front of the other. But unfortunately, many physicians do not have access to such a caring community—or, even worse, feel ashamed and do not ask for help.

It is estimated that 30 to 40 percent of physicians experience burnout—and with varying definitions of the term, the actual rate could be zero to 80 percent. More than half of medical students are already burned out. In fact, there is such a critical need for more information on this topic that on September 18 and 19, Weill Cornell Medicine is hosting the first-ever National Conference on Medical Student Mental Health and Wellbeing to identify innovative ways to foster resilience and wellbeing in our future physicians. (More information can be found at weill.cornell.edu/mentalhealth2019.) As an institution, Weill Cornell is prioritizing wellness for physicians and students. And at the Alumni Association, we too are committed to this charge.

Our many mentoring initiatives include a recently established program that connects new Weill Cornell graduates with senior alumni at their residency institutions—so these young physicians can have additional support during this difficult time. While we already have many successful programs like this one, we are eager to do more. As we work to expand our programs in this area, I encourage you to reach out to us if you have ideas for new and innovative ways in which we can address this challenge. As our healthcare landscape continues to evolve, wellbeing is becoming even more vital.

Now, when the students at Cornell University ask me about how I find work-life balance, I say to them honestly, "It's a challenge, some days more than others. But I am proud of the example I am setting for my two sons, and I love my job. I am committed to making sure I take time for my own self-care—for the sake of myself, my family, and my patients." And I hope that those students who want to become physicians still pursue that path. As many of us know, although it can be incredibly difficult at times, it is well worth it.

*Natasha Leibel, MD '98
President, Weill Cornell Medical College Alumni Association
NL121@columbia.edu*



A DAY TO REMEMBER (from left): Yoon Kang, MD, acting senior associate dean for education, celebrates Match Day with Ngozi Monu, MD '19, Dean Augustine M.K. Choi, MD, and Joshua Adjei, MD '19.

Medical College

1950s

Leon I. Hammer '48, MD '52: "I am now 94 years old. I have practiced psychiatry and psychoanalysis and worked for some time as a child psychiatrist as well. For most of those years I wanted to combine this work with some kind of physical interface with my patients, recalling that throughout history healing involved the 'laying on of hands.' I found that medium in the form of Chinese medicine that I encountered in 1971. I have practiced both, especially Chinese medicine, until recently. I have founded the Dragon Rises College of Oriental Medicine and written seven books (all of which are currently available) and published forty articles. My first book was published in 1990 and the most recent ones this and last year. I love medicine and my work. As a medical intervention, it has been very successful and rewarding and my contribution is now being taught in China."

Jerome Jacobs, MD '56: "Fran and I have moved to Kendal on Hudson, a retirement community in Sleepy Hollow, NY. We like walking in nearby Rockwood Hall Park,

theatre and museums in NYC, and concerts at Tanglewood and at Caramoor, here in Westchester County. It would be delightful to meet classmates at any of these venues. We look forward to celebrating our 63rd wedding anniversary this spring."

Michael H. Stone '54, MD '58: "I published, with co-author Dr. Gary Brucato, a psychologist at Columbia University Irving Medical Center, a book called *The New Evil*, a sequel to my *Anatomy of Evil* (2009). Published by Prometheus Books, it has chapters on cultural changes since the 1960s, serial killers, school shooters, and the serious problems besetting court evaluations in contentious child-custody cases."

Harry G. Preuss, MD '59: "After two years training with Dr. Robert Pitts in physiology, I decided to spend the majority of my time in research. I am still full-time at Georgetown University Medical Center, tenured in four departments. I recently co-authored a paper, 'A Seven-year Longitudinal Trial of the Safety and Efficacy of a Vitamin/Mineral Enhanced Plant-sourced Calcium Supplement,' that received

the Ragus Award for the year's best research paper in the *Journal of the American College of Nutrition*. I won the same award ten years ago for showing that cinnamon decreases elevated blood pressure. At present, I have over 500 medical publications, of which 270 are peer-reviewed research articles, and am now co-editing my 15th book, tentatively entitled *Dietary Sugars, Salt, and Fats*. This has committed me to write six chapters. Present research deals with diet, insulin resistance, and their effects on metabolic syndrome, non-alcoholic fatty liver disease, and aging in non-diabetics. I believe my recent studies and prior papers will significantly alter how we evaluate current acceptable values of normal blood glucose."

