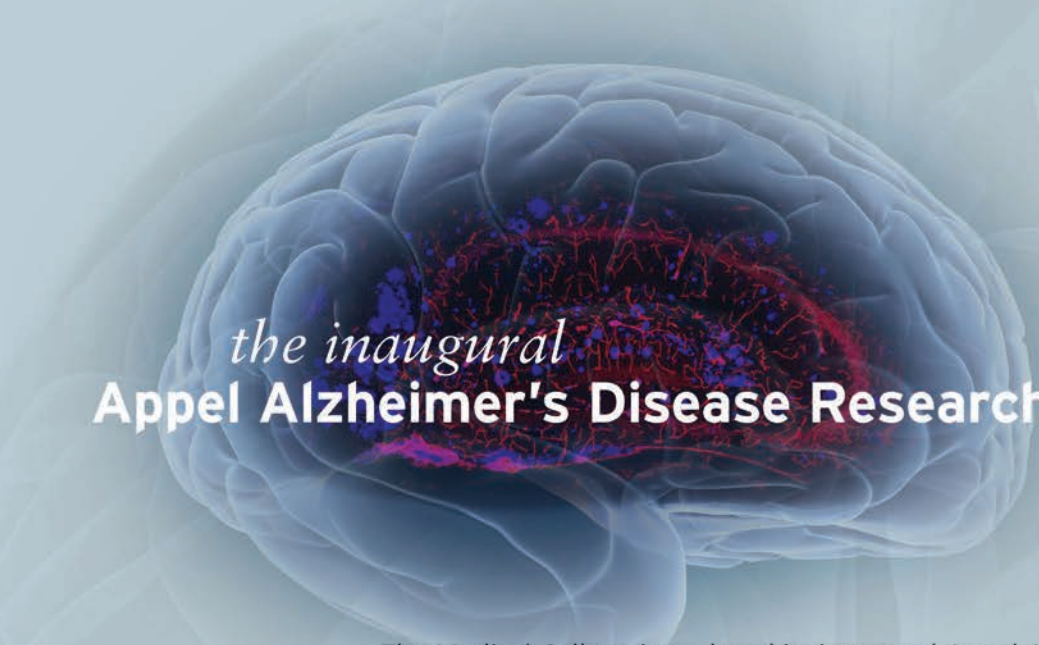
weillcornellmedicine

THE MAGAZINE OF
WEILL CORNELL
MEDICAL COLLEGE AND
WEILL CORNELL
GRADUATE SCHOOL OF
MEDICAL SCIENCES

WINTER 2013

Looking Up

In Tanzania, WCMC helps local staff improve burn care



the inaugural Appel Alzheimer's Disease Research Institute Symposium

The Medical College introduced its inaugural Appel Alzheimer's Disease Research Institute Symposium on November 1, 2012. Established in 2006 by a $15 million gift from Overseer Bob Appel and his wife, Helen, the Institute is the first of its kind, and the Appels, longtime friends and supporters of Weill Cornell, were delighted to attend the symposium.

Greeted by the director of the Institute, Steven M. Paul, MD, Burton P. and Judith B. Resnick Distinguished Professor of Neurodegenerative Diseases, over 200 attendees were educated on genetic risk factors, new treatments, prevention research, and more. Dr. Paul also presented, in addition to speakers including Costantino Iadecola, MD, the Anne Parrish Titzell Professor of Neurology and Professor of Neuroscience; Gregory Petsko, DPhil, Professor of Neuroscience; and Norman Relkin, MD, PhD, Associate Professor of Clinical Neurology and Neuroscience. The symposium concluded with a panel discussion led by Matthew E. Fink, MD, Professor and Chairman of the Department of Neurology and Neuroscience.

A dedicated institute for **Alzheimer's research is one of the most important investments we can make for our health,** and that of future generations.

The event culminated with a lively question-and-answer session, allowing guests the opportunity to learn more about developing research and treatments for the disease, which has been predicted to be one of the world's most threatening global health crises as people live longer and baby boomers move into high-risk ages. This is why a dedicated institute for Alzheimer's research is one of the most important investments we can make for our health, and that of future generations.

To learn more about how you can support research on neurodegenerative disease and related disorders, **please contact Lucille Ferraro, Campaign Director, at (646) 317-7387 or luf2003@med.cornell.edu.**

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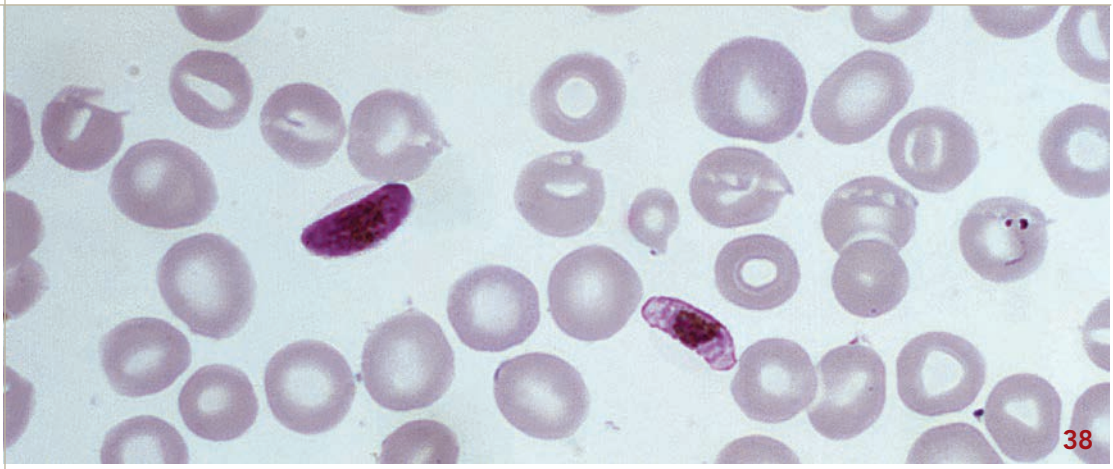

38

26

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FEATURES

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JOHN ABBOTT

12

Shahin Rafii, MD

DEPARTMENTS

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An Auspicious Beginning

Laurie H. Glimcher, MD,
Dean of the Medical College

Robert Browning said that you should measure the height of a person's mind by the length of the shadow it casts. The measure of a community, therefore, is how well it enriches the lives of all its members—and I have learned over the last year that, in this way and so many others, Weill Cornell is truly remarkable.

I assumed the deanship a year ago, drawn by a passion to make a great medical college even greater. As I said at the time, our country's health-care system is at a watershed moment, and academic medical centers face formidable challenges. But challenges bring opportunities—and Weill Cornell has the potential to lead the way in solving the most complex problems in health care today. In my first months, I laid out my vision for our College: to become among the world's best in each element of our tripartite mission—research, education, and clinical care—while holding patient care at the center of everything we do.

Since then, we at Weill Cornell have begun to execute a strategy to take our institution to new heights, building on a pioneering attitude in discovery and translational research and a culture of cooperation, collaboration, and transparency. We have sought new partnerships with other universities and medical colleges; begun revising our curriculum; worked to enrich the faculty experience; launched a robust effort to attract the finest scientific minds to strengthen our research enterprise. This list represents just a small fraction of what we have accomplished so far—and it only hints at the achievements to come.

For more than a century, the Medical College has demonstrated excellence in education, research, medicine, and patient care—and its star is on the rise. One measure of that, as I am proud to report, is that this year's incoming medical class had the highest mean GPA in the College's history. These talented future physicians and researchers will build on Weill Cornell's remarkable history; with our faculty's guidance, they will truly bend the curve in academic medicine for the twenty-first century.

LISA BERG

Last fall, I was delighted to celebrate Reunion and meet many Medical College alumni. It's thrilling to imagine, when our current students return to campus decades from now, what great things our institution will have achieved.

At Weill Cornell, we are united in the common cause of improving the health and well-being of all—bringing hope to patients and their families. As my son told me when I asked him why he had decided to switch from law to medicine: "Because I want to do something where I never have to wonder why I do it." At Weill Cornell—and in medicine at large—we are deeply fortunate to do some of the most meaningful work imaginable.

Alumni Reunion:
A Weekend of Reconnection and Education

This year's alumni reunion brought in over 400 alumni and guests from around the country on October 19-20, 2012. Alumni were treated to an event-filled weekend and the chance to revisit the campus where their careers in medicine first blossomed. Presentations were given by Dean Glimcher, Everest mountaineer Richard B. Birrer, MD '75, and Anthony S. Fauci, MD '66, Director of the National Institute for Allergy and Infectious Diseases, among many others. David J. Skorton, MD, President of Cornell University, moderated a panel discussion on cross-campus research initiatives, and Special Achievement Awards were given to four alumni, all of whom gave lectures over the weekend. In recognition of their generosity and dedication, the Alumni Association formally recognized Joan and Sandy Weill, Chairman of the Board of Overseers, with the inaugural Distinguished Fellowship award.

This was the last reunion for the current president of the association, Michael Alexiades, MD '83, whose two-year term has ended.

"Although my term as President of the Weill Cornell Medical College Alumni Association has come to an end, I look forward to remaining active in the organization under its new and very capable leadership," said Dr. Alexiades.

Alumni also had many opportunities to network, including guided tours of the Medical College showing the Clinical Skills Center, Anatomy Lab, and Weill Education Center; a cocktail reception at the Weill Greenberg Center; class dinners arranged by class leaders; and a women's networking breakfast at the Griffis Faculty Club. The weekend culminated with a reunion "picnic" lunch at the Olin Hall Gym, followed in the evening by a gala with dinner and dancing at Cipriani 42nd Street.

"As dean, it's always a treat to meet alumni and to hear about the great things they're doing," said Dean Glimcher about the weekend. "It's incredibly rewarding to know that our institution has done so much for the future of medicine, and will continue to do so."

Our alumni are among our most valued supporters; their tie to Weill Cornell makes their gifts that much more meaningful. To learn more about alumni events, contact Clara Cullen, Director of Alumni Relations and Giving, at (646) 317-7412.

Clockwise from top left:

WCMC Alumni Association outgoing president Michael M. Alexiades, MD '83, Dean Glimcher, and incoming president R. Ernest Sosa, MD '78, right, present Joan and Sandy Weill with the inaugural "Distinguished Fellowship" award.

Dean Glimcher takes time to speak with 50th Reunion alumni Bryant Barnard, MD '62, and William T. Stubenbord, MD '62.

Friends from the Class of 1986 reunite.

Leonard N. Girardi, MD '89, O. Wayne Isom Professor of Cardiothoracic Surgery, speaks about his cross-campus research on replacement aortic valves. Dr. Girardi participated in a panel moderated by Cornell University President David Skorton, MD.

Martin S. Wolfe, MD '61, Dr. Henry Kissinger, former Secretary of State, and R.A. Rees Pritchett, MD '48. Dr. Kissinger made a surprise appearance to hear Dr. Wolfe speak about his time as a traveling physician for the State Department.

Light Box

The old neighborhood: John Kuiper, MD ’61, took this Kodachrome photo on a Sunday afternoon in the fall of 1959…and then forgot about it. When he found it, more than half a century later, he sent it to *Weill Cornell Medicine*. “The 69th Street image brings back memories of Soo Lee’s, where most of us brought our shirts to be laundered and pressed; of Morris and Lou Garfinkel’s delicatessen just around the corner on First Avenue, where we occasionally lunched on pastrami on rye and cream soda; of the two or three Cuban men rolling cigars from dawn to dusk in their 70th Street storefront; of my home care patient a few streets further to the north,” writes Kuiper, a retired internist and nephrologist living in Los Angeles. “And of course, memories of a magnificent medical center, international in scope, pursuing the highest standards of medical education, research, and patient care, but always grounded in its mission to benefit the health and well-being of all mankind—as represented in my photograph by those living and working in its immediate neighborhood. In addition to being somewhat archival, it reminds us of Dean Glimcher's appeal that ‘our patients be at the center of everything we do.’”

JOHN KUIPER, MD ’61


Coca-Cola

Weill Cornell Aids Neighbors in Sandy Aftermath

AP IMAGES

State of emergency: During Hurricane Sandy, patients were evacuated from flooded hospitals to other institutions, including NYP/Weill Cornell.

While Weill Cornell emerged from Hurricane Sandy largely unscathed, several city medical institutions did not—prompting WCMC to offer aid and support in a variety of ways. After NYU's hospital and medical school suffered flooding and power outages and was forced to close, Weill Cornell created nine clerkship spots in psychiatry and pediatrics; offered space for lab samples, specimens, and research animals; and hosted displaced scientists. Student volunteers helped with medical care in shelters around the city, and PTSD expert JoAnn Difede, PhD, mobilized a team to provide free counseling at community centers.

As patients were rerouted from NYU and Bellevue—whose closure left NYP/Weill Cornell as the only Level I trauma center for half of Manhattan—the Emergency Department saw a 150 percent spike in patient visits; venues such as the Greenberg Pavilion lobby and Perelman Heart Institute were pressed into service for the care and discharge of ED patients. Said Dean Laurie Glimcher: "These acts of collaboration stand as testament to the resilience and teamwork that symbolize the Weill Cornell community."

Brain and Mind Institute Named for Feil Family

In recognition of a $28 million gift from the Feil family, Weill Cornell has named its new neuroscience center the Feil Family Brain and Mind Research Institute, in honor of Gertrude and Louis Feil. Established in September, the Institute will be a translational research hub for such diseases and conditions as Alzheimer's, Parkinson's, stroke, and multiple sclerosis. The Feil gift will allow for the recruitment of four top-tier neuroscientists; state-of-the-art equipment; training scholarships for postdocs, fellows, and clinicians; scholarships for medical students; and more. Says the Institute's director, Costantino Iadecola, MD, the Anne Parrish Titzell Professor of Neurology: "This generous gift enables the Institute to be a focus of intense multidisciplinary research that will advance the pace of discovery and the development of new treatments, and will create a greater platform for obtaining federal grants and tapping into other sources of extramural funding."

PROVIDED

Jeff Feil

The Feil family has supported Weill Cornell since the Eighties; their philanthropy includes scholarships, endowed professorships, clinical scholar awards, and the establishment of the Judith Jaffe Multiple Sclerosis Clinical Unit in the Weill Greenberg Center. The family has also supported training in neurology, cancer, and cardiology, along with programs in diabetes and metabolic disorders. In 2010, Weill Cornell named its scientific facility on 61st Street the Gertrude and Louis Feil Building in honor of Overseer Jeff Feil's parents. Says Feil: "There has never been a more critical time to advance research in neuroscience and neurodegenerative disease."

Glimcher Wins Trio of Awards for Research

Dean Laurie Glimcher was recently honored with three major awards, all recognizing her body of research in immunology and cancer: the Ernst W. Bertner Memorial Award from the University of Texas MD Anderson Cancer Center; the William B. Coley Award for Distinguished Research in Basic Immunology from the Cancer Research Institute; and the Dr. Luis Federico Leloir Prize of International Cooperation in Science, Technology, and Innovation from the government of Argentina. Glimcher's many previous honors include membership in the American Academy of Arts and Sciences, the National Academy of Sciences, and the Institute of Medicine.

Schafer Elected to Institute of Medicine

Andrew Schafer, MD, chairman of the Department of Medicine and the E. Hugh Luckey Distinguished Professor of Medicine, has received one of his field's highest honors: election to the Institute of Medicine of the National Academy. Schafer was one of seventy new members and ten foreign associates elected in 2012. Established in 1970, the IOM recognizes people who have made major contributions to the advancement of the medical sciences; at least a quarter are selected from fields outside the health professions. This recent group also included neuro-oncologist Lisa DeAngelis, MD, chair of neurology at Sloan-Kettering and a Weill Cornell professor of neurology.

AMELIA PANICO

Andrew Schafer, MD

WCMC Medical Library Turns Fifty

Last fall, Weill Cornell's medical library marked its fiftieth anniversary. The facility, known as the Samuel J. Wood Library, moved to its current location in October 1962, combining the previous Medical College and nursing libraries. The facility has undergone several renovations and modernizations in recent years, including the creation of a sunken reading room and a refurbished computer lab. Recent innovations include the development of a mobile website and an online chat service for reference assistance; plans are in the works to embed librarians in research labs and to offer study space that's available twenty-four hours a day.

WCMC Wins Three Gates Challenge Grants

Weill Cornell researchers have won three Grand Challenges Explorations grants totaling more than $1.5 million. The awards, from the Bill & Melinda Gates Foundation, support innovative approaches to problems in global health and development. A $100,000 grant went to Juan Cubillos-Ruiz, PhD, a postdoc in the lab of Dean Laurie Glimcher, MD, for work on using tailored nanodevices to understand HIV resistance. Carl Nathan, MD, chairman of microbiology and immunology, the R. A. Rees Pritchett Professor of Microbiology, and director of the Abby and Howard Milstein Program in the Chemical Biology of Infectious Disease, was awarded about $647,000 for tuberculosis research. Kyu Rhee, MD, PhD, associate professor of medicine and of microbiology and immunology, received about $783,000, also for work on TB.

