

# NYUPHYSICIAN

THE MAGAZINE OF NEW YORK UNIVERSITY SCHOOL OF MEDICINE

WINTER 2013-2014  
VOLUME 65 • NO.

# 2



*distracted*  
inattentive impulsive forgetful disorganized  
*restless* unfocused frustrated *hyperactive* overwhelmed  
disorganized forgetful impulsive restless  
frustrated *fidgeting* daydreaming

## TACKLING THE BEHAVIORAL CHALLENGES OF ADHD

A PROGRAM OFFERS THE TOOLS TO HELP KIDS WITH ADHD  
SUCCEED IN SCHOOL AND BEYOND

PLUS IS ALZHEIMER'S IN YOUR FUTURE? • IMPROVING PATIENT HANDOFFS • BRITTLE BONE DISEASE

# Help Us Make Dreams Come True

**EVERY ASPIRING PHYSICIAN DREAMS OF THE DAY SOMEONE WILL CALL HIM OR HER "DOCTOR" FOR THE FIRST TIME.** But getting there takes a lot more than hard work and dedication—it takes resources. By contributing to the NYU School of Medicine Alumni Campaign, you help ensure that our next generation of physicians will have access to the best teaching and research, along with a competitive financial assistance package.

When you make a gift, you help us guarantee that all of our students will have the means to complete our rigorous education. One day, you may even have the privilege of addressing them yourself as "Doctor."

## **MAKE A GIFT ONLINE**

Please visit [www.nyu.edu/alumni](http://www.nyu.edu/alumni).

To discuss special giving opportunities, **call Anthony J. Grieco, MD, Associate Dean for Alumni Relations, at 212.263.5390.**



**Thank you for  
your generosity.**

# NYUPHYSICIAN

New York University

**Martin Lipton, Esq.**  
Chairman,  
Board of Trustees

**John Sexton**  
President

**Robert Berne**  
Executive Vice President  
for Health

NYU Langone  
Medical Center

**Kenneth G. Langone**  
Chairman,  
Board of Trustees

**Robert I. Grossman, MD**  
Dean and Chief  
Executive Officer

**Kathy Lewis**  
Senior Vice President  
Communications  
and Marketing

NYU PHYSICIAN

**Steven B. Abramson, MD**  
**Anthony J. Grieco, MD**  
Editors, Science  
and Medicine

**Marjorie Shaffer**  
Editor

**Nicole Dyer**  
Contributing Editor

**Sherry Zucker**  
Print Production  
Coordinator

**Segal Savad Design**  
Art Direction

**Nancy E. Sherman**  
Copy Editor

COVER DESIGN:  
SEGAL SAVAD DESIGN



## COVER STORIES

**06 Getting Organized**  
The Child Study Center at NYU Langone offers an innovative program to help kids with ADHD overcome one of the condition's most overlooked but debilitating symptoms: disorganization.  
**By Kenneth Miller**

**14 Between Doctors**  
When shifts end and doctors transfer the care of their patients to another doctor, miscommunication can result in serious medical errors. A broad initiative at NYU Langone is dedicated to reducing that risk. **By Nicole Dyer**

**20 Is Alzheimer's in Your Future?**  
A radical rethinking of research ethics is occurring among Alzheimer's disease researchers. Many now believe that subjects should be told the results of studies evaluating biomarkers for the brain-robbing disease. **By Adam Piore**

**"Organizational skills training clearly worked for a large proportion of kids with ADHD."**

## DEPARTMENTS

**02 Message from the Dean**  
Our Greatest Treasure is Our Children

**03 News from Medicine**

- A Common Biochemical Thread Found in Cellular Debris
- A Combined HIV/Cocaine Vaccine?
- A Potential New Weapon Against a Deadly Cancer

**26 Faculty Conversation**  
Q & A with Dr. David Oshinsky  
A Humanistic Approach to Medicine

**28 Faculty News**

- Honoring Three Masters and One Major Benefactor on Dean's Honors Day
- A Renowned Surgeon Who Made Medical History Joins NYU Langone

**30 Medical Education**

- A range of dual-degree programs expose students to fields that intersect with medicine.
- Students survey health needs in a remote area of northern India.

**32 Student Profile**  
Curiosity and a keen interest in science lead to a prestigious student fellowship.

**34 Patient Story**  
Even bones as fragile as matchsticks couldn't stop Jessica Bernstein from standing on her own two feet.

**36 End Page**  
For Dr. Bradley Adams and his team of forensic anthropologists, there's only one question: Who are you?

# Our Greatest Treasure is Our Children

*AS ANY PARENT KNOWS, CHILDREN LIGHT UP OUR DAYS.*

Despite all the trials and tribulations of child rearing, it is one of life's most gratifying and fulfilling jobs.



There is a never-ending sense of wonder watching a child mature into adolescence and adulthood. When this process is interrupted, it is heartbreaking. This issue of *NYU Physician* magazine features the remarkable work of clinical researchers at the Child Study Center at NYU Langone, who treat one of the most common neurobehavioral disorders of childhood, ADHD. Over the past two decades, they have defined one of the most stubborn and debilitating symptoms of the condition and developed real tools to manage it, allowing children to progress in school and in their family life. The story also reveals how a summer camp offered by the Child Study Center reinforces these hard-won skills. Perhaps there is nothing more heartening than a happier and calmer child, as one parent says of her camper.

This pioneering work is emblematic of our dedication to children at NYU Langone Medical Center. We offer a full range of pediatric healthcare services, and last fall, our capabilities multiplied with an anonymous donor's \$40 million gift to establish the Institute for Family-Centered Care, which will greatly expand supportive services for children and their families. The Institute will also advance research and develop innovative education programs designed for families and staff.

Our future has never been brighter.

A handwritten signature in black ink that reads "Bob". The signature is written in a cursive, slightly slanted style.

DEAN & CEO ROBERT I. GROSSMAN, MD

# A Common Biochemical Thread Found in Cellular Debris

Researcher finds new mechanism linking chronic inflammation in Alzheimer's, vascular disease, and diabetes.

We owe our lives to the constant vigilance of the immune system. Yet this same army of cells, while orchestrating an elaborate cascade of chemicals to fight off infection, can also precipitate our decline. Kathryn Moore, PhD, professor of medicine and cell biology in the Leon H. Charney Division of Cardiology, and a senior investigator in the Marc and Ruti Bell Program in Vascular Biology at NYU Langone Medical Center, seeks a sharper understanding of what goes wrong at the cellular level when the immune system misbehaves. Her recent study in *Nature Immunology* describes a surprising cellular mechanism underlying chronic inflammation, a condition in which immune reactions refuse to quit, sustaining a persistent, painful attack on healthy tissues throughout the body.

In recent years, an onslaught of research has linked chronic inflammation to a host of debilitating diseases from cancer to autism. Dr. Moore's research focuses on three of the biggest offenders: atherosclerosis, type 2 diabetes, and Alzheimer's disease. Together these conditions affect more than 100 million Americans.

Once considered disparate, the trio is increasingly thought to have a common

biochemical thread—namely, chronic inflammation. Each disease litters the body with particulate matter. Vascular disease dumps cholesterol crystals into plaques in the blood vessels; Alzheimer's deposits clumps of protein in the brain; and type 2 diabetes is often associated with a glut of dead fat cells. In each case, the cellular debris—cholesterol plaques, protein clumps, and dead fat cells—appears to set off an immune reaction.

Dr. Moore's latest research offers an entirely new explanation for how this biochemical chain reaction works. Previously, scientists believed that scavenger cells called macrophages would attack disease debris just as they would a virus or bacterium, a process referred to as a *sterile* inflammatory response, because it happens in the absence of pathogens. But Dr. Moore's team has found that macrophages, far from helping the situation, can actually make it worse. "The debris damages the macrophages," Dr. Moore says. "And it's this damage that triggers the immune reaction."

The NYU Langone research shows that a receptor called CD36, present on macrophages, binds to debris and draws it inside the cell. Along the way soluble debris is transformed into *insoluble*

particles that never break down and accumulate in cells. "The insoluble crystals and proteins then trigger a powerful cytokine, called interleukin-1B, that causes fever and inflammation," explains Dr. Moore. When the researchers blocked the CD36 receptor in mice whose arteries were clogged with cholesterol, the interleukin-1B response declined, fewer cholesterol crystals formed in plaques, and inflammation decreased. Consequently, the mice had healthier blood vessels. This finding could translate to better ways to treat chronic inflammation in the future.

Another strategy for quelling chronic inflammation is to



block interleukin-1B. "But this approach has a major downside," Dr. Moore notes. "Blocking interleukin-1B also blocks the body's ability to respond to microbes." Targeting CD36, by contrast, stops inflammation at the source, preventing the dangerous transformation of debris while preserving the cytokine response. "It's a whole new way of thinking about chronic inflammation." ● —NICOLE DYER

▼ Inflammation is a hallmark of atherosclerosis, the buildup of plaque inside arteries. The fluorescent photomicrograph below shows the accumulation of immune cells called macrophages (red) in the plaque.

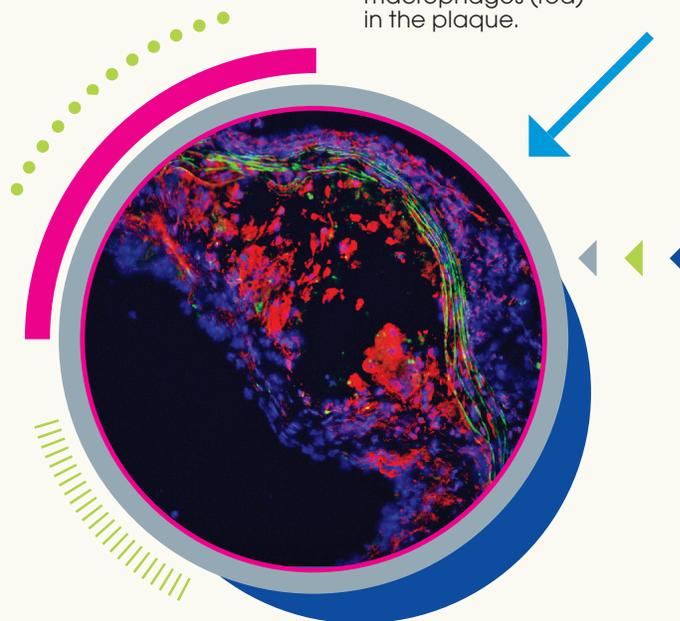


PHOTO COURTESY DR. KATHRYN MOORE'S LABORATORY

# A Combined HIV/Cocaine Vaccine?

An unconventional idea wins a prestigious award.

Last year, Timothy J. Cardozo, PhD, associate professor of biochemistry and molecular pharmacology, was designing an HIV vaccine when he noticed that it shared a key feature with another group's experimental cocaine vaccine—a carrier protein from the cholera toxin.

In very small doses, the cholera toxin's B subunit boosts immune activity, particularly in mucosal areas

of the body, which are the most prone to be initially exposed to HIV. Cholera toxin B was being used in an experimental cocaine vaccine intended to elicit immune responses to block the drug from reaching the brain and causing an addiction-reinforcing high. The decoy molecule that mimics the drug is too small by itself to provoke an immune reaction, so it has to be piggybacked onto the large cholera protein.

Dr. Cardozo's HIV vaccine, initially developed as part of a large project led by Susan Zolla-Pazner, PhD, professor of pathology, uses the cholera protein to carry small molecular additions that mimic

parts of a protein called gp120 that studs the surface of HIV. The protein is thought to be relatively vulnerable to a human antibody response, even across multiple strains of the virus.

Dr. Cardozo thought: Why not fasten onto the cholera protein toxin the molecules that mimic cocaine and produce a simple combination vaccine against HIV and cocaine? "It occurred to me that in certain populations where cocaine abuse and HIV infection are rampant and interrelated, immunization against both could have a synergistic effect," he says.

In October 2012 Dr. Cardozo applied for an Avant-Garde Award from the National Institute on Drug Abuse (NIDA) for his planned combination vaccine. The prestigious award is intended to encourage groundbreaking research that has the potential to transform the treatment of HIV among people who suffer from drug addiction. In December Dr. Cardozo learned that he was being considered as a finalist. There was just one catch: The award reviewers noted that he had no experience making antidrug vaccines. "They were a little concerned that I didn't have that background, so I looked around for potential collaborators who did," he says.

Dr. Cardozo soon found two highly experienced partners without even having to venture outside NYU Langone: John Rotrosen, MD, professor of psychiatry, and Kenneth D. Carr, PhD, professor of psychiatry, and biochemistry and molecular

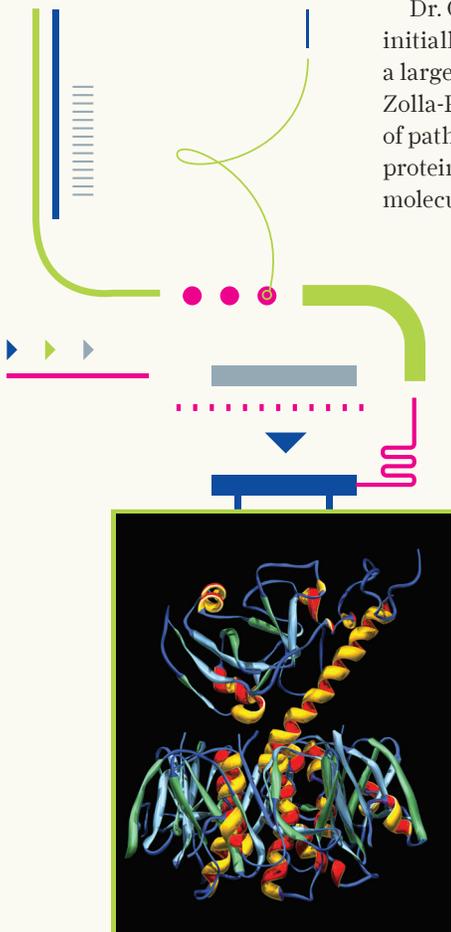
pharmacology. Coincidentally, Dr. Rotrosen had been a local investigator for a NIDA-sponsored clinical trial of the same cocaine vaccine that had inspired Dr. Cardozo's combination-vaccine idea.

