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SPRING/SUMMER 2016

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**“Residency is daunting.
It’s a trial by fire, and the
learning curve is steep.
But I feel as ready as any
fourth-year student.”**

*Devon Ryan, MD, an inaugural graduate of the
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Easing the Burden—on Medical Students and Patients Alike



NYU School of Medicine has long been at the forefront of medical education. Our Curriculum for the 21st Century, or C21, launched in 2010, forged a new approach to training physicians, one that is truly patient-centered and disease-focused. Our Institute for Innovations in Medical Education, created in 2013, has reinvented the classroom experience, putting the vast resources of biomedical information at students' fingertips.

The cover story in this issue of *NYU Physician* highlights yet another milestone of our educational mission: In May we graduated 15 physicians (about 10 percent of the class) who comprise the inaugural class of the Three-Year MD Pathway program, an accelerated curriculum that allows select students to complete their undergraduate medical studies in just three years. Why offer a shorter path? The structure of medical school has not fundamentally changed since 1910, when the seminal Flexner Report prescribed nationwide standards for educating doctors. Yet the demands on prospective doctors have changed dramatically. More than 85 percent of medical school graduates carry debt, averaging \$161,000. Breaking from the old Flexner model lets students graduate with less debt while getting more doctors quickly into communities that need them.

A recent survey of medical school deans nationwide reported that at least 35 percent of medical schools in the US have developed, or are considering, a three-year MD program. I am proud of the fact that NYU School of Medicine is at the leading edge of this trend, and once again innovating better ways to train physicians.

Enjoy the issue.

A handwritten signature in black ink, appearing to read "Bob", with a small dot above the "B".

DEAN AND CEO ROBERT I. GROSSMAN, MD

PHOTO: JOHN CARNETT

NEWS FROM MEDICINE

SPRING/SUMMER 2016

A NEW WAY TO FIGHT TUBERCULOSIS,
UNTANGLING SCHIZOPHRENIA, AND MORE

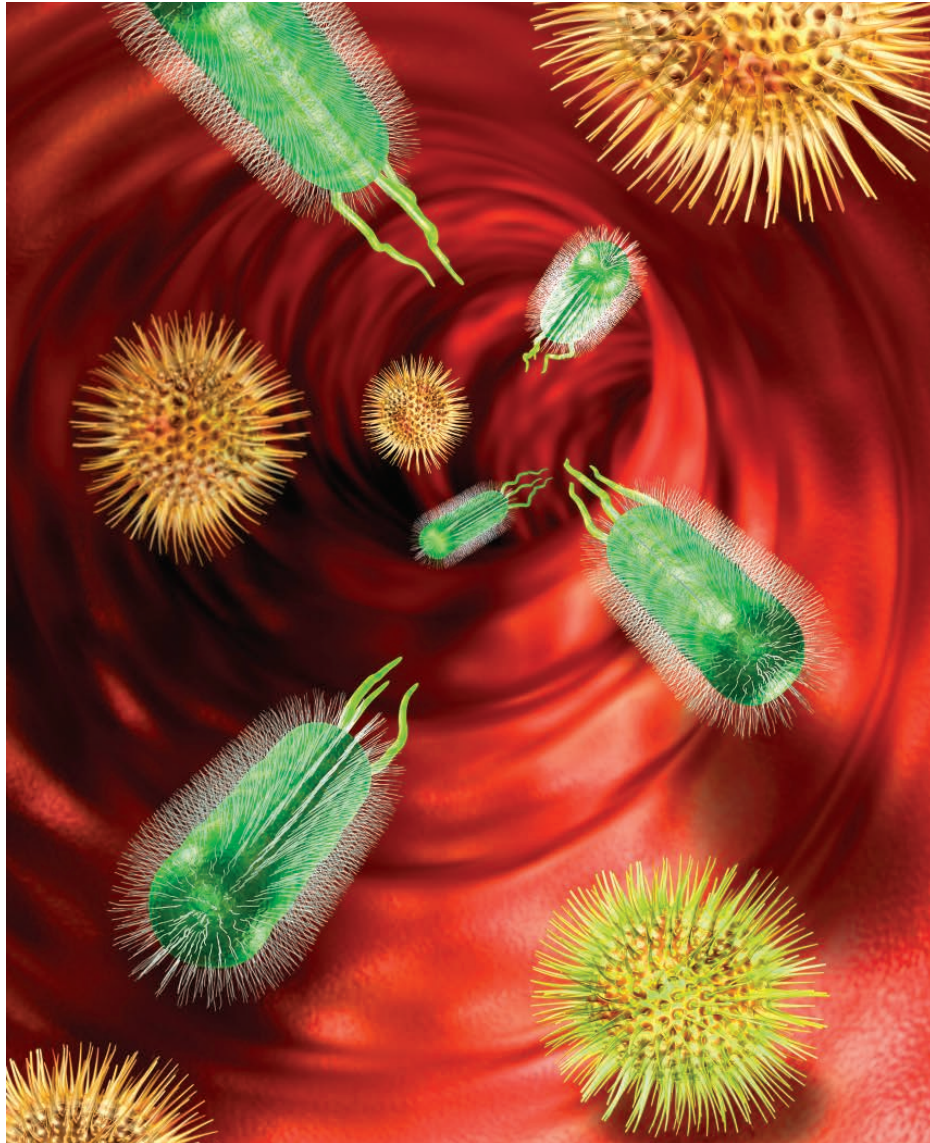


ILLUSTRATION: HARVINDER SINGH / SCIENCE PHOTO LIBRARY

**How can an intestinal parasite beat back
pathogenic bacteria in the gut?**

IN DEFENSE OF GUT PARASITES, PAGE 6 →



P'NG LOKE, PHD

IN DEFENSE OF GUT PARASITES

A soil-dwelling worm gives beneficial bacteria the upper hand against inflammatory bowel disease.

NEARLY 10 YEARS ago, parasitologist P'ng Loke, PhD, then a postdoctoral fellow at the University of California, San Francisco, received a curious phone call. The caller, a technology entrepreneur, told Dr. Loke that he had cured himself of a painfully inflamed colon by eating parasitic whipworm eggs.

Intentionally infecting yourself with parasites may sound like an extreme way to treat intestinal distress, but the idea is not without scientific merit. Epidemiologic studies have shown that people who live in countries where soil-dwelling parasites like whipworm are prevalent tend not to develop inflammatory bowel disease, or IBD, an umbrella term for chronic conditions of the digestive tract. Such disorders, which include both ulcerative colitis and Crohn's disease, currently affect more than 1.4 million

Americans. Cases of IBD are also on the rise in countries such as Japan and Korea, where the number of parasitic intestinal infections have declined in recent years—further supporting the notion that harboring worms might hamper IBD.

Given all that—and the fact that the only other treatment options for this individual were a colectomy or a grueling regimen of immunosuppressive drugs—Dr. Loke says, “Parasitic worms probably didn’t seem so bad.” Intrigued by the patient’s apparent turnaround, Dr. Loke and his colleagues took a closer look at his intestines. Their observations—which were published in 2010, when Dr. Loke had joined the faculty at NYU Langone as associate professor of microbiology—revealed that the worms were boosting intestinal mucus.

But why would a flood of mucus quell the symptoms of IBD? Now a follow-up study in mice—recently published in *Science*—offers a fascinating clue: gut bacteria. For this latest series of experiments, Dr. Loke joined forces with Ken Cadwell, PhD, associate professor of microbiology. Dr. Cadwell and his colleagues had engineered a mouse model of IBD by mutating a gene called Nod2, which is frequently damaged in people with Crohn’s disease. Like patients with IBD, these mice display a marked withering of mucus-producing cells in the small intestine. Without its protective layer of mucus, the animals’ intestines became overrun with *Bacteroides*, a family of inflammation-producing bacteria.

When the researchers then infected the animals with the mouse version of whipworm, however, their mucus production was restored and the *Bacteroides* vanished. That change “completely reversed all the abnormalities we saw in these mice,” says Dr. Cadwell. In other words, the mice experienced the same relief as the self-infected entrepreneur.

But how did the worms beat back the bad bacteria? Indirectly, it seems. According to Drs. Loke and Cadwell, the parasites provoke a particular type of immune response—one that enhances the production

of mucus. The mucus, in turn, serves as a source of nutrition for a class of beneficial gut bacteria called *Clostridia*. As these protective microbes proliferate, they outcompete the *Bacteroides*, restoring a healthy balance of bacteria to the gut.

At least that’s what happens in mice. But what about in people?

To answer that question, Drs. Loke and Cadwell teamed up with Dr. Yvonne Lim and her colleagues at the University of Malaya in Kuala Lumpur. These researchers had been following a tribe of indigenous Malaysians called the Orang Asli, who live in an environment rife with parasites like whipworm.

As predicted, the Orang Asli—most of whom harbor the parasitic worm—have fewer *Bacteroides* and more *Clostridia* than individuals from the urban environment of

1.4
MILLION
Number of Americans
living with inflammatory
bowel disease

Kuala Lumpur. When the researchers treated the Orang Asli with a drug that killed off the parasites, the bacterial balance was reversed: the bad bacteria came to outnumber the good, the same situation that prevails in people with IBD.

Worms may not provide a cure for all those suffering from intestinal ailments. But the current study suggests that the parasite could aid a subset of people with IBD or Crohn’s disease—for example, those who have impaired mucus production, an increased load of *Bacteroides*, or defects in Nod2, the



The whipworm parasite (shown here) can live undetected in the human intestine for years and may protect against inflammation.

“People who are resistant to Crohn’s disease are more likely to harbor fewer *Bacteroides* and more *Clostridia* bacteria.”

gene mutated in Dr. Cadwell’s mice.

In the meantime, Drs. Cadwell and Loke will continue to explore the mechanism that allows worms to alter the intestinal microbiome. For example, they’ve found that injecting the mice with an immune molecule that’s produced in response to parasitic infection is enough to boost mucus production and drive the growth of good bacteria.

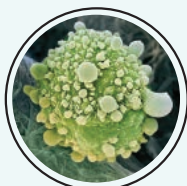
Similarly, providing mice with *Clostridia* directly can also thwart the growth of bad bacteria, an observation that, Dr. Loke says,

“opens the door to probiotics” and could send the investigators back to Malaysia. “We’d like to isolate *Clostridia* from the Orang Asli to see if the bacteria would act as a more potent probiotic,” he says.

“The premise is very simple,” adds Dr. Cadwell. “People who are resistant to Crohn’s disease are more likely to harbor fewer *Bacteroides* than *Clostridia* bacteria.”

Eliminating the parasitic middle man would no doubt be a prescription that’s easier to swallow. —KAREN HOPKIN

THE SPEED
READ →
SCIENCE IN
30 SECONDS



Aggressive pancreatic cancer cells lash out as they die, secreting a protein that fuels nearby tumor cells, according to new research led by **George Miller, MD**, coleader of the cancer immunology program at the Perlmutter Cancer Center. The work, recently published in *Nature*, may help explain why only one-fifth of patients diagnosed with advanced pancreatic cancer survive beyond a year.



DAYU LIN, PHD

THE ROOTS OF RAGE

Ready to rumble? New research pinpoints the neural circuits that may be responsible.

SOME PEOPLE are pugnacious, always itching for a fight. The same is true for mice. Now, researchers have identified a small set of cells, deep within the brain, that bristles with activity when rodents are nosing around for trouble.

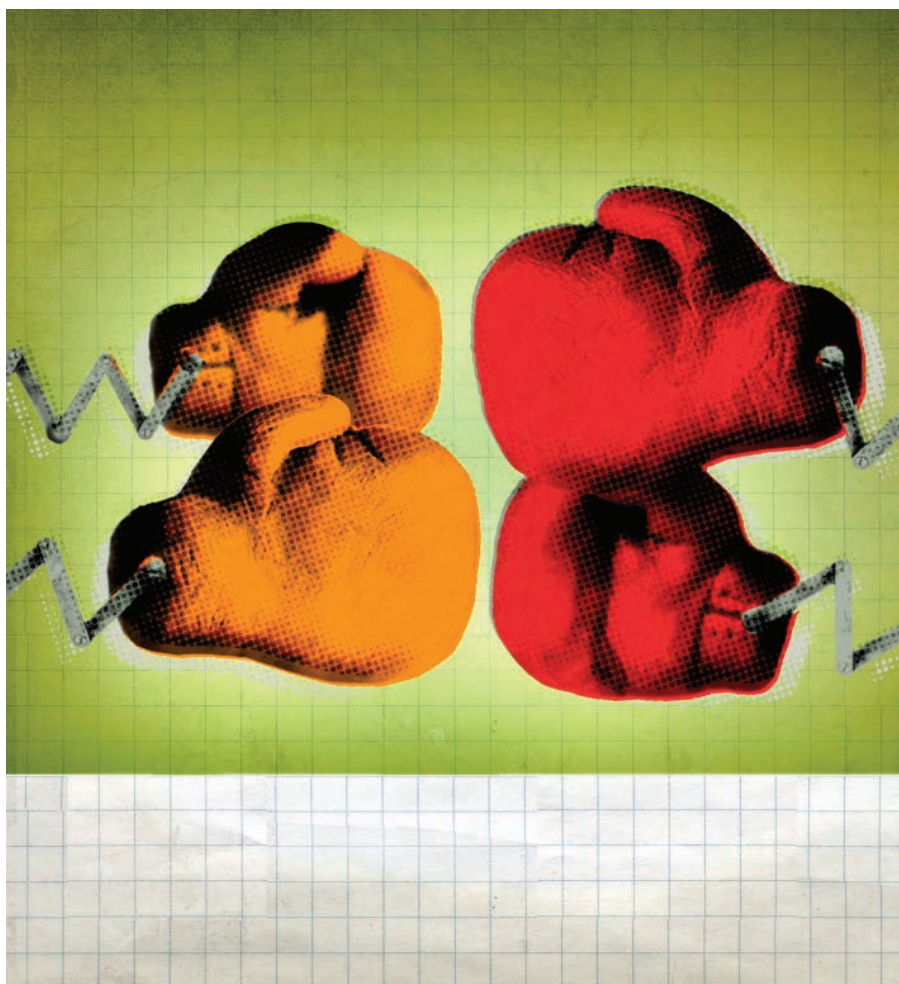
The new study, which recently appeared in *Nature Neuroscience*, is the first to link a specific brain region to premeditated behaviors, like stalking and bullying, that often precede violence. “An attack is the ultimate expression of aggression, but there are many events that lead up to it,” says senior author Dayu Lin, PhD, assistant professor at NYU Langone’s Neuroscience Institute. Uncovering the cellular circuitry that precipitates a violent encounter, she notes, “is going to be useful for understanding aggression and how to suppress it.”