TIP OF THE CAP TO...

Medical students **Sha-har Admoni**, **Nipun Verma**, and **Andrew Ji**, named Howard Hughes Medical Institute research fellows. MD-PhD student **David Roy** had his fellowship renewed for another year.

Curtis Cole, MD '94, associate professor of clinical medicine and of clinical public health, elected a fellow of the American College of Physicians.

Robin Davisson, PhD, the Andrew Dickson White Professor of Molecular Physiology, winner of the Arthur C. Corcoran Memorial Award from the American Heart Association for distinguished research on hypertension.

Peter Fleischut, MD, assistant professor of anesthesiology, and **Gregory Kerr, MD**, associate professor of clinical anesthesiology, winners of the John M. Eisenberg Patient Safety and Quality Award from the National Quality Forum and the Joint Commission.

Rainu Kaushal, MD, director of the Center for Healthcare Informatics and Policy and the Frances and John L. Loeb Professor of Medical Informatics, elected to the New York Academy of Medicine.

Professor of clinical psychiatry **Marlin Mattson, MD**, winner of the Planetree Caregiver Award, given to promote patient-centered care.

Fabrizio Michelassi, MD, the Lewis Atterbury Stimson Professor and chairman of the Department of Surgery, who received the Grand Award of Merit from the American Society of the Italian Legions of Merit, its highest honor.

Shahin Rafii, MD, director of the Ansary Stem Cell Institute and the Arthur B. Belfer Professor in Genetic Medicine, and **Xin-Yun Huang, PhD**, professor of physiology and biophysics, elected fellows of the American Association for the Advancement of Science.

William Reisacher, MD, director of allergy in the Department of Otolaryngology, and **Michael Stewart, MD**, chairman of otolaryngology and the E. Darracott Vaughan Jr., MD, Senior Associate Dean for Clinical Affairs, winners of honor awards for meritorious service to the American Academy of Otolaryngology—Head and Neck Surgery.

William Schaffner, MD '62, chair of preventive medicine at Vanderbilt University, winner of the Abraham Lilienfield Award, the highest honor from the American College of Epidemiology.

Steven Wexner, MD '82, chairman of colorectal surgery at Cleveland Clinic Florida, elected a fellow of the American Surgical Association and appointed to the board of regents of the American College of Surgeons.

Hearing hoofbeats: The oryx

GOOGLE IMAGES

WCMC-Q Maps Genome of Qatari Animal

Researchers at the Qatar branch have mapped the genome of the Arabian oryx, the first animal to be sequenced in the emirate. The oryx, a white-and-brown antelope with long, needle-like horns, is the national symbol of Qatar; its wild population fell to just a couple hundred during the Fifties and Sixties, and it's currently classified as "vulnerable." The findings, which will help strengthen genetic diversity in the nation's captive breeding program, could allow more of the animals to be released into the wild.

Dean Glimcher's Blog Debuts

Dean Laurie Glimcher has inaugurated a blog to address issues of interest to the Weill Cornell community and the wider world. Begun last fall, the blog has featured such topics as the shortage of future doctors, the role of the physician-scientist, and curriculum changes at WCMC. "In writing it," she says, "I hope to give you greater insight into my activities and news that I'm currently excited about, pondering, or simply want to share with you." The essays can be found at weill.cornell.edu/about-us/dean/blog.

Mann Publishes *Hypertension and You*

Professor of clinical medicine Samuel Mann, MD, has published *Hypertension and You*, his latest general-audience book about high blood pressure. The book, from Rowman & Littlefield, explores the drug therapies currently in vogue—and argues that older medications, or smaller doses, can often be more effective. "It is not an overstatement to say that millions of people are on more blood pressure medication than they need because their blood pressure is measured incorrectly either at the doctor's office or at home," Mann writes. "Worse, in most cases, neither the doctor nor the patient is aware that the blood pressure is being overtreated."

Pediatric Sleep Center Opens

The Komansky Center for Children's Health at NYP/Weill Cornell has opened a Pediatric Sleep Center, featuring child-friendly sleep labs and staffed by a multidisciplinary team that includes pulmonologists, otolaryngologists, neurologists, psychologists, pediatricians, and sleep specialists. "Many behavioral problems we see in children are the result of sleep problems," says Haviva Veler, MD, assistant professor of pediatrics and director of the new center. "Once you address sleep, these problems, be it moodiness or depression or even ADHD, may disappear." The facility aims to address a range of issues, from the inability of babies to sleep through the night to more serious problems such as apnea and insomnia.

Informatics Master's Program Launched

The Center for Healthcare Informatics and Policy has begun a master of science program in health informatics. Offered through the Graduate School of Medical Sciences, the program will combine the study of health systems, information systems, and research methodology to prepare students for careers in health information technology—its implementation, analytics, management, research, and policy. The thirty-credit program began accepting applications last fall and launched in January.

Prostate Cancer Center Established

NewYork-Presbyterian Hospital and the Medical College have established a comprehensive center dedicated to research and treatment of prostate cancer. The Center for Prostate Cancer at NYP/Weill Cornell will include advanced screening and diagnostic methods such as fusion biopsy, focal therapy for localized tumors, refined imaging techniques, open and robotic surgery, treatments for advanced disease, and rehabilitation for urinary and sexual issues following treatment. It will be led by Ashutosh Tewari, MD, director of the LeFrak Center for Robotic Surgery and the Ronald P. Lynch Professor of Urologic Oncology. "My main focus is to not let anyone get to an advanced cancer stage," Tewari says. "Therefore, we will use a combination of imaging, genomics, surgery, and novel therapies to augment our surgical results and thus improve survival while maintaining quality of life."

LIBRADO ROMERO/THE NEW YORK TIMES/REDUX

Rooms with a view: A brightly colored mural, entitled *Time and Time*, has replaced a bare wall at NYP/Weill Cornell, offering a cheerier view to patients on the west side of the hospital.

FROM THE BENCH

Grant Funds Study of Metabolomics in COPD

Weill Cornell researchers have been awarded a five-year, $6.5 million grant from the National Heart, Lung, and Blood Institute to investigate metabolic changes of airway epithelial cells in the lungs of patients with chronic obstructive pulmonary disease (COPD). Caused by smoking, COPD currently has no cure, few effective treatments, and no known biomarkers for early diagnosis. The study will be the first time that researchers use metabolomics to identify, analyze, and profile COPD-related changes in the lungs. Pharmacology professor Steven Gross, PhD, calls metabolomics "a powerful new approach to discover how airway epithelial cells are disturbed by smoking and how this may lead to COPD."

Electronic Health Records Improve Care

In the *Journal of General Internal Medicine*, Weill Cornell public health researchers reported that electronic health records (EHRs) can better the quality of patient care. The study, which examined data from nearly 500 physicians and 75,000 patients, found improvements across four measures: hemoglobin A1c testing in diabetes as well as screening for breast cancer, chlamydia, and colorectal cancer. "EHRs may improve the quality of care by making information more accessible to physicians, providing medical decision-making support in real time, and allowing patients and providers to communicate regularly and securely," says Rainu Kaushal, MD, director of the Center for Healthcare Informatics and Policy and the Frances and John L. Loeb Professor of Medical Informatics. "However, the real value of these systems is their ability to organize data and to allow transformative models of health-care delivery, such as the patient-centered medical home, to be layered on top." The work was conducted with the Health Information Technology Evaluation Collaborative, a multi-institutional effort directed by Kaushal and associate professor of public health and medicine Lisa Kern, MD.

ABBOTT

Rainu Kaushal, MD

Overcoming Fear Difficult for Teenage Brains

Adolescent brains have a hard time recovering from a fear response—which may explain why anxiety and depression spike during the teenage years. Researchers found that after being exposed to fear-inducing stimuli, adolescents—both human and rodent—maintained their fear response even after the stimuli were removed. "If adolescents have a more difficult time learning that something that once frightened them is no longer a danger, then it is clear that the standard desensitization techniques from fear may not work on them," says senior co-investigator Francis Lee, MD, PhD, professor of pharmacology and psychiatry. The human experiments, which paired noxious sounds with colored squares, were conducted at the Sackler Institute for Developmental Psychobiology.

Tool Reveals Antibiotic Mechanisms Inside Cells

Using mass spectrometry, scientists are now able to "see" how antibiotics target bacteria inside living cells—providing insight that may lead to the improvement of drugs for infectious diseases like tuberculosis. Associate professor of medicine Kyu Rhee, MD, PhD, and colleagues exposed the TB bacterium to the antibiotic para-aminosalicylic acid (PAS), the second-oldest TB drug on the market, and through mass spectrometry analysis discovered that PAS itself becomes toxic once inside the bacterium. Says Rhee: "The study findings show us that sometimes there is a profound disconnect between what we think a drug is doing and how it actually works inside cells."

Drug Combo Could Stem Blood Vessel Growth

A combination of two kinds of FDA-approved drugs could retard the growth of abnormal blood vessels—potentially treating such diseases as cancer, diabetic retinopathy, macular degeneration, and rheumatoid arthritis. In *Developmental Cell*, researchers described the efficacy of the two types of drugs—one (prescribed for autoimmune neurological diseases like multiple sclerosis) that targets the protein S1P1, and another (used to fight cancer and other conditions) that inhibits vascular endothelial growth factor. Says Timothy Hla, PhD, director of the Center for Vascular Biology: "This research defines one of the fundamental mechanisms of blood vessel growth that is vital to normal health and that also fuels many diseases."

Pain Drug Kills Resistant TB

The anti-inflammatory drug oxyphenbutazone has been found to kill drug-resistant TB in the lab. The drug—which dates from the Fifties and is long off-patent—would cost just two cents a day in developing countries. But Carl Nathan, MD, the R. A. Rees Pritchett Professor of Microbiology, worries it may never reach the 500,000 patients it could benefit. "It is difficult today to launch clinical studies on a medication that is so outdated in the United States, that is mainly used here in veterinary medicine to ease pain," Nathan says. "No drug firm will pay for clinical trials if they don't expect to make a profit on the agent. And that would be the case for an off-patent drug that people can buy over the counter for pain in most of the world." He adds that it faces another hurdle: the FDA requires animal testing for safety and efficacy, but mice metabolize the drug too quickly.

Carl Nathan, MD

PANICO

Praise for On-Site HIV Tests

Integrating rapid on-site HIV testing into drug abuse treatment programs is cost-effective, Weill Cornell researchers have found. Using data from a 2009 study in which 80 percent of patients offered on-site testing accepted and obtained their results, they found that earlier diagnosis and treatment paid off in terms of increased life expectancy, lower risk of transmission, and other measures. The findings were published in *Drug and Alcohol Dependence*.

WCMC-Q Launches Date Palm Research Program

Four years after mapping the date palm genome, WCMC-Q has established a formal Date Palm Research Program—aiming to make Qatar the international leader in the field. The program, a collaboration with the Qatari Ministry of Environment's Biotechnology Center, kicked off in October with video conferencing among leading experts. "Integrated research like this has not been conducted on the date palm before, and we expect that the results will directly impact this important crop in the future," says Joel Malek, PhD, director of genomics at WCMC-Q. Dates, which have been grown in the Middle East for thousands of years, are an essential part of the diet in the Arab world.

Shahin Rafii, MD

JOHN ABBOTT

Growth Potential

The Ansary Stem Cell Institute announces a major breakthrough

Like Goldilocks in the classic fairy tale, stem cell scientists have been stymied by two extremes. Embryonic (or "pluripotent") stem cells have the potential to become any cell in the body—but in some ways, they're *too* elastic. Efforts to coax them into becoming viable adult cells to cure disease or repair organ damage have not yet borne fruit. And worse: their inherent malleability puts them at risk of turning cancerous.

At the other end of the spectrum are adult stem cells, which scientists—facing severe restrictions on government funding for embryonic stem cell research—are also studying, exploring their potential to become therapeutic agents. "But that process is very inefficient," says Shahin Rafii, MD, director of the Ansary Stem Cell Institute and the Arthur B. Belfer Professor of Genetic Medicine, "and it is not clear if directly programming an adult fibroblast is clinically feasible."

But in what Rafii calls a "major, landmark breakthrough," he and colleagues at the Ansary

Institute have found a highly promising middle ground. "Could you find a cell that is not as pluripotent as a human embryonic stem cell, but is not as inflexible as an adult fibroblast? Could you find a cell that is a compromise?" Rafii asks rhetorically. "Our lab has found that cell."

That avidly sought middle ground, a mid-gestational amniotic cell, is the subject of a paper published in *Cell* in October 2012. In it, Rafii and colleagues—including Zev Rosenwaks, MD, director of the Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine at Weill Cornell and a longtime contributor to the Ansary Institute's research—describe how they have taken sloughed-off fetal cells obtained through routine amniocentesis and coaxed them into becoming endothelial cells, the essential building blocks of the vascular system. "This is going to be transformative, because we have been able to generate endothelial cells that are very close in function, phenotype, and all other features of an adult endothelium," says Rafii. "We have achieved a milestone that was set when we established the Ansary Stem Cell Institute: to generate a cell that can be translated to the clinic."

Established with a $15 million gift from Shahla and Hushang Ansary—he is a former vice chairman of the Board of Overseers and former Iranian ambassador to the United States—the Ansary Institute has engendered myriad discoveries since its founding in 2004. They include success in converting adult mouse spermatogonial stem cells to endothelial cells (published in *Nature* in 2007); work on how endothelial cells play a vital role in liver regeneration (*Nature* and *Nature Cell Biology*, 2010); the discovery that endothelial cells produce growth factors key to the creation of adult stem cells (*Cell Stem Cell*, 2010); and research on how blood vessels support lung regeneration (*Cell*, 2011).

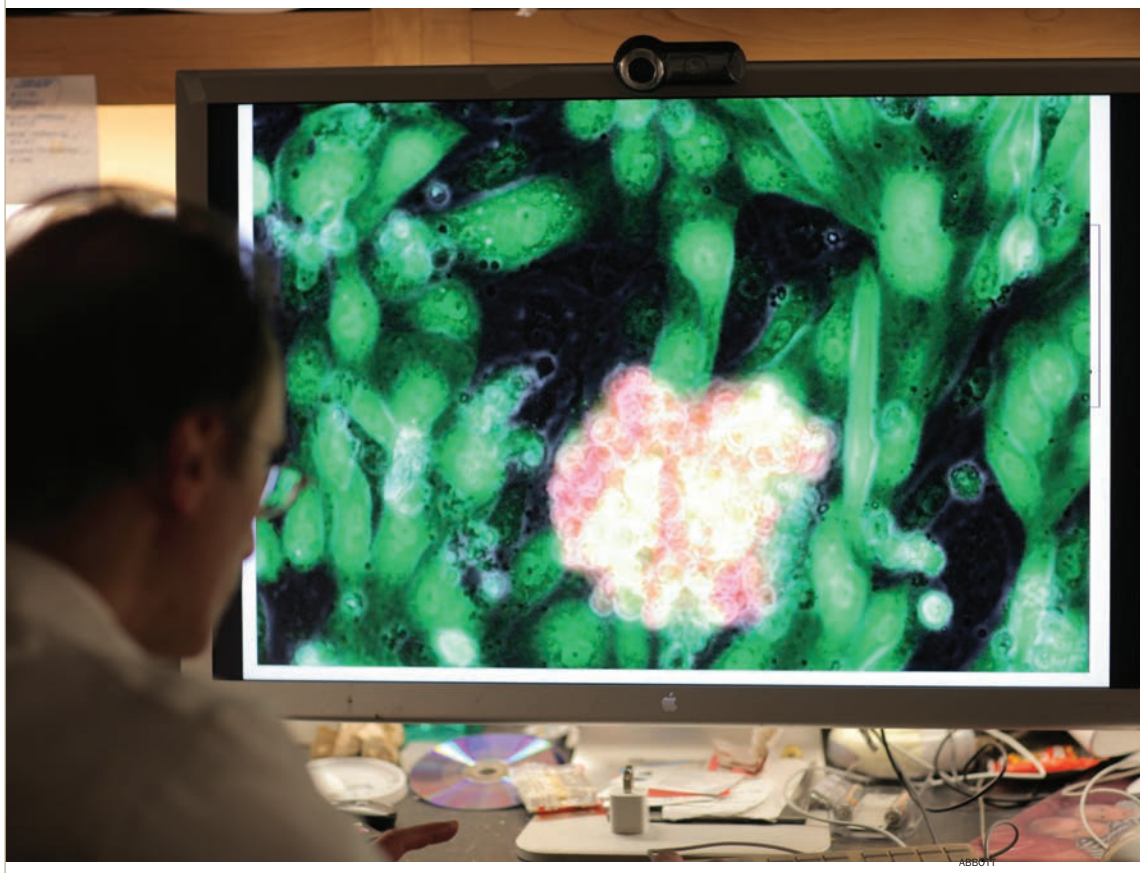
The new *Cell* paper chronicles the process by which amniotic stem cells, derived from routinely sampled amniotic fluid at sixteen weeks of gestation, are transcriptionally reprogrammed into vascular endothelial cells, or rAC-VECs. "We have designed and micro-fabricated a cell that, by reconstructing the blood supply, can benefit any organ that is damaged," says Rafii, who is also studying the cells in a mouse model. "I can envision someday that if someone has a heart attack, we can transplant genetically matched, amniotic-derived rAC-VECs that are trained and educated to behave as a cardiac endothelium."