The new collaboration impressed NIDA, which, in August, bestowed upon Dr. Cardozo the Avant-Garde Award, one of only three given in 2013. The \$2.5 million grant will fund early development of Dr. Cardozo's proposed HIV/cocaine vaccine.

"It was nice to be able to find this much expertise and knowledge here at NYU Langone, and I suspect that the involvement of Drs. Rotrosen and Carr was a key to our getting the award," he says.

Dr. Cardozo hopes to be able to test at least one experimental combination vaccine in an initial small-scale safety trial by the end of the five-year Avant-Garde funding period. So far, HIV and cocaine vaccines have each shown only moderate levels of protection in clinical trials, and he will try to boost those protection levels. "But even with marginal individual effectiveness, they could still make a major impact as a combination in those communities where rates of cocaine abuse and HIV infection are high," he says. ●

—JIM SCHNABEL



▼ This molecular model of the cholera toxin shows its two subunits, A (top) and B (bottom). Small doses of the B subunit boost immune activity.

DR. MARK J. WINTER / SCIENCE SOURCE

# A Potential New Weapon Against a Deadly Cancer

In laboratory research, a compound thwarts the relapse of prostate cancer.

The propensity of prostate cancer eventually to override standard drug therapies makes it particularly deadly. Last year the cancer killed some 29,720 men in the United States, making it the second leading cause of cancer death among men. Now, a new study by Susan Logan, PhD, associate professor of urology and pharmacology, and Ramanuj DasGupta, PhD, associate professor of biochemistry and molecular pharmacology, raises hope for an agent that can block one of the key pathways prostate cancer cells use to thwart drug therapies.

In the early stages of prostate cancer, the main driver of growth is a cellular-communication pathway controlled by the androgen receptor (AR). Prostate cells are studded with ARs, which are stimulated by testosterone and related hormones. "Prostate cells generally need the continuous stimulation of their ARs for their survival," says Dr. Logan.

A variety of drugs—called castration therapy—interfere with AR signaling in a prostate tumor, but after awhile the tumor often develops alternative strategies to activate the AR pathway and/or seeks out other pathways and begins to grow again. "At that point, there aren't many good options for patients," Dr. Logan says. "The drugs that we have now for castration-

resistant prostate cancer prolong life for only a few months on average compared to first-line therapies."

Several years ago Dr. DasGupta discovered an intriguing compound that blocked a communications pathway different from AR that is active in cancer cells, particularly those that have developed resistance to primary therapies. He subsequently found that this pathway relies on a growth-promoting protein called beta-catenin to function.

Pharmaceutical companies have been trying to develop beta-catenin blocking agents, but the protein is a difficult target because it also has beneficial effects on cells. Dr. DasGupta's compound, C3, inhibits beta-catenin's growth-driving activity but leaves its beneficial functions intact. He and his colleagues reported in 2011 that C3 and closely related compounds do a good job of killing colon cancer cells, for example, yet spare healthy cells.

"After that, we wanted to test these compounds against as many cancers as possible, to get a sense of where they could be most useful," Dr. DasGupta says. He soon sought out Dr. Logan, since the beta-catenin pathway had been widely suspected as a key factor in the relapse of prostate cancer and was known to share common elements and a mutually reinforcing cross talk

with the AR pathway.

In their new study, published in the *Proceedings of the National Academy of Sciences*, Drs. Logan and DasGupta tested C3. Applied for only a few days in modest doses, the compound stopped the growth of prostate cancer cells—or even killed them—in lab dishes and mice. This happened even when the compound was applied to cancer cells that didn't respond to AR-blocking therapies. At the same time, it appeared to have only modest effects on healthy cells.

"This is still in the proof-of-concept phase," Dr. Logan cautions. "But we're now

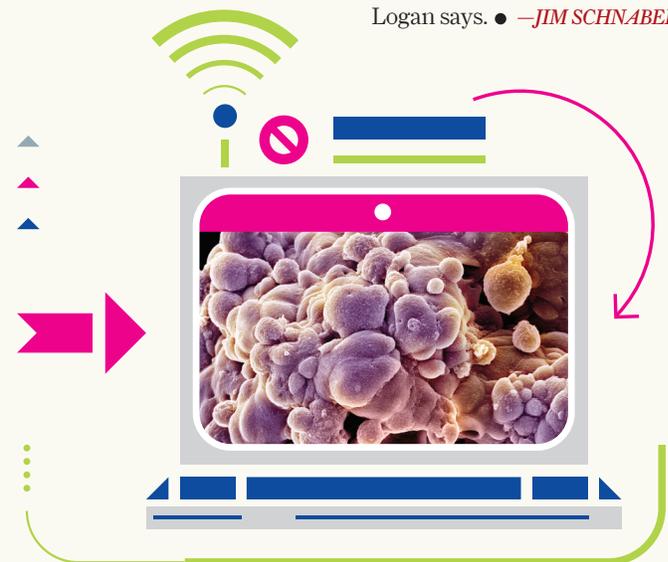
convinced that this is a very valuable approach."

Moreover, their experiments showed that C3 could shut down both the AR and beta-catenin pathways. Just as important, the compound worked well against stem-cell-like prostate tumor cells, believed by many to form a naturally drug-resistant reserve that can seed tumor relapse. "A standard AR antagonist drug did little against this cancer stem cell model, but C3 had a dramatic effect," says Dr. DasGupta, who plans to continue the preclinical development of such compounds and says more powerful ones than C3 already exist.

"A lot of us in the field hope that eventually we'll be able to use a cocktail of drug compounds like this one to manage prostate cancer," Dr. Logan says. ● —JIM SCHNABEL



▼ A colored scanning electron micrograph of prostate cancer cells.







# GETTING ORGANIZED

The Child Study Center at NYU  
Langone offers an innovative program  
to help kids with ADHD overcome one  
of the condition's most overlooked but  
debilitating symptoms: disorganization.

**BY KENNETH MILLER • ILLUSTRATIONS BY JON KRAUSE**



# ON A MONDAY AFTERNOON

in NYU Langone's Child Study Center, the chatter of children's voices fills the waiting room—a bright, airy space with a vibrant mural of a Manhattan streetscape covering one wall. As their parents look on, kids dash across the carpet, twirl in circles, or explore the toy kitchen set up in a corner. They're all here for appointments with the Center's specialists, who treat children for psychiatric troubles ranging from anxiety and eating disorders to autism and schizophrenia.

Perched on a purple chair shaped like an M&M, 9-year-old Willy Lambert (not his real name) quietly browses through a picture book. A slight boy with a Beatlesque mop of dark hair, Willy has been diagnosed with attention deficit hyperactivity disorder, which affects an individual's ability to sit still, inhibit impulsive behavior, and focus on tasks. To look at him, you might not guess that anything was amiss. His symptoms fall toward the inattentive rather than the hyperactive end of the spectrum; they can be hard for a casual observer to detect. And at the moment, a prescription stimulant helps keep him from being too distracted to read amid the hubbub.

Yet like many kids with ADHD, Willy has been struggling with a problem that pharmaceuticals often can't fix: a serious deficit in what mental-health experts call OTMP skills. The acronym stands for organization, time management, and planning—tasks whose mastery can be crucial to success in school and beyond. Even on medications like Adderall or Concerta, children with ADHD may struggle to show up for class on time. They tend to lose track of assignment deadlines and forget to bring home textbooks. When they finish a project, they may neglect to turn it in. Or they may lose it—along with jackets, keys, and cell phones. “If you look in their backpack, you'll find apple cores, misplaced permission slips, overdue homework,” says behavioral psychologist and clinical research scientist Howard Abikoff, PhD, the Pevaroff Cohn professor of child and adolescent psychiatry, and director of the Institute for Attention Deficit Hyperactivity and Behavior Disorders. “It's bedlam in there.”

That certainly was the case with Willy. “He's smart, gentle, and cheerful, but he was very scattered,” says his mother, Karen. And no matter how many lectures his parents gave him—no matter how many rewards they promised, punishments they threatened, or pills they fed him—he remained as disorganized as ever.

Then Karen and her husband discovered the Child Study Center's new Organizational Skills Training (OST) program.

Open to third, fourth, and fifth graders with ADHD-related organizational problems, the program uses an intensive system of skills building—based on more than a decade of research—to help these children develop productive habits. OST offers fresh hope to kids like Willy. And by studying the program's impact on the brain circuitry of young participants, a team of NYU scientists aims to uncover some of the deepest neurological secrets of ADHD itself.

**The survey revealed that about 50 percent of kids diagnosed with ADHD had organizational problems severe enough to impair their school performance.**

The most common neurobehavioral disorder of childhood, ADHD is sometimes apparent in preschool but is more often diagnosed later. Although estimates of its prevalence vary widely, the disorder is generally thought to affect between 5 percent and 7 percent of children, according to a review of studies published last year in the journal *Neurotherapeutics*. A recent epidemiological survey by the Centers for Disease Control and Prevention put the number even higher, at 11 percent. Among those diagnosed, boys outnumber girls by about three to one. An estimated 30 percent to 50 percent of kids with ADHD continue to have symptoms into adulthood.

As with many ailments of the mind, ADHD's nomenclature and definition have evolved over the years. In the current edition of the *Diagnostic and Statistical Manual of Mental Disorders*, the condition is divided into three subtypes, depending on which symptoms predominate. Patients classified as “predominantly hyperactive” (about 15 percent of ADHD

cases) squirm and fidget, talk too much, interrupt others, and have trouble controlling their impulses. Those labeled “predominantly inattentive” (20 percent to 30 percent of cases) have difficulty concentrating on anything that doesn’t strongly interest them; they’re easily distracted, get lost in daydreams, and often forget to finish what they start. The “combined presentation” subtype, in which both kinds of symptoms are evident, accounts for 50 percent to 75 percent of cases.

One thing all the subtypes share is a tendency toward organizational deficits. Dr. Abikoff first glimpsed this in the early 1970s, when he began his career as a psychologist and clinical researcher at Long Island Jewish Medical Center. Over the next 20 years, while treating hundreds of children with ADHD (once crudely classified as a form of mild brain damage) and observing them in classrooms, he came to realize that organizational difficulties were often their most stubborn and debilitating symptoms. “Yet there was almost no research on this aspect of the disorder,” he recalls. “We didn’t have measures to assess the problem, let alone treat it.” By 1996, when he moved to NYU as a founding staff member of the Child Study Center, he was determined to rectify the situation.

**T**he first step was to develop a way to assess children’s organizational skills. In 1999 Dr. Abikoff teamed up with Richard Gallagher, PhD, associate professor of child and adolescent psychiatry and director of special projects at the Institute for Attention Deficit Hyperactivity and Behavior Disorders. They designed a questionnaire they called the Children’s Organizational Skills Scale (COSS), to be filled out by parents, teachers, and kids. Gathering data on about 1,000 children in the New York metropolitan area, the pair were able to determine what scores were typical of boys and girls at various ages in skills such as tracking assignments, planning work schedules, and managing school materials. (The sample eventually expanded to 5,000 children, and the COSS is now used by researchers and clinicians nationwide.) The survey revealed that about 50 percent of kids diagnosed with ADHD



From left: Dr. Abikoff and Dr. Gallagher in The Child Study Center

had organizational problems severe enough to impair their school performance, more than twice the proportion of those without ADHD who had such problems.

To doctors, those results indicated that many children with ADHD were unable to learn basic life skills the way others could—by simply observing their elders and getting occasional instructions on topics such as how to arrange a three-ring binder. So in 2002, with funding from the National Institutes of Mental Health (NIMH), they designed a pilot program that would teach such skills by breaking them down into simple tasks to be learned step by step. Anecdotal evidence suggested that such methods (known to behavioral scientists as “task analysis”) could be useful in alleviating organizational deficits, but their efficacy had never been systematically tested.

The researchers enrolled 20 third- through fifth-grade students with ADHD-related organizational problems for 20 hour-long sessions. To help the lessons stick, the training took place twice a week. Parents attended part of each session, learning how to reinforce their kids’ new skills at home. After completing the program, Dr. Gallagher recalls, “most of the children showed significant improvement. Teachers reported that they were more productive in school. They had fewer problems with homework and fewer family conflicts over organizational issues.”

To prove that their method was scientifically valid, however, the team had to perform a large-scale, controlled study. That



**“If you look in their backpack, you’ll find apple cores, misplaced permission slips, overdue homework.”**



government-funded effort began in 2006, using 180 third through fifth graders with ADHD and elevated COSS scores. The kids, who attended sessions at the Child Study Center and Duke University, were divided into groups: one that received organization skills training; another that was treated with a technique known as contingency management, in which children are rewarded for achieving a desired organizational goal (without being instructed how to achieve it); and a third, the control group, which received no treatment or training.