James E. Shepard, MD '59: "In February, I testified in a case going back ten years in Edmonton. I am reminded that my first patient contact was at the then-Cornell division at Bellevue Hospital. On the way into the doctors' entrance to the hospital someone had written on the wall in crayon: 'The way to stay out of trouble... is to stay out of trouble.'"

'We had such a fabulous time at our last Weill Cornell Medicine reunion in October 2018 and plan to get together in a couple of years. New York is such a sophisticated and interesting city.'

— Ron Rankin, MD '68

1960s

Allen J. Togut, MD '60: "I am working as a volunteer in hospice and in palliative care and ethics in a hospital setting."

Jack Bagdade, MD '62: "I'm doing endocrinology six days per month at the Lane County Community Health Clinics serving the underserved, writing medical opinions for a lawyer who represents veterans seeking benefits for ailments related to their service in Vietnam and exposure to the herbicide Agent Orange, and publishing an occasional article in the lipoprotein literature."

George H. McCracken, MD '62: "In October, I received a lifetime achievement award from the Pediatric Infectious Diseases

Society of America 'in recognition of outstanding contributions to the field of pediatric infectious diseases.' And in November, I received the Mead Johnson Pediatric Lifetime Achievement Award 'in recognition of a lifetime of commitment to the health of children.'"

Stuart E. Wunsch, MD '63: "Did you know that on OB when I was a student, three residents were Fear, Hazzard, and Risk? True."

Tony Middleton, MD '66: "I'm on the faculty at the University of Utah College of Medicine in the Division of Urology. After hours, I play doubles tennis and full-court basketball three times a week. I'm still playing in a string quartet that started in our Boston/Harvard days. I volunteer at a homeless shelter in Salt Lake City. Recently, I published my autobiography, *A Wonderful Journey! The Autobiography of Anthony W. Middleton*, which is available in paperback through Amazon. I've tried to make it a fun read. Among other things, it speaks to our time together at Weill Cornell Medicine, and Medical College graduates might enjoy sharing the memories. It also speaks of my journey in medicine locally and nationally, as well as our adventures non-medically. The thing I remember most from medical school is Aaron guarding Olin Hall, while being asleep most of the time. I'd like to hear from **Mike Dosik '62, MD '66.**"

John Q. Stauffer, MD '66, is retired and living half the year in Basalt, CO, and the other half in Tampa, FL. His hobbies include painting, investing, reading, and enjoying his six grandchildren.

David Tucker, MD '66: "I am happy to report that my wife, Lynda, and I are well and still very active. As I've previously mentioned, my memoir, *The Hard Bargain*, was published in 2018 and has received some very positive reviews. It is a father-son saga about how my dad encouraged me forcefully to take a medical career path. You can learn more from my website, thehardbargainbook.com. I have also done many program events about my father's operatic legacy to enthusiastic audiences around the country. I am thrilled to be doing a Richard Tucker Program at Lincoln Center at the Metropolitan Opera Guild this coming May 14. It's so nostalgic to talk about my father's career at his second home in NYC. For those interested, check out the Met Guild's website. More importantly, my wife, who originally trained at the Cornell Nursing School



THE ENVELOPE, PLEASE: Connie Lu, MD '19, moments before learning her residency match

RESIDENCY BOUND:

Wesley Rogers, MD '19 (left), and Stephanie Chen, MD '19, proudly display their match letters.



and has been a hospice nurse for close to 40 years, has just helped to build a residence specifically for terminal care in Stamford, CT. It's a great accomplishment for her dream to provide this service to the community of Fairfield County."

