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THE MAGAZINE OF NYU SCHOOL OF MEDICINE

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NYU PHYSICIAN

ON THE COVER:
Photograph by
Michael Grecco

MICHAEL GRECCO

"It feels like a miracle," says Nancy Clayton, one of the first people in the world to receive an artificial mitral valve without invasive surgery. "I'm getting stronger every week."

FEATURES

DEPARTMENTS

NYU School of Medicine
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Medicine at Its Best

I'M ENORMOUSLY GRATEFUL to be a part of a patient-centered organization with a clear and noble purpose: we save lives. This issue of *NYU Physician* highlights two remarkable and inspiring examples. On page 12 you'll read about a landmark cardiac surgery that technically wasn't a surgery at all. Last summer, Mathew Williams, MD, director of our Heart Valve Center, and his team performed one of the first nonsurgical replacements of a diseased mitral valve anywhere. Improbably, the patient, a 73-year-old competitive rower and CrossFit buff, featured on the cover, was back on the water within a few months of the procedure, without a scar. It's an outcome that would have been unthinkable just a few years ago.

Then, on page 24, you'll meet the Doell family, whose irrepressibly jolly six-month-old, Joey, was diagnosed with a diaphragmatic hernia in the womb. At just 34 weeks, he was given a 30 percent chance of survival. Thanks to an extraordinary clinical collaboration among our maternal-fetal specialists and pediatric surgeons, Joey beat the odds. After a heroic surgery, he left the hospital four months earlier than expected and with no monitor or tubes. Today, he's thriving. "He should live a normal life," says pediatric surgeon Jason Fisher, MD, who led the four-hour operation. "Maybe he runs a 10-minute mile instead of an 8-minute mile."

These are just two examples of the outstanding care we provide at NYU Langone—exceptional cases, yet typical of how we practice medicine at its most profound and meaningful. May we never lose sight of our awesome potential to heal and transform lives.

ROBERT I. GROSSMAN, MD, **THE SAUL J. FARBER DEAN AND CEO**

JOHN CARNETT

NEWS FROM MEDICINE

WINTER 2017

ADAPTING TO A NEW FACE, VANQUISHING HEPATITIS B, SMARTER GENE SEQUENCING, AND MORE

NICOLAS ASFOURI/AFP/GETTY IMAGES

"Within one or two generations, we could eradicate hepatitis B worldwide."

CALVIN PAN, MD (SEE PAGE 6)

ONE YEAR LATER, A PROMISE UNBROKEN

Patrick Hardison isn't just adapting to his new face—he's thriving. What we're learning from his success.

BY KENNETH MILLER

Before his face transplant last year at NYU Langone, Patrick Hardison made a deal with his surgeon, Eduardo D. Rodriguez, MD, DDS. "I said, 'You do your part, and I'll do mine,' " recalls Hardison. A former volunteer firefighter from Senatobia, Mississippi, he had been severely disfigured when a burning roof collapsed on his head, destroying his eyelids, lips, ears, and nose, and leaving a mass of scar tissue from the scalp down.

As the world learned, Dr. Rodriguez and his team of over 100 came through on their end, successfully completing the most extensive face transplant ever performed in just under 26 hours on August 15, 2015. "No one had ever replaced so much tissue before, including functional eyelids," explains Dr. Rodriguez, the Helen L. Kimmel Professor of Reconstructive Surgery and chair of the Hansjörg Wyss Department of Plastic Surgery. And one year later, Hardison, for his part, is still making good on his end of the deal. "I wasn't going to let everybody else do all this work, and then suddenly say, 'Okay, forget it,' " says Hardison. "I'm not that guy."

Hardison's commitment to his new face has played a big role in his unusually smooth recovery. Of the 37 men and women who've undergone such procedures, almost all have experienced an episode of acute rejection, usually within 90 days. Hardison still hasn't had one. Aside from a brief viral illness, he has suffered no opportunistic infections or other significant adverse effects of antirejection medications. "Patrick's recovery has amazed us all," says Bruce Gelb, MD, assistant professor of surgery and director of renal transplantation, who designed Hardison's regimen of immunosuppressant medications.

Today, Hardison can perform all the ordinary functions that eluded him for more than a decade after his 2001 accident. The father of five can close his eyes, form normal facial expressions, and eat without pain. His restored ability to blink (and thus keep his eyes clean and hydrated) means he's no longer at risk of going blind. To his delight, he can drive a car again.

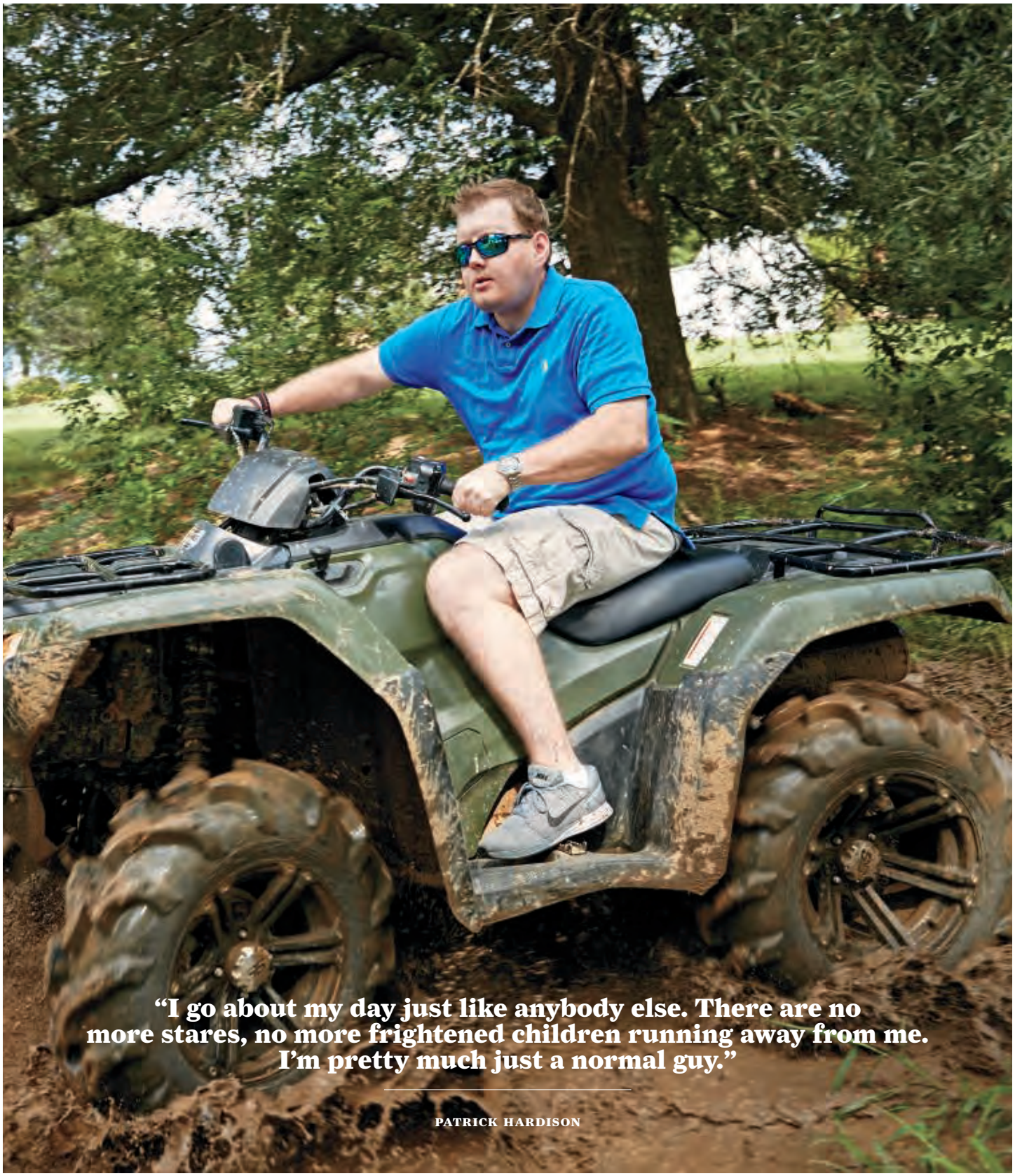
There have been struggles along the way. Hardison had to learn how to swallow and talk again following the surgery, and he's undergone revision surgeries to adjust his new eyelids, lips, and forehead. Even today, his swelling has not yet fully subsided. But compared to other face transplant patients, his progress has been remarkable.