Requiring elaborate preparation, extensive follow-up, and intricate data analysis, the study took nearly five years to complete. The results were striking: About 60 percent of children in the organizational skills training group

improved their COSS scores so significantly that they no longer qualified as organizationally impaired; their academic and homework performance rose as well. Sixty percent of kids in the contingency-management group scored similar gains on the COSS scale—suggesting that for some kids with ADHD, organizational problems reflected not a skills deficit but some other impediment (one that seemed at least partially correctible by behavior-modification methods). This group’s organizational improvement at home, however, was somewhat less. Just 3 percent of children in the control group, by contrast, showed significant improvement.

“The data were extremely encouraging,” Dr. Abikoff says. “Organizational skills training clearly worked for a large proportion of kids with ADHD.” Applying what they’d learned in their investigations, he and Dr. Gallagher launched the Organizational Skills Training program at the Child Study Center in 2012.

**S**o far, about two dozen children have completed the program (which is available at the Center’s clinical locations in Hackensack, New Jersey, and Lake Success, Long Island, as well as its headquarters at One Park Avenue, in Manhattan). Willy comes every Monday and Friday after school, making the trip from Brooklyn with one or both of his parents.

Today, in a colorfully decorated treatment room, he’s working on time management—specifically, learning to estimate how long a given task will take. Willy’s therapist-

trainer, Lauren Knickerbocker, PhD, a clinical psychology postdoctoral fellow and clinical instructor of child and adolescent psychology, asks him to think about how he would break down one of his chores at home—washing the dog. He ticks off the steps, though not in the right order: “Get shampoo. Put water in the bath. Drain the water. Put the soap on her, and then wash the soap off.” He corrects himself. “*Then* drain the water. Dry her with a towel.”

“Those are good steps,” Dr. Knickerbocker says. “You thought of them quickly.” She asks him how much time he thinks each step will take and adds up his guesses: 34 minutes and 10 seconds. “So if you know that’s how long it takes, is this something you would do before you leave the house in the morning for school?” He nods his head. “Really?” she asks. He quickly corrects himself.

The OST program uses similar techniques to teach skills ranging from filling out a planner to remembering to turn in homework. But for children with ADHD, who are often literally incapable of focusing on tasks they find boring, simply explaining and exhorting aren’t enough. For extra motivation, students receive points for practicing the skills during the sessions and for using the skills appropriately at school and at home; these credits can be exchanged for favorite activities, like watching videos, having a sleepover, or (in Willy’s case) going on a special outing with Dad. The kids also get prizes—rubber balls, Lego sets, silly erasers—the first few times they accomplish a challenging task.

Another way of engaging children’s interest is to enlist them in battle against a mythic enemy. To this end, Dr. Gallagher invented the Glitches, a set of mischievous creatures (drawn to look like videogame gremlins) that tempt people to behave in disorganized ways. There’s the Time Bandit Glitch, who distracts kids from finishing their work so he can steal their free time; the Go Ahead and Forget Glitch, who tells kids not to write down assignments; the Go Ahead and Lose It Glitch, who urges them not to bother remembering where they put things. Besides providing an element of playful combat, Dr. Knickerbocker explains, the Glitches help students face their problems without feeling ashamed. “I’ll say, ‘Oh, I left my papers on the printer, a Glitch got me.’ We let them know that everybody has these problems and that they can be defeated.”

The program relies on less fanciful measures to help children apply what they learn in OST sessions to real-life



## GROWING UP WITH ADHD

A 40-year study follows untreated children into adulthood.



The importance of adequately treating ADHD in young people was underscored by a four-decade study, the longest of its kind, published in the *Archives of General Psychiatry* in 2012. Researchers led by Rachel Klein, PhD—now the Fascitelli Family Professor of Child and Adolescent Psychiatry at NYU School of Medicine and director of the Anita Saltz Institute for Anxiety and Mood Disorders—followed a group of 135 white, middle-class males with combined-type ADHD from childhood into adulthood. The children were free of conduct problems, such as aggression, taunting, lying, and having general disregard for rules. None of the subjects were on stimulant medication after age 13, due to a belief (since discredited) that adolescents would become addicted to such drugs. In fact, few received any kind of ongoing therapy for the disorder.

The study began in 1970, when the subjects’ mean age was 8, and the researchers checked on them in late adolescence and adulthood. Conduct problems began cropping up when the boys were in their teens. By 2011, when they had reached an average age of 41, they showed significantly worse educational, occupational, economic, and social outcomes, compared to 136 controls without ADHD who came from similar backgrounds.

Only 16 percent finished college, versus 35 percent of the controls. The ADHD group earned far lower incomes: a median of \$52,000, compared to \$96,000 for the controls. A third of the men with ADHD were divorced, versus a tenth of the controls. Almost three times as many (14 percent versus 5 percent) had a substance-abuse disorder. Fully three times as many (36 percent versus 12 percent) had been incarcerated.

Surprisingly, the disorder was diagnosed in adulthood in only 22 percent of the ADHD group. Nonetheless, many continued to suffer the consequences of poor choices they had made years earlier. “Their disadvantages originated in adolescence,” Dr. Klein says. “Ordinary teenagers engage in impulsive behaviors, but these kids did so even more, and with greater variety and severity. Some were jailed multiple times and a substantial proportion continued as adults to engage in antisocial behavior. This pattern of chronic antisocial maladjustment was unique to the ADHD group. They couldn’t follow the rules even if they wanted to.”

situations. Therapist-trainers maintain regular contact with each child's teacher, who signs off on the child's daily planner. They provide accordion files for organizing homework, and checklist cards that can be pinned to a student's backpack zipper. Perhaps most important, they teach parents to break down children's tasks at home (and dole out points and rewards), using the same methods employed in the treatment room.

For Willy, who's just halfway through his 20 sessions, the effects are already visible. "He's concentrating, focusing, and organizing much better," says his father, Tom. "He got 100s on his spelling and science tests last week. He's even remembering to hang his coat by the front door."

"There's a huge difference," Willy's mother affirms.

It may be surprising, then, to hear Dr. Abikoff's verdict on OST: "It works for a lot of kids, but it's not a panacea." He points to the clinical trials he and Dr. Gallagher oversaw, in which 60 percent of children who received organizational skills training showed clinically significant improvement; that means 40 percent didn't. What's more, he observes, the results were almost equally robust—though also far from perfect—in the group that was treated using contingency management, a behavior-modification method with no skills training. Some kids with ADHD respond better to the first method, others to the second, and still others to neither. The question is, why?

Dr. Abikoff hypothesizes that differences in neural circuitry among ADHD sufferers may be partly responsible. If a child's brain is wired one way, she may have trouble learning organizational skills without intensive training; if it's wired another way, she may be able to learn such skills easily but have trouble putting them to use without behavioral therapy. The only way to know for sure, however, would be to peer inside the children's skulls.

That's what another group of researchers at the Child Study Center is attempting to do. Led by F. Xavier Castellanos, MD, the Brooke and Daniel Neidich Professor of Child and Adolescent Psychiatry and director of the Center for Neurodevelopmental Disorders, the team recently began using fMRI (functional magnetic resonance imaging) to record patterns of brain activity in 30 children with ADHD-related organizational problems before and after going through the Organizational Skills Training program. "We're looking for changes that would let us determine how the

## Learning how ADHD treatments affect brain circuitry is another important piece of the puzzle.

training affects brain circuitry," Dr. Castellanos explains. "That would give us clues as to what is producing the behavioral changes when OST is successful."

Over the past two decades, Dr. Castellanos has helped assemble an increasingly detailed picture of how the brains of children with ADHD differ from those of their unaffected peers. In 1996 he directed a brain-imaging research team at NIMH that showed the right prefrontal cortex (a brain region involved in executive functions like attention, motivation, and concentration) was smaller in kids with ADHD than in kids without it. He later found that part of the cerebellum was undersize as well. In 2002, after moving to NYU, he led a study showing that such structural differences were not caused by ADHD medications, as some experts had suspected. And his more recent research shows the differences mirror deeper neurochemical abnormalities—particularly in the mechanisms that let brain regions talk to each other. Dr. Castellanos and his colleagues, including Adriana Di Martino, MD, the Leon Levy Research Assistant Professor of Child and Adolescent Psychiatry, and Michael Milham, MD, PhD, a research psychiatrist at the Nathan Kline Institute, have uncovered evidence of faulty synchronization among areas such as the cerebellum, striatum, and prefrontal cortex in children with ADHD.

Learning how ADHD treatments affect brain circuitry—and how those effects differ in young people with different forms of the disorder—is another important piece of the puzzle. "Eventually, we hope to be able to identify which kids will respond best to which treatment," Dr. Abikoff says. "The work we're doing now is a first step toward that goal. We're searching for signals." ●



## A SUMMER CAMP'S REWARDS

Where children with ADHD learn to tackle behavioral challenges and have fun at the same time.



**ON A HOT AUGUST MORNING,** a dozen first and second graders sit on a spot of shady lawn as their counselor quizzes them on subjects they're learning in summer camp—topics that have nothing to do with archery or tying lanyards. "What's our social skill of the day?" she calls out. When a boy named Liam answers "listening," she awards him 10 points for paying attention. "And what's our coping skill of the day?" A camper named Sean pipes up: "Walking away when someone's bothering us." As the group applauds, the counselor awards him another 10 points—this time, for contributing to the conversation.

The Summer Program for Kids (SPK), a day camp offered by the Child Study Center at NYU Langone, is designed to help children with ADHD tackle the behavioral challenges that often accompany the disorder. The seven-week program—the only one of its kind in the New York metropolitan area—uses clinically tested behavior-modification techniques to improve kids' skills in areas including social interaction, rule following, problem solving, and frustration tolerance. Based at the College of New Rochelle, in New Rochelle, New York, the SPK accepts up to 55 campers, aged 7 to 11, each summer; while most are from the tristate area, others come from around the country and the world.

"ADHD is a disorder of self-regulation," says director Karen Fleiss, PsyD, assistant professor of child and adolescent psychiatry at NYU Langone. "In the classroom, these kids often talk out of turn. In social situations, they'll get too close or too excited. Other kids may reject them, which affects their confidence and self-esteem. Our goal is to work to change all that."

Along with the usual summer-camp menu of swimming, sports,

and art, the SPK provides an intensive regimen of academic reinforcement and skills instruction to help develop competence in the classroom. The 30 counselors (overseen by two clinical supervisors) are recruited from colleges and grad schools, and undergo three weeks of intensive training to prepare for the rigorously structured program. Throughout the day, they give kids constant feedback—accompanied by the awarding or deducting of points on their performance in everything from eye contact to waiting one's turn. An individualized daily report card targets specific behaviors for each child, and is reinforced with home-based rewards. Each child's progress in these areas earns them privileges such as field trips and video game sessions. An eight-week parent-training program is an integral part, providing support and behavior management strategies.

Founded in 1997, the SPK grew out of a study by the National Institutes of Mental Health, which showed that children with ADHD who took medication and went through an intensive behavioral program—including an eight-week summer camp—needed lower doses to control their symptoms than kids who took meds alone. The program's success can be gauged in part by the 40 percent to 45 percent of campers who sign up for two or three consecutive summers. "Parents tell us their kids are happier, calmer," Dr. Fleiss reports. "They say, 'I've got my child back.'"

The kids tend to agree. "I used to get super-frustrated very easily," says Antonio, a dark-eyed 8-year-old who's here for his second season. "Now it takes more for me to get upset. When someone annoys me, I take a deep breath and ignore them. I've learned a lot of good things at this camp."



# BETWEEN DOCTORS

When shifts end and doctors transfer the care of their patients to another doctor, miscommunication can result in serious medical errors. A broad initiative at NYU Langone Medical Center is dedicated to reducing that risk by overhauling the way patient handoffs are taught and performed.

BY NICOLE DYER • ILLUSTRATIONS BY PHIL WRIGGLESWORTH

---



In 1991, a commuter plane crashed in a cornfield in Texas, killing 14 people. The cause: a simple miscommunication during a shift change. In 1998, the same problem led to the explosion of an offshore oil platform in the North Sea. The death toll was 167.

Staff handovers have long been a major source of catastrophic errors and accidents. Many high-risk industries have learned this difficult truth the hard way and adapted. Today, if your job is to keep airplanes from colliding or oil pumping from the ocean floor, the process by which you convey information to the oncoming staff is subject to strict protocols.

One might expect the same kind of scenario in medicine. Patients are rarely more vulnerable than when their doctor ends a shift and transfers their care to another doctor. Yet the process of handoffs, so critical to patient care, has never been formally taught in medical schools.

“Traditionally, physicians-in-training learn how to do patient handoffs by example, using an apprentice model, with varying degrees of standardization,” says Laura Evans, MD, associate professor of medicine at NYU School of Medicine and medical director of critical care at the Bellevue Hospital Center. “While some people might do it very well and methodically, other people might be more ad hoc.”

Such inconsistency has proved dangerous. Fumbled handoffs, like a perilous game of telephone, lead to surgical mistakes, medication errors, delays or repetition of tests, and in extreme cases, even death. According to The Joint Commission, the nation’s leading hospital accreditation board, an estimated 80 percent of serious medical errors result from miscommunication during handoffs.