Ron Rankin, MD '68: "We had such a fabulous time at our last Weill Cornell Medicine reunion in October 2018 and plan to get together in a couple of years. New York is such a sophisticated and interesting city."

1970s

Eric Thomas, MD '70: "I just added superficial radiation therapy to my practice as an alternative to surgery for non-melanoma skin cancer and for keloid therapy. I absolutely love adding new things to the office, although I did have a variation of this a few years ago. This one is much better, and, best of all, this time I added a radiation tech to do the day-to-day treatments."

Frank Bia, MD '71: "Although I'm an emeritus at Yale Med, I'm still precepting Yale residents at a federally qualified health center in New Haven and attend with **Peggy Johnson Bia, MD '72**, on the medicine teams. We both still precept Yale students in free clinics for the underserved. Trying to pass on

what Eliot Hochstein taught us all before he took leave. Peggy just turned emerita after 40 years in transplant nephrology. In 2018, she received a lifetime achievement award from the National Kidney Foundation. Jesse, our oldest, received his PhD in anthropology from University College London, and Joshua is in his fourth year at the Netter School of Medicine, Quinnipiac University."

Richard Lynn, MD '71, was selected by the Society for Vascular Surgery (SVS) to receive the inaugural SVS Excellence in Community Service Award for his commitment to increase awareness of the vascular profession through state societies and mission trips in the Caribbean and South America, along with his service to the SVS and its members. The Florida Vascular Surgery Society and the Florida chapter of the American College of Surgeons have especially benefitted from his expertise and leadership, allowing them to advance their missions and strategic initiatives. The award will be presented at the Vascular Annual Meeting in June.

Allan Gibofsky, MD '73, was named a lifetime member of the American Association for the Advancement of Science.

Jon A. Perlman, MD '73, associate clinical professor of plastic surgery at UCLA, retired as of January 2019 after practicing

plastic and aesthetic surgery in Beverly Hills since 1980. Dr. Perlman was seen on ABC TV's "Extreme Makeover," where he performed 40 surgical procedures between 2003 and 2006. He is the father of Jessica, 28, and Justin, 13, and enjoys hiking, fitness, and nutrition and bicycle and motorcycle riding throughout the canyons and mountains of Southern California.

Robert J. Quinet, MD '74, is program director of the rheumatology fellowship and the retired chair of rheumatology at Ochsner Medical Center in New Orleans. His wife, Mary, is the social studies chair at St. Martin's Episcopal School.

Warrick Barrett, MD '75: "2018 was a wonderful year. Each of my sons and daughters-in-law welcomed a daughter into the world. Each of my three children now has children of their own, and I now have a total of two grand-

sons and three granddaughters. I am most grateful! I hope to enjoy more years such as 2018."

Robert Friedman, MD '76: "I'm still working in Charleston, SC. Daughter Jena is the 'most famous comedian you have never heard of.' Daughter Dora is working for Sun Life in San Francisco. Best wishes to all."

Suzanne M. de la Monte, MD '77, is a professor of pathology, neurology, and neurosurgery at Alpert Medical School of Brown University. She was appointed chief of pathology and laboratory medicine at the Providence VA Medical Center in July 2018. At the 2018 meeting of the American Association of Neuropathologists, she received the D'Armond Award and gave the keynote lecture. She is a member of the Neurotoxicology and Alcohol Study Section of NIH.



CONGRATULATIONS: Max Morin '21 (left) embraces Lauren Tufts, MD '19, after she learns her residency match.



THE BIG MOMENT: Class of '19 members including (from left) Zhenzhen Shi, Yunan Nie, and Timothy Kim retrieve their residency letters on Match Day.

1980s

Rochelle Peck, MD '80: "I'm retired from ophthalmology practice and loving retirement. I'm still in NYC; I have an 8-month-old grandson living with my daughter and her husband in San Francisco and a second daughter, newly married, in Detroit. Enjoying lots of travel, taking courses, seeing lots of theater, and visiting museums. Too little time! Looking for fellow alumni who like to ski or travel to adventurous places."