While the Ansary Institute has focused on the creation of endothelial cells, other labs could adapt the technology to other types of cells, such as neurons lost through brain disease or islet cells integral to insulin production, notes co-author Sina Rabbany, PhD. The next step for the Institute team, he says, is to work on scaling up production to clinical levels. "A typical clinical intervention would require 200 billion to 300 billion cells," says Rabbany, adjunct associate professor of genetic medicine and of bioengineering in medicine. "For instance, if the goal is to revascularize the heart of someone who has suffered a massive heart attack, you'd probably need to inject at least several hundred billion cells into it to hope for angiogenesis and regeneration of heart muscle. So the challenge would become, how could we use bioengineering modalities to produce large quantities of these cells in a short period of time?"

When the Ansary Institute was founded, one of its purposes was to offer a source of private funding to counter the strictures on federal grants for embryonic stem cell work. The researchers point out that, among its other advantages, amniotic stem cells don't involve the same kind of thorny ethical issues. "They're freely available," Rabbany notes. "There's no controversy in terms of destruction of an embryo, and we can access them from amniocentesis, which happens in hospitals on a daily basis."

In fact, the first amniotic cells used in the research came—with Weill Cornell's knowledge and permission—from Rafii's wife, who was carrying their twin boys, now aged three. With samples from some four dozen separate subjects that successfully generated rAC-VECs in the years since, Rafii can see a world in which amniotic fluid is cryopreserved and banked for future medical use, as cord blood is today. Human clinical trials, he says, could begin in as little as four years. "With the publication of this paper, we have achieved one of the biggest milestones that we promised—not only to the Weill Cornell community, but also to Mr. Ansary," Rafii says. "I hope this will be the foundation for more."

— Beth Saulnier



Studying the stuff of life: Rafii in the lab

The Geriatrics Gap

Program aims to spark student interest in treating older patients

If there's one condition that emergency physicians see often, recognize easily, and usually manage well in younger patients, it's agitated delirium. But in elderly patients, assessing an acute change in mental status can be more difficult. "With delirium in older adults, unless the patient comes in with a full medical history or family members who can speak for them, it's hard to know if that's the baseline or if they've acutely changed," says Anthony Rosen, MD '10. Once emergency physicians rule out potentially life-threatening causes of delirium such as heart attack, stroke, and liver or kidney failure, the standard next step is typically medication. "But often," says Rosen, "that's not the appropriate thing for older adults."

Rosen is a third-year resident in emergency medicine at NewYork-Presbyterian, and he has long been drawn to geriatrics. That interest deepened during the summer after his first year of medical school, when he participated in the Medical Student Training and Aging Research (MSTAR) program. Each year, forty students from around the country are selected for MSTAR, which is funded by the American Federation for Aging Research and hosted by participating centers. Weill Cornell, a host institution, also supports students through the Henry Adelman Fund, created in honor of the father of Ronald Adelman, MD, co-chief of the Division of Geriatrics and Gerontology.

The eight- to twelve-week program is designed to encourage interest in aging-related research and to expose students to clinical geriatric medicine. They typically participate after their first year of medical school—attending weekly lectures, joining the geriatrics consult and palliative care teams, shadowing the division's physicians as they make house calls, and learning to critically review literature. They also visit such sites as the Irving Sherwood Wright Center on Aging, Weill

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Anthony Rosen, MD '10, with his mentor, Michael Stern, MD '01

Cornell's outpatient facility; Dorot, a Jewish nonprofit dedicated to aging services and volunteerism; and area nursing homes and hospices.

In addition to introducing students to aging-related investigations, MSTAR exposes them to structured research in general; they begin their own projects under faculty mentorship and learn how to present their findings. Last summer nine students, from Weill Cornell and other schools, took part. "If they become geriatricians, we'll be delighted," says Adelman, professor of clinical medicine. "But with 10,000 Americans turning sixty-five every day, we just want them—in whatever subspecialty they choose—to be advocates and look after the needs of older people."

In the next two decades the population of elderly in the United States will double—and geriatricians are already in critically short supply. The reasons for the practitioner gap, while challenging, are no mystery. "Although people who do geriatrics are among the most satisfied of physicians," Adelman notes, "income for geriatricians is significantly less than it is for other subspecialties." That's compounded by the fact that medical students tend to see only the frail and sick elderly in their traditional training, a deficit the program aims to counter. "They see models of aging that dispel stereotypes—people aging successfully, even if they have a number of comorbid illnesses," Adelman says.

Students encounter patients engaged in volunteerism, exercise programs, and meaningful employment—including, for example, one nonagenarian who continues to teach and another who works on Wall Street. Such exposure shows students that with respect to health issues—as in other things—elderly patients often want to focus on function and comfort, or simply to know that someone is listening to and caring about them. "They don't necessarily want every high-tech test that can be ordered," says Veronica LoFaso, MD, associate professor of clinical medicine and co-director of the summer program, "so we really push the idea of seeing people as individuals."

LoFaso says that one particularly rewarding aspect of geriatrics is the long-term relationships that physicians develop with their patients—and those, too, can be hard for students to experience during medical school. "Unfortunately, students often see just a snapshot of the sickest patients in the hospital setting, so they may think that represents all geriatric care. We try to encourage them to come to our outpatient practice to see some of our highly functional patients as well, so they get a more rounded picture of what we do," says LoFaso, the Roland Balay Clinical Scholar. "Geriatrics requires patience and the ability to appreciate small steps of progress." She hopes that more outside specialists—such as urologists, cardiologists, and orthopaedic surgeons—will become what she terms "gero-friendly."

Anthony Rosen, with his dedication to addressing the particular needs of older patients in the ED, represents the growing number of young physicians training in many different disciplines who are becoming more knowledgeable about geriatric issues. "Caring for older adults is really about understanding that medical problems are not due to a single cause but are almost always multi-factorial," Rosen says. "The goal of care is not always curing an illness but rather improving quality of life and functional status."

Rosen credits Mark Lachs, MD, co-chief of the Division of Geriatrics and Gerontology as a key influence in his work. "Dr. Lachs was my mentor as a student," says Rosen, "and he continues to be my mentor on nursing home and outpatient projects." In the ED, Rosen is mentored by Michael Stern, MD '01, assistant professor of medicine, who preceded Rosen on a similar path years earlier. After his emergency medicine residency, Stern helped Neal Flomenbaum, MD, NYP/Weill Cornell emergency physician-in-chief, start the nation's first Geriatric Emergency Medicine Fellowship in 2005.

Scott Connors '15 aided Rosen in the emergency department this summer as an MSTAR participant. During his time there, the ED implemented a new protocol conceived by Stern and Alexis Halpern, MD, another Weill Cornell emergency physician and GEM Fellowship graduate, to help the staff better recognize agitated delirium in elderly patients. With a simple alphabetical mnemonic, the protocol is being used to train emergency physicians, physician assistants, nurse practitioners, and nurses to screen for such potential causes as lack of pain control, constipation, dehydration, and drug interactions. Connors helped with the assessment of ED personnel before and after the protocol was introduced and also with database analysis. For Connors, the balance between clinical exposure and research opportunities is precisely what makes the program so appealing. "Because geriatric patients comprise a larger and larger part of the patient population across the nation and especially in places like New York City," he says, "I thought having a greater appreciation for these issues would help me in the future."

As part of the MSTAR program, Connors and his fellow participants must submit a poster to the American Geriatric Society's annual meeting. Such research can lead to investigations that continue long after graduation. Last spring, Rosen won the award for best resident poster presentation for his study of resident-to-resident elder abuse in nursing homes—work he began as an MSTAR student.

— Andrea Crawford

'If they become geriatricians, we'll be delighted,' says Adelman. 'But with 10,000 Americans turning sixty-five every day, we just want them to be advocates and look after the needs of older people.'

Targeted Treatment

Pathologist Mark Rubin, MD, takes a multifaceted approach to the battle against prostate cancer

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Mark Rubin, MD

For doctors who diagnose prostate cancer and men concerned about the disease, these are uncertain times. The conventional wisdom that males over fifty should be screened annually using the PSA test—a measure of protein secreted by the organ—was upended in May 2012, when the U.S. Preventive Services Task Force recommended that the test no longer be given routinely. The advisory group concluded that too many patients with non-progressing or slow-growing tumors were undergoing invasive biopsies, surgeries, and other procedures following their test results, and that too few were living any longer than they would without the screen.

Enter Mark Rubin, MD, the Homer T. Hirst Professor of Oncology in Pathology, whose research on the molecular underpinnings of prostate cancer may one day help pinpoint which of the approximately 240,000 men annually diagnosed with prostate cancer truly need intervention—and how patients with the most deadly tumors can be treated more effectively. "It's not clear how many men are being overtreated—there's disagreement in the field—but it may be anywhere from fifty to one hundred or more who are being treated to save one life," Rubin says. "Obviously for that one individual

it's important. We want to have the ability to detect very early on the tumors that are going to progress, because the best way to treat a metastatic tumor is to not let it spread."

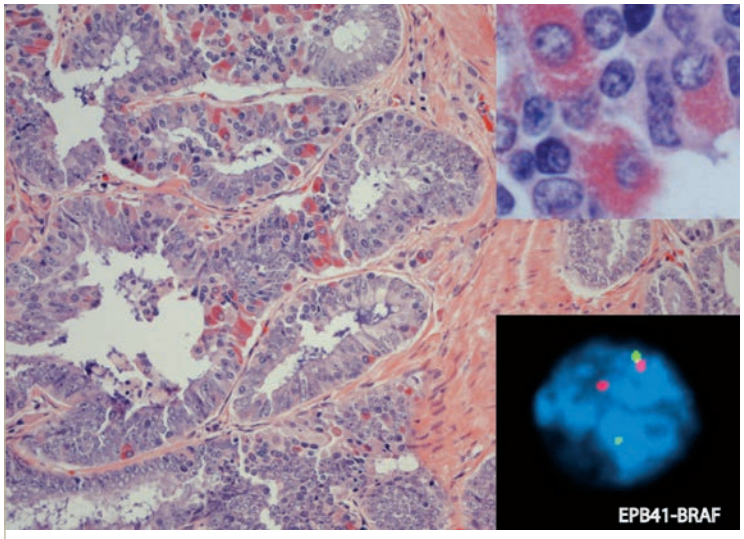
Developing the means to identify tumors by their molecular signature and then base treatment decisions on that information is at the heart of precision medicine—the targeting of treatment to the biology of an individual patient's disease—and the basic science questions that Rubin is asking. Since arriving at Weill Cornell five years ago to help develop the College's translational cancer research, Rubin has published more than fifty studies that are beginning to provide insight into the molecular distinctions between lethal and indolent (inactive or benign) prostate tumors.

Some of that work—building on his research at Harvard Medical School, where he was associate professor of pathology from 2002 to 2007—has led to the development of two clinical tests. Both incorporate discoveries Rubin made with a longtime collaborator at the University of Michigan, Arul Chinnaiyan, MD, PhD, that about half of prostate cancers contain a fusion of two genes. The fusion causes one gene that is regulated by the male hormone androgen to be over-expressed, driving tumor growth. "That represents an important class of biomarker because it's not like PSA, where it can be elevated because you have a large or inflamed prostate," Rubin explains. "It's a prostate cancer-specific mutation." A tissue test based on the finding, from Ventana Medical Systems, is available in the U.S. and Europe to classify prostate tumors and help predict how a patient will respond to treatment. And a urine test in development at Gen-Probe could more reliably diagnose prostate cancer—particularly aggressive tumors. (This work was patented by Harvard and Michigan. Rubin and Chinnaiyan are inventors and receive royalties for these commercial assays.)

Rubin's research is wide ranging. In addition to parsing the molecular distinctions between aggressive and harmless tumors and flagging the subtypes linked to specific treatment responses, he is trying to understand why therapies for metastatic prostate cancers fail and explain the genetic alterations that trigger and drive the disease's growth. In a study published in April by the *Proceedings of the National Academy of Sciences*, Rubin elaborated on the discovery of the prostate cancer fusion genes, modeling how pathways crucial to cancer progression are altered in patients with the fused genes, and suggesting that they are at risk of further mutations accumulating in their tumors if they are not effectively treated.

In several studies published in the last year, Rubin has cataloged previously unknown mutations linked to prostate cancer and explained why they may spur tumor growth. Another paper published in *PNAS* documented two copy number variations—deletions of DNA—associated with a tripling or quadrupling of aggressive prostate tumor risk, depending on which alteration a man inherits. One of the variations may trigger cancer by causing genes associated with cell growth to be over-expressed; the other's contribution to prostate tumors is still being investigated.

Mutations in another gene, SPOP, also are thought to play a role in prostate cancer, though their influence is unclear. In a paper published in May 2012 in *Nature Genetics*, Rubin, collaborating with other Weill Cornell physicians and Broad Institute scientists, reported that mutations in the gene were seen in 15 percent of prostate cancers. Scientists believe the mutations prevent the gene from carrying out its usual function of trashing no-longer-needed proteins, a factor that may allow tumors to progress. Rubin and Pengbo Zhou, PhD, professor of pathology and laboratory medicine, are now working out how the normal SPOP gene targets proteins for disposal, knowledge that may enable the development of new treatments.



PROVIDED

Closer look: A microscopic view of a prostate cancer, with a magnified image of the red granules within its tumor cells (inset, upper right). Lower right inset: A DNA test confirms that two particular genes (seen as red and green dots) are fused.

Developing medications based upon specific genomic alterations was the subject of a paper Rubin published in *Cancer Discovery*. In that study, he demonstrated that an investigational drug that targets the AURKA gene can shrink the growths in mice with neuroendocrine tumors, an especially aggressive form of prostate cancer. AURKA makes the protein aurora kinase, which is involved in cell growth and has been implicated in a variety of cancers. Millennium Pharmaceuticals is now sponsoring a multi-center clinical trial being set up by Himisha Beltran, MD, assistant professor of medicine, to see if the drug works in humans and to look for other mutations in patients with neuroendocrine tumors.