Dr. Lin first encountered this cluster of cells—located along the underside of the hypothalamus, a structure involved in regulating bodily functions such as hunger and sleep—in 2007, when she was a postdoctoral fellow in the laboratory of David Anderson, PhD, at the California Institute of Technology. Drs. Lin and Anderson discovered that stimulating neurons in this part of the hypothalamus of a male mouse would prompt the animal to attack just about anything—another male, a female, or even a random object, such as an inflated rubber glove. Suppressing activity in the region, they found, suppressed the aggression. They published their findings in *Nature* in 2011, a year af-

ter Dr. Lin joined NYU Langone.

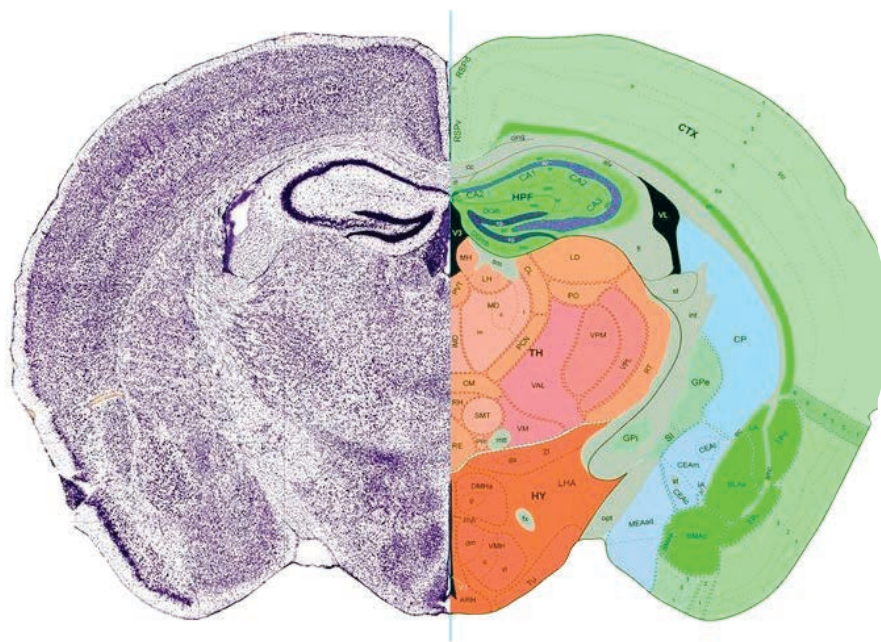
The results squarely implicated a particular set of neurons in aggression, but an important question remained: Were the cells functioning as a simple on-off switch for violent behavior, or were they involved on a deeper level, underpinning the scheming and plotting that so often precede violence? To find out, the Lin lab devised a test to assess whether a mouse was actually looking for a fight.

Dr. Lin and her postdoc Annegret Falkner, PhD, adapted a classic behavioral test in which a mouse learns to poke its nose into a hole to prompt the appearance of a reward. In their setup, the reward was a smaller mouse, whose presence in the cage repre-



PORTRAIT: THEA BRINE; IMAGES: RICHARD BERGE / ISOT, (FACING PAGE TOP): BRAIN-MAP.ORG (BOTTOM): DAVID MCCARTHY / SCIENCE SOURCE

The Lin lab has linked a small sub-region of the hypothalamus (red) to aggression in mice.



“An attack is the ultimate expression of aggression, but there are many events that lead up to it.”

sented a challenge. The trained mice, which were a bit larger than the average lab mouse, quickly learned that a nose poke would summon a weaker foe, upon which they would promptly pounce. And it was a fight, not companionship, they were seeking: When the intruder mouse was presented in a protective metal cage or was larger than the male being tested, the subjects soon lost interest in the game.

This setup provided the researchers with

1/2
of all **PSYCHIATRIC**
CASES involve aggression

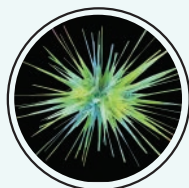
a glimpse into “the motivational state of the animal,” says Dr. Lin. In other words, the mice were not being provoked or responding to the sight or smell of a potential aggressor. “They were thinking about a fight,” she adds.

Next, Dr. Lin went back to the brain region she had previously linked with aggressive behavior—a part of the ventromedial hypothalamus—and measured the activity of individual cells as the mice were fixing to fight. She found that the very same cellular circuit that is active during an aggressive encounter is also active when an animal is merely planning to attack. Inhibiting these cells made mice less likely to seek confrontation.

With aggression involved in roughly half of all psychiatric cases, Dr. Lin’s science sets the stage for the development of more effective, possibly more humane pharmacological interventions that could diminish violent outbursts without sedation.

—KAREN HOPKIN

**THE SPEED
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Withdrawal from prescription painkillers is driving an increasing number of people to binge on over-the-counter diarrhea medications. At extreme doses, loperamide, the active ingredient in these products, can produce an opioid like high. It can also cause fatal heart arrhythmias, according to a recent report by **NYU Langone toxicologists** published in the *Annals of Emergency Medicine*.



DOLORES MALASPINA, MD

UNTANGLING SCHIZOPHRENIA

Researchers pinpoint genetic mutations that may help parse and treat schizophrenia's bewildering range of symptoms.

SCIENTISTS VIEW schizophrenia as a constellation of related mental disorders that can vary widely in the breadth and severity of symptoms, much like cancer and heart disease. Patients with the psychotic illness may experience distinctly different combinations of unbalanced thinking, disordered behavior, hallucinations, delusions, and paranoia. Standard antipsychotic drugs cannot sufficiently address such a broad range of symptoms.

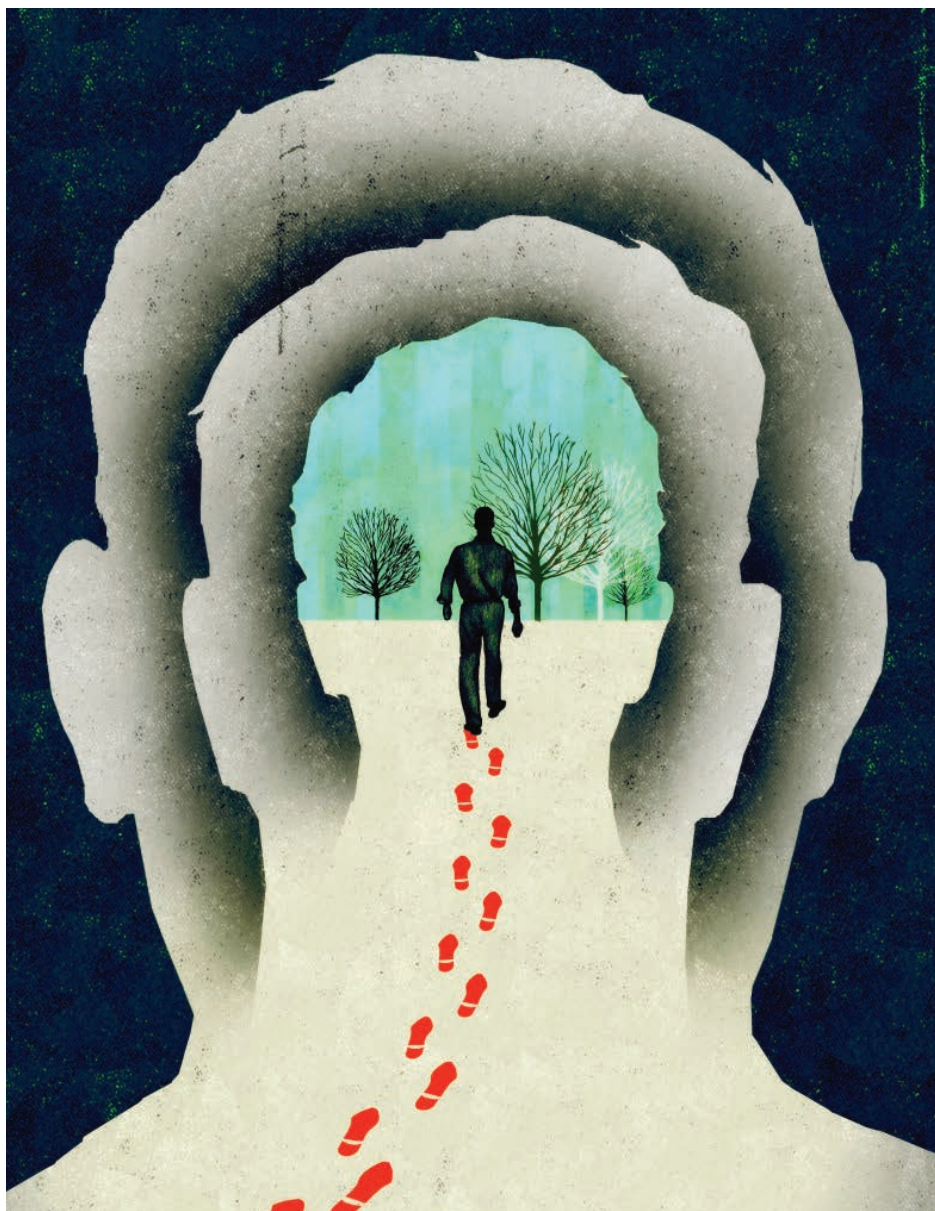
Now a team of researchers from NYU Langone has linked four subtypes of schizophrenia to specific mutations in genes involved in nerve-cell support or signaling. "Patients with these mutations differ in their course of illness, symptoms, and cognition," says study coauthor Dolores Malaspina, MD, the Anita Steckler and Joseph

Steckler Professor of Psychiatry and Child and Adolescent Psychiatry.

The findings shed much-needed light on the myriad pathways contributing to schizophrenia. "What we ideally hope is that this will set the stage for new types of treatments," Dr. Malaspina says. The study, published in a recent issue of the journal *EBioMedicine*, suggests that the gene-linked

subtypes might account for up to 30 percent of cases (there are an estimated 3.2 million in the US) and could be candidates for more targeted therapies.

Dr. Malaspina's latest discovery builds upon years of research that suggest how schizophrenia-linked mutations can arise in individuals with no family history of the disease. In a 2001 study of Israeli patients,



PORTRAIT: THEA BRINE; ILLUSTRATION: BRIAN STAUFFER / ISOT; PHOTO (FACING PAGE) NYU LANGONE

she and collaborators discovered that children with older fathers are at higher risk for sporadically occurring schizophrenia. “Sperm divides steadily over the life span of the father,” Dr. Malaspina says. “As the cells divide, there’s an opportunity for new mutations.”

For the new analysis, the NYU Langone researchers used a “candidate approach” in which they looked for sporadic mutations and very rare alterations in 38 genes

nia, but also linked the genes with specific symptoms. “It’s very interesting to us because this disorder is very heterogeneous, and that’s why so many genes are involved,” says coauthor Moses Chao, PhD, professor of cell biology, neuroscience and physiology, and psychiatry.

Thorsten Kranz, PhD, the study’s lead author and a postdoctoral fellow in Dr. Chao’s lab, says the researchers focused on 5 genes implicated in an earlier study they conducted that compared patients with schizophrenia to their unaffected parents, plus 33 genes that either encode growth factors called neurotrophins—proteins that support cellular connections throughout the brain—or proteins that interact with those growth factors. Mutations and rare alterations in some of these genes can impact nerve cell growth and disrupt the cells’ communication channels.

“The difference between our study and others is that we have a very deep knowledge of the clinical features,” Dr. Kranz says. “For a specific set of symptoms, we have a specific set of genetic variants that we identified.” One subset of patients with profound psychological symptoms from early childhood harbored mutations and rare alterations in one gene, for example, while patients who deteriorated later in life had them in another.