Dr. Rodriguez attributes his success to a variety of factors, including the exhaustive testing that was done to ensure that the donor would be a favorable match. He also credits a dose of rituximab (often used in kidney transplants, but never before in a face transplant) after the surgery to reset immunological memory in Hardison's B lymphocytes, as well as a slower-than-usual postoperative tapering of other antirejection drugs. Another new technique, transplanting portions of the donor's facial skeleton, was used to provide better support for soft tissues, and Dr. Rodriguez theorizes that the bone may be releasing stem cells that are helping Hardison's new face to thrive. Finally, there's Hardison's excellent compliance: he takes his medications faithfully, exercises regularly, and avoids alcohol and tobacco. "I do what I'm supposed to do as well as I can," Hardison notes. "That's what I promised Dr. Rodriguez."

Dr. Rodriguez and his colleagues recently published their findings in a series of articles in the journal *Plastic and Reconstructive Surgery*. The Department of Defense, meanwhile, has awarded Dr. Rodriguez $2.5 million for further research, hoping such methods can be applied to a wide range of composite vascularized allografts.

For Hardison, however, the payoff is already apparent. "I go about my day just like anybody else," he says, marveling at the idea. "There are no more stares, no more frightened children running away from me. I'm pretty much just a normal guy." ●

BEN ROLLINS



“I go about my day just like anybody else. There are no more stares, no more frightened children running away from me. I’m pretty much just a normal guy.”

PATRICK HARDISON

THE KNOCKOUT PUNCH FOR HEPATITIS B?

A landmark study describes a treatment protocol that could eliminate the transmission of the virus from mothers to infants.

BY MICHAEL EISENSTEIN

THANKS TO routine childhood immunizations introduced in the early 1990s, the transmission of hepatitis B has plummeted by nearly 90 percent in the U.S., especially from mother to infant—the most common route of infection in children. Yet the virus continues to pose a major threat globally. The World Health Organization estimates that 2 billion people worldwide have been infected with hepatitis B, which can cause cirrhosis and liver cancer.

Prevention is considered the most effective treatment, yet fewer than 30 percent of babies worldwide receive the vaccine at birth. For those who do, protection can be compromised when infected mothers have high levels of the virus replicating in their bloodstream. The consequences can be devastating: a child infected at birth has a 90 percent chance of battling the disease for life.

Now, NYU Langone gastroenterologist Calvin Pan, MD, and colleagues have validated a simple intervention that could finally put an end to hepatitis B infections, and it costs less than $10 per patient in many developing countries, where it stands to make the greatest impact. "Within one or two generations, we could eradicate hepatitis B worldwide," says Dr. Pan, a clinical professor of medicine at NYU School of Medicine, who has been researching hepatitis B for over a decade.

Dr. Pan and his team were recently struck by the fact that postnatal immunizations against hepatitis B tended to fail in infants born to mothers with high viral loads. The finding sparked Dr. Pan's interest in a widely used antiretroviral medication called tenofovir, known to reduce levels of HIV in the blood of pregnant women and prevent transmission to their newborns. The scientific literature suggested that the medication could potentially do the same for hepatitis B, but the supporting studies were limited in scope.

85%

Percentage of viral hepatitis deaths that occur in Asia, East Africa, North Africa, and West Africa

So in March 2012, Dr. Pan and colleagues set out to decisively address the question of whether tenofovir protects against maternal transmission of hepatitis B with a randomized, controlled trial conducted in five locations throughout China, where hepatitis B is endemic. The study, sponsored by Gilead Sciences, manufacturers of tenofovir, enrolled 200 pregnant women 20 to 35 years of age with high levels of hepatitis B virus. As described in a recent *New England Journal of Medicine* article, the results were striking: Tenofovir administered in the third trimester of pregnancy through one month after birth sharply reduced the mothers' viral load. Furthermore, transmission of the virus occurred in just 5 percent of the infants in the treated cohort, versus 18 percent in the control group. A closer analysis of the data suggests that the degree of protection may be even greater. "We think the transmission rate is probably less than 1 percent," Dr. Pan says.

The intervention promises to be particularly beneficial in sub-Saharan Africa and East Asia, where hepatitis B infects up to 10 percent of the population, and people often lack medical resources. Generic versions of the drug, now in use for HIV, should make this treatment accessible and affordable. "In many countries, tenofovir is as cheap as $3 for a month's worth of pills," says Dr. Pan, putting the price of prenatal prevention at just $9 per mother.

Dr. Pan is now working with American and Chinese officials to expand the treatment. "My prediction is that this will be a seminal study that will change the way we treat hepatitis B globally," says Mark Pochapin, MD, the Sholtz/Leeds Professor of Gastroenterology and director of the Division of Gastroenterology and Hepatology at NYU Langone. "It's a very big deal." ●

HARRY CAMPBELL

AMPED UP

Can mild electrical zaps to the brain, administered at home with online supervision, alleviate some of the debilitating symptoms of multiple sclerosis? A first-of-its kind study aims to find out.

BY KAREN HOPKIN

The woman sits alone at her desk, a laptop before her and a large plastic tackle box at her side. She pops open the box and removes a headset wired to a handheld device by a set of red and black electrical cables. After snapping a pair of moistened sponges to the front of the headpiece, she slips the rig over her head. On the laptop, a technician supervising the setup via a video link conducts a safety check, then provides the woman with a four-digit code that will unlock the device. Once activated, it sends a mild pulse of electricity into her brain.

It may sound like a scene from a high-tech spy thriller, but this setup is actually part of a first-of-its-kind experimental treatment offered by NYU Langone's Multiple Sclerosis Comprehensive Care Center. The goal is to relieve the debilitating fatigue and cognitive impairment commonly caused by multiple sclerosis (MS), a neurodegenerative disease that affects an estimated 400,000 Americans and 2 million people worldwide. "We're always looking for new ways—especially nonpharmaceutical ways—to treat these symptoms and enhance quality of life in patients with MS," says clinical neuropsychologist Leigh Charvet, PhD, the center's research program director, who—along with the center's director, Lauren Krupp, MD, the Nancy Glickenhaus Pier Professor of Pediatric Neuropsychiatry—joined NYU Langone last year from Stony Brook Medicine.