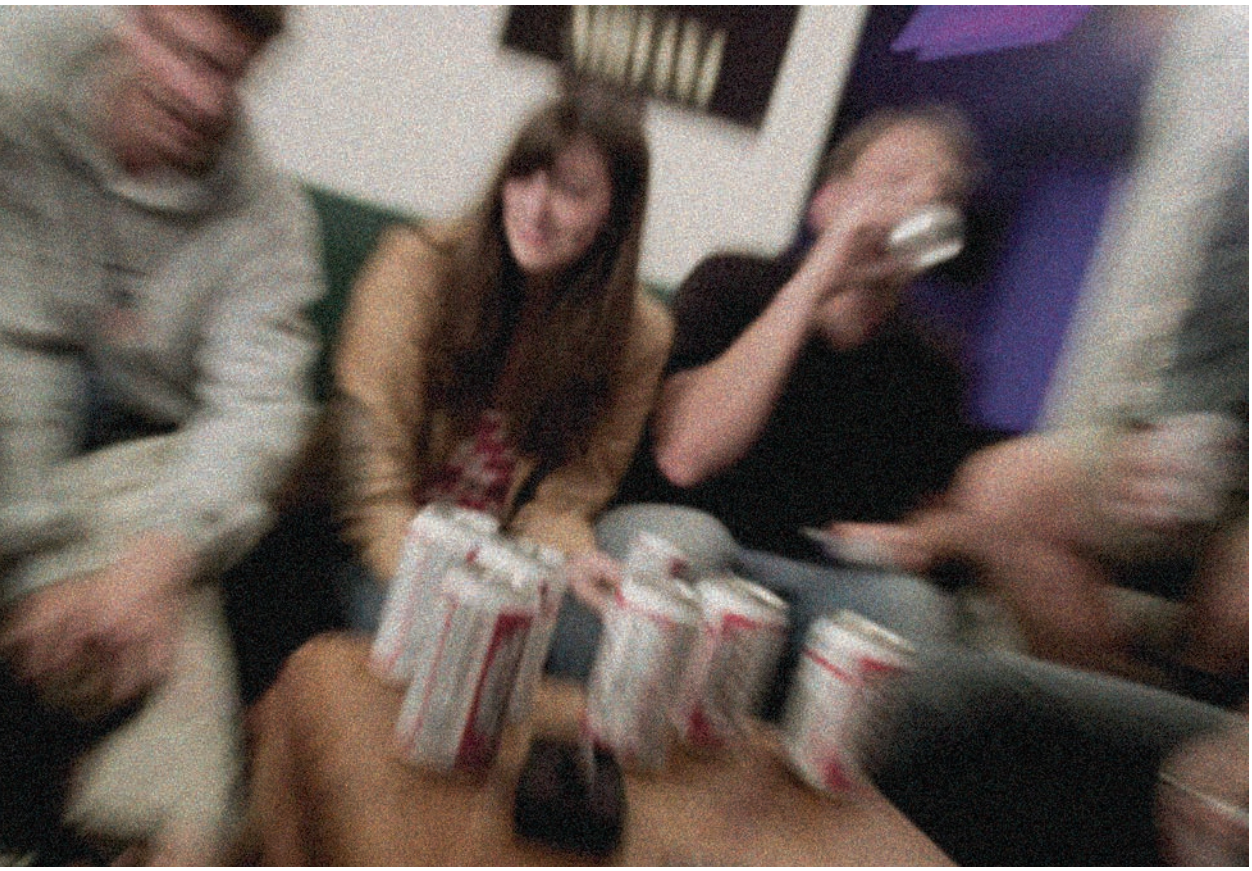
That this complex lab work has real-world impact on patients, especially the 28,000 men who die of prostate cancer annually, is never far from Rubin's mind. In April 2012, he was made part of a "dream team" of prostate cancer investigators from seven centers who were awarded $10 million by the nonprofits Stand Up to Cancer and the Prostate Cancer Foundation. Over the next three years, the team will sequence the tumors of 500 men participating in clinical trials for so-called castration-resistant prostate cancer, a lethal type of the disease that even the best new hormone therapies ultimately cannot cure.

"We have many men being put onto these clinical trials for metastatic prostate cancer," Rubin says. "They're treated, they fail, and they go on to the next drug in the regimen. To date we haven't learned much from that experience." The team will try to understand what mutations such patients have, with a goal of understanding why their treatment failed and what drugs might be more effective. "We'd love to cure prostate cancer," Rubin says, "but in the meantime, we want to decrease the suffering of men with advanced disease."

— Jordan Lite

Drinking Problems

Jennifer Epstein, PhD, studies how to prevent teens from using drugs and alcohol



STOCK PHOTO

It's a scenario that plays out innumerable times on any given weekend: an underage student goes to a party and is offered alcohol. While young people may see such behavior as a rite of passage, psychologist Jennifer Epstein, PhD, points out that for some who wind up drinking again and again due to peer pressure, it can lead to excessive consumption and possible alcohol dependence. That poses its own health risks and raises the likelihood of drunken driving, assaults, unprotected sex, poor academic performance, and other ills.

"It's a national concern," says Epstein, an assistant research professor in the Division of Prevention and Health Behavior in the Department of Public Health, "because the rate of binge drinking among college students is in the range of a third." But for many students, it's hard to say no—even if they might be inclined to abstain. "The transition to the first year of college, in particular, is a critical age and life period of increased independence," Epstein says, "when health and well-being are put to the test by the convergence of opportunity and peer pressure to drink heavily."

In an effort to combat alcohol abuse among college students, Epstein is meeting millennials on their own turf: the virtual world. With a three-year, $500,000 grant from the National Science Foundation, Epstein and computer scientist Charles Hughes, PhD, of the University of Central Florida are designing virtual reality scenarios in which students confront thorny situations and practice negotiating them—say, to opt for water rather than binge drinking. "You could simulate scenarios that would be high-pressure situations, like a party off campus," Epstein says. "That would allow students to try out these experiences without really being in them. They could even make mistakes and learn from them."

The project, which is currently under development and will begin enrolling subjects in the fall, is Epstein's latest work in the field of youth substance abuse prevention. For the past two decades, she has studied how students in middle school, high school, and college make decisions about using alcohol, tobacco, and illegal drugs—with an eye toward curbing those risky behaviors. Such habits, she stresses, can become entrenched and cause long-term damage, both medical and social. "The younger you start drinking, the more likely you are to become alcohol dependent," Epstein says. "So some of it is a matter of delaying initiation."

Epstein's work mainly focuses on economically

disadvantaged youth; she notes that when she came to the field, much of the existing research had been done on white, suburban teens. She has published dozens of papers on a wide range of topics, including

'The younger you start drinking, the more likely you are to become alcohol dependent. So some of it is a matter of delaying initiation.'

the relationship between linguistic acculturation and alcohol, smoking, and drug use among Hispanics; the effect of family drinking on alcohol use in inner-city teens; the perceived social benefits of smoking and drinking among rural youth; the relationship between alcohol consumption and use of social media; risk factors for suicidal ideation and suicide attempts; and how peers and parents influence addictive behaviors and computer use.

Epstein was drawn to the field during her graduate work at Columbia, where she collaborated on a smoking cessation study; she came to Weill Cornell in 1992. She notes that while tobacco use has dropped steeply since her student days, public health officials haven't had the same success with adolescent drinking—and while girls traditionally drank much less than boys, the gender gap is closing, yet remains palpable for frequent alcohol use and binge drinking among high school seniors. "Alcohol usually is the drug of choice in this country," Epstein says. "Even though prevalence rates have gone down, they're still unacceptably high."

— Beth Saulnier

ABBOTT

Robert Allan, PhD, and Jeffrey Fisher, MD

Heart and Mind

Exploring the connection between well-being and coronary disease

One evening in the early Eighties, cardiologist Stephen Scheidt, MD, drove from Manhattan to Long Island to observe a group therapy session for patients with coronary heart disease. Robert Allan, PhD, the psychologist who ran the group, recalls that at the end of the session, Scheidt looked around the room and said, "I just want you folks to know that there's not a shred of scientific evidence to support what you're doing."

They set out to change that. In 1983, Scheidt (who died in 2007 after a nearly forty-year career at Weill Cornell) and Allan co-founded the Coronary Risk Reduction Program at what was then the New York Hospital; in 1996 they published *Heart and Mind: The Practice of Cardiac Psychology*. Now, Allan has co-edited a new edition of *Heart and Mind* with cardiologist Jeffrey Fisher, MD, a clinical professor of medicine at Weill Cornell. Summarizing the growing body of research about the connection between psychosocial

factors and cardiovascular disease, the new book includes a review of cardiology geared toward mental health professionals, enumerates psychosocial risk factors, and highlights important recent trials.

What has changed in the fifteen years since the first edition? "Data," says Allan, a clinical assistant professor of psychology in medicine. "A mountain of data." Where the initial book gathered empirical evidence into just one chapter, Allan and Fisher have distilled some 59,000 papers on the subject, more than half pertaining to the major psychosocial factors—depression, social isolation, anger, anxiety, distressed personality, post-traumatic stress disorder—that have been linked to coronary heart disease, the leading cause of death in the U.S.

The connection between heart and mind has been explored since antiquity. One of the book's contributors describes the case of an eighteenth-century English surgeon who believed, somewhat presciently, that anger could cause his death—and then fulfilled his own prophecy after arguing with colleagues. In the twentieth century researchers began to find an empirical basis for the anecdotal evidence; in 1959, Meyer Friedman, MD, and Ray H. Rosenman, MD, originators of the type A behavior pattern, first reported a link between psychological stress and myocardial infarction.

In the current literature, depression shows the strongest connection to increased risk of heart attack and stroke. It is associated with generalized inflammation throughout the body, a tendency for the blood to clot more avidly, and less heart-rate variability, a factor associated with increased mortality. Anxiety and depression stimulate "sympathetic tone," raising blood adrenaline. Increased sympathetic tone contributes to atherosclerosis—"hardening of the arteries"—and the transient surge in adrenaline can lead to rupture, causing heart attacks and acute heart failure in "broken heart syndrome."

"Anxiety and depression need to be treated as much as high blood pressure and high cholesterol," says Fisher. These physiological factors are also exacerbated because people suffering from depression are less likely to follow doctors' orders and adhere to healthy lifestyles, and more likely to self-medicate with alcohol, drugs, and fattening food.

Psychosocial factors contribute to cardiovascular disease in two ways, both as long-term effects and as a trigger. "The hypothesis is that various stress factors, such as anxiety or easily aroused anger, damage arterial linings and make arteries more susceptible to plaque accrual, just as such standard risk factors as elevated cholesterol or high blood pressure do," says Fisher. As for emotions triggering a cardiac event, evidence has emerged showing that the heart muscle can be damaged by a sudden release of adrenaline. "Cardiologists have had to come to grips with the fact that an emotional event or trauma can cause a 'broken heart,' " Fisher says.

Acceptance of cardiac psychology has indeed been growing. In 2008, the American Heart Association began recommending that cardiac patients be screened for depression, and in 2010, Medicare approved coverage for the program established by Dean Ornish, MD. His Lifestyle Heart Trial, published in 1990, showed actual regression of coronary plaque in patients who incorporated diet, exercise, and lifestyle changes, including support groups and an hour a day of yoga and meditation. Time spent in meditation showed the strongest connection.

Still, the field of cardiac psychology remains "scientifically imbalanced," Allan and Fisher write, with tens of thousands of epidemiologic studies and only forty-three randomized clinical trials. And some longstanding work has come under criticism in recent years. "We have this absolute paradox that type A isn't studied epidemiologically anymore," says Allan, "but the most robust clinical trials have made extensive use of the theory."

While much research remains to be done, both men emphasize that clinical care of patients with coronary heart disease needs to include psychosomatic approaches—otherwise, internists and cardiologists are too often treating outcomes rather than causes. Group therapy, Allan says, is the treatment of choice for much of this population. One investigation, the Stockholm Women's Intervention Trial, provided 237 cardiac patients with one year of group therapy; following up seven years later, enrolled patients had one-third the mortality of controls.

Incorporating into his practice an investigation of the psyche as well as the soma, Fisher says he cannot fully treat his cardiac patients without knowing their emotional state. "I don't take their inner worlds for granted," he says.

— *Andrea Crawford*

Convenient Care

Nyack clinic offers specialty treatment for local MS patients—no bridge or tunnel required

By the early Nineties, New York City police officer Richard Fernandez was noticing some weakness in his right leg, particularly after going on long runs. He was also having balance problems; on a ski trip, his friends once wrongly assumed that he'd had a few cocktails before hitting the slopes. Then, after scuffling with a perpetrator while on duty on Manhattan's Upper West Side, he suffered a minor back injury. "My back was fine by the time I saw a doctor," Fernandez recalls. "But I told him about my right side and he said, 'I think you should see a neurologist.' " The diagnosis: multiple sclerosis.

On one level, Fernandez was fortunate: the year he was diagnosed, 1993, was the same one in which the FDA approved Betaseron, the first MS-specific drug. His disease remained relatively well-controlled for the next two decades, with symptoms progressing slowly. He rose to the rank of sergeant and stayed with the NYPD until October 2011, when he put in his retirement papers. "In the last three years in particular I've noticed shifts in my health," says Fernandez, who was honored with the force's

Theodore Roosevelt Award, given to officers who serve despite medical hardship. "I thought it was best to pack it in."

A Rockland County resident, Fernandez had long seen MS specialists in Manhattan—but around the time that he retired from the NYPD, he learned that he could get treatment closer to home. Weill Cornell had just opened an MS clinic at Nyack Hospital; Fernandez could get checkups, drug infusions, imaging scans, and rehab sessions a half-hour from his home in Stony Point. "It's extremely convenient to have quality MS care locally," says the forty-five-year-old. "That's not a knock on other local neurologists, but they're also seeing someone with stroke, with Parkinson's; it's nice to have a nearby location that has MS experts."

Established in August 2011, the center is a joint effort between Nyack Hospital and NYP/Weill Cornell's Judith Jaffe Multiple Sclerosis Center, under the direction of Timothy Vartanian, MD, PhD. The Nyack center is headed by Jai Perumal, MD, an assistant professor of neurology and the Feil Family Clinical Scholar in Multiple Sclerosis II. Based in Manhattan, Perumal spends one day a week in Nyack. Jennifer Reardon, a Nyack Hospital nurse practitioner with specialized training in MS treatment, is at the clinic three days a week, while an administrator works full-time to coordinate patient care. In its first year the practice grew to some 200 patients from throughout the New York metro area; plans are in the works to expand the clinic hours with an eye to being open Monday through Friday. "Patients seem very grateful we're here," Perumal says. "It's great for us to do this, because there's nothing like this close by. It's gratifying for us. We're seeing patients across the spectrum—from the newly diagnosed to those who have been seen at other centers and want to transfer their care."

Having an easily accessible care provider is more than just a matter of convenience for MS patients, who often grapple with fatigue and limited mobility. The Nyack facility is one of a handful of dedicated MS centers in the region that are outside New York City; others are located in White Plains and Teaneck, New Jersey. "Patients in this area have a reluctance to go into Manhattan," Perumal says. "If they have gait issues, it can be difficult." Says Reardon: "They may need someone to drive them to the city. Then they have to find parking, see the provider, and drive home. It's half a day for one doctor's appointment, for someone who already has fatigue."

Natasha Adams, a forty-one-year-old who works in quality assurance, was diagnosed in 2008 after a bout of optic neuritis, another common MS symptom. Shortly after the Nyack clinic opened, the Nanuet resident transferred her care from a practice in Manhattan. "Now everything is

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Walking tall: Treatment has helped MS patient Richard Fernandez (with nurse practitioner Jennifer Reardon) retain his mobility.

right there," says Adams. "I no longer have to travel across the bridge; the specialist is ten minutes from my home. It's awesome." She praises the clinic staff for their attentiveness, not only in terms of practical issues (like obtaining ice packs to counter the heat sensitivity that the disease sometimes causes), but in helping her cope with the depression that MS patients often suffer, both for psychological and neurological reasons. "There have been times where I was an emotional wreck and called Jen and she was very concerned about me," Adams says. "She suggested I see a therapist and followed up with me. Whenever she says she's going to call you back with information, she does it—every time. Any time I need her, she's right there for me."

For patients diagnosed with MS, the prognosis has improved dramatically over the past two decades. The advent of new drug therapies like Tysabri has made MS a livable, manageable disease—particularly if it's caught early, monitored closely, and treated appropriately. "People have an image of MS as a disabling disease, but as we're starting patients on treatments earlier, we're seeing that less and less," Perumal says. "It has changed from a field where you couldn't do much to a field where you can make a big difference. Often MS patients are young—diagnosed in their twenties and thirties—so if you treat them effectively you're making a difference, not only in terms of how they live now, but in their long-term outcome."

'People have an image of MS as a disabling disease,' Perumal says, 'but as we're starting patients on treatments earlier, we're seeing that less and less.'

Adams has remained active—working, rearing two children, and leading a team ("Tasha's Troopers") that has raised more than $15,000 through MS walks. Although Fernandez has begun using crutches, he works out regularly on a stationary bike and aims to launch a new career, possibly in the nonprofit sector. "There are always challenges in life," he says. "You can complain about it, or you can do your best. Some people have perfect health, but they can't go out and do anything because they have no job or money. The glass is half full or half empty—it depends on how you look at it."

— Beth Saulnier

Follow the Leaders

Weill Cornell is in the vanguard of training students in leadership skills

When MD-PhD student Megan Riddle found out who was in one of her problem-based learning groups a few years ago, she was thrilled—at least at first. "I thought, This is going to be phenomenal; I like them all, they're really intelligent," recalls Riddle, who recently defended her dissertation on the neuroscience of eating disorders. "But I found that a number of them had very strong, outspoken leadership styles—and when everyone was in the room together, we couldn't all be leaders at once. I thought, This is not working. It has to change. Some people are speaking all the time and others are not being heard."

In retrospect, Riddle says, she wishes she'd had some training not only in the content they were grappling with, but in how to handle the contentious dynamics of the group itself. "When you take these intelligent, driven folks and put them together, it can sometimes lead to conflict with all those strong personalities," she says. "With more training in group dynamics, that might be mitigated."