The hope is that clinicians could one day tailor treatments based on these genetic subdivisions. If a patient’s schizophrenia symptoms are linked to a mutation in a gene that promotes inflammation, for instance, it may make more sense to treat that patient with an anti-inflamma-

“Little by little, we’re unpacking the symptoms of schizophrenia and finding the differences in biology,” says Dr. Dolores Malaspina.

tory drug rather than an antipsychotic drug that can produce severe side effects, Dr. Kranz says. The collaborators are now testing the functional implications of some of the mutations by investigating their effects in rat nerve cells grown in the lab.

In a separate essay in *The American Journal of Psychiatry*, Dr. Malaspina recently reflected on how her sister’s struggle with schizophrenia motivated her to learn all she could about the disease. If she and her colleagues can match individual mutations to specific clinical consequences, the remaining schizophrenia cases may also prove easier to understand. “So little by little, we’re now unpacking the symptoms of schizophrenia and finding the differences in biology,” Dr. Malaspina says.

30%

Estimated percentage of schizophrenia cases newly linked to mutations in genes that help brain cells develop or communicate

that they and others had tentatively linked to the disease, and focused on a pool of 48 schizophrenia patients in New York. In all, the study found that 15 of the patients carried extremely rare alterations or newly identified mutations in four genes.

The results not only added to the list of genes potentially at play in schizophre-

**THE SPEED
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SCIENCE IN
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Tuberculosis is among the oldest, deadliest, and most pervasive diseases in history. Now, a new study led by **Kathryn Moore, PhD**, the Jean and David Blechman Professor of Cardiology and Cell Biology at NYU Langone, sheds light on the bacterium’s notorious hardiness. In a paper published in *Nature Immunology*, she and her colleagues describe a clever survival strategy whereby TB disarms macrophages and transforms them into fat-producing machines for their own nourishment. The next step is investigating whether cholesterol-blocking medications can interfere with this process.

When Three Equals Four:

The New Math *of*
Medical School

Susanna Nguy, MD,
from New York, New York,
is a resident in radiation
oncology at NYU Langone.

Devon Ryan, MD, from
Bedford, Massachusetts,
is a resident in
orthopaedic surgery at
NYU Langone.



This summer, 15 newly minted doctors entered their residencies after just three years of training at NYU School of Medicine. Will these trendsetters become the new norm?

By Gary Goldenberg

Amy Ou, MD, from Endicott, New York, is a resident in internal medicine at NYU Langone.

Rae Rokosh, MD, from New York, New York, is a resident in surgery at NYU Langone.

Travis Hill, MD, from New York, New York, is a resident in neurosurgery at NYU Langone.

Susan Creighton, MD, from New York, New York, is a resident in primary care at NYU Langone.





NEARING THE END of his third year at NYU School of Medicine, Devon Ryan, MD, still hadn't given any thought to the residency match, the angst-ridden process that consumes much of the last year of medical school. In fact, he never bothered with his fourth year. Dr. Ryan didn't abandon his dream of becoming a physician. Rather, he headed straight into a residency in orthopaedic surgery, as part of an accelerated curriculum that allows select students to complete their undergraduate medical studies in just three years.



Jenna Conway, MD, from Toronto, Canada, is a resident in neurology at NYU Langone.



Brian Sanders, MD, from New York, New York, is a resident in otolaryngology-head and neck surgery at NYU Langone.

One of the benefits is a slot in the residency of their choice at NYU Langone, provided they maintain a strong academic performance and apply through the conventional "match" process, by which a nationally standardized algorithm matches residents to residency programs.

"I'm a bit nervous, sure," says Dr. Ryan, a native of Bedford, Massachusetts. "Residency is daunting. It's a trial by fire, and the learning curve is steep. But I feel as ready as any fourth-year student."

If Dr. Ryan sounds confident, he has every reason to be. Before starting his medical studies, he took time off to conduct research in orthopaedic surgery at NYU Langone. Since his first days in medical school, he's been participating in various activities in the Department of Orthopaedic Surgery, from rounds to skill sessions to teaching conferences, gradually acculturating to life as a resident.

"I have no doubt that Devon is prepared for the next step in his training," says his mentor, Kenneth Egol, MD, professor of orthopaedic surgery and director of the department's residency program. "He might be the most prepared intern in the U.S."

NYU School of Medicine launched its accelerated pathway in 2013 as part of a broader effort to address the changing demands on prospective doctors. Today, the average medical student will graduate with more than \$165,000 in educational debt. The three-year option reduces that burden by enabling qualified medi-



Lauren Statman, MD, from Valley Village, California, is a resident in internal medicine at the University of Pittsburgh.



Yasaman Yaghoubian, MD, from New York, New York, is a resident in obstetrics/gynecology at NYU Langone.

cal students to graduate with less debt and begin practicing one year earlier than traditional students.

Not everyone agrees on the perceived merits of accelerated learning, however. Critics point to a series of shaky experiments in the 1970s, when dozens of medical schools began offering three-year MDs. The majority of students and faculty participating in those programs felt overwhelmed by the rapid pace of learning, and schools eventually abandoned them.

NYU School of Medicine, however, has taken a different approach, offering accelerated study only to a select group of students who know which specialty they want to pursue. Three-year graduate Sarah “Rae” Rokosh, MD, for one, knew she wanted to be a surgeon when she was only a high schooler in Winnipeg, Canada. Fellow graduate Danielle Lo, MD, who will pursue a residency in ophthalmology, knew her future specialty at age 15 when she first watched her father, an ophthalmologist, perform cataract surgery.

The accelerated pathway saves a significant chunk of time by simply eliminating the exhaustive process of applying for residency programs. “Most of the fourth year is spent traveling for residency interviews and doing ‘away’ rotations, which are more or less auditions for residency,” explains Dr. Egol. “If you eliminate these activities, you can shorten the curriculum by several months.” Students also forgo their first summer break, using that time for an eight-week elective. In the third year,

“By and large, many students are prepared to begin residency by the end of their third year,” says Steven B. Abramson, MD, vice dean for education, faculty, and academic affairs.

they waive the 12-week clinical research concentration, 10 weeks of electives, and 4 weeks of concentrated study. Overall, the new pathway features 130 weeks of instruction—18 weeks fewer than the traditional four-year program.

So far, the compressed schedule has not impacted performance. “Third-year students actually outperformed fourth-year students in terms of clinical skills and knowledge on tests conducted in our simulation center last spring,” says Steven B. Abramson, MD, vice dean for education, faculty, and academic affairs and the chair of the Department of Medicine. “I suspect that this is because the former were fresh from their core clerkships, while the latter had been focusing on electives and traveling around doing residency interviews. After some instruction, the fourth-year students recalibrated very quickly. But the point is that, by and large, many

students are prepared to begin residency by the end of their third year.”

LIFELONG LEARNING

The potential benefits of accelerated study are substantial. By shortening their stay in medical school, students not only save tens of thousands of dollars in tuition fees and housing costs, but also launch their careers a year earlier—no small advantage considering that the path to practice for some doctors lasts eight years beyond medical school. “People have this mistaken impression that earning the MD degree is the end of your training as a doctor, when it’s essentially a ticket to the next phase of training, which is residency,” says Dr. Abramson. “And the learning should continue after that.”

One big advantage of the accelerated pathway is that it

smoothes the stressful transition from medical school to residency, thanks to a special emphasis on mentorship and departmental engagement. “I have a pretty good impression of what to expect as a resident,” says Dr. Rokosh, who begins her residency in general surgery at NYU Langone this July. “I’ve been doing research in the Department of Surgery, going to departmental meetings, and spending my free time in the OR. I’m as ready as I’m ever going to be.”

Elisabeth Cohen, MD, professor of ophthalmology, oversees mentoring for all of the accelerated pathway students, ensuring that their specific progress and concerns are carefully addressed. In a testament to the program and the student selection process, Dr. Cohen says students have come to her not for help with crises, but rather for assistance with everyday practicalities and the occasional pep talk. “In any new venture, it’s a little uncomfortable to be in the vanguard,” says Dr. Cohen. “In most cases, they just needed assurance that when they encountered any problems, we were open to improvements.”

For Dr. Danielle Lo, who’s following in her father’s footsteps to become an ophthalmologist, Dr. Cohen’s mentorship was the cornerstone of her three-year education. “It was the best part of the program,” she says. “Dr. Cohen met with all of us multiple times throughout the year and really got to know us as people.”

Mark Hochberg, MD, professor of surgery, serves as mentor to three accelerated students, including Dr. Rokosh. “Everyone thinks that surgery is just

what happens in the operating room,” says Dr. Hochberg. “That’s important. But the major thing we teach our residents is how to evaluate symptoms, lab tests, and imaging studies to determine the diagnosis, and then how to decide whether the patient needs an operation, and when. The three-year students I’ve been mentoring have been getting that experience on a weekly basis.”

Amy Ou, MD, feels similarly prepared. “I received a lot of mentoring and advice about what activities I should be doing to prepare for residency,” says Dr. Ou, who is pursuing a residency in medicine before subspecializing in gastroenterology. “It provided a framework for learning how to think from an internal medicine perspective. And during my subinternship at Bellevue Hospital, where I’m spending a lot of time as a resident, the previous residents were helpful in teaching me how everything functions, all the day-to-day nuances you have to know to facilitate your patients’ care.”

SUCCESS IN NUMBERS

The graduation rate for the inaugural class has exceeded expectations—15 of the 16 students enrolled in the accelerated program have stayed with it. “I anticipated that we might lose a third of the original group,” says Dr. Abramson. “But only one student did not remain in the accelerated program, and all those who have done so have done quite well.” Indeed, every-



Xinlin Chen, MD, from San Jose, California, is a resident in psychiatry at NYU Langone.



David Rhee, MD, from Tenafly, New Jersey, is a resident in internal medicine at NYU Langone.



one sailed through the first two years of the curriculum (graded on a pass-fail basis), and all have passed the first two phases of the U.S. Medical Licensing Examination. Two of the 15—Drs. Ryan and Rokosh—were accepted into Alpha Omega Alpha Honor Medical Society, which recognizes the top medical students around the country—a similar ratio seen among students in the conventional pathway.

No substantive changes have been made for students who are following in their footsteps, with one key exception: while the members of the first class had to be accepted into the pathway and a residency on day one, any student can now apply for accelerated study midway through the first year. Being able to “opt in” later is proving popular. In the second class, 12 students were accepted at the start of medical school and 10 more opted in. (Conversely, students in the pathway can “opt out” at any time if they find that accelerated study is not right for them.) Roughly 15 percent of the second and third classes are doing accelerated study. Program administrators expect that enrollment in the new pathway will peak at about one-quarter of the student body.

NYU School of Medicine is also pilot testing a three-year pathway for those who come to medical school with a PhD in hand. “This is especially attractive to students whose ultimate goal is to do research,” says Joan Cangiarella, MD, director of the Three-Year MD Pathway program and associate dean for education and fac-



Shu Liu, MD, from Chantilly, Virginia, is a resident in radiology at NYU Langone.



Jina Park, MD, from Duluth, Georgia, is a resident in neurology at NYU Langone.

ulty affairs. "Our whole focus is on individualized pathways."

SHAPING THE FUTURE OF MEDICAL EDUCATION

Leaving nothing to chance, NYU School of Medicine will continue to evaluate students in the accelerated program and follow graduates as they move through their residencies. "This program isn't just a fast track," says Dr. Cangiarella. "It's a unique opportunity to follow and assess learners across the continuum of undergraduate-graduate medical education."

Indeed, the next leg of the journey represents a critical test of the program. If graduates handle their residencies as well as expected, their success will help ease any lingering doubts about the competency and preparedness of three-year graduates and encourage more medical schools to pursue their own accelerated programs. In fact, at least 35 percent of U.S. medical schools have or are considering developing a three-year MD program, according to a 2014 survey of medical school deans. Robert I. Grossman, MD, the Saul J. Farber Dean and CEO of NYU Langone, expects that number to boom in the coming years. During a speech in May honoring the inaugural three-year graduates, Dr. Grossman predicted that the accelerated pathway will become "a tsunami in medical education."

Inspired by this positive trend, eight medical schools have formed a consortium to identify and share best practices for accelerated pathways

"This program isn't just a fast track," says Joan Cangiarella, MD, director of the Three-Year MD Pathway program. "It's also a unique opportunity to follow and assess learners across the continuum of undergraduate-graduate medical education."