With the number of handoffs predicted to increase as physicians work shorter and more frequent shifts, Dr. Evans and her colleagues at NYU School of Medicine are part of a growing national effort among physicians, institutions, and accrediting bodies to overhaul the ways trainees learn how to communicate during sign-outs. After adding “transition of care” to its national Patient Safety Goals in 2006, The Joint Commission now requires hospitals to create a standardized process for patient handoffs. The Accreditation Council for Graduate Medical Education (ACGME), which oversees

residencies for 111,000 young doctors in the United States, is following suit.

For NYU School of Medicine’s part, Dean and CEO Robert Grossman, MD, commissioned several task forces last summer to address the evolving ACGME requirement. Dr. Evans led the task force focusing on how transitions between doctors-in-training are taught and performed. Dr. Evans brings unique perspective to the job. In 2012, she developed a new handoff protocol for first-year residents working in the intensive-care units at Bellevue Hospital. The protocol is now one of several in place for first-year residents at Bellevue and Tisch Hospitals.

This recent shift in attitudes about handoffs stands in sharp contrast to the earlier days of medicine, when sign-out lapses were easier to brush aside. “Veteran physicians will say, ‘Well, we never did patient handoffs because we were just there all the time,’” Dr. Evans says. But medicine has changed. Today’s physicians find themselves handing off responsibility for their patients more than ever before. A widely cited study published in 2006 in the *Journal of Hospital Medicine* reported that the average patient hospitalized over five days is passed between doctors more than 15 times.

The situation is even more troubling for young doctors. The same study, led by Vineet M. Arora, MD, at the University of Chicago, found that the average intern, restricted to shifts no longer than 16 hours, will transfer care of 300 patients in one month.

Many veteran physicians are concerned. “I’m an old-time surgeon from the era of the 120-hour workweek,” says Ronald Simon, MD, chief of the Division of Acute Care Surgery and professor of surgery and anesthesiology at NYU Langone. “Obviously, the connection that one has for their patient is different if you have cared for the patient for 24 hours. Once you hand off a patient, some portion of that connection is lost.”

**Y**et it’s hard to say which is more dangerous—handoffs or physician fatigue. The tradeoff has been the subject of heated debate since the 1980s when the Libby Zion case threw a national spotlight onto the issue of intern fatigue. Zion was an 18-year-old college freshman who died in 1984, allegedly at the hands of overworked residents and interns at the New York Hospital in Manhattan.

By 1989, the state of New York, spurred by the case, restricted trainees to an 80-hour workweek with 10 hours of rest between shifts, and shifts no longer than 24 continuous

**“Each handoff in each situation has the same overall goal, which is to transfer situational awareness from one provider to another.”**

---

hours. The ACGME took similar action in 2003, issuing national guidelines that echoed New York’s. In 2011, it went even further, revising the guidelines to limit intern shifts to just 16 continuous hours.

The hour restrictions, many contend, present a whole new set of dangers. “I recognize that there are lifestyle and fatigue issues, but I think we’ve traded one set of problems for another set of problems,” says Dr. Simon. Shorter shifts mean more handoffs, and more handoffs mean more medical errors, leaving many to wonder whether patients are any safer now than they were before the rule change.

Michael Ambrosino, MD, associate professor of radiology and dean for graduate medical education at NYU School of Medicine, doesn’t necessarily disagree with the backlash against duty-hour reform, but he accepts that limited intern shifts are here to stay. The only way to move forward, he believes, is to address the problem at hand. “We should look at the new rule on duty hours as a kind of stress test,” Dr. Ambrosino says. “It’s just brought attention to something that needed to be fixed in the first place.”

**T**he big question is how to formally teach what has traditionally been an informal practice subject to physician preference and circumstance. When the ACGME scaled back intern hours for the second time in 2011,

the accrediting organization also required medical schools to develop handoff curriculums and institute policies to help minimize the number of patient handoffs. Doubling down on that mandate, this year it is rolling out a new on-site review program that will evaluate residency programs based on six core areas of learning, including handoffs, every 18 months.

That mandate inspired Dean Grossman’s handoff task force to pursue the broadest possible approach to the problem, taking into account the multitude of settings in which handoffs occur. The interdisciplinary team, representing all fronts of the handoff, from physicians and nurses to technicians and administrators, has spent months reviewing the latest literature on staff transitions, consulting experts in the field, and comparing handoffs across disciplines. The goal is to determine the essential ingredients of an effective handoff, regardless of the environment in which it’s performed, and incorporate those core elements into a universal teaching model.

The task force is still drawing up its recommendations, but what it’s discovered so far has been reassuring. New protocols for handoffs are emerging across the country—an indication of medicine’s resolve to make handoffs a priority. The American Medical Association website lists at least seven models. The variation makes sense since every specialty signs out differently. “All pilots have checklists, but the checklist for a pilot flying a Boeing 747 will be different from a checklist for a pilot flying a commuter plane,” says Dr. Simon. But the models also share many basic elements.

“We’ve found that different systems may have different names with nice little mnemonics, but they all share the same core elements: Who is the patient? Why are they here? What’s going on? What do we need to do?” Dr. Evans says. “Each handoff in each situation has the same overall goal, which is to transfer situational awareness from one provider to another.”

The concept of transferring situational awareness is nothing new to other high-stakes fields, such as aviation, space exploration, and the military. In 2012, when Dr. Evans and colleagues set out to design a protocol for first-year physicians working in the intensive-care units at Bellevue, they looked to handoff practices in those fields for inspiration. “Air-traffic controllers have codified the verbal communication so that it follows the same structure each time,” says Dr. Evans. “The goal is to transfer situational

**New protocols for handoffs are emerging across the country—an indication of medicine's resolve to make handoffs a priority.**



awareness based on three things: perception, assessment, and prediction,” she says.

Her team also looked to nursing units. More accustomed to shorter shifts and therefore more handoffs, nurses have long practiced more formalized procedures for transferring patient information. Borrowing from these successful models, Dr. Evans, her team, and Amit Uppal, MD, clinical instructor of medicine and director of the medical intensive care unit at Bellevue, developed an acronym of their own: SHARE, for System to Improve Handoffs and Reduce Errors. With this system, residents receive a formal lecture on handoffs, help design shift schedules, and follow a standardized electronic checklist, also repeated verbally, that moves from head to toe.

The checklist, as simple as it seems, acts as a powerful mnemonic. The repetition of information in a predictable sequence helps residents remember details, detect errors and omissions, and improve decision making. Moreover, SHARE handoffs are conducted face-to-face, free of interruptions, and include a clinical summary and a rationale for patient management—all core elements of an effective sign-out.

Joe Kingsbury, MD, an intern at Bellevue, says the SHARE model has helped make the ICU less overwhelming. “It breaks down the major issues by system—brain, cardiovascular, respiratory, endocrine, infectious disease—then outlines the problems within each system, sets a plan of action, and provides a to-do list,” Dr. Kingsbury says. “It really helps you think about the greater picture of the patient. If something goes wrong, you’re better equipped to address the problem.”

What’s more, despite the fact that SHARE takes a bit longer to complete than a conventional sign-out, it actually saves time in the long run. “It’s a dynamic sign-out that doubles as your daily progress note,” says Dr. Kingsbury. “It’s very efficient.”

**K**atherine A. Hochman, MD, assistant professor of medicine and director of the Hospitalist Program at Tisch Hospital in the Department of Medicine, incorporated similar elements into a handoff model she developed in July 2012 to help bridge the gap between her weekday and weekend staff. A hospitalist is an attending physician who specializes in the care of hospitalized patients from admission to discharge and who communicates with all members of the healthcare team, including primary care doctors. But even a hospitalist can’t live at the hospital. For Dr. Hochman, the Friday to Saturday transition was

particularly challenging. “In the past, most of the action happened on weekdays,” says Dr. Hochman, who coleads a separate task force on quality improvement, another area targeted by the new ACGME’s on-site review program. “Then the weekend happened, and there was little advancement of care. Without knowing what a cellulitis looked like on Friday, a physician is unlikely to discharge a patient on Saturday, even if it was indeed better. That patient typically hung around until Monday.”

Dr. Hochman’s solution was the four-hour handoff, a unique model where the weekday hospitalist rounds at the bedside of patients with the weekend hospitalist each Friday. As with SHARE, the handoff happens face-to-face without interruption—a core element. It also happens in front of the patient. “It’s empowering for the patient to hear the story that’s given from one provider to another,” says Dr. Hochman. “They can point out omissions or mistakes and add to the narrative.” Dr. Hochman has also created a pamphlet, with pictures of the entire hospitalist team, to aid in the handoff process. “It is important to convey to patients that we have an entire team who is caring for them 24/7,” she says. “Pictures really help.”

The model, although expensive due to staffing overlap, has been well received. On the administrative end, the number of weekend discharges has gone up, along with patient satisfaction scores, and the average length of stay has gone down. “Patients like the model because they can actually see who their doctor is on the weekend,” says Dr. Hochman, “and weekday hospitalists like it because they know their patients will be well cared for. Weekend hospitalists like it because they don’t just walk into the weekend with a list of patients. They know their faces, they have met their families and understand the details of their patients’ illnesses. Moreover, it also models good handoff practices to the house staff. There are a lot of wonderful side effects.”

**T**he reality is that even the smoothest transition between physicians still carries risk. “It’s just the nature of the beast,” says Dr. Simon, a veteran of many handoffs throughout his long career. “No matter how thorough you are in presenting things, you can’t hand off every piece of information.”

Knowing which information to pass along and why is a vital skill. The hope is that teaching better handoff practices will help every young physician master it. ●



# Is Alzheimer's in your future?

A radical rethinking of research ethics is occurring among Alzheimer's disease researchers. Many now believe that subjects should be told the results of studies evaluating biomarkers for the brain-robbing disease, but worry whether such information will bring clarity or extreme distress.

**BY ADAM PIORE**





The mild delusions were the first clue that something was wrong with Margarita De Young's mother, Victoria Suazo. She was about 80 the first time she unleashed an irrational rant, accusing a dear childhood friend of stealing a miniature teacup from her collection. Then came the episodes outside. Suazo, always a strong, independent woman, let herself out of the house, forgot where she was, and wandered around the neighborhood lost until someone recognized her and brought her home. Soon after, police picked up Suazo downtown, disoriented and bleeding badly from the head. She could not tell them who she was or where she lived.

It's been more than seven years since Suazo finally succumbed, at 93, to Alzheimer's disease, the most common form of dementia. But lately, De Young has been thinking a lot about her mother's heartbreaking final years. One of hundreds of volunteers enrolled in clinical studies at NYU Langone Medical Center looking at aging, mild cognitive impairment, and Alzheimer's disease, Suazo recently turned 70 herself. Now, every time she loses her keys, forgets where she parked the car, or finds herself at the bottom of the stairs trying to remember what it was she came down to do, she can't help but confront terrifying questions: Is she experiencing a totally predictable, completely innocuous "senior moment"? Or are these *her* first clues? Will she, too, get Alzheimer's disease?

"I've noticed this more in the last three years or so," says De Young, who signed

Previous page:  
Margarita De Young  
is part of a long-term  
research project  
studying biomarkers for  
Alzheimer's.

up for a long-term research project that asks some of these very same questions. The study, called the Alzheimer's Disease Neuroimaging Initiative (ADNI), is the largest and most comprehensive Alzheimer's research endeavor of its kind, supported by a \$40 million grant from the National Institutes of Health. De Young is one of 1,000 volunteers enrolled at 55 different sites in the United States and Canada, including NYU Langone, who are helping to determine whether imaging of the brain every six months can help predict and monitor the onset and progression of Alzheimer's disease. It's just the sort of information that could bring clarity to De Young's future. "I am worried," De Young adds. "If I am going to get it, I want to begin planning before it's too late."

De Young has already undergone an exhaustive battery of diagnostic tests, including spinal taps, blood work, brain scans, and surveys to evaluate her cognitive performance. Taken together, they provide, at the very least, some indication of the probability De Young will develop Alzheimer's. These tests search for what are known as

"biomarkers," physical traces correlated with the prevalence of Alzheimer's, like abnormal levels of certain proteins in the cerebrospinal fluid and blood, genetic variations, and structural changes in the brain.

The irony is that while all of these tests may well benefit Alzheimer's research, they may do very little for De Young because she'll never see most of the results. The ADNI study policy, like most clinical trials, prohibits researchers from revealing data to patients. The rationale behind the policy is well intentioned: The tests are experimental, after all, and their results can be inconclusive. Moreover, in the case of Alzheimer's disease, even if the results were perfectly predictive, they would do nothing to save patients from the disease, as there are currently no drugs to prevent Alzheimer's.

But attitudes about patient disclosure are changing quickly. A growing number of clinicians and researchers are challenging the mandate to shield participants from bad news. Indeed, a significant number *already* ignore it. In a recent anonymous survey of 139 investigators participating in ADNI and published in the journal *Neurology*, Melanie B. Shulman, MD, clinical associate professor of neurology and psychiatry at NYU Langone, and colleagues found that 14 percent of respondents admitted to sharing diagnostic data with their patients. Participants also had the opportunity to express their opinions more fully in comments to the authors, and these complicated, more nuanced responses are being used to help create more sophisticated disclosure policies, says Dr. Shulman.