Riddle has gone on to become a student leader at the Medical College; she's executive co-director of the Weill Cornell Community Clinic and past co-director of the Female Association of Clinicians, Educators, and Scientists (FACES), a support and mentoring group for women in the MD-PhD program. She is also serving on a student-faculty committee working to integrate leadership training into the curriculum. The effort is part of an overhaul spurred in part by the Accreditation Council for Graduate Medical Education, which has called for curricular innovation in the wake of the Flexner 2.0 report that re-evaluated the field a century after the landmark study that established the current system. "Medicine is different than it was a hundred years ago," says Joseph Abularrage, MD, MPH, MPhil, professor of clinical pediatrics and liaison for curricular projects, who is heading the effort for leadership training at Weill Cornell. "Our students already have significant leadership experience prior to coming to the Medical College. These students will go on to become leaders in medicine. There are definable skills that will help them fulfill their potential as successful leaders. We believe that leadership skills are important for success, and they can be taught. Some people say, 'You're either a leader or you're not.' But we all have the potential to lead."

Chairman of pediatrics at New York Hospital Queens, Abularrage has long given weekly leadership seminars to Weill Cornell students and pediatric residents. Last academic year, under a pilot program, he spearheaded a required leadership module for first-year medical students. It included a self-assessment exercise, called the Personal and Company Effectiveness (PACE) Palette, designed to promote self-awareness and empathy for others. It categorizes personality types into four colors—from the adventurous (red) to the introverted (green)—and offers insights into how people with those temperaments can best work together. Such knowledge is aimed to facilitate interpersonal dynamics—whether in the classroom, on the wards, at a scientific conference, in a professional society, or in the exam room. "Leadership skills are part of the portfolio

Joseph Abularrage, MD, MPH, MPhil

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that every student who graduates from our Medical College should have, at least at a basic level," says Carol Storey-Johnson, MD '77, senior associate dean for education. "We're attempting to produce the future leaders of medicine, whatever our students go into. They need to understand what dynamics are useful to foster change."

In addition to the self-assessment exercise, students did a module on conflict resolution, conducted by Sally Klingel from the faculty of Cornell's School of Industrial and Labor Relations. Clinical Skills Center director Yoon Kang, MD, a member of the leadership curriculum committee, notes that such training would have come in handy when treating a past patient, a Jehovah's Witness whose religious beliefs put strict limitations on his care. "Some of the negotiation skills that we learned from this brief conflict resolution pilot would have been helpful to me in terms of interacting with this patient and his family," says Kang, the Richard P. Cohen, MD, Associate Professor of Medical Education. "Also, it would have helped to understand that beyond different expertise on the medical team there were different perspectives based on personalities. Everybody had the same goal of taking care of the patient, but they were coming from different angles in the way they were thinking about the clinical content." A tool like the PACE Palette, she says, "would have helped put me in their shoes in terms of the way they were viewing the situation."

Abularrage points out that although some residencies and fellowships have a leadership training component—and some institutions offer it to faculty at various career stages—Weill Cornell is now the only medical college requiring students to participate in a curriculum designed around training in leadership. "We did a literature review on teaching leadership in medical schools in the U.S." he says, "and it turns out that there was none." But just as new doctors have long been told to go forth and teach—without having received any dedicated instruction in pedagogy—they're expected to have the innate ability to guide others and work well in groups. "All of a sudden, someone taps us on the shoulder and says, 'OK, we'd like you to run this,' " Abularrage says. "But nowhere in our education do we get trained in leadership skills."

Fourth-year student Matthew Goodwin, PhD, has been an enthusiastic supporter of Abularrage's efforts. He calls leadership training vital to countering "an outdated hierarchical system" in which those at the bottom are expected to follow orders unquestioningly at the potential expense of optimal outcomes. "More people are looking at other industries like aviation and saying, 'There are better ways to do things,' " he says. "They're starting to realize that medicine is behind the curve on finding innovative solutions to our problems."

Starting this fall, all first-years will undergo the PACE self-assessment training, and second-years will have the conflict resolution module in the spring; instruction on public speaking is also in the works. Abularrage's committee is weighing further development of leadership training in the curriculum, while other teams are working on enhancing mentoring, offering teacher training, dissolving boundaries between basic science courses and the clinics, adding more humanities instruction, and other curricular issues. "Sometimes as students, if we're not specifically learning about medicine, we think that maybe it's not as important," says Riddle. "But leadership is one subject that's critical regardless of where you end up. Whether it's private practice, public policy, consulting, or academics, this is going to help you along the way."

— Beth Saulnier

'We believe that leadership skills are important for success, and they can be taught,' says Abularrage. 'Some people say, "You're either a leader or you're not." But we all have the potential to lead.'

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Anthony Sauve, PhD

Magic Pill?

Pharmacologist Anthony Sauve, PhD, investigates a form of vitamin B that could aid healing, prevent aging, and combat obesity

One group of test subjects ate a high-fat diet, and—as expected—gained weight, developed diabetes, had higher cholesterol, lost muscle fiber, and suffered other ill effects. Another group ate the same thing but received a special supplement. They gained significantly less weight, maintained strength and endurance, and did not develop negative health effects.

What was this supplement that sounds like a magic pill—something that produces the benefits of a low-calorie diet and exercise without requiring one to engage in either? It was the molecule nicotinamide riboside (NR), a natural form of vitamin B that exists in very small amounts in milk, as well as beer and other foods made from yeast, which secretes the compound. "What has happened here," says Anthony Sauve, PhD, associate professor of pharmacology, "is that we've discovered a super-vitamin."

In a study that appeared in the June 2012 issue of *Cell Metabolism*, Sauve and colleagues from the Polytechnic School in Lausanne, Switzerland, showed that, when given in high doses, NR produced these remarkable effects in mice—with no toxicity—by stimulating key anti-aging pathways in cells. NR appears to improve the function of mitochondria, the source of most energy in cells; mitochondrial decline is associated with diseases of aging, including cancer and neuro-degeneration. "The compound was able to stimulate physiology in such a way as to resist metabolic syndrome, make the animals healthier and improve their stamina, and correct the toxic effects of this high-fat diet," says Sauve, a pharmacologist and organic chemist.

Sauve's investigations of NR began in anti-aging research. He and other colleagues were trying to understand how anti-aging enzymes known as sirtuins get upregulated, or increased, by factors such as extreme low-calorie diets or exercise. The enzymes, they found, are highly dependent upon nicotinamide adeine dinucleotide (NAD), a metabolite central to counteracting metabolic syndrome and protecting cells from oxidative stress.

Others had theorized a connection between NR and NAD years ago; while working on NAD metabolism in the Fifties, Nobel Laureate Arthur Kornberg recognized that NR could play an important role. But he tested NR on cells that had been broken open in a test tube, and these early tests produced no interesting results. More than five decades later, Sauve and his team posed the same question but used a different approach. "We threw NR on whole cells—and what happened? The cells made a lot of NAD," he says. "It took fifty-five years for people to actually answer the question, 'What does NR do in cells?' "

To answer that question, however, Sauve first needed to procure large enough quantities of NR. He invented a method to synthesize NR in highly pure form and in the large multi-gram amounts required for testing. He published this synthesis in 2007, and in the same paper showed for the first time that NR is, indeed, a super NAD enhancer.

Still, it was not clear that increasing NAD would make the anti-aging sirtuins work better. With this latest research, he says, they've now shown "that NAD gets it done." In the past two years, Sauve and his Swiss colleagues proved that by increasing NAD genetically they could stimulate the correct pathways: mice with genetic modifications to increase NAD proved resistant to the effects of a high-fat diet. Now, they have achieved the same results without manipulating any genes but by delivering NR directly to the mice in their food.

The findings demonstrate the potential of NR—both as a natural compound and in novel derivatives for pharmaceutical uses—not only to fight obesity and metabolic disorders, but also to play a role in treating conditions such as spinal cord injuries, Parkinson's disease, and mitochondrial disorders. "People have known for a long

time that some of the same things that protect you from metabolic syndrome also give you protection against neuro-degeneration and sarcopenia, or muscle-wasting, two debilitating conditions of aging," Sauve says. He showed, in a 2007 paper written with Harvard's David Sinclair (known for his research on resveratrol, the beneficial substance in red wine) and other colleagues, that increased levels of NAD in mitochondria protect cells from dying. "NR has this special property. It hits the magic organelle—the mitochondria—and makes it have more NAD," he says. "This is exactly what you want to target in order to get these protective effects."

In one example of this potential, Sauve has collaborated with Samie Jaffrey, MD, PhD, another faculty member in the Department of Pharmacology, and Brett Langley, PhD, whose lab at the Burke Rehabilitation Center seeks ways to protect and regenerate cells of the nervous system. They are now in the fourth year of a five-year grant from the New York State Spinal Cord Injury Center of Research Excellence to study whether NR could be given at the time of spinal cord injury to arrest cell death and axonal degeneration. "The studies look fantastic," says Langley, assistant professor of neurology and neuroscience at Weill Cornell. "These compounds are able to protect cells from dying."

When the spinal cord is injured, a number of chemical and physical barriers prevent regeneration from occurring. Many of these inhibitory factors come from the myelin, the insulation around axons (the nerve fibers that project from the cell body and transmit the electrical impulses of the nervous system), which plays an important role in maintaining axonal integrity. "We've modeled growth inhibition factors *in vitro*, and when we increase NAD by giving NR we can actually get axons to grow through barriers they normally wouldn't grow through," Langley explains. They are now testing the response in animals and expect to publish their findings in 2013. "Prior to Dr. Sauve's work, no one really had good ways of increasing NAD in cells. He was able to find ways of synthesizing NR in large enough quantities that we can actually use it both as an investigative tool and as a therapeutic drug," he says.

Sauve's method for synthesizing NR has been patented by Cornell's Center for Technology Enterprise and Commercialization and licensed to ChromaDex Corporation. The company is now working to manufacture it on a scale required for formulation in products for human consumption, pending safety approvals. Before long, NR could be available as a dietary supplement. "There are a lot of important bioactive compounds in food—possible new vitamin forms or other nutrients that are packaged by nature in ways that affect their potency and how well the body can convert them into something beneficial," Sauve says. "It's only in recent years that we've had the analytical capabilities to begin to interrogate more complex actions of vitamins and nutrients. With greater attention and NIH research funding, we'll see more of these kinds of discoveries."

— Andrea Crawford

The New Normal

PhD grad pioneers nonprofit for rare genetic diseases

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Nearly 26 million Americans have diabetes. More than 5 million have Alzheimer's disease and a million have Parkinson's. Each condition has a clear diagnosis and a cadre of scientists delving into its mechanisms and exploring potential treatments. If only people with rare diseases were so lucky.

The constellation of rare diseases comprises some 8,000 conditions, each affecting fewer than 200,000 people. Symptoms often emerge in infancy, but accurate diagnoses—and effective treatments—can be hard to come by. And because most rare diseases are caused by genetic mutations, as many as 30 percent of the people who have them die before they enter kindergarten. Few reach old age. "Identifying potentially causative genes is the first step," says Naira Rezende, PhD '12. "The second step is to use that information to design a treatment that makes sense."

In 2011, Rezende partnered with fellow medical and graduate students at Johns Hopkins, Washington University in St. Louis, Yale, and Harvard to form the Rare Genomics Institute (RGI), a virtual nonprofit staffed exclusively by volunteers—many, like Rezende, former Howard Hughes scholars. "It's possible to use genome sequencing to help people with a whole spectrum of diseases," says Rezende, who earned a PhD in stem cell biology under Lorraine Gudas, PhD, the Revlon Pharmaceutical Professor of Pharmacology and Toxicology. "We want to make sure every family that needs it has access to this technology."

Through its website, RGI recruits patients with genetically based diseases, clinical scientists investigating those conditions, and donors willing to help fund the effort. The nonprofit's eighteen volunteers facilitate introductions. "As I finished my PhD, I noticed that I didn't have much contact with the patient community," says Rezende, who now works as a scientific associate at the law firm of Wilson, Sonsini, Goodrich & Rosati in Manhattan and leads RGI's patient advocacy team. "I wanted to be in contact with the families we were working at the bench to benefit."

Already, the nonprofit has facilitated sequencing for three children; twenty more are being evaluated for sequencing through RGI partnerships. "The families provide a great motivation," says Rezende. "There were days in graduate school where I wondered, 'Why am I doing this?' It's been humbling, connecting with these amazing families who put all of their money, time, and energy into helping their children."

— Sharon Tregaskis


BRAINLAB

Brain Storm

New techniques, agents, and technologies have sparked a revolution in neurosurgery

By Andrea Crawford

Photographs by John Abbott

The pons, as medical students learn, is the bridge-like part of the brainstem that connects the brain with the spinal cord. Tumors found there, called diffuse intrinsic pontine glioma (DIPG), strike children and grow aggressively among the key cranial nerve structures responsible for sensory and motor functions such as equilibrium, chewing, swallowing, and respiration. Upon diagnosis of DIPG, patients receive radiation as palliative care. There are no other options.

For years, Mark Souweidane, MD, director of the Weill Cornell Pediatric Brain and Spine Center, has seen the disease take its toll on patients and their families. "You watch a child succumb to a tumor the size of a walnut—you watch the angst, turmoil, and frustration it causes the family," he says. "You receive their continuous questions as to why there's nothing better. There's no stronger motivation than that to look for a better way."

Twelve years ago, Souweidane set out to look for that better way. He scoured the literature, collaborated with bench scientists, and assembled a team. They devised a treatment concept, found a promising therapeutic agent, and created a surgical procedure to administer it directly into the tumor, bypassing the blood-brain barrier. This past spring, with the opening of a clinical trial, Souweidane's team may have finally changed the par-

Mark Souweidane, MD

Philip Stieg, MD, PhD

adigm, offering hope where there had been none. "We had to start at ground zero, amid a lot of criticism that what we were doing was unfathomable," Souweidane says. "We wanted to infuse things into the brainstem that no one had ever tried before, and when we began there was no evidence that you could do this."

In May they operated on a four-year-old girl, the first attempt at surgical treatment for a patient with DIPG. In July they operated on a second child with the disease.

The current phase-one clinical trial is designed to look at safety and feasibility, and over the next one to two years the team plans to administer the treatment to a minimum of twelve patients between the ages of three and twenty-one. While it will be a long time before they can begin to assess efficacy, the surgery offers the first glimmer of hope for treating a disease long considered inoperable.

During the surgery, a radioimmunotherapeutic agent reaches the tumor through a method called convection-enhanced delivery (CED), a pressure-driven infusion through a surgically placed cannula. The agent, known as 124I-8H9, consists of an antibody produced by mice, which binds to the tumor to administer a radioactive substance to kill its cells. The technical feat alone is challenging because the tumors are small lesions, nine centimeters beneath the surface of the brain, which the team targets using interoperative MRI, a recently FDA-approved navigation system, and specially designed micro-catheters.

With its combination of innovative surgical technique—in which the team treated an area of the brain that had never before been accessed—and its novel application of an agent that uses antibodies to attack the tumors with radiation, the work on DIPG demonstrates

'Patients undergoing treatment today have no comparison to how it used to be—thank goodness. They're beneficiaries of an amazing amount of innovation.'

some of the ways in which neurological surgery is in the midst of a revolution. Minimally invasive techniques have radically altered how neurosurgeons work, and the emerging field of molecular medicine—using surgery to deliver agents such as genes, cells, drugs, or antibodies to targets in the nervous system to treat a variety of diseases—is changing the way surgeons think about clinical care.

As the field redefines itself, the traditional role of the neurosurgeon is evolving as well. When Philip Stieg, MD, PhD, chairman of the Department of Neurological Surgery and of the Weill Cornell Brain and Spine Center, entered the field three decades ago, he says, "neurosurgeons were considered iconoclasts, unfriendly and inaccessible. Today neurosurgeons at NYP/Weill Cornell are part of a large team of physicians who take care of complex neurologic disorders." That approach extends from the operating room to the laboratory, as surgeons do their part not only in bringing scientific breakthroughs to their patients, but in taking ideas from the OR back to the lab—and helping to generate those breakthroughs.

Technology has driven much of the revolution. "When I started, I was operating with an incandescent light bulb," Stieg says, "and an advanced OR was one that had a microscope." Now he and his team of neurosurgeons use computer-guided instruments and three-dimensional technology. They get much better visualization of the brain's structures with bright illumination and magnification in extremely high resolution, advances that enable them to look around corners, around the brain stem, and at the complex relationships between compressive structures like blood vessels on nerves. "Our ability to visualize pathology has changed dramatically," Stieg says.