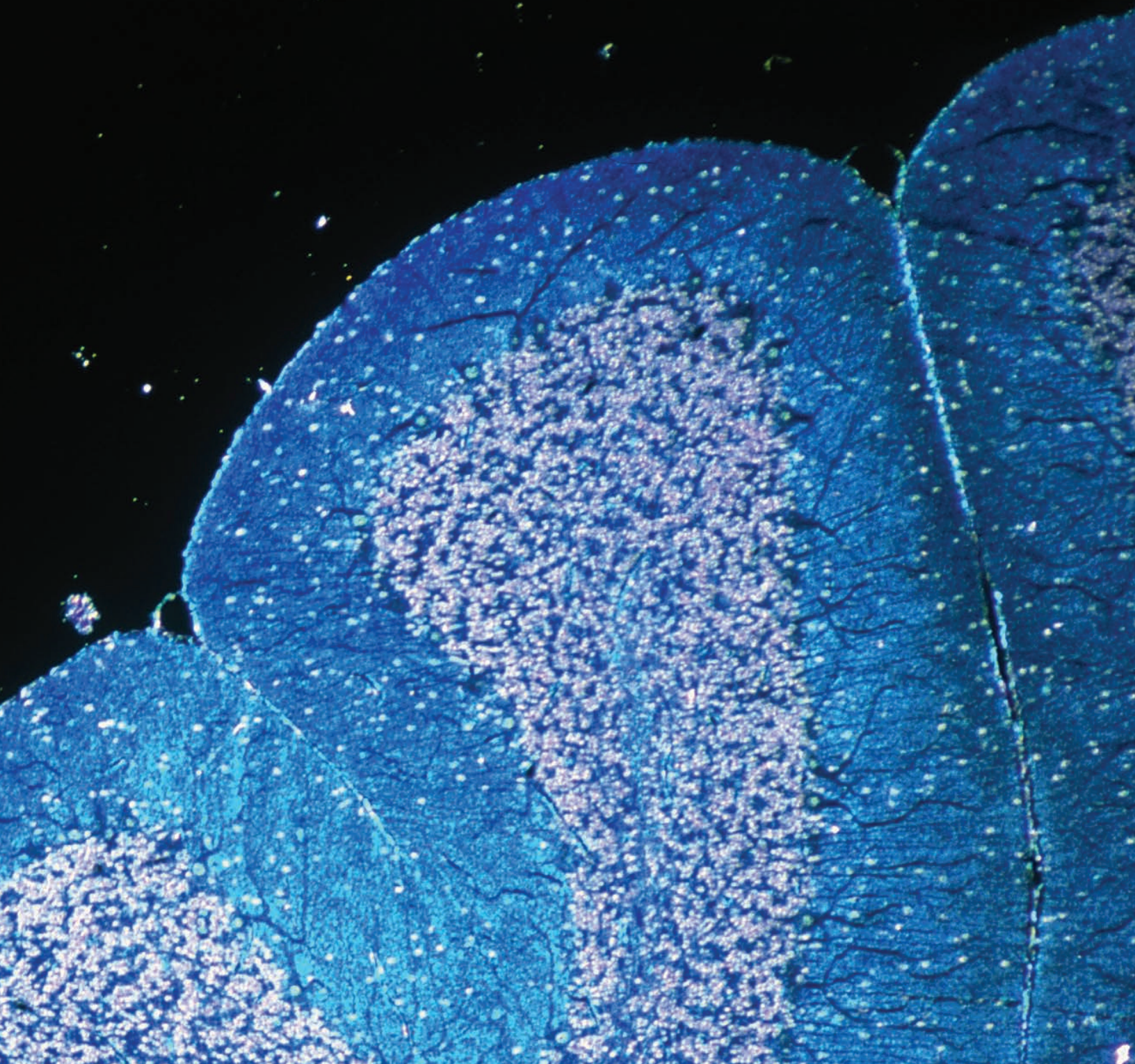
to the medical degree. The consortium, funded by a four-year, \$250,000 grant from the Josiah Macy Jr. Foundation, includes medical schools that have implemented or plan to implement accelerated pathways. (While NYU School of Medicine was not the first to offer a three-year curriculum, it is the only one to offer residencies in all medical specialties.)

"Our big goal over the next few years is getting the rest of the medical profession to accept the notion of accelerated pathways," says Dr. Abramson, who is coleading the Macy grant along with Dr. Cangiarella. "Right now, the old guard doesn't want to think about changing an educational system that has remained largely the same since 1910."

But a growing number of students see things differently. "I'd recommend this program to others—if they have strong feelings about what they want to do in medicine," says Dr. Rokosh. "The final six months are pretty jam-packed, but I've never questioned my decision."

Dr. Ryan is similarly positive. "The fourth year is known for being relatively relaxed, with less in the way of clinical obligations," he says. "At times, I've been a little jealous of that. But from what I gather, the match process is brutal, it's expensive, and there's tons of uncertainty. I think that most of my peers, if given the opportunity, would like to be done 2 months from now, rather than in 14 months." ●

This tiny slice of brain
tissue, packed with
thousands of neurons,
consists mostly of water.





THE CRANIAL CLEANSE

A newly discovered network of drainage channels in the brain has profound implications for understanding the damage wrought by strokes, heart attacks, and neurodegenerative diseases such as Alzheimer's. **BY BRYN NELSON**

IMAGE: PONGSAKORN JIJN / ISTOCK BY GETTY IMAGES; (FACING PAGE) INNERSPACE IMAGING / SCIENCE SOURCE



THE IMAGERY IS LIKE SOMETHING OUT OF A HAZY DREAM:

Shadowy escorts push molecular garbage through a thicket of tiny blood vessels enveloping the brain. Enzymes hack the trash into ever-smaller bits. Mysterious interconnected tunnels dramatically swell in size overnight to flush it all away and then shrink back at dawn.

Researchers have long struggled to understand why only certain molecules can

enter or leave through the tangle of capillaries that form the blood-brain barrier and selectively block access to the brain. Others have sought to understand how toxic proteins can be chopped into harmless pieces and whether the clear cerebrospinal fluid coursing through the brain and spine might also play a role in flushing out waste.

After years of obscurity, the brain's murky disposal system may finally be coming into focus. The emerging science, influenced by decades of research at NYU Langone, suggests that overlapping networks within the brain haul away the daily detritus of the body's most energy-hungry organ. These systems, according to recent studies, may falter with age, sleep disruptions, disease, or injury. By uncovering their mechanisms and weak points, though, scientists may gain a critical understanding of how to minimize the damage inflicted by strokes, heart attacks, traumatic brain injuries, and neurodegenerative diseases such as Parkinson's and Alzheimer's.

The big question is how the body removes all kinds of brain garbage, says Mony de Leon, EdD, director of the Center for Brain Health and professor of psychiatry at NYU Langone. "It's every breakdown product.

It's a thousand things. It's not one," he says. "So the question is, What is the network by which stuff gets out?" And what happens if that network fails?

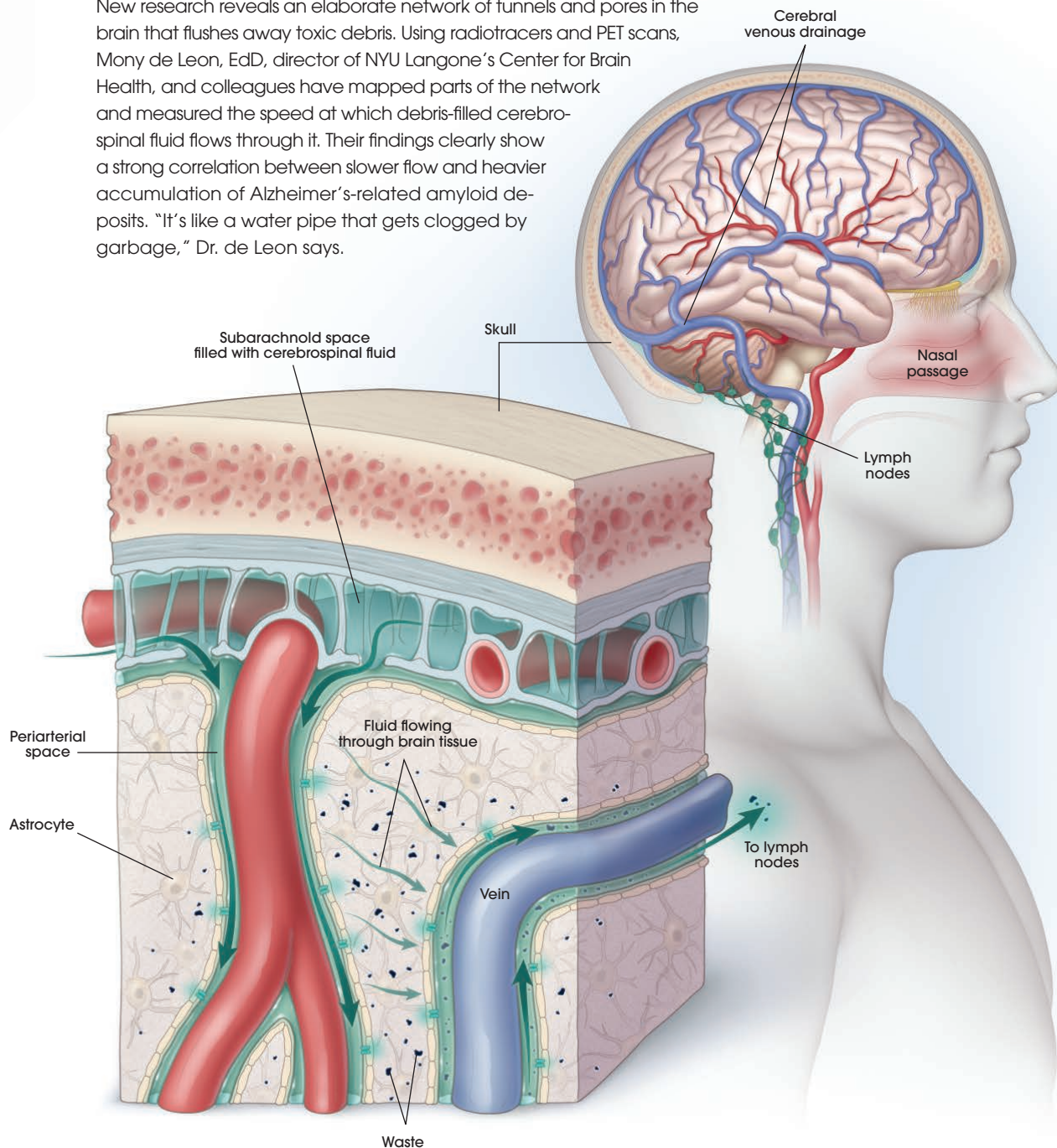
NYU Langone researchers have taken a particularly keen interest in the fate of a protein fragment called amyloid-beta that plays a central role in the development of Alzheimer's disease. Although the protein's normal function isn't well understood, it usually dissolves in cerebrospinal or interstitial fluid and can be carted away by a variety of mechanisms. Some of these same mechanisms may clear other Alzheimer-related proteins such as tau, making the brain's exit routes critical to understanding the buildup of pathological proteins.

Blas Frangione, MD, PhD, professor emeritus of pathology and psychiatry, conducted some of the first studies to examine how amyloid-beta travels through a mouse brain. More recent experiments by Jorge Ghiso, PhD, professor of pathology and psychiatry, have identified two enzymes that may be critical in hacking up the protein into smaller, nontoxic bits. Other studies have illuminated how certain molecules then escort the pieces through the blood-brain barrier. Once out of the brain and into the

IMAGE: OKEA /ISTOCK BY GETTY IMAGES; ILLUSTRATION: FACING PAGE, SCOTT LEIGHTON

THE BRAIN'S ELEGANT GARBAGE DISPOSAL

New research reveals an elaborate network of tunnels and pores in the brain that flushes away toxic debris. Using radiotracers and PET scans, Mony de Leon, EdD, director of NYU Langone's Center for Brain Health, and colleagues have mapped parts of the network and measured the speed at which debris-filled cerebrospinal fluid flows through it. Their findings clearly show a strong correlation between slower flow and heavier accumulation of Alzheimer's-related amyloid deposits. "It's like a water pipe that gets clogged by garbage," Dr. de Leon says.



bloodstream, the chunks can be safely removed from the body through urine.

Many scientists, however, believe that if amyloid-beta isn't cleared fast enough, the partially folded protein can begin to stick together, form the toxic telltale clumps, or plaques, of Alzheimer's, and clog the plumbing.