The study's findings are just one

De Young holds a picture of her mother, who died of Alzheimer's. De Young worries if she, too, will get the disease.



indication of a radical rethinking of research ethics and protocol in the field of Alzheimer's studies, a process that echoes previous debates in other medical fields, most notably cancer. In Alzheimer's, the issue is being brought to a head by events in Washington: In the spring of 2012, the Food and Drug Administration approved the use of an injectable radioactive dye made by Eli Lilly that stains clumps of sticky proteins called beta-amyloid in the brain—a classic correlate of Alzheimer's—and renders them visible for the first time through a PET scan instead of an autopsy. The landmark FDA decision finally delivers a verifiable tool to help diagnose and study Alzheimer's, a disease afflicting some 5 million Americans, or one in nine Americans over 65. With the population aging, that number is estimated to increase to as many as 16 million by 2050, as old age is one of the biggest risk factors for the disease. Controversy flared in September 2013 after Medicare said it would pay for the amyloid test only if patients were enrolled in a research study. Eli Lilly and the Alzheimer's Association objected to the ruling, arguing that Medicare should pay for the test, which costs between \$3,000 and \$5,000, without any restrictions.

Nevertheless, the FDA's seal of approval brings with it widespread publicity that

can spur patient demand for the test and raise expectations about its prognostic powers. "People with very mild problems especially want to know what the future holds," says Dr. Shulman, who serves as associate director of the Pearl Barlow Center for Memory Evaluation and Treatment at NYU Langone.

Many of the patients she sees, Dr. Shulman notes, have been diagnosed with "amnesic mild cognitive impairment," which carries a "very ambiguous prognosis." "It just means isolated memory trouble," she says. "Two-thirds of those who receive that diagnosis will go on to get dementia, but one-third can remain stable or even reverse. It's very unsettling to get the information. Biomarkers can provide some information."

In her ADNI survey, Dr. Shulman queried more than 150 investigators, many of whom also serve as personal physicians to subjects in ADNI studies. Almost three-fourths (73 percent) said they considered results from the amyloid-imaging test clinically relevant enough to share with patients who have mild cognitive impairment. About 58 percent supported providing the results to participants with healthy cognition.

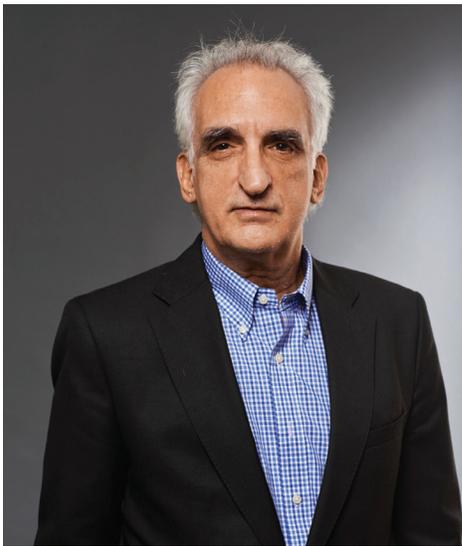
The benefits to disclosure are, of course, easy to see. It can lead to improved lifestyle changes, planning for the future,

eligibility for intervention studies, the survey participants said. Most of all, some noted in comments submitted to Dr. Shulman and her colleagues, patients have a right to know.

"I think saying nothing but 'Thanks for participating in the study' causes people a lot of stress and frustration, and causes people to go elsewhere to get the information," says Mony de Leon, EdD, professor of psychiatry and the founder and director of the Center for Brain Health at NYU Langone. Dr. de Leon, an ADNI researcher, is a principal investigator on five studies funded by the National Institutes of Health to develop biomarkers for Alzheimer's.

On the other hand, some survey participants argued, disclosing ambiguous results with no consensus on how to interpret them may do more harm than good. A person who learns they have amyloid plaques in their brain might suffer years of anxiety even though they may never develop dementia. (The plaques do not always neatly correlate with mental decline; in fact, up to one-third of cognitively normal elderly men and women have amyloid in their brains.) What's more, the disclosure can bias the trial results.

"It's a tug of war because you want the research to be as clean as possible," says



Dr. Mony de Leon and  
Dr. Melanie B. Shulman.

Dr. Shulman, who notes that one recent study found that subjects in aging studies who are informed of their APOE genotype (a genetic marker for Alzheimer's disease) subsequently do worse on memory tests. "But as a clinician caring for people, you want to help them."

Perhaps the most widely repeated argument against revealing the biomarker test results is that at least for now, there is not much one can do to treat Alzheimer's disease. As a result, some have warned, disclosing the information is not only cruel, it might also detract from the patient's quality of life—even lead them to commit suicide.

It's a prospect that some Alzheimer's researchers argue is likely overstated. Several pointed to a study conducted by Robert C. Green, MD, MPH, a geneticist at Brigham and Women's Hospital and Harvard Medical School and a collaborating author on Dr. Shulman's paper. Dr. Green followed individuals who had discovered through genetic testing that they had a gene highly correlated with Alzheimer's disease. Six months after receiving the information, most of the subjects he surveyed had no discernible change in depression or anxiety. Most, however, did make lifestyle changes and purchased health insurance.

"Most people do not react cataclysmically," Dr. Shulman says. "They incorporate the information like they incorporate other information."

However, integrating that kind of

information could move someone to make a conscious decision to end life on one's own terms. That is precisely what Margarita De Young says she plans to do if she learns that she is, in fact, afflicted with Alzheimer's.

"I work with Alzheimer's patients as a physical therapist, and I know what it is like," De Young says. "I know what it was like with my mother. It was awful. I do not want to go through that and put my family through that. I want to be able to live healthy as long as I can. I want to be able to see my grandchildren finish school and get married. But I want to make a decision when I am aware enough to make a decision."

**A**rthur L. Caplan, PhD, the director of NYU Langone's Division of Medical Ethics in the Department of Population Health, notes that doctors have been grappling with similar issues in the field of cancer research and treatment for more than a decade.

Around seven years ago, for instance, doctors discovered they could use genetic markers to identify who might respond negatively to a cancer drug called Tassigna, one that could potentially have particularly bad, even fatal, side effects. The discovery set off a serious ethical discussion that echoed in the current discussion over Alzheimer's. How accurate did the genetic markers have to be to base a choice on them? Did you need to be 100 percent sure that a patient

would respond negatively to deny them potentially lifesaving treatment? Or was 80 percent enough?

"At what point do you say the potential risk from the drug outweighs the potential benefit, and how sure do you have to be before you say we're not going to give you the standard of care?" Dr. Caplan says. "There is a lot of uncertainty on how to approach this."

The situation with Alzheimer's is quite similar. "The question has always been, even today, what do biomarkers actually tell you? Biomarkers are not the real thing. They are surrogates," says Dr. de Leon. "How precise are the measurements? How accurate? Can the information be of value to an individual? Can it guide clinical work? Those are important questions, and not all of them have been answered."

In the cancer and Alzheimer's fields, groups met, professional societies met, there was a lot of debate back and forth, and guidelines were finally created. In the case of Tassigna, doctors agreed that once the tests became accurate enough, the information should guide treatment.

A similar process is under way with the FDA-approved Alzheimer's brain-imaging test. After Dr. Shulman reported her preliminary results before the summer 2012 meeting of ADNI, a subcommittee changed the group's official policy to allow amyloid-imaging results to be disclosed to those suffering dementia. It was a modest step but a first one forward, which Dr. Shulman hopes will be followed

up in future meetings with a new policy allowing disclosure to even those with mild cognitive impairment.

While the new amyloid-imaging test has rekindled the debate over patient disclosure, it's not even the most accurate test available. The amyloid test has "limited utility," Dr. de Leon says. "Even if you have amyloid in your brain—and a lot of it—it doesn't mean you are going to have Alzheimer's disease. You can have amyloid without any clinical symptoms. Your risk is increased certainly, but there are many, many exceptions."

A combination of other biomarker tests is a far more accurate gauge of a person's likelihood to develop the disease, says Dr. de Leon. A spinal tap that detects markers for both amyloid and another protein deposit, twisted fibers known as tau, coupled with the detection of small memory changes, is far more predictive. Some studies, Dr. de Leon says, have found them to be 80 to 90 percent predictive of future decline.

But since these tests require a spinal tap—a procedure most people are reluctant to undergo—it's unlikely to find commercial backers willing to finance the clinical trials needed to win FDA approval. For his own part, Dr. de Leon

supports disclosure of some sort, with the caveat that it should be delivered carefully and in context.

"In general, people like to know what they are doing and why they are doing it, and if it means explaining to somebody that the results are statistical, my inclination is to make it as user-friendly as possible," he says. "I don't think it should be given in terms of a specific number, but to use statements such as 'your levels are high or low, and this translates into high risk or low risk in some individuals.'"

Dr. Caplan also notes that one of the main arguments against sharing biomarker data—that there is nothing one can do to fight Alzheimer's disease—appears to be changing. At least three clinical studies of drugs to treat individuals with no memory problems but some of the biomarkers associated with Alzheimer's are under way. Dr. Shulman is the lead NYU Langone investigator in one of those studies, called A4, slated to begin in 2014, which will test a vaccine to clear amyloid from the brains of cognitively healthy people over 65 whose brain imaging demonstrates the presence of amyloid.

Meanwhile, she is continuing to do studies aimed at developing a meaningful

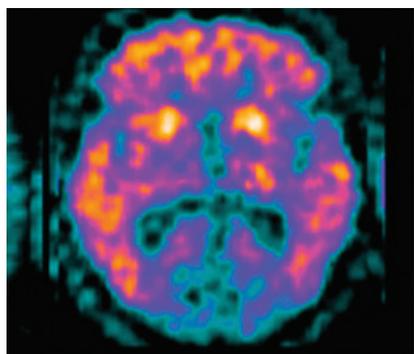
disclosure policy, including research into the effect of disclosure on patient mood and anxiety, the best way to educate patients about the meaning of the tests, and what kind of support they might need once informed.

"It isn't black and white," Dr. Shulman says. "People have a right to information. But they have a right to be given the education to understand the information. That's the challenging thing. It's about how to design a disclosure process as subtle as informed consent so that it is meaningful and somebody can take positive actions."

**M**argarita De Young is also hoping the official policy will change. Though she says she understands the need to withhold information to prevent biasing research, she disagrees with any contention that it's somehow in her best interests—even if the implications of the biomarkers themselves are not yet considered definitive. Most people, she argues, would want to get their finances in order, make decisions about who will look after them, and where they might want to live.

"I think I have the right know," De Young says. "I think that if a person wants to plan for the future, it's useful information." The concern that a person might wish to end her life, she argues, is not sufficient reason for denying her rights.

"I would not end my life because I was depressed," says De Young. "I'm not afraid of dying. I'm afraid to vegetate, emotionally, mentally, and eventually physically. I'm afraid to get to the point where I don't have any awareness or consciousness of what's happening to me, and don't even recognize my relatives. I don't think that is living anyway." ●



This PET scan image shows clumps of amyloid in the brain of a patient with Alzheimer's disease. The bright orange and yellow clumps are stained with a radioactive tracer called Pittsburgh compound B. It was the first tracer to be tested in the study of Alzheimer's and remains a benchmark for amyloid testing.

# A Humanistic Approach to Medicine

The new director of the division of medical humanities discusses how medicine seen through the perspective of history, literature and the arts, contributes to being a better doctor.

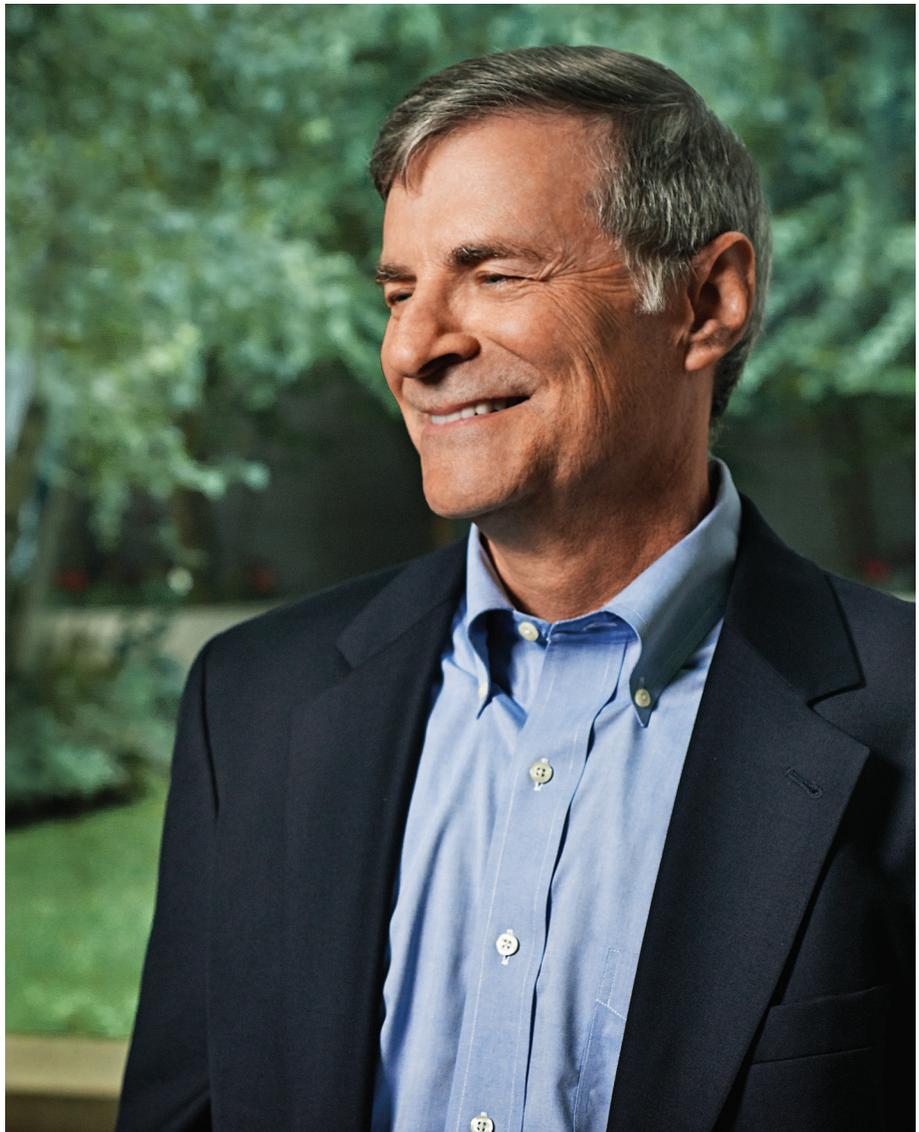
BY GARY GOLDENBERG

It is the rare book that has any measurable effect on public health. Two examples that readily come to mind are Sinclair Lewis's exposé of the meatpacking industry, *The Jungle*, and Rachel Carson's prescient warning about the dangers of pesticides, *Silent Spring*.