Leona Chen, MD '81: "A group of us from the Class of 1981 (**Joel Solomon, Neil Rosenthal, Mike Robbins, Sam Spigelman**, and myself along with our significant others) get together monthly for dinners and yearly for a group trip. We are proud to say that we have been thrown out of some of the nicest places in NYC!"

Jonathan Javitt, MD '82: "After a 30-year career in ophthalmology, public health, and public service, I was sufficiently captured by my brother Daniel's discoveries in the role of NMDA antagonists for treating suicidal depression that I joined with him to found

NeuroRx, a clinical-stage biotechnology company. My decision was driven by the suicide of Mitchell Max, whom many of us remember as **Fred Plum [MD '47]**'s chief resident in neurology and then **Kathy Foley [MD '69]**'s fellow in pain management at Memorial. We are entering phase 3 for our first drug, NRX-101, under an FDA Special Protocol Agreement and hope to file for approval of a lifesaving drug for patients whose only currently approved treatment is ECT by 2020. The Javitt family has not abandoned ophthalmology, however. Matthew Javitt has taken a break from the fourth year of medical school to spend a research year at the Bascom Palmer Eye Institute in Miami."

David Brams, MD '87, was recently named chairman of the Division of General Surgery at Lahey Hospital and Medical Center, where he has worked since 1996.

Theresa Rohr-Kirchgraber, MD '88: "**Paul Kirchgraber, MD '88**, and I are in Indianapolis, though our children have moved on. We are looking forward to meeting our granddaughter when she arrives in May. Paul keeps busy bringing new drugs to market as

'I'm retired from ophthalmology practice and loving retirement. Enjoying lots of travel, taking courses, seeing lots of theater, and visiting museums. Too little time!'

— Rochelle Peck, MD '80

'We recently visited the campus with our 13-year-old daughter, Ella, and could not believe how much it has been developed. We love Weill Cornell and wish the best for our fellow alumni.'

— Erin E. Kershaw, MD '97

the vice president and global general manager of Covance Central Labs. He seems to enjoy traveling while I enjoy using his miles for vacations. Working on bringing sex and gender into every discussion and lecture about medicine and disease—my current positions allow me many opportunities to do this. Will be in NYC for the upcoming American Medical Women's Association annual meeting and look forward to seeing some of you there."

1990s

Daniel B. Jones '86, MD '90, is a professor of surgery at Harvard Medical School and vice chair of surgery and of the Office of Technology and Innovation, as well as chief of minimally invasive surgery, at Beth Israel Deaconess Medical Center. He is the series editor of the *Atlas of Robotic Surgery*.

Cynthia Fray McNamara, MD '91, is an assistant professor of clinical medicine at Yale University School of Medicine and an internist in the Veterans Administration Hospital Connecticut Healthcare System. She is honored to provide primary care for our country's veterans

and to teach trainees in clinical medicine, global health, and cross-cultural issues. The mother of four biological children, she has also been a guardian and mentor for two refugee boys from Burundi who were displaced after the Rwandan genocide and came to the US with their family as adolescents. She has received two Yale/Stanford Johnson & Johnson Global Health Scholar awards to serve as a teaching physician in Uganda and Rwanda and has also worked providing primary care in areas of Central America.

Erin E. Kershaw, MD '97: "I am currently serving as chief of the Division of Endocrinology at the University of Pittsburgh. I remain happily married to my husband, Dave Demoise, who also works at the University of Pittsburgh Medical Center in the Division of General Internal Medicine. We both completed our residencies in internal medicine at NewYork-Presbyterian/Weill Cornell in 2000. We recently visited the campus with our 13-year-old daughter, Ella, and could not believe how much it has been developed. We love Weill Cornell and wish the best for our fellow alumni."



SEVEN FUTURE DOCTORS: Class of '19 grads Micha Thompson, Kelsey Young, Elizabeth Gilbert, Cara Berkowitz, Lisle Winston, Lindsay Mandel, and Emily Lebowitz on Match Day



THE NEXT STEP: Katherine Li, MD '19 (center), is all smiles on Match Day, along with her boyfriend (left) and classmate Aditi Gupta, MD '19.