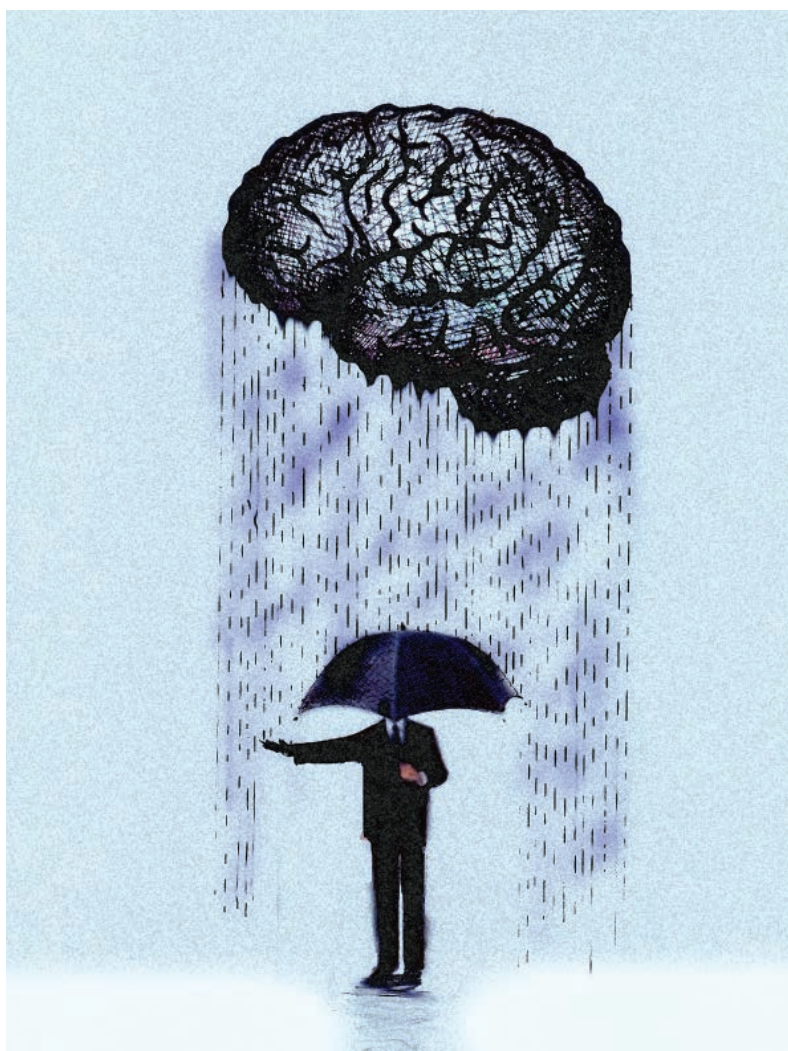
The recent discovery of a kind of hydraulic disposal system that may use pressurized cerebrospinal fluid to wash away amyloid-beta and other debris has added another wrinkle to the investigations. Until recently, the idea that materials can flow in bulk through the brain had been a vague concept. "Now we're coming to see this as probably being quite important to many things," says Charles Nicholson, PhD, professor emeritus of neuroscience and physiology. Like a river, he says, the flow may be crucial for hauling waste over vast distances.

DR. NICHOLSON has spent more than four decades studying the fluid- and scaffolding-filled gaps between brain cells, known as extracellular spaces. Stocked with proteins, polymers, and electrically charged molecules, the narrow but complex spaces facilitate cellular communication by conducting electrical currents. By Dr. Nicholson's widely accepted measurements, these spaces account for a remarkable 20 percent of the brain by volume.

Scientists long believed that molecules moved through the extracellular channels randomly, like drops of ink dispersing in water. But recent evidence points to an additional mysterious force that sweeps along compounds of various sizes at the same clip, creating a flow that's far more rapid than diffusion's slow creep. Could the channels do more than just facilitate cellular communication? Could the molecules be subject to both short-range diffusion and flow across longer distances? And for what purpose?

About 30 years ago, researchers first described the tubing that envelops blood vessels in the brain and courses with cerebrospinal fluid. The hypothesis that such hollow cavities—known as the perivascular

The brain generates an estimated three pounds of debris a year. "So the question is, What is the network by which stuff gets out?" says Mony de Leon, EdD, director of the Center for Brain Health at NYU Langone.



space—may help drain fluid from the brain, however, remained controversial for years, until Dr. Nicholson's lab helped to measure the phenomenon of expanding and contracting space between brain cells.

"How do you change the size of the extracellular space? The only way you can really do it is by swelling or shrinking the cells that form the boundaries of the extracellular space," Dr. Nicholson says. Brain cells tend

ILLUSTRATION: GARY WATERS / GETTY IMAGES; IMAGE (FACING PAGE): OKEA / ISTOCK BY GETTY IMAGES

to expand dramatically after a heart attack or stroke; they lose the ability to control their volume and swell with an influx of water, squeezing off the space beyond. He and his collaborators found that a heart attack or stroke can reduce the brain's extracellular space from 20 percent to 5 percent, for example. As that volume shrinks, the movement of water and molecules slows considerably, thwarting electrical communication between cells.

A separate group of researchers at the University of Rochester Medical Center was investigating how the brain deals with its own waste—and what happens when it doesn't. Brain cells are exquisitely sensitive to even minor changes around them, says Maiken Nedergaard, MD, codirector of the university's Center for Translational Neuromedicine, who has collaborated closely with Dr. Nicholson for years. For age-related diseases that involve a loss of mental abilities, she says, "it's very clear that they're diseases of a dirty brain, that you accumulate proteins in the brain."

The rest of the body deals with its disposal needs through the lymphatic system, a network of lymph nodes, ducts, and vessels. The system uses a clear fluid called lymph to circulate disease-fighting cells and flush toxins and waste products from body tissues to blood vessels and on to the liver, where they can be detoxified. Dr. Nedergaard began to ask why no similar system existed in the brain, given that its energy demands exceed those of any other organ. She estimates that the brain generates about three pounds of debris every year.

Maybe, she thought, a similar disposal network occupied the little-studied perivascular space around the brain's blood vessels. Dr. Nicholson's research had suggested that the complexity of the brain's cells and their branchlike projections greatly hindered the movement of molecules in the fluid surrounding brain cells. Within the relatively open, less-cluttered perivascular spaces, however, the movement improved significantly.

The first major insight arrived when Dr. Nedergaard and her lab injected fluo-

rescent dye into the cerebrospinal fluid of mice. Instead of a one-way flow out of the brain, the fluid unexpectedly and quickly recirculated back into the brain and traced a route through the tunnel-like perivascular spaces. The return voyage hinted at a more complicated kind of plumbing. Subsequent experiments suggested that the cerebrospinal fluid hauled away more than half of a mouse's normal output of amyloid-beta protein—far more than previously thought—and dumped it into larger lymphatic vessels

in the neck before making the return trip back into the brain.

The evidence led Dr. Nedergaard and colleagues to propose a new waste disposal network dubbed the "glymphatic system." Instead of lymph flowing through lymphatic vessels, they suggested, cerebrospinal fluid courses through the brain's perivascular tunnels and into brain tissue via star-shaped brain cells called astrocytes. The researchers soon realized that the footlike extensions of the astrocytes bunched together to form the



outer layer of tubing that defines the perivascular space surrounding every vein, artery, and capillary.

Dr. Nedergaard's research suggested that the big-footed cells act as gatekeepers to control the flow of water in or out of the perivascular space. Each astrocyte harbors a series of conduits, or pores, formed by a protein called aquaporin-4 that directs water back and forth across the cell. Both the bulk flow and amyloid-beta clearance slow significantly in mice that lack the conduit.

Dr. de Leon's findings generally match the main ideas of this "glymphatic system." In experiments to track the impact of various diseases on how well radiotracers leave the brain, he and his colleagues have found that the size of a molecule doesn't seem to matter once it gets into the brain's intercellular fluid. "It's like being dumped into a river," Dr. de Leon says. Whether a leaf or boat, all are carried along by the flow, which is powered by the heart and lungs. Thus, cardiovascular and pulmonary disease can slow the flow, Dr. de Leon believes, and allow debris to accumulate in the brain.

Other studies suggest that the river can be widened or narrowed by drugs, sleep, disease, and other factors that alter the water concentration within the adjacent brain tissue. Dr. de Leon and colleagues have observed this effect themselves in experiments measuring how two radiotracers move through the brain. The novel system is based on an imaging technique called positron emission tomography, or PET, and compares the tracers' activity within Alzheimer's patients. One labeled protein measures flow through the brain while the other measures the location and amount of accumulated amyloid-beta protein.

The radiotracer technique, Dr. de Leon says, can estimate the relative clearance ability of every part of the brain, down to millimeter-size units of observation called voxels. "That's done over time, which has allowed us to make maps of how long it takes for the tracers to move, and which areas of the brain are most effective in the movement," he says. For the first time, the

"If loss of deep sleep can increase the risk of Alzheimer's disease, then we could theoretically use new drugs to enhance deep sleep and protect against the disease," says Dr. Ricardo Osorio.

team has used the approach in humans to identify several areas with optimal clearance activity and has shown a "very, very strong" correlation between lower clearance and higher accumulation of Alzheimer's-related amyloid deposits. He compares the problem to a river system that can efficiently move ships and other traffic until it's choked off by a big pile of garbage.

Dr. de Leon's PET-based collaboration at the Center for Brain Health with radiologist Yi Li, MD, research assistant professor of psychiatry, and mathematician Henry Rusinek, PhD, professor of radiology and psychiatry, has a direct bearing on Alzheimer's disease and the stagnation hypothesis of amyloid-beta accumulation. Even so, Dr. de Leon adds that measuring the rate of clearance could help illuminate the physiological impact and treatment of other conditions such as head trauma, stroke, cardiovascular disease, Alzheimer's, and Parkinson's—all marked by inflammation.

With an assist from Dr. Nicholson, Dr. Nedergaard's research has added yet another twist to the concept of brain clearance by suggesting that sleep-wake cycles in mice may regulate expansion and contraction of the glymphatic system. Although her group performed its initial studies in anesthetized mice, technical advances allowed them to implant a sort of window into the brains of lab mice and train them to sit still on the platform of a powerful two-photon microscope. The mice become so comfortable, in fact, that several dozed off. "They would ac-

tually fall asleep, and you could then start to look at the movement of these cerebrospinal fluid tracers in awake and sleeping mice," Dr. Nedergaard says.

When the animals fell asleep, fluorescently dyed molecules injected into a cavity at the back of the brain flowed freely with the cerebrospinal fluid through the extracellular space. Every time the animals woke up, however, the molecules virtually stopped. "This was such a dramatic decrease that I doubted it," Dr. Nedergaard says. She and her lab repeated the same experiment over and over, using different techniques. Each time, they got the same result.

Dr. Nedergaard sometimes calls Dr. Nicholson the "landlord" of the brain's extracellular space: one of the key people in the field and the first to call if you encounter anything unexpected. "As soon as we had made the discovery, we basically had to tell Charles, 'This is what we have found. Can you make sense out of it?'"

One of Dr. Nicholson's main methods for measuring the size of the brain's extracellular space uses two tiny electrodes placed a small distance apart. The technique exploits the electrodes' electrical signals to measure how long it takes for a small molecule to travel from one to the other, like timing a swimmer from a starting wall to the finish line. The method and accompanying software developed by the Nicholson lab have allowed researchers to estimate the relative hindrance of a molecule's forward progress and the size of the space it's moving through

between the start and end points—like gauging whether the swimmer is moving through a wide channel or narrow chute.

Dr. Nicholson agreed to help train members of the Nedergaard lab, set up the experiments, and verify the incoming data on the size of the extracellular space in sleeping and fully awake mice. The result was a breakthrough 2013 study by the NYU Langone and University of Rochester labs, in the journal *Science*. “We found that in the sleeping state, this extracellular space is about 24 percent of the total volume of the brain. And then as soon as the mice wake up, it goes to about 14 percent. So it’s a very dramatic change,” Dr. Nedergaard says. “We have since repeated it in maybe 200 animals, and it always happens. It’s a very solid observation.”

The finding raised an intriguing new question: Why did sleep improve the drainage so much? “For the brain, which has an incredibly high metabolic demand and makes all of this waste product, maybe sleep is for a basic housekeeping function,” Dr. Nedergaard says.

Dr. Nicholson describes the hypothesis like this: “You’re so busy during the day, tending to your cell phone and various other things, that toxins tend to build up in the brain. There’s not enough time to remove them all.” During sleep, however, the enhanced clearance process is able to wash them out. “We don’t really know to

what extent that’s true, but it’s an interesting idea,” he says.