In MS, the body's immune system mounts an attack on the protective myelin sheath that covers the nerves in the central nervous system. The symptoms—wide ranging and often debilitating—include muscle weakness, muddled thinking, severe exhaustion, and depression. With the cause of MS unknown, therapies are aimed at managing the symptoms, with varied success. "There is no FDA-approved therapy for fatigue or cognitive impairment associated with the disease," notes Dr. Krupp. Antidepressants are notoriously hit or miss.

This is where the electrodes come in. Some studies suggest that a mild form of electrical stimulation called transcranial direct-current stimulation, or tDCS, can boost brain activity and improve cognition and mood. But the supporting science is limited. Most of the trials to date have included very few subjects or used only one or two sessions. Moreover, few studies have tested the technique on people with MS—owing, perhaps, to the nature of the disease. "It's a real drain for patients to travel in for therapy day in and day out," explains Dr. Charvet. "Many of them juggle work and family obligations or are so disabled that they are dependent on a caregiver or don't have access to transportation."

As a solution, Dr. Charvet has sought to adapt the procedure so that it can be performed in the home with online supervision from a technician. Remote monitoring is not only easier for patients, but it has enabled her team to conduct a large number of treatment sessions—enough to see meaningful results—while maintaining the standards of an in-clinic visit.

Initial tests indicate that remote monitoring works. In a recently completed trial, participants were sent home with computers and asked to play customized brain-training games as members of Dr. Charvet's team tracked their progress from the clinic. The results showed that participants displayed a significant improvement in mental function, and just as important, demonstrated that remote monitoring can be used successfully to provide cognitive rehabilitation outside a clinical setting.

To test this approach with tDCS, Dr. Charvet has since collaborated with a biomedical engineer and medical device manufacturer to custom-design a device and a headset tailored to people with MS. The apparatus delivers a mild current to the dorsolateral prefrontal cortex, a part of the brain, just behind the forehead, involved in mood, alertness, and some aspects of cognition. The stimulation program runs for 20 minutes, during which subjects are observed as they engage in a variety of cognitive exercises on the computer.

The debut trial, conducted on 25

Researchers Leigh Charvet (on screen) and Kai Sherman

"We're always looking for new ways—especially nonpharmaceutical ways—to treat these symptoms and enhance quality of life in patients with MS."

LEIGH CHARVET, PHD, CLINICAL NEUROPSYCHOLOGIST

patients, demonstrated that the method was safe and feasible. "We had over 96% compliance, and we never had to discontinue a session because of pain or tolerability issues," says Dr. Charvet, who published her findings last year in the journal *Neuromodulation*. The study also showed positive effects on information-processing speed, mood, and fatigue. "These are the kinds of things that people with MS really struggle with," explains Dr. Krupp. Some participants even showed improved gait and overall physical activity. "That was totally unexpected," she adds. "So I think there's a tremendous amount of promise with this approach, which is offered only at NYU Langone."

How much of the benefit stems from electrical stimulation instead of, say, the daily online interaction with a supportive technician or the simple feeling of being helped? To find out, the team recently extended their study to include a placebo condition.

Whatever the mechanism, Dr. Charvet believes the at-home protocol could potentially help mitigate symptoms from a broad range of conditions. She's now collaborating with researchers at NYU Langone's Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders to test whether it can be adapted for use in Parkinson's disease. "This tool is perfectly aligned with our clinical mission to enhance patients' potential and minimize their symptoms," says Dr. Krupp. ●

PETER ROSS

SEEING EVERY MISTAKE

A high-fidelity DNA sequencing technique developed at NYU Langone spots mutations that can give rise to superbugs and cancer much sooner than traditional tools.

BY BRYN NELSON

Most hospitals work hard to contain infections, but bacteria often work harder to outwit them. One in 15 patients admitted to a hospital in the U.S. will catch a bacterial infection during their stay. More than 800,000 patients a year will pick up methicillin-resistant *Staphylococcus aureus*, better known as MRSA, a superbug that defies nearly all antibiotics. While medical centers rely on sophisticated DNA sequencing methods to detect the spontaneous mutations that give these nasty pathogens their deadly edge, some mutations are so uncommon that even the best sequencing methods fail to see them. "Nobody has been able to directly monitor these rare mutations in real time," says Evgeny Nudler, PhD, the Julie Wilson Anderson Professor of Biochemistry in the Department of Biochemistry and Molecular Pharmacology at NYU Langone Medical Center.

Now, he and colleagues have developed a potentially industry-changing technique, dubbed maximum-depth sequencing, that can detect exceedingly rare DNA variants in cell populations. The method allows researchers to identify and monitor DNA mutations as they occur in the population, even those that are quickly corrected or that condemn the cells to die, says Dr. Nudler, an investigator with the Howard Hughes Medical Institute. The unbiased and highly sensitive technique, which he and his group recently described in the journal *Nature* and are in the process of patenting, could help researchers pinpoint mutational hotspots and new sources of antibiotic resistance, as well as reveal hidden DNA repair pathways. The high-fidelity sequencing may even help researchers pinpoint cancer-prone cells well before they form tumors.

Instead of sequencing the cell's entire collection of DNA, the new method uses molecular barcodes to tag smaller, more strategic stretches of the DNA, which can then be directly tracked and independently copied. The approach, developed in the Nudler lab by MD/PhD student Justin Jee and postdoctoral fellow Aviram Rasouly, PhD, enriches the number of true mutations while eliminating errors introduced during the sequencing process. "Because our method is so sensitive, we are seeing things that people haven't seen before," Dr. Nudler says.

Using maximum-depth sequencing, the researchers have discovered that specific regions of the *E. coli* genome acquire mutations 10 times as fast as other regions. Moreover, the group found that the mutation rate was far higher for bacterial genes that produce proteins less often, unexpectedly suggesting that protein-manufacturing machinery, including the cell's ribosomes, may put the brakes on DNA mutations and play an important role in maintaining genomic stability. Uncovering the basis of such error-prone sites and stabilizing mechanisms, in turn, might reveal new ways to disrupt dangerous microbes.

The study also directly supports a hotly debated hypothesis that antibiotic exposure may actually speed up the rate of bacterial mutation. Based on his research, Dr. Nudler believes a class of antibiotics that disrupt the outer cell wall of some bacteria, such as ampicillin, may in fact suppress DNA repair. "If you inhibit this process, then the mutation rate goes up," he says. In other words, certain antibiotics may be indirectly fueling the mechanism that defeats them.

Maximum-depth sequencing isn't just limited to bacteria. It could also help researchers identify rare cancer-linked mutations in body fluids. Dr. Nudler's lab is exploring this avenue with biopsy and blood samples from cancer patients. "The point is to see whether we can accurately and consistently detect mutations not in the tumor but in the bloodstream," he says. If so, the technique might provide a powerful new tool for early cancer diagnoses and for monitoring anticancer therapies.