2000s

Jian Shen, PhD '99, MD '02: "I published three clinical papers on endoscopic spine surgery in 2018."

Demetris Delos, MD '06, is in private practice with Orthopaedic and Neurosurgery Specialists in Greenwich, CT. He resides in Greenwich with his wife and four children.

2010s

Erica Greenberg, MD '10: "I became director of the Pediatric Psychiatry OCD and Tic Disorders Program at Massachusetts General Hospital in Boston, MA, in July 2018."

Charles K. Vorkas, MD '11, joined the faculty of the Division of Infectious Diseases at Weill Cornell Medicine and successfully competed for a K08 award to study the innate immunology of tuberculosis.

Blossom P. Samuels, MD '13: "After receiving my medical degree from Weill Cornell, I decided to remain for residency in physical medicine and rehabilitation. After graduating, a special interest in bone health led me to join the metabolic bone disease fellowship at Hospital for Special Surgery,

where my skill set broadened to encompass treating osteoporosis and providing non-operative management for pelvic, vertebral, and stress fractures, among other bone conditions. Today, I am an assistant professor of rehabilitation and regenerative medicine at Columbia University Irving Medical Center, providing comprehensive bone care at New York's Regional Bone Center located at Helen Hayes Hospital. I am enjoying a recent appointment as principal investigator for the New York State Osteoporosis Prevention and Education Program, through which I will be helping to prevent fractures and promote skeletal wellness for patients statewide through education and outreach."

Jessica Clemons, MD '15, a psychiatric resident at NYU Langone Medical Center, has more than 50,000 followers on her @AskDrJess Instagram profile. She shares personal stories and inspirational quotes, as well as a weekly live stream where she answers viewers' questions. She writes: "I had this idea to try to normalize conversations about mental health. It came out of my own feelings of not being able to really do the work in psychiatry the way that I felt strongly committed to, which is supporting communities of color."

Graduate School of Medical Sciences

Thomas P. Hopp, PhD '77: "I have been consulting with a biotechnology company, Metrodora, that is about to launch a clinical trial in Australia of a new bacterial vaginosis treatment based on the immunomodulating protein lactoferrin. I also write novels, and will launch my latest thriller, *The Great Seattle Earthquake*, this spring, as a sequel to *Rainier Erupts!*, which was my best selling novel to date, published in 2016."

Vladimir Drozdoff, PhD '88, is chief patent counsel at Cold Spring Harbor Laboratory and works in business development and technology transfer.

Lore vonHoffen, PA '88: "I'm celebrating 25 years at NYU Winthrop Hospital in Mineola, NY, as well as a new promotion to PA/NP educator in the Department of Surgery. This is my second year as director of our surgical summer internship shadow program at NYU Winthrop. I'm taking my final certification exam before retirement. Congratulations to this year's graduates as they enter a gratifying, fulfilling career as a professional healthcare practitioner."

Chad May, PhD '01, was recently promoted to senior vice president of research and development at Maverick Therapeutics, where he has been working the past two years. Previously, he spent seven years at Pfizer working on immunotherapy treatments. He lives in the Bay Area.

Gianina Panaghie Meltzer, PhD '06, is an associate director for global regulatory strategy at Bristol Meyers Squibb. She lives in New Jersey.

Brad Chernock, PA '10, a fourth-year medical student at Rutgers New Jersey Medical School, and his sister were featured in the online publication *New Jersey Stage* for coordinating a three-day exhibit at Sotheby's in New York City in February. The exhibit, "The Art of Choice," featured work by artists who reside at the Matheny Medical and Educational Center, a hospital and educational facility for children and adults with developmental disabilities.

Kathryn Bambino, PhD '14, is a senior scientist for science communication at the Estee Lauder Companies.