A more recent example is David Oshinsky's 2005 Pulitzer Prize-winning book, *Polio: An American Story*, which documents the history of the epidemic and the drive to find a cure. Dr. Oshinsky's tale caught the eye of Bill Gates, persuading him to launch a major initiative to rid the world of this pathogen once and for all. "Reading Oshinsky's book a few years ago," Mr. Gates wrote on his blog in 2011, "broadened my appreciation of the challenges associated with global health issues and influenced the decision that Melinda and I made to make polio eradication the top priority of the foundation, as well as my own personal priority."

Dr. Oshinsky recently joined NYU School of Medicine as director of the division of medical humanities in the Department of Medicine. He is also professor of medicine, a member of the Department of History, and a distinguished scholar-in-residence at New York University, and he serves as publisher of the Bellevue Literary Press and editor of the *Bellevue Literary Review*.

Among his books are *A Conspiracy So Immense: The World of Joe McCarthy*, which won the Hardeman Prize for the best book



DR. DAVID OSHINSKY

about the U.S. Congress, and *Worse Than Slavery*, which won the Robert F. Kennedy Prize for distinguished contribution to human rights. In 2009 PBS aired a documentary, *The Polio Crusade*, based upon his book, and Dr. Oshinsky received the Dean's Medal from the Johns Hopkins Bloomberg School of Public Health for his distinguished contributions to the field. His articles and reviews appear regularly in the *New York Times*. He was formerly the Jack S. Blanton Professor of History at the University of Texas at Austin, where he received the university's Raymond Dickson Centennial Teaching Award.

We spoke to Dr. Oshinsky in July before he departed for the NYU campus at Abu Dhabi to teach Disease and Medicine on a Global Scale.

***How do you define medical humanities, and why is it important?***

Medical humanities is medicine as seen from the perspective of history, literature, art, and other disciplines. The idea is to provide medical students and physicians a supplement to the increasingly technical world of healthcare. In my experience, medical humanities expands the imagination, promotes self-reflection, and, perhaps most important, enhances communication with patients. Doctors with a humanistic approach to medicine are more attuned to the full demands of their profession.

***Can you provide an example of how this perspective improves the practice of medicine?***

I always mention Dr. John Snow and the Ghost Map, which has to do with the huge cholera epidemics in London in the mid-1800s. By talking to people, by gaining an understanding of the neighborhood and those who lived there, Snow was able to trace the source of the disease to a single water pump and stop the spread in its tracks—decades before Robert Koch identified the causative agent. It wasn't conventional science or medicine that stopped this epidemic—it was the personal

**“What In my experience, medical humanities expands the imagination, promotes self-reflection, and, perhaps most important, enhances communication with patients. Doctors with a humanistic approach to medicine are more attuned to the full demands of their profession.”**

approach of a single physician with deep ties to his community.

***How about a current example?***

The anti-vaccine movement particularly troubles me. This group dominates the vaccine conversation today. We in medicine have not done enough, in the past or currently, to explain how vaccines have saved more lives than any other medical intervention in history. We have to teach people about the polio epidemics that struck America in the previous century, crippling thousands of children each year. We don't see polio epidemics today in the United States because the vaccines have done their job so well. But if we stop vaccinating we'll see these epidemics again, as we're seeing outbreaks of measles and whopping cough and other vaccine-preventable diseases. Doctors have to be educated, too. Most have never seen a case of polio. To them, polio is a vaccine, not a virus. And that's where medical history and story telling can play an enormously effective role.

***New York City, it would seem, is the perfect backdrop for these lessons.***

Yes, I would like to take all incoming medical students on a trip to Roosevelt Island [originally Blackwell's Island, then Welfare Island] in the East River. That's where public health began in New York City. You had the Lunatic Asylum,

Immigrant's Hospital, the Smallpox Hospital, the Penitentiary Hospital, and more—all on that small spit of land. Some of the building shells are still there. And of course, right next door there's Bellevue, the nation's first public hospital. I want to give students a feeling for the continuity of medicine, a sense that they come from a long tradition of service to public health. NYU has been a bit too modest in highlighting its extraordinary role in the development of antiseptic medicine, pathology, psychiatry, and infectious disease prevention, to name a few. The developers of the two polio vaccines, Jonas Salk and Albert Sabin, both graduated from our medical school. Both were extremely well-read beyond their fields, men of great humanity and vision.

***Do you have other plans for improving the teaching of medical humanities?***

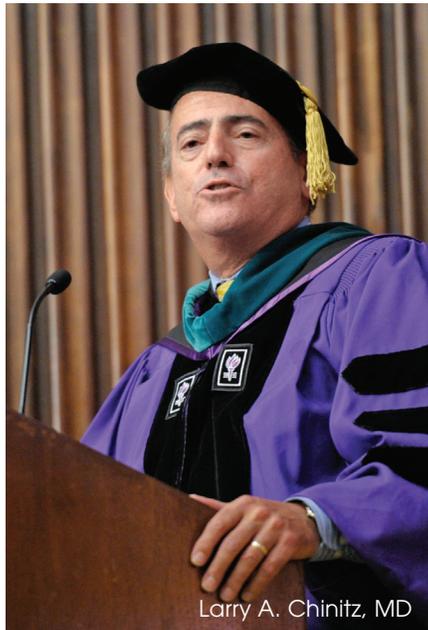
I would like to further involve our students in current global health issues—not unlike what I'm teaching at the Abu Dhabi campus. Here we discuss three diseases: smallpox, which has been wiped from the earth; polio, which we are very close to eradicating; and AIDS, which is still raging in parts of the world. By seeing what we've done in the past—the breakthroughs, failures, and strategies—we hope to figure out what to do best in the future. There are endless public health issues to contend with, from vaccination to disease

CONTINUED ON PAGE 33

# Honoring Three Masters and One Major Benefactor on **DEAN'S HONORS DAY**

On Monday, September 30, 2013, faculty, benefactors, and friends gathered in Farkas Auditorium for Dean's Honors Day. Dean Robert I. Grossman, MD, led a platform that included Kenneth Langone, chairman of the NYU Langone Medical Center Board of Trustees; John Sexton, PhD, JD, president, New York University; and Steven B. Abramson, MD, vice dean for education, faculty, and academic affairs.

Alice M. Tisch, a trustee of NYU Langone Medical Center, received the Valentine Mott Founders Award named for the father of modern surgery and cofounder of NYU School of Medicine. Mrs. Tisch, who has been involved with the Medical Center for more than 20 years, serves as the chair of KiDS of NYU, a leadership group of parents, physicians, and



Larry A. Chinitz, MD



Alice M. Tisch

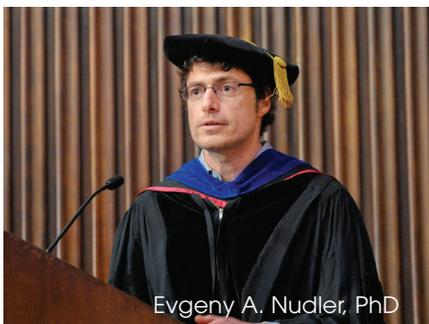
friends that works through philanthropy and community service to enhance pediatric care and promote a nurturing environment for children and families at the Medical Center. Mrs. Tisch and her KiDS colleagues recently raised more than \$1 million at the 2013 KiDS of NYU Langone's Springfling Gala. Her leadership has helped make this annual event a celebration of the transformational care children receive at Tisch Hospital and across the Medical Center.

Larry A. Chinitz, MD, the Alvin Benjamin and Kenneth Coyle, Sr., Family Professor of Medicine and Cardiac Electrophysiology, received the Master Clinician Award. Dr. Chinitz currently serves as director of the Cardiac Electrophysiology Program and the Heart Rhythm Center. He developed the Division of Cardiology's groundbreaking clinical cardiac electrophysiology program and was also a driving force in the establishment of the NYU Heart Rhythm Center, which provides state-of-the-art cardiac rhythm

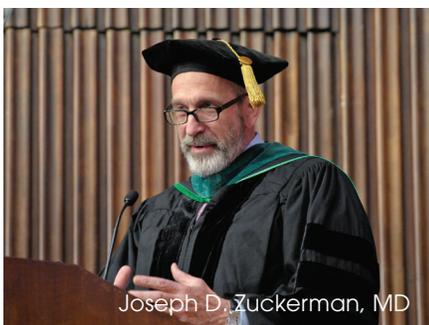
management, cutting-edge research, and a renowned training and mentoring program in clinical electrophysiology.

Joseph D. Zuckerman, MD, the Walter A. L. Thompson Professor of Orthopaedic Surgery, was named Master Educator. A revered teacher, Dr. Zuckerman serves as chair of the Department of Orthopaedic Surgery at NYU Langone Medical Center and surgeon-in-chief of NYU Langone's Hospital for Joint Diseases (HJD). He is an internationally recognized expert in shoulder surgery and hip and knee replacement. Dr. Zuckerman has dedicated himself to providing superior education, a hallmark of his career. Residents have conferred their Teacher of the Year Award on Dr. Zuckerman five times, more than on any other faculty member in the department. He is renowned for always having time for medical students and residents.

Evgeny A. Nudler, PhD, the Julie Wilson Anderson Professor of Biochemistry, was named Master Scientist. A trailblazing biochemist with an insatiable sense of



Evgeny A. Nudler, PhD



Joseph D. Zuckerman, MD

PHOTOS: DAVID LUBARSKY

wonder and curiosity, Dr. Nudler became the youngest full professor in the history of NYU School of Medicine in 2005.

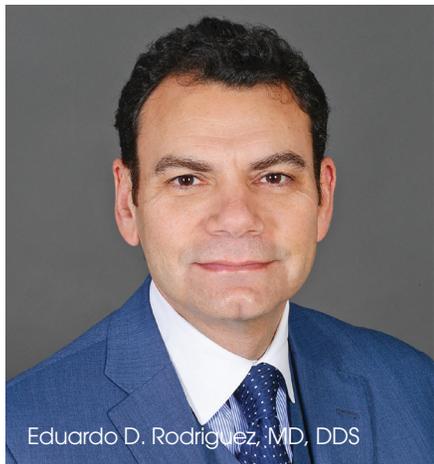
Dr. Nudler was selected as a Howard Hughes Medical Institute investigator in 2013 for his work on the role of bacterial gases in antibiotic resistance and the interplay between RNA transcription and cellular response to stress. ●

From left: Dean Grossman, John Sexton, PhD, JD, Kenneth G. Langone, Robert Berne, PhD, and Steven B. Abramson, MD



## A RENOWNED SURGEON WHO MADE MEDICAL HISTORY JOINS NYU LANGONE

In November, the NYU Langone Medical Center welcomed Eduardo D. Rodriguez, MD, DDS, as the new chair of the Department of Plastic Surgery and the Helen. L. Kimmel Professor in Reconstructive Plastic Surgery. If the name rings familiar, it may be because Dr. Rodriguez recently made medical history. In 2012, he earned international acclaim when he performed the world's most extensive face transplant, leading a team of 150 medical experts through a marathon 36-hour surgery at the R Adams Cowley Shock Trauma Center at the University of Maryland School of Medicine, where he was chief of the Division of Plastic, Reconstructive, and Craniofacial Surgery and professor of surgery.



Eduardo D. Rodriguez, MD, DDS

The successful procedure broke new ground in plastic and reconstructive surgery, and transformed the life of patient Richard Norris, now 38, who lost much of his face during a shotgun accident 15 years ago.

For this and other distinguished achievements, Dr. Rodriguez has received numerous awards and honors, including the prestigious Harry Strusser Memorial Award for Promoting Public Health Awareness from his alma mater the NYU College of Dentistry. Most significant, he has also earned the gratitude of his patients, including Richard Norris.

Thanks to the transplant, Norris can now recognize himself in a mirror and venture outside without drawing ridicule and stares. "Unless they know me personally, they don't know I am a face transplant patient," Norris told the press. "That right there is the goal we had."