To help expand the "high potential" of maximum-depth sequencing, Dr. Nudler says, his lab developed the necessary molecular biology methods as well as computational tools to streamline the analysis. "Now the community can take advantage of both of them," he says. ●

LAURENT CILLUFFO

"Because our method is so sensitive, we are seeing things that people haven't seen before."

EVGENY NUDLER, PHD, JULIE WILSON ANDERSON PROFESSOR OF BIOCHEMISTRY IN THE DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR PHARMACOLOGY

Nancy Clayton, just a few months after receiving an experimental mitral valve, prepares for her morning workout.

Back

(and Better Than Ever)

Doctors at NYU Langone are pioneering a revolutionary approach to heart valve replacement—one that requires no surgery.

AT 10:00 ON a bright August morning, Nancy Clayton met her rowing coach at a marina in Newport Beach, California. The two exchanged a long hug. "I can't believe you're back," exclaimed the coach, a fit young woman named Jill Clapp. "I can't, either," Clayton said. ■ Together, they carried Clayton's single-scull racing boat to the dock and slid it into the water. Clayton climbed aboard the low-slung craft, moving carefully to keep the narrow hull from tipping over. Then, she pushed off into the bay, her legs pumping and her seat sliding back and forth with each sweep of her oars. Clapp followed in a motor launch. ■ Other boaters out that day might have been shocked to learn that the rower skimming past them—with her stylish blond bob and sleek athletic togs—was 73 years old. But there was something even more astonishing about Clayton: just five weeks earlier, doctors had replaced a diseased valve in her heart.

By Kenneth Miller

Photographs by Michael Grecco & Jonathan Kozowyk

“This technology represents the future. Someday, I hope we can offer it to everyone.”

DR. MATHEW WILLIAMS

As she paddled, she recalled her two previous valve procedures, open-heart surgeries that required months of grueling recovery. This time, she'd traveled across the country to NYU Langone Medical Center, where she'd volunteered for a groundbreaking experiment: a mitral valve replacement involving no surgery at all. Now, here she was, propelling herself through a light chop, pelicans wheeling overhead, and so far, she'd barely broken a sweat.

A few hundred yards offshore, Clapp pulled alongside. "Ready for some drills?"

Clayton felt a surge of anxiety. This would be her first major workout since the operation. How would her newly mended heart behave? There was only one way to find out. "Let's go," she said.

NANCY CLAYTON HADN'T planned to make medical history in January 2016, when she phoned Aubrey Galloway, MD, the Seymour Cohn Professor of Cardiothoracic Surgery and chair of the department. All she wanted was a second opinion from a physician who years earlier had amply earned her trust.

Born with a malformed aortic valve, Clayton had been defying the odds for seven decades. As a girl, she'd ignored her worried mother's ban on exercise and become an avid fitness buff. After valve-repair surgery in her early 30s, she went back to the gym as soon as she was able. When the repair gave out, she was 58 years old and living in New York City. She needed a mechanical replacement valve and a pacemaker, along with a procedure to enlarge her aortic root so that the new valve would fit. Clayton's husband, Zane Miranda, MD, a dermatologist who'd done his residency at NYU Langone, had heard from a colleague that Dr. Galloway was a leader in his field.

In a dramatic twist, the operation took place on September 11, 2001, as the towers collapsed five miles downtown. Dr. Galloway had just connected Clayton to a heart-lung machine and was sawing open her chest when the second plane hit. Every few minutes someone rushed into the operating room with an update. "Please keep the door shut," Dr. Galloway said sternly. "What's happening is horrible, but we can't do anything about it right now. We've got to take care of our patient."

Fourteen years later, after following her son and two grandchildren to Southern California, Clayton was in the best shape of her life. Most days, the nonprofit marketing specialist spent an hour practicing with her competitive rowing team or an hour doing CrossFit training—or both. But one morning in late 2015, she felt unusually winded as she labored at the oars. Over the following weeks, her shortness of breath worsened, and she developed a chronic cough.

When Clayton's doctor ruled out bronchitis, she went to see her cardiologist. The tests came back with distressing news: this time, the problem wasn't with her aortic valve. Instead, she had mitral valve regurgitation—a disorder in which the valve fails to close completely, causing some blood to flow backward into the heart's upper chamber. Eventually, the condition can lead to congestive heart failure. Clayton had begun to reach that stage.

The question was how to treat it. For an elderly patient who'd already undergone two open-heart surgeries, a third could be debilitating, even fatal. But while far gentler alternatives had been developed for the aortic valve, such options for its mitral counterpart were severely limited.

So she called Dr. Galloway. Soon afterward, Clayton returned to NYU Langone for another brush with history—this one more auspicious.

THE MITRAL VALVE serves as the heart's gatekeeper, regulating the flow

Dr. Mathew Williams, the first person to receive dual training in interventional cardiology and cardiac surgery, has performed more catheter-based aortic valve repairs than any surgeon in the U.S.

It Takes a Village

The team behind Nancy Clayton's landmark heart-valve procedure: (1) Rachel Vania-Velasco, RN, circulating nurse (2) Maurice Singleton, RN (3) Muhamed Saric, MD, PhD, director, noninvasive cardiology (4) Cezar Staniloae, MD, assistant director, Heart Valve Center (5) Rosemarie Harrington, surgical technologist (6) Hasan Jilaihawi, MD, associate director, Heart Valve Center (7) Michael Querijero, physician assistant, director of operations and program development, Heart Valve Center, and Tara Collins, senior clinical physician assistant (8) Maurice Singleton, RN, Rachel Leibovici, RN, Michael Concepcion, surgical technologist, Michael Bautista, surgical technologist, and Candice Crispino, RN (9) Peter Neuburger, MD, assistant professor of anesthesiology, perioperative care, and pain medicine.


8


7


Maurice


9

Aubrey Galloway, MD, a pioneer of minimally invasive cardiac surgery, with patient Nancy Clayton last summer. Dr. Galloway, who operated on Clayton's aortic valve on September 11, 2001, referred her to Dr. Mathew Williams when her mitral valve began to fail 14 years later.

of oxygenated blood from the left atrium into the left ventricle. Because it handles higher pressure levels than the other three cardiac valves, it often gives out first. At its top, a fibrous ring called the annulus supports two leaflets, whose motion is controlled by cordlike tendons. Mitral valve regurgitation (MR) occurs when the leaflets don't meet properly, allowing blood to flow backwards.

MR is the most common form of valve disease, affecting an estimated 4 million Americans. The type Clayton had—known as degenerative MR—often results from simple wear and tear. Although mild cases can often be controlled with medication, the only effective treatment for severe MR may be to repair or replace the errant valve. Yet of the 1.7 million patients who become eligible for mitral-valve surgery each year, only 30,000 undergo it.