When Souweidane arrived at NYP/Weill Cornell in the mid-Nineties, no one had ever used an endoscope in the brain; today, 20 to 30 percent of the neurosurgeries they do are endoscopic. He points out that on a recent day he performed four operations: two tumor removals, one procedure to treat hydrocephalus (the overproduction of cerebral spinal fluid inside the brain's ventricles), and one biopsy of a tumor in the brain stem. In the not-too-distant past, each of those surgeries would have required traditional craniotomies, yet he had done each through a "burr hole," a quarter-inch opening in the skull. "These techniques

Michael Kaplitt, MD '95, PhD, with Dr. Stieg

have hugely impacted the field," Souweidane says. "Patients undergoing treatment today have no comparison to how it used to be—thank goodness. They're beneficiaries of an amazing amount of innovation." Stieg agrees, noting the improved speed and ease of recovery. "With less invasive surgeries," he says, "patients get better faster with the same outcomes."

In addition to making surgery easier on patients, endoscopic and minimally invasive techniques have also broadened what surgeons can do—changing the way they treat congenital malformations, brain tumors, and cystic structures such as colloid cysts, benign but potentially deadly tumors located deep in the central part of the brain. Weill Cornell neurosurgeons are removing tumors previously considered inoperable. For example, Theodore Schwartz, MD, a professor of neurological surgery who directs the center for epilepsy surgery and specializes in anterior skull base approaches for the treatment of pituitary tumors, uses endoscopes to take out types of tumors that very few surgeons would be able to remove, his colleagues say.

Spinal surgeons such as Roger Härtl, MD, the Leonard and Fleur Harlan Clinical Scholar and the neurosurgeon on call for the New York Giants, and Eric Elowitz, MD, assistant professor of neurological surgery, use computer navigation guides, resulting in much less destruction of muscle tissue, which is key to recovery and rehabilitation. Technological advances also allow interventional radiologists Pierre Gobin, MD, professor of radiology in neurological surgery, Athos Patsalides, MD, the Alvina and Willis Murphy Assistant Professor of Neurological Surgery, and Jared Knopman, MD, assistant professor of neurological surgery, to more safely, efficiently, and effectively treat intracranial vascular lesions such as aneurysms and arteriovenous malformations. Technology has reached the point where even noninvasive procedures are available. Susan Pannullo, MD '87, director of neurosurgical radiosurgery, delivers radiation to tumors and other targets through instruments that use beams and do not require incisions.

Perhaps the most surprising shift in neurosurgery has been in the emerging field of molecular techniques and treatments. In 2003 Michael Kaplitt, MD '95, PhD, associate professor of neurological surgery and vice chairman for research, was the first person in the world to administer gene therapy to the brain. Last year, he concluded a phase-two study of that work in treating Parkinson's disease—the first time that a randomized, double-blind study showed positive results for any type of biological therapy in a neurological disease. In 2009 John Boockvar, MD, associate professor of neurological surgery, in collaboration with Gobin and Patsalides, was the first to infuse the chemotherapeutic agent Avastin directly into a glioblastoma tumor, bypassing the blood-brain barrier—work featured in the *New York Times*.

"If you had asked about the future of neurosurgery twenty years

Jeffrey Greenfield, MD ’02, PhD

RENE PEREZ

ago, almost everybody would have said it was in new types of devices and hardware,” says Kaplitt. “Our current approaches would have been unthinkable then. Yet now there’s not a field of neurosurgery where there aren’t people actively taking leadership roles in both basic and translational research to apply molecular therapies or molecular techniques to novel problems.” Jeffrey Greenfield, MD ’02, PhD, assistant professor of neurological surgery in pediatrics and the Victor and Tara Menezes Clinical Scholar in Neuroscience, agrees. “Molecular medicine may not have changed our day-to-day practice of neurosurgery, but it’s starting to make inroads in how we think about our patients, how we plan our surgeries, and how we think about their postoperative care,” says Greenfield.

In an effort to allow clinicians and scientists at Weill Cornell to conduct more research into ways to attack rare tumors, last year Souweidane and Greenfield launched the Children’s Brain Tumor Project. It grew out of conversations Greenfield had had with a patient, who was a college sophomore in 2010 when she learned she had gliomatosis cerebri—an inoperable, diffuse, and highly aggressive tumor—in almost every lobe of her brain. The patient died in May 2012, and that summer, using her tumor, Greenfield’s team finished the first complete DNA mapping of gliomatosis cerebri, a vital step in finding potential therapies.

Over the eighteen months of treatment, Greenfield had to tell his patient and her family that physicians know virtually nothing about gliomatosis cerebri. “It was quite frustrating to be forced to admit that there’s not a lot of research on rare diseases because there’s no NIH funding impetus to take care of a disease that affects 200 people a year,” he says. A foundation established by the patient’s family helped to launch the Children’s Brain Tumor Project. “We’re going to figure out what we can do to offer hope to those patients,” Greenfield says. “That’s what the patient wanted.”

Recently, we have seen the first surgery to attempt to treat DIPG, the first genomic analysis of gliomatosis cerebri, and now the first attempt to treat addiction through neurosurgery. This past summer, Kaplitt received FDA approval for a phase-one trial to treat cocaine addiction by stimulating the reward center of the brain. His work demonstrates how research in neurological surgery is further revolutionizing the field by changing the definition of what constitutes a neurosurgical case. His long-standing research on Parkinson’s—and in treating its non-motor symptoms such as depression, addictive behaviors, and memory problems—has led to advances that could

'Our department on the whole is incredibly translational, and everyone, top to bottom, is running basic science labs that are taking things from the operating room into the lab and vice versa.'

benefit millions who suffer from major depression, drug addiction, and metabolic diseases.

A few years ago, working with the Rockefeller University's Paul Greengard, PhD, the 2000 Nobel laureate in medicine, Kaplitt found that a protein known as P11 acts as a shuttle to bring neurotransmitter receptors to the surface of the cell, thus influencing its response to serotonin and dopamine. In a paper published in *Science* two years ago, they showed that when P11 is knocked out with gene therapy in the nucleus accumbens, a reward center in the brain, depression-like behavior occurred in animals; when they overproduced P11, normal behavior returned. The findings were corroborated in human samples from the brain bank of collaborator Carol Tamminga, MD, of Southwestern Medical Center. "So there's a human proof of principle that suggests that low P11 levels in this area of the brain may be one of the causative factors that define human depression, which we can potentially reverse genetically," Kaplitt says.

More recently, he has determined that P11 also has a profound influence in a second region of the brain, the subgenual cingulate cortex—an area currently being closely studied in relation to depression—and that its effects there may be opposite from what it does in the nucleus accumbens. "It seems to do very different things in these two regions, which highlights the value of focal neurosurgical interventions because drugs would influence the pathway only in one direction or another," says Kaplitt, who is preparing to publish his findings. "It's interesting in a way that fits nicely with what's known about depression through brain imaging technology."

Kaplitt has similar data showing how parts of the brain may influence metabolism, which Stieg notes could have application for treating eating disorders. That's just one example, Stieg says, where "we're waiting for the molecular biology, whether it be the creation of viral or genetic or chemotherapeutic agents, to catch up with the surgical technique." Neurosurgeons have therefore become important participants, even leaders, in helping to push the molecular biology. "We believe that neurosurgeons have a lot to offer in the scientific realm, and that the historical biases about neurosurgeons—that they may be smart but they operate and that's it—are fundamentally flawed," says Kaplitt, noting that almost half of the department's current residents have PhDs. "We believe that neurosurgery is completely compatible with quality science."

Each member of the department has numerous patient-centered trials where they're not only operating but also attempting to push the envelope for the entire field. "Our department on the whole is incredibly translational, and everyone, top to bottom, is running basic science labs that are taking things from the operating room into the lab and vice versa," says Greenfield. Kaplitt cites Souweidane as a prime example. With no formal background in research science, he simply had a strong desire to help his patients with intractable brain tumors. "So of his own volition he started a research effort," Kaplitt says. "He focused on a problem that was a strong unmet need in his field, and that evolved from an idea to the point where, now, he's treating patients."

His fellow surgeons give credit to Stieg, under whose leadership the department has supported its members' efforts to bring new therapies to patients. Even as its traditional surgical volume has grown dramatically in the last decade, the department had been structured to support research to an unusual degree, creating an environment where ideas flourish, says Kaplitt.

A prime example of Stieg's leadership and focus on mentoring his faculty was the department's launch of a Brain Summit in June 2011. Under the direction of Boockvar—working with Stieg, WCMC Dean Laurie Glimcher, MD, and NYP President Steven Corwin, MD—the Brain Summit brought together top neuroscientists from across the country and representatives of biotech firms to help drive scientific collaboration to accelerate cures. In addition, the forum provided an opportunity to expose promising research approaches to potential funders.

Stieg's drive for scientific collaboration also resulted in taking his whole department to Ithaca to meet with biomedical engineers, sparking several collaborations that continue to bear fruit. Weill Cornell's Härtl and Cornell's Larry Bonassar, PhD, associate director of the Department of Biomedical Engineering, for example, are working to bioengineer artificial spinal disks. These could offer treatment for patients with degenerative spinal disease with a substance that, unlike plastic or metal, mimics the qualities of human disks. Similarly, they are working to create tissue to repair annular defects, which currently have no treatment. "There are so many opportunities now, so much interest," Kaplitt says. "Smart, creative, energetic people with the right institutional backing and the right idea can start pushing these things into the clinic."

Stieg's mission to share his team's expertise globally and build a world-class collaborative teaching facility led to the launch in 2010 of the Surgical Innovations Lab, the only one of its kind in the world. Demonstrations of advanced neurosurgical techniques pioneered by Stieg and his team are shared in real time with other medical professionals via multimedia technology. Recently, Chinese, Arab, and Italian neurosurgeons watched and commented as Stieg taught residents how to perform complex surgical approaches to the skull base.

Recent scientific and technical advances are greatly broadening the range of what neurosurgeons are able to treat, even as an aging population increases the frequency with which surgeons see the conditions they have long treated, such as back pain, stroke, and movement disorders. But as vast as neurosurgery's scope may be today, Stieg says, its mission lies at the historic foundation of medicine: "We're always thinking about how to alleviate pain and suffering." ●

Mother courage: A woman and her children at Weill Bugando Medical Centre. Only a lucky few in the nation get appropriate treatment for burn injuries; many others endure a lifetime of disfigurement and disability.

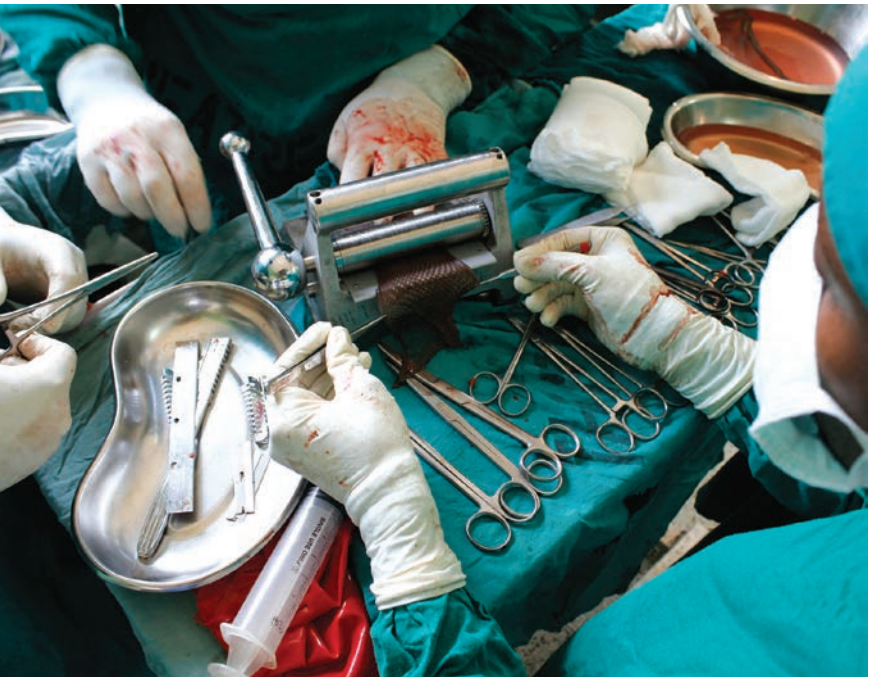
More Than Skin Deep

On a service trip to Tanzania—where burn injuries are common and physicians are few—Weill Cornell surgeons and nurses aimed to help colleagues at Weill Bugando

By Beth Saulnier

Photographs by David Chalk

His name was Charles, and he'd survived a horrific accident that had killed most of his family: their home had been destroyed when a tank of propane cooking fuel exploded, taking the lives of his parents and four of their seven children. Suffering third-degree burns over some 25 percent of his body including his chest, hands, and entire face, the twelve-year-old had traveled 170 miles to Weill Bugando Medical Centre in Mwanza, Tanzania, for treatment—but given its limitations of equipment and training, there was little the staff could do but clean and cover his wounds. By the time burn surgeon James Gallagher, MD, saw Charles, eight days after the explosion, his bandages were tinged green with infection. "His life was definitely threatened," says Gallagher, the leader of a Weill Cornell team that visited Mwanza last March.



Medical mission: (Clockwise from above) A young patient; Weill Cornell's James Gallagher, MD, and Katrina Mitchell, MD, confer with Bugando's Geofrey Giiti, MD; Gallagher in the operating room; burn surgery instructions; a Bugando OR.

Gallagher and his colleagues—including surgical resident Katrina Mitchell, MD, three nurses, and a rehabilitation therapist—spent three weeks working side by side with Bugando staff. They demonstrated approaches such as employing tourniquets to minimize blood loss during surgery, the use of skin grafting instruments, and the vital role of rehab in recovery. "Everyone knows that Africa is suffering and that there aren't enough doctors—but what does that mean?" muses Gallagher, who spent a year doing general surgery in the sub-Saharan region a decade ago, before specializing in burns. "Well, it means that things present very late. In the hospital there are lots of kids with open burn wounds who've been there for months, but the surgeons don't operate on them because they don't have the proper tools, they have no track record of success, and the hospital has many patients with other surgical problems needing care. The surgeons focus their time and effort on problems they know they can solve, and the burn patients often get discharged with open wounds."

Even in the developed world, extensive burn injuries can be devastating. In addition to requiring multiple surgeries and intensive postoperative care, such injuries often raise difficult emotional and practical issues. Despite successful treatment, burns—especially to the face—can mean permanent disfigurement, with all the psychological damage that entails. Burns to the hands can cause dexterity problems that impede patients from performing everyday tasks or even earning a living.

And if burns aren't properly treated in the hours, days, and weeks following injury—as they rarely are in the developing world—the outcomes are infinitely worse. Patients endure chronic wounds in which granulation tissue—which, under normal circumstances, plays an essential role in the healing process—is never covered by healthy skin; they suffer contractures in which scar tissue forms and hardens, fusing fingers together or even sealing limbs to the body. "The granulation just keeps growing; we've seen adults with chronic wounds remaining from childhood," Gallagher says. "It's pretty terrible. In the community you see all of these horrible contractures, and the anatomy underneath is completely deformed."

Gallagher and his team hoped to counter that—not by sweeping in and treating a few lucky patients over the course of a few weeks before jetting home again, but by helping Bugando's staff develop its own burn-treatment infrastructure. "The best thing you can do," Mitchell says, "is try to strengthen the local institution by improving care protocols and the ways they educate themselves and their colleagues." In fact, Mitchell notes, these days one-off "mission trips" by Western medical teams—while clearly gratifying to the participants themselves—are increasingly understood to be of limited benefit; they can even be counterproductive, by introducing conflicting treatment protocols or providing equipment that local staff aren't trained to use or maintain. "Traveling to a place for a few days, taking care of a few patients, and leaving does very little to improve an institution or local health care," she says. "It is more important to direct funding and human resources into sustainable projects that will affect hundreds or even thousands of patients into the future."

In a video chronicling the Bugando trip, Gallagher notes that while there is one doctor for roughly every 350 people in the developed world, in Africa the proportion is one for every 33,000. Only a fraction of those MDs are surgeons—and severe burn injuries are

surgical cases. Tanzania has just one dedicated burn unit, located in the capital city of Dar es Salaam, more than 1,000 miles from Mwanza. "Apart from the paucity of human resources," says Geofrey Giiti, MD, a lecturer and general surgeon at Weill Bugando who is spearheading the improvement of burn treatment at the hospital, "there are inadequate facilities for resuscitating acute burn injury, consumables for dressing burn wounds, shower tables, proper surgical instruments, and facilities for rehabilitation therapy."