Iva Dincheva, PhD '14, is a full-time technical specialist in the intellectual property department at WilmerHale. This fall, she will begin Fordham Law School to become an intellectual property lawyer.

Hui "Heather" He '11, PA '14, is a physician assistant at Stanford Health Care. She coordinates care for patients with benign and malignant breast diseases as part of an interdisciplinary team including breast surgeons, medical oncologists, radiation oncologists, plastic surgeons, and genetic counselors. She bridges care plans between breast surgeons and plastic surgeons to marry disease treatment and reconstruction. She also helps empower women to feel whole again after breast disease and reconstruction by providing 3D nipple areolar tattooing.

Alexandra Kreins, PhD '14, completed her pediatric residency in Zürich, Switzerland, and was recently appointed a clinical research fellow in thymus transplantation at Great Ormond Street Hospital in London, England.

Ralitsa Petrova, PhD '14, is a Larry L. Hillblom Foundation Postdoctoral Fellow at the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF.

Matthew Sung, PhD '14, is a principal scientist in oncology R&D at Pfizer.

Rob Frawley, PhD '16, is working in the education lab at the Columbia Zuckerman Institute, teaching K-12 students in a hands-on science setting through a nonprofit called BioBus. His role is as a teacher and student-facing scientist conducting ongoing research in environmental science, biodiversity, and chemistry. In his free time, he enjoys coaching the swim team at the New York Athletic Club.

Christy Tzu-yun Kuo, PhD '17, is a senior scientist in functional genomics at Pfizer Oncology.

Adam Horn, MS '18, is a business analyst at Ready Computing and lives in NYC.

During her doctoral studies in computational biology, **Tamar Melman, PhD '18,** developed improved statistical methods for EEG signal processing, with the aim of better understanding the conditions of severely brain injured patients. She now works as a data scientist at ClimaCell in the Boston area.

'I'm taking my final certification exam before retirement. Congratulations to this year's graduates as they enter a gratifying, fulfilling career as a professional healthcare practitioner.'

— Lore vonHoffen, PA '88

'47 MD—Lester J. Schnell of Garden City, NY, November 1, 2018; obstetrician/gynecologist; practiced at Nassau Hospital (now Winthrop Hospital); captain, US Navy and US Air Force; served as a physician on the island of Saipan; sports fan; enjoyed bridge, gardening, golf, tennis, reading, swimming, classic cars and boats, and theater; active in community and professional affairs.

'51 MD—Allan M. Levy of Woodcliff Lake, NJ, April 8, 2018; chief of sports medicine, Pascack Valley Hospital; team doctor of the New York Giants; also worked as a family physician; US Navy medic; volunteered with the Living Heart Foundation, which helps former sport team players; active in community and professional affairs.

'47 BA, '52 MD—Gerald S. Barad of Flemington, NJ, January 16, 2016; obstetrician/gynecologist; chairman of obstetrics and gynecology at Hunterdon Medical Center; advocate for sex education and family-centered childbirth; US Army Medical Corps veteran; co-wrote a book for expectant parents with Lamaze pioneer Elisabeth Bing; horticulturist; member of the Philadelphia Cactus and Succulent Society; active in community and professional affairs.

'53 MD—Earnest M. Curtis Jr. of Atlanta, GA, November 27, 2016; leader in developing minimally invasive surgery; helped establish Kaiser Permanente in Georgia; retired from Emory University; veteran; author; photographer; painter; active in community and professional affairs.

'56 MD—Ramon R. Joseph of Sun City West, AZ, February 17, 2016; gastroenterologist, Henry Ford Medical Center; professor of medicine, University of Michigan; chief of medicine, Wayne County General Hospital; established free clinics for indigent patients; author; enjoyed ballroom dancing, gourmet cooking, singing, and acting; active in professional affairs.

'60 MD—Joseph C. Dougherty of Harlingen, TX, January 1, 2017; medical director of the Watson W. Wise Memorial Hemodialysis Center and the Valley Diagnostic Medical and Surgical Clinic; also practiced at Scranton State Hospital, Mercy Hospital, Audie L. Murphy

Memorial VA Hospital, Bexar County Teaching Hospital, and Montefiore Hospital; veteran; flight surgeon; active in professional affairs.