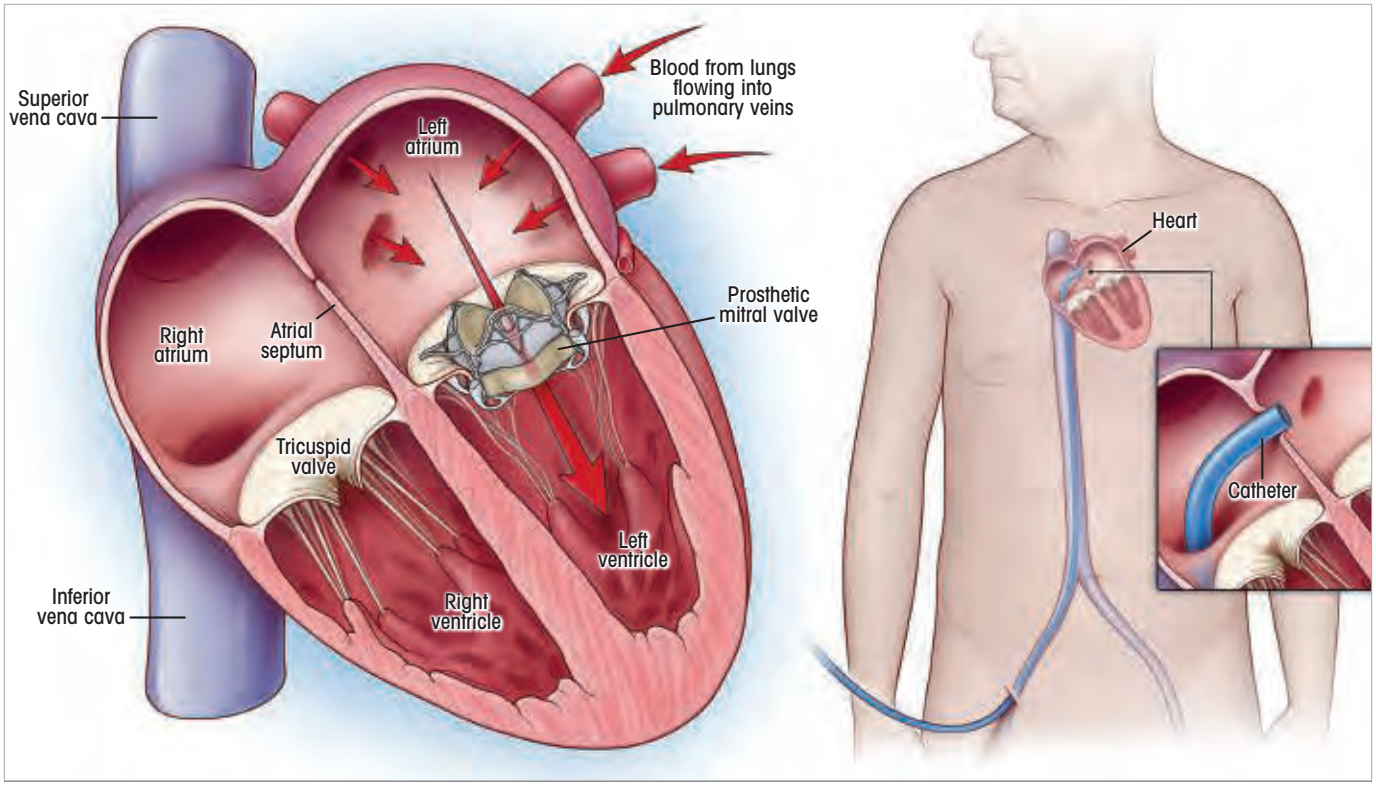
One important reason for this, many studies suggest, is that MR is strongly associated with advancing age—and older people tend to be poor candidates for the rigors of open-heart surgery. Some are too frail to survive such a procedure; others may be unable or unwilling to weather the months of painful recovery that follow. "These surgeries work very well, but they're not for everybody," says Mathew R. Williams, MD, associate professor of cardiothoracic surgery and medicine, and director of the Heart Valve Center.

Over the past two decades, researchers have developed an array of techniques aimed at reducing the impact of valve repair or replacement procedures on patients' bodies. Such methods are usually reserved at first for those at high risk of dying from surgery, but they may be approved for a broader population as technologies are refined and data on safety and efficacy accrue. One of the most widely used forms of minimally invasive cardiac surgery was pioneered in the 1990s by Dr. Galloway. Known as the minithoracotomy, it provides access to the heart between the ribs instead of through the breastbone—shrinking the incision, decreasing the trauma, and lessening the likelihood of complications. But even that approach, which still requires stopping the heart and using a heart-lung bypass machine, may be too taxing for many patients.

More recently, advances in imaging and other technologies have enabled a growing number of cardiovascular procedures to be performed percutaneously—that is, through a skin puncture rather than an incision. The best-known example may be transcatheter aortic valve replacement (TAVR), which has given a new chance at life to as many as 50,000 desperately ill patients in the U.S., and thousands more abroad. Guided by live imaging, an interventional cardiologist typically inserts a catheter through a puncture in the groin, snakes it through the femoral artery, pushes the old valve out of the way, and seats the substitute in its place. Because the heart continues to beat, no heart-lung machine is necessary. The FDA approved TAVR for inoperable patients in 2011, for high-risk patients in 2012, and for moderate-risk patients in August of this year. Trials are under way for the low-risk cohort. About 30% of aortic valve replacements are now performed by this method.

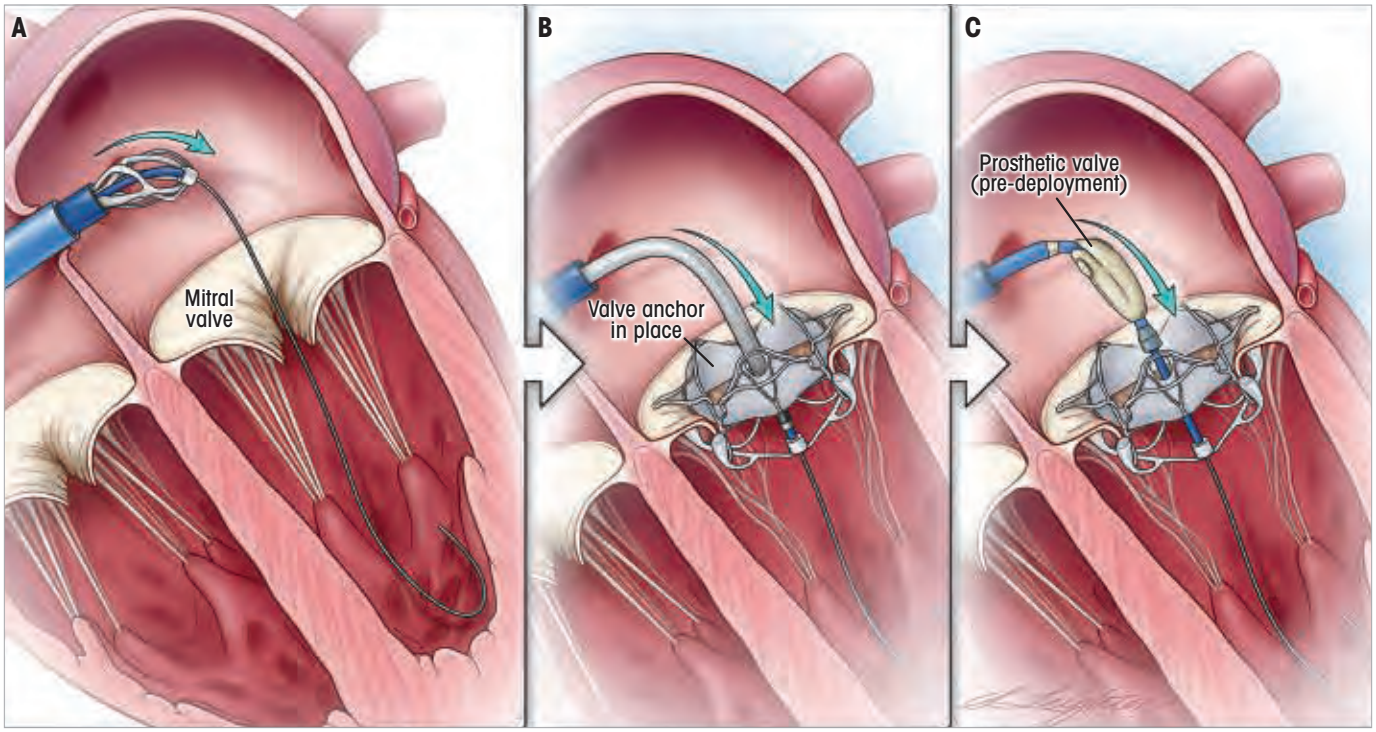
"TAVR has changed the standard of care for aortic valve disease in older patients," Dr. Galloway observes. "If we can do something similar for mitral valve disease, it will be transformative."