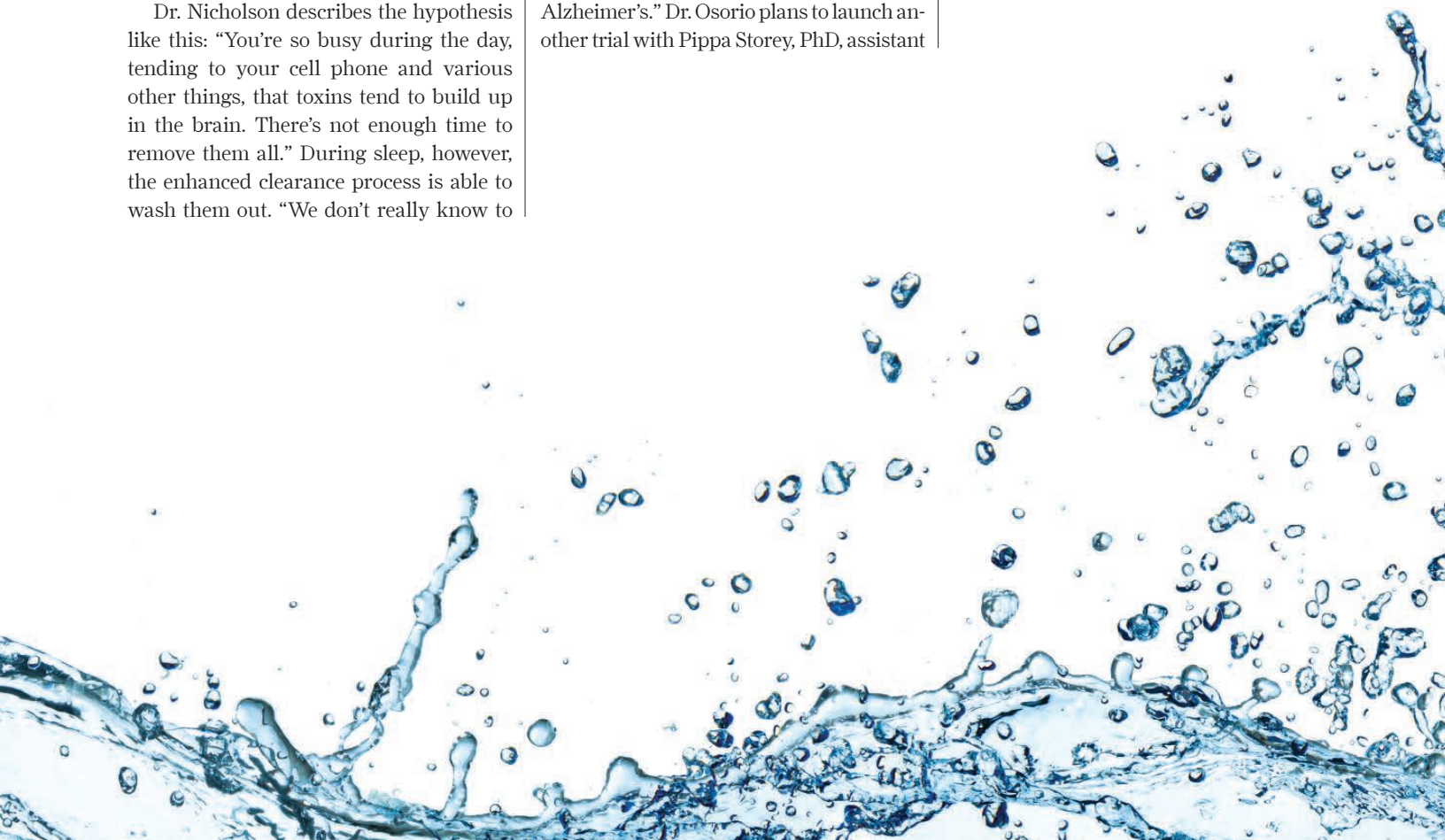
Intriguingly, recent data suggest that brain activity dips while clearance rates rise during deep sleep, also known as slow-wave sleep, which decreases with age. In a study of 36 healthy volunteers with an average age of 68, the Center for Brain Health’s Ricardo Osorio, MD, assistant professor of psychiatry, reports that adults with shorter periods of deep sleep have more amyloid-beta proteins in their cerebrospinal fluid. The link bolsters Dr. Nedergaard’s observation that mice that miss deep sleep clear away less of the toxic protein. “This could be one of the mechanisms by which age increases the risk of developing Alzheimer’s,” Dr. Osorio says.

If further studies pan out, he says, clinicians could contemplate prevention trials. “If loss of deep sleep can increase the risk of Alzheimer’s disease, then we could theoretically use new drugs to enhance the deep sleep and protect against the disease,” says Dr. Osorio. “The idea would be to not cure Alzheimer’s, but improve the sleep quality and, by doing so, delay the age of onset of Alzheimer’s.” Dr. Osorio plans to launch another trial with Pippa Storey, PhD, assistant

professor of radiology at NYU Langone, using MRI scanners to investigate whether reduced slow-wave sleep alters the nighttime expansion of the brain’s drainage channels.

The science is moving quickly. Just last year, researchers discovered the presence of lymph vessels in outer tissues surrounding the brain, revealing yet another potential disposal system. At the least, Dr. Nicholson says, the mounting evidence has solidified the idea that diffusion is far from alone in clearing away the brain’s clutter. If plenty of disagreement remains over the fine details of the disposal process, he says, the new discoveries have reinvigorated the field.

“From my perspective, as a basic scientist who’s interested mainly in the extracellular space and has always been concerned about how we might study flow, I think it’s really brought everybody back to thinking about this problem, which is very exciting,” he says. ●



DE- CON- STRUCT- ING ADDIC- TION

A psychiatrist trained in anthropology investigates the socioeconomic forces that shape how we treat substance abuse.

BY KENNETH MILLER

HERE'S A MEDICAL RIDDLE: Ed and Jonathan are heroin addicts in their 20s, with a history of severe mood swings. When Ed seeks treatment for his drug dependency, he's referred to a substance-abuse clinic, where a psychiatrist diagnoses him with bipolar disorder. He's put on methadone to control his addiction and prescribed powerful antipsychotics to stabilize his moods. Jonathan, meanwhile, consults a psychiatrist in private practice, who diagnoses him with depression and prescribes a popular antidepressant. For his addiction, Jonathan receives buprenorphine, an opioid similar to methadone but with fewer risks of overdose and addiction. Unlike methadone, it's prescribed in a doctor's office and dispensed by most pharmacies. If both men have similar symptoms and drug habits, what explains the differences in diagnoses and therapies?

To Helena Hansen, MD, PhD, who followed Ed and Jonathan for years as part of her wide-ranging research on addiction and mental health, the answer is clear: Ed is a Latino living in a poor section of Brooklyn, while Jonathan is a middle-class white man from suburban Queens. But what drives such disparities in care, Dr. Hansen argues, isn't racial prejudice on the part of individual clinicians, most of whom want only the best for their patients. Rather, it's a complex web of factors ranging from neighborhood resources to federal drug-enforcement policies.

"The social influences on health are incredibly important," says Dr. Hansen, assistant professor of psychiatry at NYU Langone. "Yet our understanding of how those forces impact health is amazingly

ILLUSTRATION: ROY SCOTT / GETTY IMAGES



underdeveloped.” Over the past decade, this physician-scientist—whose PhD is in cultural anthropology—has dedicated herself to deepening that understanding. Her fieldwork, supported by the National Institutes of Health and the Robert Wood Johnson Foundation, among others, has taken her to shooting galleries and crack houses, corporate suites and legislative headquarters, upscale doctors’ offices and rundown drug-treatment centers. A prolific author of journal articles and book chapters, she speaks on the social dynamics of addiction and recovery at conferences and seminars across the country.

Dr. Hansen is also a leading proponent of “structural competency,” a new philosophy of medical education that calls on clinicians to learn how socioeconomic inequalities affect the people they treat—and to incorporate those insights into every aspect of care. “Helena is trying to move a whole generation of healthcare providers to think more deeply about mental health,” says social epidemiologist Chau Trinh-Shevrin, DrPH, associate professor of population health and medicine, who serves with Dr. Hansen on the Medical Center’s diversity committee. “She’s asking important questions and getting doctors to see what’s happening beyond the clinic walls.”

HELENA HANSEN’S education in racial and class disparities began in childhood. Her mother was African-American, her father an immigrant from Norway; both studied psychology at the University of California, Berkeley. When the couple separated, the kids stayed on with their mother, who later became a social worker in Oakland.

Dr. Hansen spent much of her youth shuttling between the Berkeley campus and the low-income neighborhoods where her family lived. “I took public buses to school starting in first grade,” she recalls. “This was in the 1970s, when California was closing its mental hospitals, and the streets were filling up with deinstitutionalized patients, who were now homeless. I remember walking

“The social influences on health are incredibly important,” says Dr. Hansen. “Yet our understanding of how those forces impact health is amazingly underdeveloped.”

past them on the way to the bus stop and developing relationships with some of them.”

Some of her loved ones wound up on the street as well. Three of Dr. Hansen’s uncles grappled with substance-abuse and mental-health issues; two died as a result. “They were talented young black men who got tragically sidetracked,” she says. Meanwhile, thanks to her mother, Dr. Hansen grew familiar with ongoing theoretical debates over addiction and public healthcare, and the joys and frustrations of professionals on the front lines.

Such experiences had a profound influence on her formal education. After graduating from Harvard University in 1992 with a degree in biology and an abiding interest in social policy, she later enrolled in Yale University’s MD-PhD program, persuading the admissions committee to accept her as its first social-science student. Her pitch, she notes, formed the rationale for much of her subsequent work: “Just as we need basic science to be translated to the bedside, we need social science to be translated to the clinic.” Her doctoral research included six weeks in Cuba investigating the government’s response to the AIDS epidemic, and a year in Puerto Rico studying Pentecostal street ministries that were founded and run by recovering addicts.

The biggest turning point in Dr. Hansen’s career came during her last year of medical school, in 2005, when she assisted in a clinical trial of buprenorphine, the first prescription narcotic for addiction that could be prescribed in a doctor’s office instead of a clinic. “People were very excited about this new medication, which was supposed to change the culture of medicine by allowing addic-

tion to be treated in primary care settings” she recalls.

By then, after decades of debate, experts commonly described addiction as a chronic brain disease, rather than a failure of morals or will; the goal, some argued, should be medical management, as with diabetes or asthma. The problem was how to manage the management. The Harrison Narcotics Act of 1914 had prevented doctors from using opioids for addiction treatment. Since 1972, an exception had been made for methadone, which satisfies narcotic cravings without producing an intense high. But that medication, introduced under the Nixon administration, was subject to heavy restrictions: it could be administered only at clinics overseen by the Drug Enforcement Agency, with staffers watching to ensure doses weren’t smuggled out for street sale.

Buprenorphine, meanwhile, could be prescribed in a doctor’s office. More difficult to abuse than methadone, it was intended to provide the older medication’s benefits without its inconveniences and stigma. Yet three years after its approval by the FDA, Dr. Hansen discovered, it was rarely available in minority communities, even as its sales surpassed blockbuster medications like Viagra. She decided to find out why.

In the fall of 2005, Dr. Hansen enrolled in the psychiatry residency program at NYU School of Medicine. Soon afterward, aided by an American Psychiatric Association fellowship, she began researching buprenorphine in more depth. She interviewed prescribers, policymakers, and the developers of buprenorphine maintenance, as well as bu-

prenorphine patients at Bellevue Hospital—then the only public medical facility in New York City with an outpatient buprenorphine service—and elsewhere. She also began observing the daily lives of methadone patients, whom she met while leading group therapy programs at Bellevue.

Since then, Dr. Hansen has published her findings in a series of groundbreaking papers, weaving together a detailed analysis of what she calls the “racial politics” of addiction treatment. In this accounting, the methadone/buprenorphine divide is just one of many disparities. Methadone, she learned, was initially presented to the public as a tool for lowering crime in black and Latino communities. Accordingly, methadone clinics were mostly located in those areas. Then, in 1996, the introduction of OxyContin, a prescription painkiller as powerful as heroin, changed the face of opioid abuse. By the start of the new millennium, media reports warned of an epidemic of OxyContin addiction sweeping suburban and rural America.

Buprenorphine maintenance, Dr. Hansen found, was aimed expressly at this new, overwhelmingly white cohort of substance abusers. The National Institute on Drug Abuse, alarmed by the dramatic uptick in the rate of death due to prescription painkillers, awarded the medication's manufacturer \$23 million in grants for clinical trials and advocated for the Drug Abuse Treatment Act of 2000, which paved the way for buprenorphine to be prescribed by private physicians for addiction treatment. Because the law required buprenorphine prescribers to complete an eight-hour training course and obtain a special registration number, Dr. Hansen's interviewees told her, it favored physicians in more affluent communities, who could spare the time and expense. When buprenorphine came on the market, ads portrayed the typical user as a white, middle-class dad who'd become addicted to painkillers after a back injury and wanted to return to coaching his son's baseball team. Even now, many buprenorphine providers accept only private insurance or out-of-pocket payments—unlike meth-



Dr. Helena Hansen in
Bellevue's Sobriety Garden

A SPACE FOR HEALING

Although Dr. Hansen focuses primarily on research and education, she also co-leads two therapy groups in Bellevue's outpatient addiction program. The first is a community performance workshop, which puts on plays, dance shows, and other events for the hospital population. “Many addicts are disconnected from their families and other support systems,” she explains. “To recover, they need sources of community besides their drug-use networks, and activities that feel meaningful besides the search for drugs. The performance group provides both.”

In the second group, participants create short videos about themselves. “Addiction treatment is all about rescripting one's life,” Dr. Hansen notes. “This group enables them to do that literally.” The video workshop also inspired Dr. Hansen to create her own documentary, *Managing the Fix*, which weaves together the experience of three patients undergoing methadone or buprenorphine therapy with material illustrating the social, economic, and political forces that affect addiction and its treatment.

These and other therapy groups often meet in Bellevue's Sobriety Garden. Built in 1989, the space is decorated with sculptures crafted by former substance-abuse patients, and planted with flowers and vegetables that current patients cultivate themselves. “Gardening requires patience, attention, and collective effort,” Dr. Hansen says. “It can be really helpful for some patients who don't respond well to talk therapy or medication.”

In New York City, Dr. Hansen's research shows, buprenorphine treatment rates were highest in the zip codes with the highest incomes and highest percentage of white residents, while methadone treatment rates were highest in zip codes with low-income, largely black or Latino residents.

adone clinics, which rely mostly on Medicaid reimbursements.