'61 MD—Robert F. Lindberg of Ketchum, ID, April 30, 2013; orthopaedic surgeon, Sun Valley Orthopaedic Clinic; also practiced in the Straub Clinic & Hospital, Honolulu; US Army surgeon in Vietnam; enjoyed chess, classical music, literature, hiking, running, backpacking, sailing, skiing, rollerblading, choir singing, and horseback riding; active in community and professional affairs.

'61 MD—James E. Standefer of Marine on St. Croix, MN, December 28, 2018; ophthalmologist; founder, Associated Eye; clinical professor of ophthalmology at the University of Minnesota; US Navy flight surgeon; performed cataract surgery, treated glaucoma, and taught others to perform procedures in more than 31 developing countries; recognized with the International Blindness Prevention Award from the American Academy of Ophthalmology; enjoyed collecting Asian art, beekeeping, bird watching, gardening, scuba diving, rowing, cross-country skiing, and bicycle racing; active in community and professional affairs.

'60 BA, '64 MD—Peter D. Tyler of Kalispell, MT, October 23, 2018; orthopaedic surgeon; founded the Center for Bone and Joint Disease in New Port Richey, FL; chief of staff, Community Hospital, New Port Richey, FL; battalion surgeon and paratrooper, US Army; pilot; scuba diver; marathon runner; traveler; historian; avid reader; active in community and professional affairs. Phi Delta Theta.

'67 MD—Delbert G. Ririe of Provo, UT, December 29, 2018; retired ophthalmologist;

practiced at the Eye Clinic of Provo; veteran; president, Utah Ophthalmology Society; instrumental in starting the Covey Center for the Arts; enjoyed classical music, gardening, woodworking, raising orchids, astronomy, sailing, model building, and reading; active in community, professional, and religious affairs.

'68 MD—J. Patrick Rooney of Stockton, CA, November 9, 2015; cardiothoracic surgeon; US Navy veteran; sports fan; active in professional affairs.

'69 MD—Robert S. Modlinger of Cranford, NJ, July 23, 2018; chief of hypertension, VA Hospital, East Orange, NJ; assistant clinical professor of medicine, University of Medicine and Dentistry of New Jersey; chief of endocrinology, Mountainside Hospital; author; active in professional affairs.

'72 MD—Daniel L. Leary Jr. of Newburyport, MA, July 6, 2018; cardiologist and internal medicine specialist; president of the medical staff, Anna Jaques Hospital; Marine captain; Vietnam veteran; foreman on an archeological expedition in search of early man; World War II history buff; outdoorsman; mountain climber; skydiver; bungee jumper; author; worked on oil rigs and cattle ranches in his youth; active in community and professional affairs.

'75 MD—John W. Stakes III of Winchester, MA, October 16, 2018; neurologist, director of specialty care and development, director of the sleep lab, and senior adviser and physician director of network development integration at Massachusetts General Hospital; taught at Harvard Medical School; sailor; active in professional affairs.

We want to hear from you!

Share your news with your classmates

Email Chris Furst:
cf33@cornell.edu

Send by mail to:
Weill Cornell Medicine
401 East State Street
Suite 301
Ithaca, NY 14850

Write a letter to the editor

Weill Cornell Medicine welcomes comments and correspondence from readers. Letters may be edited for length, clarity, and civility. We may not be able to publish all correspondence received, but we would like to hear from you. Please write to: wcm@med.cornell.edu.