But it won't be easy. The mitral valve presents a gauntlet of obstacles. Unlike the aortic valve, it can't be accessed directly through an artery; instead, the catheter must penetrate the wall of the heart, creating major technical challenges for device designers and operators. The aortic valve, moreover—with its round annulus at the end of a gently curving tube—is a much simpler structure. The mitral valve's annulus is large and



Replacing a Mitral Valve without Surgery

Nancy Clayton is one of the first people in the world to receive a new catheter-based device designed expressly to replace a diseased mitral valve. It's a two-stage design, with an anchoring ring installed separately from the valve itself. Each part can be withdrawn and repositioned repeatedly for a better fit. "With other devices, once you've placed it, you're done," explains Clayton's surgeon, Mathew Williams, MD, a pioneer in heart valve repairs. "There's no retrievability." Mitral valve regurgitation, in which the valve's leaflets fail to close properly, is the most common form of valve disease, affecting an estimated 4 million Americans. Of the 1.7 million candidates who are eligible for mitral-valve surgery each year, only 30,000 undergo it, largely because they are too frail to endure invasive surgery.



SCOTT LEIGHTON

saddle-shaped, and contracts each time the leaflets close. The atrium above it is a tight space, with little room to maneuver.

That's why progress on transcatheter treatments for mitral valve disease has been comparatively slow. In this country, the sole device available for percutaneous repair of MR is the MitraClip, approved by the FDA in 2013 for high-risk patients with the degenerative form of the disease. The clip works by gripping the edge of the leaflets, pulling them closer together. But while it reliably reduces severe regurgitation to a more manageable level, it seldom eliminates the condition completely.

For patients like Nancy Clayton, who would benefit from mitral valve replacement rather than repair, the transcatheter option is available only through a clinical trial. Dr. Williams, who has performed nearly 3,000 TAVRs, more than any other U.S. surgeon, is one of just a handful of surgeons worldwide authorized to conduct such studies.

"I'm getting stronger every week, and I absolutely expect to get back to where I was before. It feels like a miracle."

WHEN CLAYTON contacted Dr. Galloway early this year, he suggested that she might be a candidate for a MitraClip instead of surgery, and referred her to Dr. Williams. After examining her test results, Dr. Williams told Clayton, "We may have something else for you."

Clayton flew to New York a week later. Dr. Williams explained that there were three possible alternatives for treatment. The first was the MitraClip, which could stabilize her condition but might not enable her to return to the active way of life she cherished. The second choice was open-heart surgery. Dr. Williams, the first physician in the U.S. trained in both interventional cardiology and cardiac surgery, felt confident that he and his colleagues could safely replace her mitral valve by this method, as they had done for many other high-risk patients. But he warned that she was at elevated risk for complications largely due to her prior surgeries, and her recovery would likely be even more challenging than it was 15 years earlier, when she endured six weeks of chest pain and exhaustion.

Then came the third choice: transcatheter mitral valve replacement, or TMVR. About two dozen manufacturers were developing such devices, Dr. Williams said, and a few had begun human trials. The results so far had been less than stellar, with 30-day mortality rates ranging from 25% to 50%. In part, this reflected the advanced age and severe illness of most trial participants; many died of causes unrelated to their valve replacement soon after the procedure. But in other cases, the devices themselves may have contributed to the problem. All of the implants were designed to be delivered through the apex of the heart. This is the most direct route to the mitral valve, but it requires entering through an incision in the chest and placing stitches in the apex, both of which are physiologically stressful.

Dr. Williams, however, had been selected to test a new device that took a fully percutaneous approach. As with the MitraClip, the catheter was inserted through the groin and up the femoral vein, then pushed through a tiny puncture in the atrial septum—the inner wall that separates the upper right and left sides of the heart. Although more difficult for clinicians, transseptal delivery was far easier on patients.

The new device had other potential advantages, as well. Unlike other TMVR

CROSSFIT

systems, it was expressly designed for the mitral valve, rather than repurposed from an aortic device. An anchoring ring was installed separately from the valve itself, which made for less bulk. Each part could be withdrawn and repositioned repeatedly for a better fit. "With other devices," Dr. Williams explained, "once you've placed it, you're done. There's no retrievability."

Thanks to recent changes in FDA policy, he added, the artificial mitral valve would be the first TMVR device to begin early feasibility studies in the U.S. rather than Europe or elsewhere in the world, and Clayton could become the first human subject to receive the implant. She asked for some time to deliberate, and flew back to California.

"I was up every night, stressed to the max," Clayton recalls. The conventional options were unappealing, she thought, but their risks were known. With TMVR, Dr. Williams had cautioned her, the potential complications were similar—stroke, fluid buildup around the heart, or dying during the procedure—but no one could gauge the odds.

Clayton's family rallied to help with the decision. After speaking with Dr. Williams and Dr. Galloway, her son, a veterinary cardiologist, thought TMVR was the right decision. Her husband agreed. But it was her own research that finally convinced her. "I googled Dr. Williams," she recalls, "and people were calling him a genius." She told him she was willing—though she preferred to be the second subject, not the first.

A woman in her 80s preceded her, on June 15. The procedure went perfectly.

CLAYTON'S TURN CAME on July 7. At 8:30 a.m., she was wheeled into NYU Langone's newest state-of-the-art hybrid OR (one of two at the Medical Center equipped for both cardiac surgery and interventional cardiology) and placed under general anesthesia. More than a dozen clinicians joined Dr. Williams around the movable operating table, which was encircled by a C-arm fluoroscope. A bank of wide-screen monitors glowed overhead. With Clayton mostly hidden under surgical drapes, the procedure that followed looked more like a video game than surgery, albeit one with a real life at stake.

As Muhamed Saric, MD, PhD, associate professor of medicine and medical director of noninvasive cardiology, inserted a special camera scope down Clayton's throat, a video of her mitral valve appeared onscreen—the regurgitation clearly visible. After inspecting the anatomy on display, Dr. Williams pushed a catheter roughly the width of a permanent marker into Clayton's right groin, using a control handle studded with dials and switches to slowly thread it up the vein. He used other controls to continually reposition the table and C-arm, enabling the X-ray camera to follow the action. On the monitors, the catheter appeared as a sinuous gray form, silhouetted against a tracery of blood vessels.