While treatment resources are few, the need is acute: burn injuries are heartbreakingly common in Africa, where cooking is mainly done around open fires. Those fires are often low to the ground—at child height—and many pediatric injuries involve scalding by hot water, tea, or porridge. "You have unprotected kitchens, and you also have the fact that people are boiling water to make it drinkable," Gallagher says. "So there's a lot of boiling going on and a lot of cooking in what we would call unsafe conditions. When I lived in Africa the first time, the conclusion I drew is that for much of the population it's like long-term camping. If you picture yourself camping, sleeping on the ground and cooking over an open fire—that's what it's like to live in much of Africa."

The Mwanza burn efforts began with a meeting between Gallagher and Mitchell, who was in New York on leave from a two-year stint at Weill Bugando, where she was working on surgical education development. Gallagher, with his dual interests in burn medicine and global health, asked about the state of burn treatment at Bugando—an institution that is not only affiliated with Weill Cornell but shares a common benefactor in Sanford Weill. "She said, 'There's really nothing going on with burns,' " he recalls. "But she knew a surgeon who would be a good candidate to lead the charge and be the person who invites us—because we want to work with the surgeons on the ground and say, 'What do you guys need? We're your partners.' " Giiti signed on, and in August 2011 Gallagher and Mitchell—who eventually opted to stay in Tanzania for a third year to work on the burn project—took a two-week fact-finding trip to assess the state of burn treatment at the hospital, from operating rooms to nursing staff to the kitchens that provide nutrition; they even visited the local fire department.

During the March trip, which also included a volunteer photographer, the team focused its efforts on a half-dozen severely injured pediatric patients. They included Charles—on whom they performed successful skin grafts, including a dramatic repair of his face—and a girl of toddler age who'd fallen face-first into hot coals; after two months in the hospital, her skull remained exposed. During their second week in Mwanza, a woman came into Sekou Toure Hospital, a nearby facility that the team also visited; a household maid, she'd been accused of stealing from her employers. "She denied it, and they took her to a witch doctor, who poured an accelerant on her and said if she was innocent she wouldn't go on fire," Gallagher says. "Quite naturally she went on fire, and suffered third-degree burns to both of her legs." Under the guidance of the Weill Cornell surgeons, the Tanzanian staff did skin grafts just three days after her injury. "Normally it would be months in the hospital, contracted," Gallagher says. "I'm not exaggerating. She would've ended up a cripple, because she would've had chronic wounds for months, or more likely permanently."

Gallagher points out that while burn injuries can be devastating, their treatment is often fairly straightforward: dressing changes, possibly skin grafts, and rehabilitation. That means that with training and the proper surgical instruments—which are generally low-tech—it's realistic to expect that surgeons and support staff in developing countries could treat them successfully. "At the hotel in Mwanza you'd run into other visiting physicians, and many of them were overwhelmed and frustrated that they can't change anything," Gallagher says. "I'm grateful that I don't feel that way. I'm excited because I feel that we have a practical solution and can help the local African surgeons to ease the suffering from burn injury in their people."

According to Giiti, Weill Bugando has indeed begun to make progress in bettering its burn treatment since the March trip. "Dr. Gallagher's burn team demonstrated to us the role of a multidisciplinary approach in treating burn injuries," he says. "We have started to involve other specialties like rehabilitation therapists in managing burn patients. In deep burn, we are advocating early surgery by tangential excision and early skin grafting. In the past, the practice was to delay surgery until after skin granulation had taken place, which was associated with long hospital stays and bad aesthetic outcomes."

The ultimate goal, Giiti says, is to establish a dedicated burn unit in Mwanza. Weill Cornell will continue to offer training and support, including the development of surgical simulators; Gallagher is currently conducting a study on the efficacy of a low-tech simulation system for evaluating and training burn surgeons. In November, he and his team learned that they'd been awarded a $191,000 grant from the ELMA Foundation for the pilot phase of developing a pediatric burn unit, including reorganizing surgical spaces and establishing care protocols for nursing and rehabilitation; Dean Emeritus Antonio Gotto, MD, DPhil, has pledged to spearhead fundraising of an additional $120,000. "Over the next few years, quarter by quarter, it will build upon itself and be a model or proof of concept that can be taken anywhere," Mitchell says. "To say, 'If you're a care provider interested in burns, this is the stepwise way to go about establishing a burn center anywhere in a resource-limited environment.' " Now a senior resident in the Weill Cornell general surgery program, Mitchell ultimately plans to practice internationally, most likely in trauma and critical care surgery. "It's challenging in a different way than working in the States," she says of practicing in developing countries. "It makes you think more practically and utilize all your resources. Most of all, it's incredibly rewarding. Patients are grateful, you have wonderful relationships with your colleagues across disciplines, and it brings your work back to its roots. In Africa, I felt like medicine was a joy." ●

Treating and training: (Clockwise from top left) Rehab specialist Sam Yohannan works with a pediatric patient; Mitchell and Yohannan with local children; Mitchell outside the OR; Gallagher lectures to Bugando staff.

Infectious Enthusiasm

Professor Linnie Golightly, MD '83, is dedicated to battling malaria and other devastating diseases, in the developing world and at home

By Kristina Strain & Sharon Tregaskis

Linnie Golightly, MD '83, was at the end of her second year of medical school when a class founded by legendary professor of tropical medicine and public health Benjamin Kean, MD, introduced the Detroit native to the roster of diseases common in developing countries. At the end of that year, she traveled deep into the Brazilian rain forest with Warren Johnson, MD, now the B. H. Kean Professor of Tropical Medicine at Weill Cornell. "There was no doctor, no health-care professional," recalls Golightly, now an associate professor of clinical medicine and of medicine in microbiology and immunology at the Medical College. "When we were there, people would come from miles around because there was somebody who could help them."

JOHN ABBOTT

Johnson still laughs, recalling the day—the ground slick with mud from a recent downpour—when he sent Golightly out with their host, parasitologist Philip Marsden, MD, a British expatriate who had established clinics throughout Brazil. When they returned, Johnson asked how things had gone. "Philip says, 'She nearly killed me—you didn't tell me she was a runner! She's as sure-footed as a mountain goat!' " That same energy still infuses Golightly's work, says Johnson, who recruited his protégé to join Weill Cornell's faculty in 1997. "It's symbolic of her perseverance," he says. "There were a certain number of patients to be seen that day, and Linnie was going to see them."

Until then, Golightly had imagined she might train as a neurosurgeon, then return home. Intrigued by basic science, she rotated in the laboratory of Ira Black, MD—then chief of Weill Cornell's Laboratory of Developmental Neurology, the Nathan Cummings Professor of Neurology, and a stem cell pioneer—who was investigating the molecular pathways of nerve regeneration. But a return to Brazil with Johnson at the end of her fourth year of medical school cemented her course in international medicine.

In the intervening three decades, Golightly has gone on to investigate the molecular basis of drug resistance in *Plasmodium falciparum*—the parasitic strain responsible for the most deadly form of malaria—and the genetic underpinnings of its life cycle. "Parasitic diseases were the diseases nobody was studying, yet they cause so much mortality worldwide," she says. "I decided I wanted to do something about it." Today, Golightly is still pursuing her longtime interest in neuroscience and infectious disease, tackling a variety of seemingly disparate projects linked by their shared potential to help people throughout the developing world. Traveling among Manhattan, Ghana, and Haiti, she seeks clues to such diseases as malaria, West Nile virus, dengue fever, and cholera. "Sometimes it sounds exotic, doing medicine abroad," says Golightly, who also oversees medical students testing their own interest in such a career, "but it's not a vacation."

Every year nearly one million people die of malaria—the vast majority of them African children under the age of five. The disease causes a constellation of symptoms including alternating fever and chills, nausea, diarrhea, listlessness, and even coma. Yet few African children in malaria's throes see a health-care professional. On average, there is just one doctor, nurse, or midwife available for every 2,000 people on the continent; by contrast, there is one health-care worker for every seventeen Americans.

Instead, in a region where malaria is perhaps the most deadly cause of such pediatric symptoms, health-care providers and families often skip straight to treatment—if the medicine is available and relatives have the resources to pay for it. "If a child comes in to NewYork-Presbyterian suspected of having malaria, we do blood smears to verify the diagnosis and blood cultures to assess for bacterial infections—and if the child is in a coma, we perform lumbar punctures and CT scans or an MRI," says Golightly, who travels regularly to Accra, Ghana, a malarial hotspot just a nine-hour flight from Manhattan. "It's the standard of care in the U.S., but in Africa sometimes people don't even have money for a smear to verify that the child in fact has malaria." On a continent where malaria claims nearly 3,000 lives daily, doctors working in remote areas often rely on a subjective history of fever alone to begin treatment. But in combating

CDC

Tiny invaders: A blood smear containing *Plasmodium falciparum*, the parasite responsible for malaria

the panoply of parasitic, bacterial, and viral diseases—all characterized by fever—that are rampant throughout sub-Saharan Africa, Southeast Asia, and India, conflating fever and malaria poses its own hazards, including high rates of misdiagnosis.

For people with limited means living far from a dispensary, getting the right treatment is critical. Not only are anti-malarials expensive, they don't combat other infections with similar symptoms—leading to increased morbidity and mortality when a patient gets the wrong treatment. And the hazards extend far beyond a single patient's recovery: overuse of the few reliable anti-malarials exacerbates the public health challenges associated with increasingly drug-resistant strains of the disease. "In the U.S., we do blood cultures to see if there might be a bacterial infection along with the malaria," says Golightly. "There, all too often, they assume it's malaria, give them malaria drugs, and will only go back to look for bacterial infections if they don't improve."

ABBOTT

Rapid detection: David Tay and registered nurse Lorraine Pierre-Destine, technicians in Golightly's lab, with the cell phone-based device that helps diagnose malaria

In a pilot project funded by the Bill & Melinda Gates Foundation, Golightly and collaborator Alberto Bilenca, PhD, a senior lecturer in biomedical engineering at Israel's Ben-Gurion University of the Negev, aim to deploy cell phones to speed affordable front-line diagnosis. "In remote areas you don't have the infrastructure to diagnose malaria with a microscope and complicated staining methods, but cell phones are everywhere in Africa," says Bilenca, who found Golightly in an online search for clinicians expert in the basic science of malaria, then called her about the possibility of collaborating. "You don't need to be trained to use a cell phone."

The biology behind Golightly and Bilenca's cell phone solution is relatively simple. Inside red blood cells, *Plasmodium*—the parasite responsible for malaria—moves fast. To avoid detection by the spleen, the only organ in the body equipped to detect the abnormally shaped infected cells, *Plasmodium* generates a sticky surface protein that causes infected blood cells to cling to the walls of the blood vessels they traverse, much like cholesterol hardening an artery. Vessels compromised by this buildup change from red to orange to white as the plaque of infected cells gets thicker; eventually, circulation shuts down completely.

Meanwhile, hungry for food to fuel its conquest, the parasite devours the oxygen-carrying hemoglobin at the core of each red blood cell. As calling cards go, the crystalline product that results—hemozoin—is unmistakable. It's known as the "malaria pigment" for its reddish-brown hue and can provide scientists with a diagnostic cue that the parasite is present.

The crystalline hemozoin molecule bends light. "If there's hemozoin in the blood, it will affect the amount of light we're detecting," says Bilenca, an expert in optics. "When light shines directly through the crystal, it rotates; hemozoin changes the polarization." Capitalizing on the crystal's unique optical properties, Bilenca and Golightly are developing a cell phone application sensitive to its light-bending ways. Outfitted with a $15 lens accessory, the phones become diagnostic tools, confirming a case of malaria by detecting the presence of hemozoin and even determining the severity of a case by gauging the extent of adhesion in the blood vessels. "Measuring blood flow with a cell phone, non-invasively, sounds like a fiction," says Bilenca. "But it works."

In young African children who have yet to develop resistance to the parasite, *Plasmodium* can affect

the blood-brain barrier. That leads to cerebral malaria, which wreaks havoc in the vessels that supply oxygen and nutrients to the core of the nervous system. "You don't know which child is going to get it. They suddenly develop seizures and go into coma," says Golightly, "and we can't predict who's going to recover." Children treated with anti-malarial medications may still develop cerebral malaria—and those who recover may appear well but have lifelong neurocognitive defects. More than a quarter of the children who develop cerebral malaria never come out of coma and die.

Even worse, the finger prick and blood smear that reveals the presence of *Plasmodium* doesn't indicate whether the infection has spread to the brain. "There's currently no simple diagnostic test for cerebral malaria," says Golightly. As a workaround to scarce, high-tech equipment that can reveal *Plasmodium*'s influence on blood flow to the brain, scientists have turned their attention to the eye, where a dilated pupil provides a window into cerebral vascular tissue. For nearly a decade, they've known that a specialized ophthalmic exam can reveal the severity of a malaria infection and whether the patient has cerebral malaria. But finding a trained ophthalmologist in sub-Saharan Africa is no easier than finding a laboratory set up for conventional malaria smears or blood cultures.

Now, by aiming Bilenca and Golightly's cell phone camera at a malaria patient's eye, the diagnosing physician could be anywhere. "This is telemedicine," says Bilenca. "Basically, a regular person does the medical measurement and transmits it to an MD in some other part of the globe." This year, Golightly and Bilenca will submit their work to the Gates Foundation in a bid for an extension of their $100,000 Grand Challenges in Global Health Explorations award—an additional $1 million in funding. "It's a long road," says Golightly, who is currently testing the device *in vivo* in mice at Weill Cornell.

In the Fifties and Sixties, there were aggressive public health campaigns to wipe out *Plasmodium*—first DDT to kill mosquitoes, then the anti-malarial drug chloroquine mixed into table salt in tropical countries—but *Plasmodium* has persisted and rebounded whenever the campaigns were withdrawn. The indiscriminate use of chloroquine and other anti-malarials has led to tougher, drug-resistant parasites that are gaining ground around the world as scientists like Golightly race to understand how they breach the blood-brain barrier to cause cerebral malaria. "Somehow a parasite inside a red blood cell on the other side of the vascular lining affects the brain," says Golightly. "Nobody knows how."

Working with Shahin Rafii '82, MD, the Arthur B. Belfer Professor of Genetic Medicine and co-director of the Ansary Stem Cell Institute, and collaborators at the Noguchi Memorial Institute for Medical Research in Accra, Golightly has focused her investigations on the possible role of circulating endothelial progenitor cells (CEPCs)—the small population of stem cells responsible for regenerating and repairing blood vessel linings—in recovery from cerebral malaria. In a 2009 article in the *American Journal of Tropical Medicine and Hygiene*, the NIH-funded team documented that African children who develop cerebral symptoms have lower levels of CEPCs than those with malaria whose brains hold *Plasmodium* at bay.

The team's current work may determine whether pharmaceutically boosting CEPCs—a strategy proposed to promote circulatory health in people with cardiovascular disease—could treat or even protect against cerebral malaria. "If the hypothesis proves true and repair mechanisms [like CEPC] are important in cerebral malaria, then you might be able to use drugs to augment repair," says Golightly. "But first we have to prove that we're correct."

For more than a decade, Golightly's research has toggled between the search for greater insight into the molecular basis of malaria and the quest for better, faster tools to diagnose the panoply of infectious agents—dengue virus, West Nile virus, even food-borne pathogens—that afflict the developing world. The latter has drawn heavily on the expertise of colleagues Davise Larone, PhD, professor of clinical pathology and laboratory medicine, and Francis Barany, PhD, professor of microbiology and immunology and the inventor of groundbreaking gene amplification and detection techniques including the universal array. Two forthcoming papers examine the effectiveness of using two of Barany's techniques—polymerase chain reaction and ligase detection reaction—to reveal the presence of viral diarrhea and hemorrhagic fever agents. Much faster than a conventional culture, which can take eighteen hours or longer to deliver a result, this rapid diagnostic system has the potential to aid physicians combating the spread of a particularly fast-moving contagion such as cholera or even a bioterror agent.

The trio began collaborating in the aftermath of 9/11, motivated by conversations about what they might do to help. As anthrax scares made headlines and the threat of further bioterror agents—many of them common diseases in developing countries—loomed large, Golightly, Barany, and Larone applied for funding from the National Institute of Allergy and Infectious Diseases to develop molecular methods using Barany's gene amplification technique to speed diagnosis. Rather than waiting a full

PROVIDED BY DR. LINNIE GOLIGHTLY

Field work: Golightly (center) with collaborators at a hospital in Ghana

day to identify a hazard like bubonic plague, doctors would be able to use the trio's high-speed approach to zero in on pathogens in just minutes.