Follow us on:



Nothing Up His Sleeve

Northwestern professor Ricardo Rosenkranz, MD '90, taps his passion for magic to help his students become better doctors



SEEING IS BELIEVING: Rosenkranz attired for his magic act (left) and (at left in above photo) working with a student

Ricardo Rosenkranz, MD '90, is a successful professional magician—but one of his greatest feats is giving medical students valuable insights into the doctor-patient relationship. For the past decade, Rosenkranz—a neonatologist and assistant professor of clinical pediatrics at Northwestern University Feinberg School of Medicine—has tapped his prestidigitation skills to teach a course he designed entitled *Medicine and Magic*. Offered to first- and second-years and fulfilling a humanities requirement, the five-week course features Rosenkranz and fellow (non-physician) magicians performing illusions that underscore various concepts related to medical practice, from empowering people to navigate the healthcare system to establishing a relationship with a new patient.

During one particularly memorable lecture, a guest magician performs a “mind reading” act, and Rosenkranz uses the students’ reactions as a window into how beliefs are formed. “After the applause, I ask how many of them believe he could actually read their mind,” he says, “and invariably over 50 percent of the class raises their hands.” As he goes on to explain, in a time when medicine has increased in complexity, patient beliefs and perceptions truly matter; it’s vital for future doctors to understand how beliefs are formed, so they can communicate with patients effectively. Says Rosenkranz: “For these students to go through an experience as meaningful as suddenly believing that somebody can read their mind—it’s a very powerful moment for them.”

Rosenkranz discovered his love of magic in the late Nineties, after he wandered into a magic shop in his native Mexico City and was inspired to learn a few tricks. He has gone on to establish a thriving part-time career, performing his one-man show, *The Rosenkranz Mysteries: Physician Magician*, across the U.S.; he has appeared at Los Angeles’s legendary Magic Castle and been featured on TV shows like “Penn & Teller: Fool Us.” In one of his signature illusions, Rosenkranz has individual audience members hold a box of alphabet blocks and think of the place they’d most like to go; he tells

them that they have the power to rearrange the blocks with their mind—and when they open the box, they’re astounded to find the name of their dream destination spelled out. “I’m very proud of that number, which is about empowerment,” says Rosenkranz, who also impresses on his medical students the importance of encouraging patients to educate themselves about their own conditions and to advocate for themselves within the healthcare system. “If a doctor isn’t able to empower his patients, he fails.”

As Rosenkranz sees it, his two passions have a surprising amount in common. “The history of magic and medicine is connected, anthropologically speaking,” he explains. “The very first physicians and healers were shamans, and shamans were also entertainers and magicians.” Today, he says, successful magicians and physicians share some fundamental skills, such as the ability to relate to and

During one particularly memorable lecture, a guest magician performs a ‘mind reading’ act, and Rosenkranz uses the students’ reactions as a window into how beliefs are formed.

engage with people. “In magic, it’s all about the audience members’ experience,” he observes. “Hospitals and other organizations are very interested in understanding the patient experience—they’re looking more and more at patient satisfaction—and this is what we performers do.”

At the end of Rosenkranz’s course, students are given a choice: they can write a fifteen-page paper on a topic relating to the connection between medicine and magic, or they can put their own magical skills to the test by developing a trick that they perform in a show for their peers. “In ten years,” Rosenkranz says, “I’m happy to say that no one has ever written the essay.” ■

— Alexandra Bond

PHOTOS: PROVIDED

A Legacy Gift Inspired by a Special Bond

“Psychiatry has completely changed my life,” says Brooks Betts, at left. To honor her longtime Weill Cornell Medicine psychiatrist, Judith Tanenbaum, MD '88, at right, and to support the careers of future psychiatrists, Ms. Betts created a bequest in her will to establish the endowed Betts Tanenbaum Chair in Clinical Psychiatry at Weill Cornell Medicine.



**What will your legacy be?
We can help.**

Contact our planned giving specialists at (646) 962-9567 or at plannedgiving@med.cornell.edu.



Weill Cornell Medicine

give.weill.cornell.edu/planned-giving

Weill Cornell Medicine
1300 York Avenue, Box 144
New York, NY 10065

PRSR STD
US Postage
PAID
Permit 302
Burl., VT. 05401



Take a look at our digital version!

iPad, iPhone, and Android apps too.



www.weillcornellmedicine-digital.com