When the tip of the catheter reached the heart, the full-color, computer-enhanced echocardiography became crucial. Dr. Saric kept up a constant dialogue with Dr. Williams, changing the angle and focus of the echo camera as needed to ensure millimeter-scale accuracy. Entering the right atrium, Dr. Williams used a retractable needle to pierce the septum. He advanced into the left atrium, steering sharply downward toward the mitral valve. Then, he loaded the two-stage device—its components rolled like umbrellas—into the catheter.

The anchoring unit emerged first, slipping down into the diseased valve. As the unit unfurled, a network of metal-alloy braces spread across the underside of the annulus. On top of the annulus, a cloverleaf-shaped receptacle unfolded. Using a tiny grasping tool, Dr. Williams positioned the anchor for maximum stability and locked it into place. Finally, he deployed the replacement valve (a metal frame with three porcine-tissue leaflets sewn into the middle) and attached it to the anchor. In an instant, Clayton's new mitral valve was opening and closing smartly with each heartbeat.

At 12:30 p.m., Dr. Williams called out, "That's it! Thanks, everyone." As Clayton was rolled out to the recovery room, the sense of relief was palpable. She had survived the operation. But no one could say what would come next.

SADLY, THE FIRST patient to receive the experimental mitral valve died a month after the procedure, of noncardiac problems that the device was not meant to solve. Clayton, however, was up and walking less than two hours after the procedure. She was discharged from the hospital four days later (she could have gone home after just one day if her blood thinners hadn't needed adjusting), and she was back on the treadmill the next morning. Within two weeks, she was walking two miles a day. Three weeks after that, she returned to Newport Bay.

Clayton ran through a series of exercises emphasizing the upper or lower body, as Coach Clapp shouted, "Square your blade! Straighten your back!" She tried to pay attention to her form, but waves of joy kept distracting her. Although she had to stop and catch her breath every 10 minutes or so, she managed to keep going for a half-hour before Clapp suggested they head back to shore. "How did that feel?" the coach asked as they stepped onto the dock. Clayton just grinned.

Today, she has resumed her old exercise schedule, functioning at what she gauges to be 80% of her potential capacity. "I'm getting stronger every week," Clayton reports, "and I absolutely expect to get back to where I was before, and then some. It feels like a miracle."

That miracle was made possible by techniques that could hardly have been imagined until recently. "If you'd told me 10 years ago that we could replace mitral valves percutaneously, I would have said, 'You're crazy,' " Dr. Saric says with a laugh.

Yet such wonders aren't likely to remain rare for long. "These devices are in their infancy, and we still need to see which ones will work best," says Dr. Williams. "But this type of technology represents the future. Someday, I hope we can offer it to everyone." ●

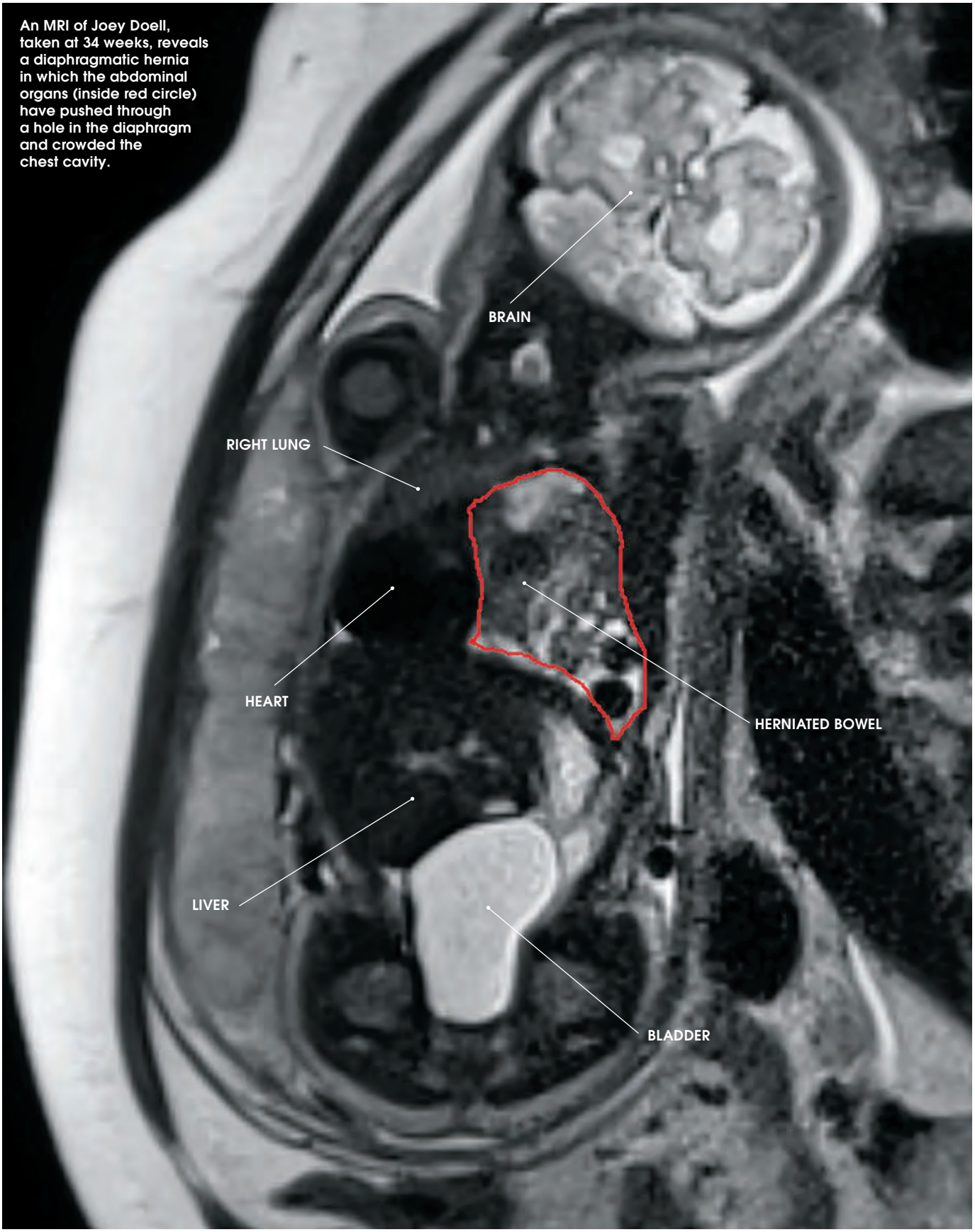
Hope Comes Early

An extraordinary clinical collaboration at NYU Langone is helping pregnant mothers and their babies survive birth defects and prenatal complications once deemed too complex to treat.