Since the first partial face transplant was performed in 2005, 28 people have undergone similar procedures. But none rival the complexity of Richard Norris's case. To prepare Norris for his new face, Dr. Rodriguez and team had to contend with cement-like layers of scar tissue built up from previous surgeries. Then, they rebuilt the bone structure beneath Norris's eye sockets, including his jaw and teeth. They also restored

Norris's tongue, all before grafting on the new face, donated by the family of a 21-year-old man who recently died in car accident.

Dr. Rodriguez' qualifications for the historic surgery are rare. He is board certified in plastic and reconstructive surgery as well as in oral and maxillofacial surgery, and his wide-ranging specialties include craniofacial surgery, oral surgery, and reconstructive microsurgery. Moreover, he has authored more than 102 peer-reviewed journal articles and 21 book chapters.

The son of Cuban immigrants, Dr. Rodriguez was born and raised in Miami, Florida. He earned his bachelor of science in neurobiology from the University of Florida in 1988, followed by a degree in dentistry from New York University in 1992. He completed his residency in oral and maxillofacial surgery at Montefiore Medical Center–Albert Einstein College of Medicine in 1997 and received his medical degree from the Medical College of Virginia in 1999. In 2003, he graduated from the combined plastic surgery program at Johns Hopkins Hospital–University of Maryland Medical Center. Dr. Rodriguez went on to practice as a fellow of reconstructive microsurgery at the Chang Gung Memorial Hospital in Taipei, Taiwan.

Dr. Rodriguez is also a clinical consultant of plastic and reconstructive surgery at the Walter Reed Army Medical Center, where he has helped soldiers recover from disfiguring wounds. ●

# Broadening Undergraduate Medical Education

A range of dual-degree programs expose students to fields that intersect with medicine.

**W**hen Superstorm Sandy slammed into New York City in the fall of 2012, Steffen Haider got a chance to use the knowledge he had gained as a student in NYU School of Medicine's dual-degree MD/MPH program. In the battered Far Rockaways, the fourth-year medical student worked with Doctors Without Borders, which was coordinating the disaster response with government agencies and private relief organizations.

"I understood exactly what the team leaders were talking about and could better participate in the planning," says Haider, "because I had learned concepts like supply chain failures and successes and other concepts in my MPH classes."

Haider's medical school training also served him well during the relief effort. He took vital signs, spoke with people who had chronic diseases, and coordinated with pharmacies to bring medications to patients stranded on the higher floors of apartment buildings. "We set up a mobile clinic in a laundry room on the ground floor of one of the buildings," Haider says. "There was only emergency power for lighting the main floor."

The melding of medical skills and knowledge from other disciplines that Haider used during Sandy is an example of how students can benefit from a recently broadened range of dual-degree programs offered by the School of Medicine. In addition to the long-standing MD/MPA in Health Policy Management, four other



From left: Joseph Oppedisano, director of student affairs, Steffen Haider ('14), Lynn Buckvar-Keltz, MD, associate dean for student affairs, and Kylie Birnbaum ('14).

dual-degree programs have been developed since 2006: an MD/MPH in Global Public Health in both a four- and five-year track; an MD/MS in Clinical Investigation; an MD/MA in Bioethics; and an MD/MBA, which admitted its first students in 2013. All of the dual degrees take five years to complete, with the exception of the four-year MD/MPH.

"The dual-degree programs were started as a way to give our students the best exposure to fields that intersect with medicine but are not fully represented in our core curriculum," says Lynn Buckvar-Keltz, MD, associate dean for student affairs, who oversees the programs. "They provide our students with the necessary tools to succeed as future physician leaders in public health settings across the globe,"

she says. Twenty-eight students are enrolled in the programs; the MD/MBA is the most popular, with nine students entering in 2013, followed by the MD/MS in Clinical Investigation, with five students.

The School of Medicine can draw on the wide range of academic disciplines at the Washington Square campus, Dr. Buckvar-Keltz says. The MD/MBA degree partners, for example, with the Leonard N. Stern School of Business, which "will dramatically increase our students' understanding of the business of healthcare and position them to be future leaders in medicine," she notes, while the MD/MPH program takes advantage of NYU's partnerships with medical institutions around the world. During his MPH year, Haider participated in an effort to improve emergency medical care

PHOTOGRAPH JOHN ABBOTT

at a hospital in Ghana. Other students are doing research in Dubai and Abu Dhabi.

The dual-degree programs are an integral part of the School of Medicine's Curriculum for the 21st Century, or C21, which provides students a patient-centered and disease-focused medical education, and a more individualized approach to medical school.

The programs, says Steve Abramson, MD, senior vice president and vice dean for education, faculty and academic affairs,

the Frederick H. King Professor of Internal Medicine, and chair of the Department of Medicine, help students pursue their passions by allowing them to choose master's programs that align with their interests and career paths.

Kylie Birnbaum, who completed her MA in Bioethics in 2013, decided to enter the program because she believed it would make her a well-rounded physician and help achieve her goal of doing policy research.

"The chance to step back for a year and examine bigger issues gave me a broader perspective than you typically get in medical school classes," says Birnbaum, who completed her thesis on organ donation.

Haider's experience during Hurricane Sandy reinforced his decision to make a commitment to the program. "It made me realize how critical it is for physicians to have a wide range of skills beyond what you learn in medical school," he says. ●

—SASCHA BRODSKY

## In the Mountains of Northern India

Four medical students help survey health needs in a remote area.

**B**lasting snow and bitterly cold temperatures force people living in remote and impoverished villages in the Indian Himalayas to spend much of the winter indoors, burning dung to cook and to keep warm. In cramped enclosed spaces, smoke from the dung can cause a condition called hut lung that may lead to emphysema, as well as other lung diseases.

Hut lung is among the conditions surveyed by four students from NYU School of Medicine who traveled this summer to the mountainous Zaskar region of Ladakh in northern India to study local health conditions during a six-week stay. They assisted a medical team led by Ladakhi physician Tsering Norboo, MD.

The isolated region, wedged between Tibet and Pakistan, lacks Western

medical care, and snow-filled roads cut off some villages from the outside world for months at a time. During the summer the roads are passable, and the group drove for hours in a truck convoy carrying food and equipment to three villages nestled high in the mountains at elevations exceeding 11,000 feet.

"The journey was challenging as we were constantly jostled, so we could understand exactly why the villages are so seldom visited," says Amelie Pham, a second-year medical student, who traveled with fellow students Gabrielle Sandler, Adria Simon, and Collette Abbott. "We stayed with local people who were incredibly welcoming and happy to see us."

The medical team brought their own generators to power an EKG and an ultrasound

machine, which was used so often that it began to overheat.

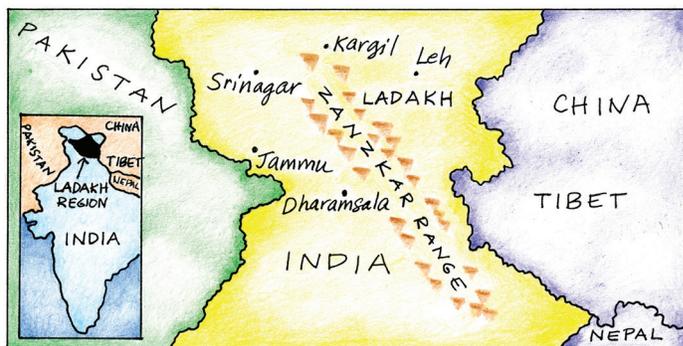
Reached by telephone, Dr. Norboo said that hut lung is common in the region and one of a wide range of health problems villagers face owing to poverty and a harsh climate. "Livestock rearing is their main occupation" says Dr. Norboo, who has conducted many health surveys in the region over the last two decades. "Due to the harsh weather, high altitude, and arid environment, agriculture and horticulture are not possible in most of these areas, and so nutritional problems occur."

The School of Medicine's International Health Program sponsored the outing.

It provides students the opportunity to travel abroad and participate in research, public health initiatives, and clinical education programs. Richard Novick, MD, the Recanati Family Professor of Science and a member of the Skirball Institute of Biomolecular Medicine, and Dr. Norboo developed the idea for the Ladakh stay. He met Dr. Norboo in 1993, while he was studying peptic ulcer disease in the region.

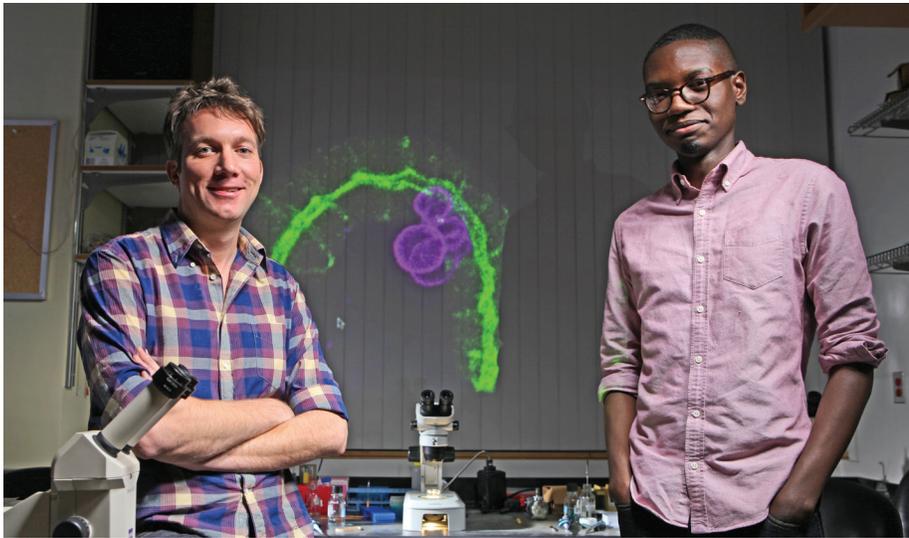
"Dr. Norboo is doing wonderful work in an area that is incredibly underserved by Western medicine," Dr. Novick says. "The students who went over there had a very rewarding and enlightening experience." ●

—SB



# An Independent Thinker

Curiosity and a keen interest in science lead to a prestigious student fellowship.



**G**rowing up in Nigeria in the 1990s, Yusuff Abdu was surrounded by the mysticism of the Yoruba culture and its traditional religion, Ifa, but by the age of nine he had grown skeptical of magical explanations for natural phenomena. He credits his mother, a single parent, for promoting his curiosity and aptitude for critical thinking.

During childhood, his keen interest in science sparked a love for science fiction, especially the classic British television show *Doctor Who*, a cult favorite that originally aired from 1963 to 1989, before returning to the screen in 2005. The eponymous Doctor, a humanoid alien, traverses time and the universe in a blue London police box called the TARDIS. Young Abdu spotted the science behind the fiction.

Today, his ability to explore and think critically has led to a coveted Howard Hughes Medical Institute (HHMI) International Student Research Fellowship in the laboratory of Jeremy Nance, PhD, associate professor of cell biology and

Dr. Jeremy Nance (left) and Yusuff Abdu (right) flank a projection of a roundworm embryo.

developmental genetics, where Abdu is earning his PhD, studying the developmental genetics of simple organisms that could yield important findings about cancer.

Abdu first found his inspiration at the University of Connecticut. In a genetics class, “it was like all the stars aligned, and I just knew,” Abdu says. “We would talk about genetic diseases, and how a gene mutation led to a molecular pathway being dysregulated, and that led to the phenotype of the disease, and I was just fascinated.”

His interest deepened during a summer break from college that he spent in a lab at Cornell, studying cell specification in sea squirts. Standing immobile on the ocean floor, painted in vivid pastels, tie-dyed purples, and luminescent blues, sea squirts resemble table decorations at a wedding banquet. (That’s why they’re also

known as sea vases.)

The early development of the sea squirt’s heart cells particularly intrigued Abdu. “Its cells are all born in what will become the tail,” he explains. “But after that, two of them migrate away and become heart cells. The other two sister cells stay behind in the tail and become muscle cells. I wanted to understand the mechanism that programs that migration.”

Thus inspired, Abdu began his graduate studies at NYU in the sea squirt lab of Lionel Christiaen, PhD. Financial aid through the Tuition Incentive Program, which matches scholarships for incoming graduate students, and a scholarship from the Nigerian government covered virtually all of his tuition and fees for his master’s degree.

Abdu spent two years in Dr. Christiaen’s lab. Each week new sea squirts would arrive from the West Coast and new sea squirt embryos would be created through in vitro fertilization. Minutes later an electric current would be run through the sea water to draw a modified gene into the fertilized egg, creating transgenic embryos for further study.

Sea squirts, like the roundworm (*Caenorhabditis elegans*), are often used to discover how genetic programming can go awry in development because many of their genes have human counterparts, their short life spans make experimentation easier—scientists don’t have to wait years for results—and they are transparent.

“What makes a cell cancerous? They overproliferate, they refuse to die, they migrate, and they invade other tissues,” says Abdu. “Cell proliferation, programmed cell death, and cell migration are all things that happen during the development of an embryo as well—but they’re controlled. By studying model organisms, we can find situations where cells undergo more

cell division than they're supposed to, and identify the genetic mutation that causes it."

In Dr. Nance's laboratory in the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center, Abdu is focusing on the development of the *C. elegans* embryo. Cancer-promoting genes in the cell death pathway such as those in the BCR-ABL family—linked to lymphoma, breast and prostate cancer, melanoma, and leukemia—were originally discovered in studying *C. elegans* development.

Choosing Abdu as a PhD student was an easy decision for Dr. Nance. "He was already mature, an independent scientist, and a deep thinker about his project," Dr. Nance says. "He would come up with his own ideas, rather than rely on me, which is

exceptional for new students."