The statistics bear out this troubling combination of regulatory and socioeconomic factors: an earlier nationally representative study found that buprenorphine patients are more likely than methadone patients to be white (92% vs. 53%, according to the Substance Abuse and Mental Health Services Administration), employed (56% vs. 29%), and to have some college education (56% vs. 19%). In New York City, Dr. Hansen's research shows, buprenorphine treatment rates were highest in the zip codes with the highest incomes and highest percentage of white residents, while methadone treatment rates were highest in zip codes with low-income, largely black or Latino residents.

Where patients live and how much money they earn even influences how they may be treated for underlying psychiatric disorders, Dr. Hansen has found. In 1996, just as OxyContin hit the market, Congress passed legislation to limit lifetime welfare benefits to five years and eliminated drug addiction and alcoholism as qualifications for Social Security disability payments. For tens of thousands of addicted people, the only way to keep from falling through the social safety net was to qualify for Social Security benefits under the new rules—which typically meant securing a diagnosis of chronic, severe mental illness.

Many addicts do, of course, have psychiatric disorders of various kinds. But because schizophrenia and bipolar disorder were the conditions most likely to be judged disabling by Social Security examiners, Dr. Hansen's research indicates, clinicians in poor minority neighborhoods were often willing to provide such a diagnosis (rather than, say, depression or borderline personality disorder) to help vulnerable patients gain desperately needed support. By 1999, psychiatric disabilities accounted for the largest number of Social Security awards, and the proportion has continued to grow.

There are costs, Dr. Hansen says, to this bureaucratic approach to psychiatric medicine. "Social Security application reviewers frequently look for consumption of antipsychotics as a sign that applicants qualify as disabled," she explains, "even though antipsychotics carry the risk of serious side effects, like obesity, diabetes, and elevated cholesterol. In private practice, a doctor has the flexibility to tailor treatment, including medication, to the individual. The Social Security review system forces the clinician's hand."

In Dr. Hansen's view, the U.S. has developed a "two-tiered" system of addiction treatment. For addicted people in private care, most of whom are white, therapy is designed to minimize stigma and get the patient back to work or college; buprenorphine is used as a means toward those ends. Addicted people in public care—which

covers most poor and nonwhite patients—are administered methadone under stringent supervision, steered into perceiving themselves as permanently disabled, and prescribed psychotropic medications that may further compromise their health.

None of this is necessarily the result of malice. "Addiction scientists didn't see that buprenorphine would lead to greater disparities," Dr. Hansen says. "It wasn't their intention. To understand inequalities in healthcare, we have to examine how treatment technology interacts with institutions, policies, and economics."

LEADERSHIP AT NYU Langone quickly realized that Dr. Hansen's insights would be of value to her fellow trainees. In 2008, during her third year of residency, the training director invited her to develop a curriculum in cultural issues for psychiatry residents. She accepted the challenge, envisioning something both broader and more probing than the kind of "cultural competency" course that has been widely offered at medical schools for the past two decades.

"The concept of culture in clinical medicine was tied to an individual patient's beliefs and behaviors," she explains. Doctors were taught that an African-American woman might not consider obesity to be a problem, for example, or that a Mexican-American man might have dietary preferences that raised his risk for diabetes. "As an anthropologist, I knew you needed a fuller picture. What kinds of neighborhoods were people going home to? How did those neighborhoods work? Were there places to exercise safely or buy healthy food?" Dr. Hansen encouraged students to ask such questions and to experiment with novel interventions—from partnering with community organizations to promote a healthier environment to teaming up with law students to aid a patient facing eviction.

Not long after launching the curriculum, she and psychiatrist-historian Jonathan Metzl, MD, PhD, began to popularize the concept of "structural competency," which calls on clinical practitioners to act outside

of clinic walls to address systemic barriers to health through collaborations with community organizations, nonhealth institutions such as law enforcement and schools, and with policymakers. In order to create a network of colleagues who are implementing this approach in clinical training, Drs. Hansen and Metzl have hosted three national conferences, edited two special journal issues, and advised two national webinar series on the subject of structural competency (see structuralcompetency.org).

Dr. Hansen's advocacy work caught the attention of the Brownsville Partnership, a coalition of agencies and community groups based in one of Brooklyn's poorest neighborhoods, which asked her to help improve its delivery of mental health ser-

vices. In response, she created a new resident program, called the NYU Elective in Community Mental Health and Structural Intervention, which provides fourth-year residents with hands-on experience in systems-based healthcare. Since 2012, participants have worked with the Brownsville Partnership to conduct community depression screenings, create trauma support groups, and map usage of mental-health emergency services to enhance preventive strategies. "Every clinician can benefit from an opportunity like this," says Dr. Trinh-Shevrin. "Besides building professional skills, it fosters humility and raises awareness of unconscious biases."

ONE EARLY, cool evening in April, Dr. Hansen strolled along the cobblestone

pathways of the Sobriety Garden outside Bellevue, admiring the blooming springtime flowers. The air was crisp and fragrant. Dr. Hansen visits the garden often, and not just for the peace and quiet. It's tended by patients from the hospital's chemical dependency outpatient program, where she works. The dozens of charming stone animal sculptures scattered throughout the plot were also made by patients. For many people in the program, Dr. Hansen notes, the garden does what years of talk therapy cannot: it delivers a sense of connection and accomplishment. "It's a vision of what addiction therapy could and should be," she says. "It's about forging social bonds, and planting and harvesting what you've seeded." ●

STATEN ISLAND: A MICROCOSM OF AMERICA'S DRUG CRISIS

As a researcher, one of Dr. Hansen's central concerns is addiction treatment in minority communities. Recently, however, she's turned her attention to a place with very different demographics: Staten Island. This primarily white, middle-class borough has the highest opioid overdose rate in New York City, with 74 deaths in 2014—up from 64 the previous year. "In a way, Staten Island is a microcosm of the United States, where opioid overdose has contributed to the recent decline in life expectancy among whites," she says. "I wanted to find out what's going on, and how clinicians are dealing with the problem."

In 2013, Dr. Hansen began interviewing physicians on the island, asking whether and why they decided to treat patients with buprenorphine—an addiction medication that, unlike methadone, can be prescribed by private practitioners. As in other parts of the country, she learned, rising heroin use is helping to drive the overdose uptick. As new regulations have made OxyContin and other opioid painkillers harder to obtain, and manufacturers have changed formulas to make abuse more difficult, many prescription-medication addicts have turned to illicit drugs. Also, as in other communities, most doctors in Staten Island shun buprenorphine, unwilling to take on the challenges of treating addicts or the legal monitoring imposed on the medication's providers.

Yet a sizable minority do offer buprenorphine maintenance—a proportion higher than in any other borough. "These providers tend to speak of addicts as their neighbors and family members," says Dr. Hansen. "Most lack specialized training in addiction therapy, but they feel a responsibility to do whatever they can."



The Hidden Curriculum

David Stern, MD, PhD, vice chair for education and faculty affairs, on the science of teaching students the unwritten rules of medicine

BY DAVID H. FREEDMAN

NEARLY A QUARTER of a century ago, David Stern, MD, PhD, was among a handful of doctors in the U.S. pursuing a doctoral degree in education, having become determined to conduct rigorous research into how to improve medical education. But the doctorate program, at Stanford University, had gotten off to a slow start for him. “I was listening to the lectures on how children learn, and wondering what it could have to do with medicine,” he says.

Things suddenly perked up for Dr. Stern when he found himself pondering a question: How do first-grade students learn to raise their hands in class? “When the teacher asks what one plus one equals, students don’t just blurt out ‘two,’” explains Dr. Stern. “They know they have to raise their hands and be called on before answering. But raising hands isn’t part of the explicit curriculum. Where do they learn it?”

Dr. Stern, now professor of medicine at NYU Langone and chief of the Medical Service at the Veterans Administration New York Harbor Healthcare System, learned that the answer lies in what educators call the “hidden” curriculum. In the case of medical school, the term refers to the many ways students learn the unspoken rules and culture of medicine, not through textbooks and formal lectures but through everyday exchanges in informal settings such as hallways and hospital cafeterias. It was an insight that inspired a long-standing fascination with how doctors learn.

Now, Dr. Stern’s journey is starting to change the way medical residents at NYU Langone learn and work, to the benefit

of patients. Part of his role at the Medical Center, in addition to his more traditional clinical and managerial responsibilities, is to introduce new routines for residents that subtly teach the hidden rules and culture of medicine. One of those new practices took hold this past summer during the monthly rotation in medical-resident assignments, when hundreds of NYU Langone patients were introduced to the incoming residents taking over their cases by the outgoing residents, who briefed their replacements on the nuances of their care.

Though most of the patients wouldn’t have known it, incoming residents nor-

tients,” says Dr. Stern. “Those are values that are hard to communicate in a classroom.”

The hidden curriculum that transmits these subtle lessons is usually informal and ad hoc, but it’s critical to medical education, insists Dr. Stern. “It’s how physicians learn professional values, like responsibility for patients, and respect and collaboration,” he says. “We add material about these values into medical school courses, but lectures are not really effective. Interns and residents learn values in hospital hallways and elevators and cafeterias, during rounds and during breaks. It happens in the ‘interstitial fluid’ of daily

“Interns and residents learn values in hospital hallways and elevators and cafeterias, during rounds and breaks,” says Dr. David Stern. “The lessons can be far more powerful than learning about values in the classroom.”

mally introduce themselves and pick up the case details guided only by a written summary from the previous resident. The “warm handoff,” highly unusual in medical centers, was a first for NYU Langone.

“It’s a change to the structure of the residency program, and it teaches important lessons to residents about teamwork and making a personal connection with pa-

work. And the lessons can be far more powerful than learning about values in the classroom.”

After his PhD, Dr. Stern, then on the faculty of the University of Michigan, set out to prove the importance of the hidden curriculum and pin down examples. He spent hundreds of hours shadowing interns and residents in hospitals in the 1990s, listen-



David Stern, MD, in his office at the Manhattan VA Medical Center

ing for informal teaching moments. He found that what doctors heard and saw on the job tended to override what they were told in classrooms and handbooks.

"You can tell medical students until you're blue in the face that they need to have 15 minutes of open-ended bedside conversation with each of their patients," says Dr. Stern. "But if they see the attending physician talking for only five minutes from the patient's doorway, that's probably what they'll end up doing, too."

The warm handoff is just one of the ways in which educators at NYU School of Medicine are working to change the environment to promote professional values. Another is a "geographic ward" program that assigns residents to specific wards.

"Residents used to live, eat, and sleep near the patients, doctors, and nurses in a single ward, until the practice was lost to the drive for efficiency," says Dr. Stern. "But staying with one ward means patients don't have to wait for nurses to hunt down the

on-call physician, reinforcing a sense of the urgency of patient needs, and it fosters interprofessional collaboration and respect."

Dr. Stern notes that the NYU Langone community has expressed only excitement for these new routines. "Everyone here is looking for an opportunity to be innovative and to nurture professional values that lead to even better safety, quality, and value," he says. "Now I'm looking for more ways to enhance the hidden curriculum. That would be a beautiful thing for patients and for medicine." ●

Pushing the Boundaries of Transplantation

Robert A. Montgomery, MD, DPhil, director of the new Transplant Institute, discusses pig organs, tissue rejection, and how to make organ donations less invasive. **BY GARY GOLDENBERG**



PHOTO: JOHN ABBOTT

ROBERT A. MONTGOMERY, MD, DPhil, one of the nation's foremost kidney transplant surgeons, joined NYU Langone in March as director of its new Transplant Institute. His charge is to broaden the Medical Center's existing expertise in transplantation and advance surgical approaches that address the needs of a growing and increasingly diverse patient population. Most recently, Dr. Montgomery professor of surgery, served as chief of the Division of Transplantation and director of the Comprehensive Transplant Center at Johns Hopkins Hospital. A relentless innovator, he has helped pioneer minimally invasive surgery to remove donor kidneys, novel techniques to reduce the risk of organ rejection, and "domino" kidney transplants, which involve multiple pairs of donors and recipients. In 2010, Dr. Montgomery led a 10-way domino transplant, earning a citation in the *Guinness Book of World Records* for the most kidney transplants performed in a day.

What brought you to NYU Langone?

I wrote a white paper about the future of transplantation and what it would take to realize that vision here at the Medical Center. When the leadership read my proposal, which called for a unification and expansion of the various transplant programs, they said, "Okay, let's do it." I was floored by the offer to lead this effort.

What is the value of unifying these different programs?

NYU Langone has some key strengths in transplantation, such as the liver transplant program—one of the first in the nation to implement a living-donor program—and the pioneering face transplant program. But to move to the next level, we must shift from traditional, siloed services to a single institute. By working together, we can reduce fragmentation and inefficiencies, manage costs, expand services, and collaborate on research and training.

Do you plan to perform any new types of transplants?

We plan to begin heart, lung, and pancreas

"If I have a talent, it's that when I see something, I can tell right away whether it's going to be important. That's what I felt when I saw my colleagues remove a diseased kidney laparoscopically."

transplants, as well as bone marrow transplants, which are increasingly being used alongside other tissue transplants to reduce rejection.

Each year, just 20 percent of patients on the transplant waiting list get a donor kidney. What can be done to improve the odds?