In 2007, the *Journal of Clinical Microbiology* published a description of the result: an assay to detect twenty infectious agents common worldwide, including those that cause anthrax, tularemia, bubonic plague, and Malta fever. More recently they've refined the technique to identify West Nile virus, dengue fever, and drug-resistant *Staphylococcus aureus*, the cause of many hospital-acquired infections. "This is very translational work," says Barany. "The idea is to aid in our country's defense against bioterror agents but at the same time help people in developing countries." For instance, when a cholera outbreak followed the catastrophic earthquake that struck Haiti in January 2010, Golightly asked colleagues at the Weill Cornell-affiliated GHESKIO clinic for stool samples. She, Barany, and Larone retooled their diagnostics to analyze the samples, finding that multiple pathogens—not just cholera—were present.

One of Barany's favorite anecdotes about Golightly stems from an incident a few years ago, when he spent a Saturday night in an emergency room with a friend suffering severe stomach pains. Says Barany: "At six on Sunday morning, I called Linnie and said, 'I hate to wake you, but something's not right here.' Golightly listened to his description of the symptoms, agreed, and immediately called a gastroenterologist friend—who, at her request, sprang into action. "He was visiting his mother," Barany recalls, "but he got in the car and drove ninety minutes to see a patient whom Linnie had never even met." Within hours, Barany's friend was in emergency surgery, which saved her life. "Linnie is a real humanist," he says. "She always goes all out to help individuals in need." ●

Notebook

News of Medical College and Graduate School Alumni

R. Ernest Sosa, MD '78

Dear fellow alumni:

I am pleased to be writing my first letter as president of your Alumni Association. As 2013 begins, we look back at what has been a very exciting time for Weill Cornell.

Over the past year, Dr. Laurie Glimcher, Stephen and Suzanne Weiss Dean, has immersed herself in the many exciting and innovative developments happening at the Medical College, while crafting her vision to position it as one of the world's leading academic medical centers. She is enthusiastic to strengthen biomedical research on campus, and her continued support in this area of growth is evident.

In August we welcomed the Class of 2016 to York Avenue. The 101 incoming students received their white coats and stethoscopes at the annual ceremony and have been hard at work since. As always, we thank the Buster Foundation for its support of this ceremony, which has become a tradition at Weill Cornell, and its continued funding of the Paul F. Miskovitz, MD '75, Stethoscope Initiative, which generously provides students with that essential medical instrument.

During the weekend of October 19–20, more than 400 alumni and guests gathered in New York for Reunion 2012. In addition to reconnecting with old friends and colleagues, meeting current students, and touring Weill Cornell's facilities, alumni had the opportunity to meet Dean Laurie Glimcher and hear from Cornell University President David Skorton, MD, who moderated a panel of alumni involved in cross-campus research initiatives. The weekend concluded with a gala dinner dance at Cipriani 42nd Street, where we reminisced about old times and discussed the exciting changes taking place at Weill Cornell.

I am happy to say that alumni remain generous supporters of the Medical College, especially in the area of scholarship. Our medical students will incur, on average, more than $147,000 in debt upon graduation. This is lower than the national average, but still a daunting number. To find out more information about the various giving opportunities at Weill Cornell or to join the Dean's Circle, please contact the Office of Alumni Relations at (646) 317-7419.

We look forward to the new and exciting initiatives and increased research opportunities in the year ahead. Through these developments, alumni will continue to play a welcome and valuable role in the continued growth of our medical school.

Once again, thank you for your support of Weill Cornell Medical College, the Alumni Association, and our students.

Best and warmest wishes,

R. Ernest Sosa, MD '78
President, WCMC Alumni Association
drsosa@nyurological.com

1950s

Marjorie F. Hughes '47, MD '50: "I retired in 1992. I'd been a doctor for the Arlington Public Schools for 36 years. Two years ago, I entered a retirement home just across the Potomac River from Washington, DC."

Stanley Birnbaum, MD '51: "I am still in gynecology practice and live in Manhattan with my wife, Michele. We now have two grandchildren: Spencer, 6, and Riley, 3."

Lowell L. Williams, MD '51: "Although I retired in 1995, I am keeping current in my research interests of epigenetics and new findings in immunology."

Bernie Siegel, MD '54: "Since graduating, I have had an interesting life experience. I am now the author of twelve books and noted to be in the top twenty of living spiritual healers on the planet. Still doing teaching, lecturing, and running support groups for cancer patients. Survivor behavior, human potential, and self-induced healing are not accidents. My next book will contain many drawings to show how they and dreams reveal somatic aspects of health and disease and the wisdom of therapeutic choices. No medical school tells its students that Carl Jung diagnosed a brain tumor from a patient's dream. I have done the same things with patients' drawings. My website (http://berniesiegelmd.com) has a webinar sharing some examples."

Joseph E. Johnston, MD '55, was featured in a recent issue of the magazine *Our South*, highlighting his 57 years of practice in Mt. Olive, Mississippi. Before his retirement in 2012, Dr. Johnston served patients in his home clinic, the Green Tree Family Medical Clinic, area hospitals, and nursing homes. His son, Dr. Word Johnston, joined his father's practice in 1984, and his granddaughter, Eden, is a student at the University of Mississippi Medical Center. Dr. Johnston's professional honors include runner-up for national Family Physician of the Year, past president of the Mississippi Academy of Family Physicians, and the John B. Howell Memorial Award.

Jay Cohn, MD '56: "I remain active as a professor of medicine and director of the Rasmussen Center for Cardiovascular Disease Prevention at the University of Minnesota. I have received local, national, and international awards in recent years—probably a tribute primarily to my persistence and longevity. My mission currently is to convince the world that early detection and therapy of asymptomatic cardiovascular disease can greatly prolong healthy life and profoundly reduce health-care costs. We are developing screening centers to provide communities with access to this evaluation. Syma and I spend eight months a year in Minneapolis, but enjoy an alternative winter lifestyle on Longboat Key in Florida."

WCMC

Cutting a rug: Cardiologist Charles Stone, MD '81, and his wife, Tanya, on the dance floor at Reunion 2012

James K. Van Buren '55, MD '59: "I continue to enjoy family, golf, travel, and medical conferences at Emory. I miss seeing patients, but don't miss the paperwork, computers, and 'productivity' that go with the practice and art of medicine as we learned it. Mary and I look forward to any visits."

1960s

Anthony A. Goodman, MD '65 has a new novel, *None But the Brave*, that tells the story of the surgeons, nurses, and medics who risked their lives to tend the wounded in World War II. Dr. Goodman is an adjunct professor of medicine at Montana State University and an affiliate professor at the University of Washington School of Medicine. He served as a surgeon in the US Army Medical Corps during the Vietnam War and on the Project HOPE hospital ship.

Edgar J. Kenton III, MD '65, was appointed director of the Stroke Program and director of the Neurology Department, Geisinger Health System in Danville, PA.

Kermit Dewey '63, MD '67: "**Bruce Lidston, MD '67**, and his wife, Carolyn, stopped overnight on their way home after visiting their son and grandson in Maine. We had a great time

WCMC

Facebook photos: Dorothy Zimmerman Jones, BS Nursing '47, and Rudolph Jones, MD '45, view some vintage images at Reunion 2012.

catching up on 40-plus years, and my wife, Valerie, finally got to meet them."

1970s

Daniel M. Hayes, MD '72: "I have retired from my medical oncology practice of 36 years. Phyllis is getting used to my being around more, and I'm adjusting with many interests, some professional, as we both await formalized travel plans. Our three daughters live in Maine, and a son and daughter-in-law and two grandchildren in New York keep us moving a lot. You can reach me at: hayesd @ mccm.org."

James S. Reilly, MD '72: "I'm a pediatric otolaryngologist at Nemour-DuPont Hospital for Children in Wilmington, DE. After hours I spend time in Ocean City, NJ, at the summer home that my wife, Barbara, and I have redone. I remain happy working as a clinician and hospital leader and enjoy my grandchildren. I remember most the physical diagnosis introduction classes with Dr. Elliot Hochstein."

George C. Ellis, MD '74: "In the spring of 2013, I am changing my mode of practice into one in which I will be caring for only 50 families. I'm partnering with Dr. Mark Brown, who I trained with at the Medical College. We are joining an organization called MD² (www.md2.com). Our new office will be at 860 Park Avenue."

Gerald Kolski, MD '76: "I'm semi-retired, working one day a week in Huntsville, TX. Susan and I are near our daughter Andrea and granddaughter. Our son, Brian, completed a cardiology fellowship at UCSD and is doing interventional cardiology. Melissa is working in Chicago, running educational programs for RIC and writing a book on pain management."

Samuel Silver, MD '79: "I'm professor of internal medicine in hematology/oncology and assistant dean for research at the University of Michigan Medical School. I was just elected as a Master of the American College of Physicians."

1980s

Rosemary Meisner Klenk, MD '80: "I've worked almost 30 years in full-time pediatric group practice in Stamford and New Canaan, CT. I'm proud that my son Colin has just started Columbia Medical School and is doing well so far. My youngest son, Kevin, is a 2012 graduate of West Point and is training as a tank commander at Fort Benning, GA. To have a little fun on Saturday night in NYC, go to KaraKlenk.com and see my eldest daughter host a weekly standup comedy show at 8:30 p.m. at UCB East."

Ann Engelland, MD '81: "As a proud Medical College alumna, I had every intention of getting to the reunion, but I broke my leg three days before! So sorry to have missed my old friends. You may know that my work as an adolescent medicine physician was featured in *Weill Cornell Medicine* in the Winter 2008/09 issue. Since then I have moved into school and college health and have been an advocate for good management of head injury. I have just published *It's All in Your Head: Everyone's Guide to Managing Concussions*. This book helps all members of the community to recognize and respond to concussions. Many specialties and their patients—from pediatrics to internal medicine, neurology, orthopaedics, and psychiatry—will benefit from it."

Sharon Strong, MD '81: "I really enjoyed see-

ing lots of classmates at the reunion in October. My husband, **Phil Bossart, MD '81**, continues to work in the ER and has become involved with medical school admissions. I enjoy palliative care and geriatrics. We enjoy travel, tennis, and bridge. Son Chris is a second-year med student. Daughter Abby is majoring in Spanish and saving money to travel to South America. Son Matt is a college junior studying engineering."

Grace Makari-Judson, MD '82: "One of our sons, Tim, is a Weill Cornell second-year student living in Lasdon. When **Peter, MD '82**, and I visit, we get quite nostalgic."

Barnaby Starr, MD '82: "I'm continuing to run an old-fashioned general pediatric practice in Baltimore. I employ five people including a part-time pediatrician and a pediatric nurse practitioner. I miss all my old classmates and wish you all well."

Perry Kamel, MD '84: "Elena and I have two kids in college this year. Only one child left at home."

Alexander Babich, MD '88, received an award for his virtual artwork "Ethiopian Bride" at the 7th Virtual Medical Complex Art Shows at the Weill Cornell Medical Library. Both the virtual and physical shows opened on November 5, 2012, and continued until January 31, 2013. Here is a link to the "Art in the Library" page, which features the virtual show: http://library. weill. cornell.edu/Art/. Other alumni in the show included **Edgar Figureroa, MD '00**, **Gerald Cordani, MD '70**, **Muriel King Taylor '58, MD '62**, and **Gus Kappler '61, MD '65.**

1990s

Scott Tarantino, MD '94: "I'm continuing in orthopaedic surgery practice in Maryland. I have three great kids—Lucia, 15, Jack, 12, and Maya, 6—and my wonderful wife, Bonnie. I'm coaching Lucia's basketball team and Jack's travel baseball team. Life is good."

Jeffrey Yao, MD '99: "I was recently promoted to associate professor of orthopaedic surgery at Stanford University Medical Center."

2000s

Josh Dines, MD '01: "I'm the youngest member named to the American Shoulder & Elbow Surgery Society and team doctor for the US Davis Cup tennis team."

Rafael Vazquez, MD '06, started working as a staff anesthesiologist at Massachusetts General Hospital. He works primarily in the vascular service providing high activity care to patients undergoing complex thoracoabdominal aneurysm repairs.

In Memoriam

'39 MD—Augustus W. Sainsbury of Canandaigua, NY, November 3, 2012; general surgeon; veteran; singer.

'48 MD—Robert J. Oehrig of Minneapolis, MN, October 16, 2012; medical director, Home Life Insurance Co.; geriatric physician, Christian Medical Center; veteran; medical missionary; lay minister; active in religious affairs.

'48 MD—Warren G. Sarrell of Birmingham, AL, September 27, 2012; retired cardiologist and internist; co-founder and president, Anniston Medical Clinic; established the first heart catheterization lab, Regional Medical Center, in 1972; co-founder, Regional Medical Center Foundation; helped found the Sarrell Dental Clinic; veteran; president, Alabama Heart Association; active in professional affairs.

'52 MD—Sterling W. Obenour of Zanesville, OH, October 17, 2012; general and vascular surgeon; veteran; served on the staffs of Bethesda and Good Samaritan hospitals; president, Muskingum County Academy of Medicine; governor, American College of Surgeons; pilot; photographer; musician; active in community, professional, and religious affairs.

'54 MD—Herbert A. Kroeze Jr. of Madison, MS, June 10, 2012; physician.

'57 MD—Anne Shannon Morgan of Westmoreland, NH, April 5, 2012; physician.

'70 MD—Richard T. Nist of Anchorage, AK, October 28, 2012; obstetrician; active in community affairs.

Post Doc

Mission of Mercy

Seeking a kidney for their child, parents travel 9,500 miles

Daaniya Zaidi

JOHN ABBOTT

Daaniya Zaidi is an energetic three-year-old with dark hair, deep brown eyes, and a sunny disposition. Colorfully clad in tie-dye and polka dots, she careens around her family's Upper East Side living room with her toddler brother one afternoon in late October. "I like to do dress up," the little girl announces, describing her preferences for fairies and princesses and her plan to wear a ladybug costume for Halloween. "I like to go to the playground."

But not long ago, Daaniya didn't have as much time or energy for play. Despite her young age, she can speak in detail about life before her June kidney transplant. "I had to go to dialysis all day, and I had to stay there," she says. "Now," she adds to the exhausted amusement of her mother, Samareen Shami, "I can run all over the house."

A year ago, Shami and her husband, Salman Zaidi, could scarcely have hoped to see their daughter so healthy. Around age two, Daaniya was diagnosed with a congenital condition that leads to kidney tumors and renal failure. "In six months, her kidneys went from 100 percent function to 25 percent," says Shami, who stopped working as a consultant in the oil and gas industry when her daughter was diagnosed. Daaniya, who went on dialysis, needed a transplant as soon as possible—but family members weren't viable matches and a Facebook campaign proved fruitless. And there was another hurdle: the family was living in Singapore, where Zaidi worked as a banker. "We were in a country where the waiting list for a kidney is nine years," Shami says. "Donation—especially live donation—is not something that happens there very often. So we had to make a choice."

The couple opted to move halfway around the globe—to an apartment just blocks from NYP/Weill Cornell—so their daughter could have the best chance for a transplant. After Zaidi's bank transferred him to New York, the family relocated in February. "It's extremely unusual," says Sandip Kapur, MD '90, chief of transplant surgery and director of the Kidney and Pancreas Transplant Programs, whom the couple chose to do the operation after an international search. "I've been doing this for eighteen years, and it's the only time I've seen a family pick up and move here for their child." Father and daughter became part of a transplant chain—a system that allows someone to give a kidney to a stranger while his or her relative gets an organ from a donor in the same situation. "They don't donate directly to their loved one," Kapur says, "but they allow their loved one to get a nicely matched, well-functioning, live-donor kidney."

Since Daaniya's condition can cause malignant tumors, surgeons removed her kidneys while she awaited a transplant; meanwhile, her father underwent donor testing. In June, they became part of a chain of nine recipients and ten donors, with the extra donor forming the first link in a future chain. Daaniya received an organ from a thirty-three-year-old woman in California—it was shipped via red-eye—and her father gave a long-awaited kidney to a forty-eight-year-old New Yorker who'd been difficult to match. "It's not quite the same as donating to your child," says Zaidi, who has suffered no ill effects, "but it's a very close second."

Daaniya has been doing extremely well since the transplant—growing, gaining weight, and bursting with energy. "It was very successful," says Valerie Johnson, PhD '76, MD '77, associate professor of clinical pediatrics, director of the Division of Pediatric Nephrology, and a member of the patient care team of the Phyllis and David Komansky Center for Children's Health at NYP. "You'd hardly know this is the same child."

Although Daaniya will need anti-rejection drugs and regular checkups throughout her life—and will likely require another transplant in her late twenties—she's essentially a normal, healthy preschooler. After the long months of dialysis, dietary restrictions, and bans on activities like bathing, swimming, and rough play (due to her catheter), the girl can snack and romp with her peers. "Seeing her healthy, happy, growing—just being a child—is fantastic," Zaidi says. "You forget some days that she went through an enormous amount to get where she is. Sometimes, you're in the happy position of taking it for granted."

— Beth Saulnier

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