Abdu is studying the development of primordial germ cells (PGCs), which are set aside at the earliest stage of development to become gametes, the reproductive cells. When he first joined the lab, Abdu's PGC project idea was exploratory, Dr. Nance says. "But he cracked it open and saw something that I hadn't seen before. He noticed that germ cells in the embryo undergo a dramatic morphogenesis, in which they change their shape, and we think that this is important for their eventual ability to make gametes. There was very little known about this process. On his own, he started looking at it and trying to figure out the genes involved."

Abdu's work has already revealed the fate of specialized structures in PGCs

called lobes, which appear in the early development of gametes, but disappear by the time an embryo emerges. No one had previously tried to find out what they did, or where they went. He and Dr. Nance found a way of studying these structures that allowed them to observe what happens to them and helps explain their function.

Abdu learned in August that he was one of 42 international students chosen from among 400 applicants for an HHMI International Student Research Fellowship. The award is worth nearly \$130,000 over years three, four, and five of his PhD program.

"I didn't open the email for at least 10 minutes, because I was too afraid," Abdu says. "It's such a great honor and opportunity. ● —GINA SHAW

## FACULTY CONVERSATION

CONTINUED FROM PAGE 27

surveillance, to clean water and prenatal care. These issues need to be studied and addressed.

Another plan is to upgrade NYU's online Literature, Arts & Medicine database, which is an incomparable resource for teaching and research. If you Google medical humanities, the site will usually come up first. It's a bit technologically challenged at the moment, but its range and potential are enormous. We need to upgrade it in a number of ways—to make it valuable to anyone who wants to use it.

### *Are NYU students receptive to the medical humanities?*

For the most part, yes. I know how hard medical students work and how valuable each moment is to them. But I don't want students to view our program as an add-on to an already full curriculum. That's not going to work. Medical humanities needs to be threaded through students' time here, so it becomes an essential part of their medical education and later, career.

### *Are the country's changing demographics making it even harder for physicians to identify—and thus communicate—with patients?*

It's more of a challenge, no doubt. I grew up in an America where immigration laws were very restrictive and quotas were in place. By 1950 the United States had the highest percentage of white, native-born people than at any time since the colonial era. This, of course, is no longer the case. Today the patient base is more ethnically and culturally diverse, not to mention older, and in need of different kinds of care. Will a more humanistic approach to medical education be an asset in dealing with these changes? I believe it will.

### *The Journal of the American Medical Association recently ended its long tradition of featuring classical art on its cover. Does this trouble you?*

It's minor stuff. What's much more important is that one of our students just had a think piece accepted by *JAMA*. That is

what we want to encourage. Many students are eager to discuss medical humanities and they need platforms for doing so.

### *How do you choose the topics for your books?*

I often write about subjects that have had a personal impact on my life, such as McCarthyism or polio. I have vivid memories of what life was like every summer before the vaccines. Kids in wheelchairs and leg braces; photos of iron lungs lined wall-to-wall in hospital corridors; beaches and movie theaters closed; newspapers' box scores of children with the disease. Each summer was a nightmare, especially for parents. Mine always sent my brother and me to the mountains, far from the supposedly contaminated cities, even though they couldn't really afford to.

### *What's the topic of your next book?*

Bellevue. I'm telling the story of public health in New York City through the lens of America's oldest and most important public hospital. ●

# Unbroken

Even bones as fragile as matchsticks couldn't stop Jessica Bernstein from standing on her own two feet.

BY GARY GOLDENBERG



**L**ike most newborns, Jessica Bernstein started life with a full-throated cry, the body's way of kick-starting the lungs for life outside the womb. But her first cries were also mixed with howls of pain. One of her legs was severely twisted against her shoulder. X-rays showed that both of Bernstein's legs had broken and healed sometime before she was born. Those findings, along with her slight facial abnormalities—drooping eyes and low, small ears—suggested a genetic abnormality. Tests later revealed that she had osteogenesis imperfecta (OI), an incurable genetic disorder. Also known as brittle bone disease, OI primarily alters the formation of collagen, leaving the bones as fragile as matchsticks.

An estimated 20,000 to 50,000 Americans suffer from the disease.

At 8½ months of age, Bernstein's leg broke spontaneously while she was sleeping. It was her first break since birth, followed by so many more that her parents lost count. There was little doctors could do to protect her, short of wrapping her in a cocoon. In any case, the little girl would have none of it. Unable to crawl or walk, she would sit on her bottom and pull herself along the floor with her arms. Concerned that she might hurt herself, her grandfather built her a scooter. "We put it under her belly," recalls her mother, Christine Cino. "I'd hold my breath, and off she'd go. She had no fear."

When Bernstein turned four, Cino began shuttling her daughter to Montreal for experimental infusions of bisphosphonates, a class of drugs that had originally been developed to treat osteoporosis but which had yet to be tested in the United States as a treatment for OI. The infusions quieted her pain, but her bones remained as brittle as ever. In time, Bernstein learned to walk using crutches and braces.

Later, in a series of rodding procedures, surgeons in Canada implanted metal rods within her femurs and tibias, shoring up her legs, at least for a while. The rods eventually loosened, causing her bones to split. Several rounds of surgery stabilized her legs, but she was confined to a wheelchair for a year, in

PHOTOGRAPHS: KARSTEN MORAN

constant pain. “In all these years,” says her mother, “never once did she ask, ‘Why me?’”

Eager for a fresh approach to her daughter’s care, Cino made an appointment at NYU Langone Medical Center’s Hospital for Joint Diseases (HJD). Under the direction of Patricia Poitevien, MD, clinical assistant professor of pediatrics and orthopaedic surgery, and medical director of inpatient pediatric surgery, a team of orthopaedic surgeons, physiatrists, nurses, physical therapists, and psychologists at HJD’s Center for Children began crafting a treatment plan to get Bernstein back on her feet.

The turning point came in 2010, when Bernstein, then 15, suffered yet another fracture, this one around the rod in her lower left leg. She also had a “nonunion”—a previous break hadn’t fully healed—in her right femur. These complications were not unexpected, says Jenny Frances, MD, assistant professor of orthopaedic surgery. “As children outgrow the rods,” she explains, “their legs tend to bow and break.”

In a series of operations, Dr. Frances replaced the old rods, realigned the bones, and bolstered the nonunion with a metal plate, using small incisions that dramatically reduced recovery times. Bernstein needed two more procedures over the next year or so, each time returning to her exercise regimen within a couple of months, each time feeling better and stronger. Meanwhile, bisphosphonate treatments kept her pain in check.

Dr. Frances has high hopes for Bernstein, now 18, and Bernstein’s mom has high praise for the team at HJD. “They’re angels,” she says. “They’re the most amazing people I’ve ever come across, and they take care of me, too.”

Dr. Frances reports that Bernstein hasn’t needed bisphosphonates for two years. “She’s probably the first child with OI I’ve seen who is exercise crazy,” she says of her patient.

Bernstein’s old fearlessness seems to have resurfaced. “I don’t think I’ll go mountain climbing—not because I’m afraid, but because I can’t do it physically,” she says.



Despite having a condition known as brittle bone disease, Jessica Bernstein flawlessly executes a straddle press handstand and walks without crutches at Rockaway Beach (at left).

Bernstein can walk without any aids, but outdoors, she uses a single crutch for safety. She enjoys riding her three-wheeled bike, swimming, and practicing yoga, which she taught herself from the Internet. She can even execute a straddle press handstand, one of the most challenging poses.

Through daily exercise and a healthy diet, Bernstein, who’s just over four feet tall, has lost 50 pounds (she’s down to 74), which enables her to stretch her limits even further. At nearby Rockaway Beach, she decided one

day to cast aside her crutch because it was too hard to use in the sand. For the first time in her life, she walked on her own two feet, without any aids, achieving a seemingly impossible goal. “Guess what I did today?” she later told her mother. “Even though I didn’t witness it,” says Cino, “it was like seeing my child take her first steps. I couldn’t be more proud of her. She’s my hero.”

This summer, Bernstein’s mom drove her to Kingsboro Community College in Brooklyn so that she could sign up for culinary classes. She has her sights set on a career as a pastry chef. Unconcerned that it may require long hours on her feet, Bernstein says matter-of-factly, “I’m used to standing now—and I have a lot of standing to make up for.” ●

# Coaxing Mute Bones to Speak

For Dr. Bradley Adams and his team of forensic anthropologists, there's only one question: Who are you?

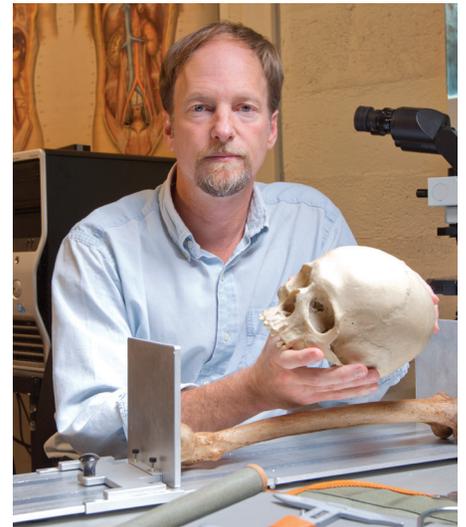
**W**hen the Suffolk County Police Department asked Bradley Adams, PhD, director of the Forensic Anthropology Unit (FAU) for New York City's Office of the Chief Medical Examiner (OCME), to meet them on a desolate stretch of Ocean Parkway one frigid morning in December 2010, they were trying to solve a human puzzle: A few bones were missing from a skeleton discovered two days earlier. "We know the human anatomy so well," says Dr. Adams, referring to his team of eight forensic anthropologists, who are often tapped for their expertise, "that we can immediately tell whether it's the bone of a human or an animal."

As it turned out, the additional bones found that day were not only human, they also belonged to multiple individuals. "The police discovered a second body, then another, and another," recalls Dr. Adams, clinical assistant professor of forensic medicine at NYU Langone Medical Center. Four skeletons were eventually recovered from the undergrowth. Once Dr. Adams and his colleagues examined them in their laboratory on First Avenue and 30th Street, they determined that all were young adult females. That's when investigators knew that, in all likelihood, they were looking for a serial killer.

About 50 times a year in New York City, unidentified remains are recovered. Forensic anthropologists dedicate themselves to solving the most human of all mysteries: answering the question, who are you? The ability to glean information—facts and clues—from skeletal remains is what makes a forensic anthropologist

a detective's detective. They determine gender by evaluating skull features, bone size, and, most important, the pelvis, which in females is configured for childbearing. The upper jaw and eye sockets offer clues to ethnicity. "We can tell the age of children's skeletons by bone and teeth development," Dr. Adams explains. "With adults, we examine wear and tear in the spine, ribs, and pelvis. We also have one of the country's few bone histology labs, where the age of a bone can be estimated." But if the scientists are uncertain, they'll say so. "What we don't want to do," says Dr. Adams, "is send investigators down the wrong path."

Dr. Adams's interest in the field dates back to the childhood summers he spent in his grandfather's funeral home in Salina, Kansas. He was appointed the FAU's sole scientist in 2004, after years of traveling the globe with the U.S. Army's Central Identification Lab, identifying the remains of missing troops. Today, the FAU is the nation's largest unit of its kind, outside the Department of Defense. Its growth is due partly to its enhanced responsibilities following 9/11, when Dr. Adams's predecessor, Amy Zelson Mundorff, supervised dozens of forensic anthropologists brought in from all over the country to sift through the debris to identify human bones and bone fragments. The expanded unit has since carried out two large identification efforts after significant additional pockets of 9/11 remains were discovered during construction in 2006. A forensic anthropologist from the unit is stationed full-time at Ground Zero, just in



Dr. Bradley Adams

case new remains are uncovered.

All this is in addition to the unit's everyday duties: examining unidentified remains found within the five boroughs, consulting with the OCME's forensic pathologists on trauma-related deaths, assisting in field recoveries, training medical students and residents, and conducting research. The unit is also auditing the city's archives of unidentified remains—exhuming skeletons for updated examinations—and assisting other jurisdictions in New York State through a grant from the Department of Justice. It was one such extracurricular assignment that brought Dr. Adams to Ocean Parkway that December, and the following spring, for a second search that turned up six more human skeletons (including two in nearby Nassau County). As with the first group of bodies, the mission of Dr. Adams and his team remains the same: coaxing mute bones to speak.

"It's tough to get an investigation going if you haven't identified the victim," Dr. Adams explains. "That's why every piece of information we can give the police is helpful. It's gratifying to be able to say 'This is what we know about this person,' and then watch the wheels start turning." ●

# Change Change Change Change Change Change Change Change Change

the world...

**One patient at a time.** When you include a bequest in your will to NYU Langone Medical Center you help us deliver outstanding health care to the many patients and families who rely upon us to improve their lives. Superb physicians, an award-winning nursing staff and internationally ranked scientists make the difference.

**Join our community, and create your legacy today.**

To learn more about making your planned gift to NYU Langone, please contact Marilyn Van Houten at 212.404.3653 or [marilyn.vanhouten@nyumc.org](mailto:marilyn.vanhouten@nyumc.org).



Sasha Nialla



[www.NYULMC.org](http://www.NYULMC.org)



NYU LANGONE MEDICAL CENTER

Office of Communications and Public Affairs  
550 First Avenue, New York, NY 10016