It's depressing. People are waiting on average four to six years, with a mortality rate around 30 percent. Deceased donations are flat, despite significant public outreach. One possible solution is xenotransplantation—transplanting organs from genetically modified animals. People are always saying it's just around the corner. But with transgenic pigs, it just might be.

Another factor driving the shortage is the need for retransplants, which account for one in five kidney transplants. Are there ways to reduce this percentage?

Retransplants occur for a number of reasons: clots, infection, recurrence of the disease that caused the patient's own kidney to fail, and most often, rejection of donor tissue. We are beginning to reduce rejection with "allogenic" cell and organ transplants, in which a related donor gives their bone marrow along with a kidney. Since the bone marrow determines the immune system, this reduces both rejection and the need for immunosuppression. This is critical for young transplant recipients,

who might need three or four transplants over a lifetime.

One of your innovations—desensitization therapy—has helped increase access to kidney transplants. Can you elaborate?

One of the big challenges was that up to 30 percent of patients were essentially untransplantable because they had become sensitized, that is, they developed antibodies to other people's tissues, usually because of a previous transplant, a pregnancy, or a blood transfusion. In 2001, we developed a treatment protocol in which we remove the problematic antibodies from the patient's blood prior to the transplantation. Our research shows it reduces the risk of rejection and doubles life expectancy, compared to those who remained on dialysis.

Do you ever feel conflicted about operating on perfectly healthy people who've chosen to donate an organ?

Kidney transplants actually started with donations between relatives in the 1950s, not with cadaver kidneys. Medical ethicists long ago agreed that it's ethical for an individual to undergo an operation that will only benefit someone else. Altruistic donations in which the donor does not even know the recipient are just an expansion of that concept. People can be connected in very powerful ways that

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don't involve blood ties. In a way, altruistic donation is purer. There's no possibility of family coercion.

What was your role in the development of laparoscopic live-kidney donation?

If I have a talent, it's that when I see something, I can tell right away whether it's going to be important. That's what I felt when I saw my colleagues remove a diseased kidney laparoscopically. My colleagues at Hopkins and I spent two years figuring out how to tweak the operation so we could remove and preserve a healthy kidney for transplantation. It has changed the calculation for donors. Many more people now donate because the operation is less traumatic.

And you pushed that idea even further with nephrectomies using vaginal extraction.

One of the drawbacks of laparoscopic nephrectomy is that while most of the work is done through three tiny incisions, at the very last moment, you have to make a larger incision to remove the kidney. My colleagues and I were always thinking, How can we do this better? One day at grand rounds, I overheard two residents debating a novel approach for removing an appendix or gallbladder through natural body openings. That gave me the idea of removing a kidney through the vagina. It was a eureka moment. We did the first case in 2009, requiring only a few tiny abdominal incisions. It went amazingly well. The next step is to eliminate those external incisions entirely. I think it's going to be increasingly common, as laparoscopic and robotics techniques get even more sophisticated.

What was your most difficult case?

A 43-year-old woman with end-stage renal disease and just about every imaginable complication that would

normally preclude a transplant: loss of vascular access for dialysis, chronic thrombosis, sepsis, and near-total sensitization. Without a transplant, there was no chance she was going to survive. We were able to identify a live donor at the end of a domino chain with a good tissue match. The option for a living donor transplant gave us the flexibility to control the timing of the operation and prepare her for transplant with a novel combination of treatments and medications. She survived.

Africa loomed large in your early life.

Could you describe those experiences?

When I was a little kid, I dreamed about traveling to Africa. My first actual visit came in college, when I did a health-related summer program in The Gambia with Operation Crossroads Africa—a model for the Peace Corps. I went back just before medical school under a Thomas J. Watson Fellowship, which allowed me to spend a year backpacking around Africa, studying the interface between Western and traditional medicine. Africa gets under your skin. I've been back many times since.

Did that experience affect you as a physician?

Yes, and it was reinforced in medical school at the University of Rochester, the vortex of psychosocial medicine, which takes into account the whole universe around the patient. That's also what appealed to me about transplant surgery. You care for patients who are very medically complex, and you follow them, in most cases, throughout their lives.

You've done more than 1,000 kidney transplants. Does it ever get routine?

Never. It's always magical when you let blood go into that organ and something so lifeless suddenly animates. I wax poetic every time I see that. ●

FACULTY NEWS



HELEN EGGER, MD

HELEN EGGER, MD, has been named chair of the Department of Child and Adolescent Psychiatry and director of the Child Study Center at NYU Langone's Hassenfeld Children's Hospital of New York. She joins NYU Langone in September from Duke University Medical Center, where she is currently chief of the Division of Child and Family Mental Health and Developmental Neuroscience. In addition to her study of anxiety disorders in children from birth to age five, Dr. Egger's current research focuses on developing innovative tools to gather and analyze information about a child's behaviors. Among these tools is a ResearchKit iPhone app that allows clinicians to screen young children for autism and other disorders.

Dr. Egger's appointment coincides with NYU Langone's rapid expansion of children's services as it prepares to open the Helen L. and Martin S. Kimmel Pavilion in 2018, several floors of which will be devoted to a state-of-the-art inpatient unit for Hassenfeld Children's Hospital. At Duke, Dr. Egger has also served as vice chair for integrated pediatric mental health in the Department of Psychiatry and Behavioral Sciences. She held secondary appointments in the Departments of Pediatrics, and Psychology and Neurosciences.

A cum laude graduate of Yale University School of Medicine, Dr. Egger completed an internship at Georgetown University Medical Center and a residency, as well as postdoctoral research, in child and adult psychiatry at Duke. ●



MARY PAT GALLAGHER, MD

MARY PAT GALLAGHER, MD, has been named director of the new Robert I. Grossman, MD, and Elisabeth J. Cohen, MD, Pediatric Diabetes Center at NYU Langone. Dr. Gallagher, assistant professor of pediatrics, previously served as codirector of the Pediatric Diabetes Program at the Naomi Berrie Diabetes Center at Columbia University Medical Center. After earning an MD from the University of Medicine and Dentistry of New Jersey, Dr. Gallagher was chief resident in pediatrics and then a fellow in pediatric endocrinology at Columbia University Medical Center. Her articles have been published in numerous peer-reviewed journals, including *Diabetes*, *The Journal of Pediatrics*, and *Pediatric Diabetes*.

As part of Hassenfeld Children's Hospital of New York at NYU Langone, the Pediatric Diabetes Center will provide com-

prehensive care and support for children and families living with diabetes, one of the most common chronic diseases seen in school-age children. Both type 1 and type 2 diabetes are on the rise among children and young adults in the U.S., according to the National Institutes of Health. Working closely with the Sala Institute for Child and Family Centered Care, the center will also provide comprehensive psychosocial support and wellness services.

Made possible by an anonymous \$10 million gift, the center is named in honor of Robert I. Grossman, MD, the Saul J. Farber Dean and CEO of NYU Langone, and his wife, Elisabeth J. Cohen, MD, professor of ophthalmology. "Elisabeth and I are enormously humbled by this extraordinary gesture of support for the work we do in pediatric medicine," says Dean Grossman. "The Department of Pediatrics has long been a galvanizing leader in the field, and this gift can only serve to strengthen its outstanding clinical, academic, and research programs." ●



ITAI YANAI, PHD

ITAI YANAI, PHD, has been named the inaugural director of NYU Langone's Institute for Computational Medicine, a hub for multidisciplinary research applying the tools of computational biology to modern medical challenges.

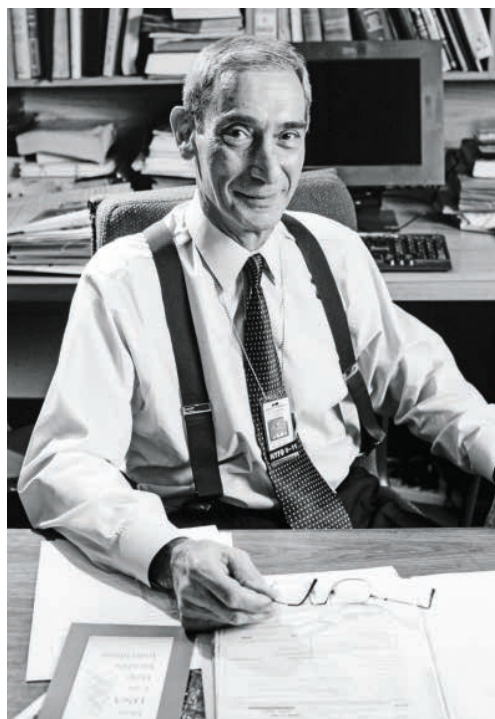
Dr. Yanai, professor of biochemistry and molecular pharmacology, comes from the Technion-Israel Institute of Technology, where he investigated the evolution of gene regulation in embryonic development. His research combines experimental approaches in embryology, molecular biology, and computational biology. At the Technion, his lab pioneered a popular method for analyzing gene expression in single cells, which his team is now using at the Medical Center

to study the progression of cancer and the process of infection.

Widely recognized for his contributions to science, Dr. Yanai was honored with a 2014 fellowship at the Radcliffe Institute for Advanced Study at Harvard University and the Krill Prize of the Wolf Foundation for excellence in scientific research. In 2002, he became the first person to earn a PhD in bioinformatics from Boston University.

Dr. Yanai is also the coauthor of *The Society of Genes*, a book about the evolution of genes, written in language accessible for a general audience with colleague Martin J. Lercher, PhD, a professor of bioinformatics at the Heinrich Heine Universität Düsseldorf in Germany. ●

Charles S. Hirsch, MD



AT THE 2013 retirement celebration for Charles S. Hirsch, MD, the longtime chief medical examiner of New York City and chair of the Department of Forensic Medicine at NYU School of Medicine, his colleague Barbara Butcher noted, “It has been my privilege in 22 years to get know him—just a little,” triggering a knowing chuckle that rippled across the room.

Charles Hirsch the private citizen and private man was a mystery to most, even his closest colleagues. Dr. Hirsch the physician, however, was a well-known quantity: an exemplary forensic pathologist, a tireless public health advocate, a visionary scientist, and an inspiring role model for countless medical students and medical examiners.

Dr. Hirsch died on April 8 in Westwood, NJ, from complications of several illnesses. He was 79.

Shortly after taking the helm of the Office of the Chief Medical Examiner (OCME) in 1989, Dr. Hirsch transformed a city agency known for its squalid facilities, bungled autopsies, and insensitive treatment of families into a model for forensic medicine specialists worldwide. He overhauled field investigations, replacing per diem physicians who had little expertise in forensics with specially trained physician assistants. He spearheaded the first studies of West Nile virus in North America. He guided the creation of a DNA laboratory within OCME, now regarded as the finest public facility of its kind.

Early in the AIDS epidemic, he started testing bodies for HIV, allowing the city to notify significant others that they may have been exposed to the virus and to recommend testing and counseling. “It’s a misconception that the medical examiner’s job is all about death and violence,” Dr. Hirsch once said. “What we do is more about public health. It’s about preventing death.”

Many in the field came to regard Dr. Hirsch as the father of modern forensic pathology. He was perhaps best known for his role in 9/11. Minutes after the first attack, he raced to the World Trade Center with six members of his staff to set up a temporary morgue. As the south tower collapsed, he reportedly used his own body to shield one of his coworkers from falling debris, and only after getting her to safety did he tend to his own injuries. He returned to work that same day, launching the monumental effort of cataloging and identifying the remains of the victims and working with the grieving families.

Dr. Hirsch treasured opportunities to

share his knowledge with the next generation of physicians, through fellowships in neuropathology and cardiovascular pathology at OCME (the first and only ones of their kind) and an elective in forensic medicine for medical students, one of the School’s most popular courses.

Today, his influence endures. One-fifth of the nation’s 500 board-certified medical examiners trained under his tutelage, including his successor at OCME and NYU Langone, Barbara Sampson, MD, PhD, clinical professor of forensic medicine and pathology. “He was the ultimate role model, showing me how to treat grieving families at the worst time of their lives and how to interact with colleagues, detectives, district attorneys, and politicians,” says Dr. Sampson. “Anytime somebody says to me, ‘That’s exactly what Dr. Hirsch would have said or done,’ it’s the biggest compliment, because then I know I’m doing it right.”

Jonathan Hayes, MD, a senior chief medical examiner at OCME once described Dr. Hirsch as “a perfect storm of competence. He combined tremendous experience with a broad knowledge of medicine, a keen analytical mind, zero tolerance for obfuscation, endless empathy, a strong sense of social responsibility, loyalty to his staff, political astuteness, and a killer sense of humor.”

Steven B. Abramson, MD, vice dean for education, faculty, and academic affairs, and chair of the Department of Medicine, notes that role modeling is the dominant influence that shapes the behavior of young physicians. “Dr. Hirsch,” he says, “was gracious and dignified, the kind of doctor you wanted to be.”

Dr. Hirsch was known to be gentle even with his harshest critics. “There’s a small group of people who have been dissatisfied with everything that we’ve done [related to 9/11],” he said a few years ago. “Those people have my sympathy, because that’s how they’re dealing with their grief. . . . I feel sorry for them and wish there were some way to bring them peace.”

Dr. Hirsch is survived by his daughter, Sophie Ghiraldini, and two grandsons. ●

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