BY AMY ENGELER — PHOTOGRAPHS BY WALTER SMITH

JUST WHEN her last two months of pregnancy seemed like a final lap, 29-year-old JACLYN DOELL's water broke. At first, it was just a few drops during breakfast with husband, Nick, her college sweetheart, in their home in Little Falls, New Jersey. Then came the deluge at a staff meeting at a nearby community hospital, where Doell works as a pediatric intensive care nurse. Alarmed but calm, she went upstairs to see her obstetrician—and suddenly a routine pregnancy became a crisis.

The Doell family at their home in Little Falls, New Jersey.



An MRI of Joey Doell, taken at 34 weeks, reveals a diaphragmatic hernia in which the abdominal organs (inside red circle) have pushed through a hole in the diaphragm and crowded the chest cavity.

An ultrasound showed the baby's heart pushed too far to the right. Then, an MRI confirmed a rare, devastating birth defect: a congenital diaphragmatic hernia (CDH), in which the stomach, intestines, spleen, and other organs squeeze through a breach in the diaphragm, crushing into the chest cavity where the lungs would normally develop. Of the estimated 1,600 babies diagnosed with this condition each year in the U.S., nearly half do not survive. For the Doells' baby boy, the prognosis was considerably worse. He was given a 33 percent chance of survival, and he would almost certainly require a heart-lung bypass machine at birth. "I work with critically ill children," says Jaclyn. "I've seen a lot. But being on the other side was a complete shock."

Since the hospital wasn't equipped to care for such a critically ill newborn, Jaclyn was transferred to NYU Langone Medical Center, where she was admitted to the new Fetal Diagnosis and Treatment Program, a tightly knit team of some 50 obstetric and pediatric specialists who handle the most precarious high-risk pregnancies and life-threatening congenital defects. She was put on bed rest at Tisch Hospital under the watch of Ashley Roman, MD, clinical assistant professor of obstetrics and gynecology, and director of the Division of Maternal Fetal Medicine.

Nationwide, one in 33 newborns suffer from a birth defect. Of the 6,200 babies delivered at NYU Langone last year, about 200 fell under the care of the Fetal Diagnosis and Treatment Program. Two-thirds of the cases had critical congenital heart defects requiring surgery within six months of birth. Others had lung or chest masses, obstructed or perforated bowels, oral-facial clefts, or congenital diaphragmatic hernias, like baby Doell. There were more than a dozen cases of distressed twin or triplet pregnancies. Left untreated, many of these conditions would have proved fatal.

Overall, the program can handle about 95 percent of all fetal abnormalities and maternal complications, according to Dr. Roman. Such exceedingly complex pregnancies require a high level of collaboration, so the program taps into more than a dozen different specialties, including ones in maternal-fetal medicine, neonatology, pediatric surgery, pediatric cardiology, pediatric neurosurgery, genetics, and social work. Team members assemble twice each month, under the direction of Dr. Roman, to discuss cases and devise treatment strategies. Every detail is worked out in advance: What is the optimal time for birth, allowing the best possible outcome? Does the baby need surgery within minutes or days after delivery? Who needs to be present? Is prenatal surgery feasible or beneficial?

"This is not something that is done at all hospitals," explains Dr. Roman. "This program exists because studies show that when you get everyone in a room together and come up with a plan as a team, patients get better care."

Jason Fisher, MD, had a plan. If Jaclyn could make it one more month, to 36 weeks, the baby's lungs would theoretically be strong enough to maximize his chances for survival. "The goal was to reposition the baby's organs and patch the hernia within the first few days after birth, as long as the heart and lungs were strong enough to withstand surgery," says Dr. Fisher, a pediatric surgeon at NYU Langone's Hassenfeld Children's Hospital of New York. But it was a calculated risk. With her amniotic sac broken, Jaclyn's womb was no longer a sterile environment. Even on bed rest, the "clock of infection" was ticking.

"Those days were hard for us. I think Nick and I cried every day, all day. We were grieving for the child we could lose."

Jaclyn rested and tried to prepare herself emotionally. She and her husband canceled their baby shower. "The last thing we wanted was a room full of baby things if he didn't make it," she recalls. "Those days were very hard. I think Nick and I cried every day, all day. We were grieving for the child we could lose."

Another week passed. Joey's lungs were roughly the size of pea, but there was no way to predict how well his lungs would function, or estimate the baby's resilience. That meant the Doells needed to make some decisions. "Dr. Fisher took time to make sure we fully understood what we faced," says Jaclyn. "Ultimately, we didn't want the baby to suffer unnecessarily. If the heart-lung machine could help him survive, then go ahead. If his function was poor, and his heart stopped or he had a stroke, don't let him suffer."

Then, quite suddenly, the plan changed. The next Sunday afternoon, just 34 weeks into the pregnancy, Jaclyn went into labor. When four hours passed with little progress, the vaginal birth she once hoped for became impossible. "I just did not have the capacity to cope," she says. "It was too much."

Dr. Fisher's team assembled that evening at 11:00 p.m. and stood by as Shilpi Mehta-Lee, MD, assistant professor of obstetrics and gynecology, performed the cesarean. "Look up, look up," Dr. Mehta-Lee urged Jaclyn as she held the baby momentarily over the drape, giving the mother a glimpse of her newborn son, Joey. Then, she handed him to a team from the KiDS of NYU Neonatal Intensive Care Unit, which intubated him before he could let out a cry.

Joey was gravely ill. His heart, squeezed by the displaced organs, struggled to keep up. With uneven pressure between the heart chambers, it raced up to 200 beats per minute. But somehow he was strong enough to get by without the heart-lung bypass machine—a sliver of encouraging news. Nick sat at Joey's bed and watched a constant stream of people come in and out to help. "I don't think Dr.

Fisher left his bedside for two weeks," says Jaclyn. "It seemed like he was there 24 hours a day, keeping everyone on the same page."

Staying close to the baby was crucial. "Patients with CDH are very fragile," Dr. Fisher explains. "Pediatric surgeons are typically very possessive of them from birth to the repair."

Five days after his birth, Joey was still too compromised to endure a move to the operating room and unlikely to grow stronger, so Dr. Fisher and his team, including fellow pediatric surgeon, Keith Kuenzler, MD, prepared for surgery in the NICU, a rare arrangement reserved only for the most delicate cases. With the equipment required to sustain Joey leaving little room to maneuver, all 15 members of the team assumed assigned positions around Joey's bassinet.

Joey's weight at birth was just shy of five pounds, and one of the biggest concerns was that his belly would be too small to accommodate all of his displaced organs after the hole in his diaphragm was patched. In that case, there would be no alternative but to leave the incision open for several weeks, posing a risk for infection, until Joey grew larger. Fortunately, this scenario never came to pass. The four-hour surgery proceeded smoothly, and all the organs fit into his abdomen. Afterward, Joey remained remarkably stable.

Even Jaclyn, a medical professional, was stunned by the success of the operation, given its complexity and Joey's precarious condition. "Joey was on an oscillator that vibrated his tiny body," she recalls. "I was amazed that anyone could perform such a delicate procedure under those conditions."

"I don't think Dr. Fisher left his bedside for two weeks. It seemed like he was there 24 hours a day, keeping everyone on the same page."

JACLYN DOELL

As techniques for keeping vulnerable fetuses alive improve, pediatric specialists find themselves with younger and younger patients. Today, the first pediatric checkup essentially occurs with the first routine ultrasound. "In the past 10 to 15 years, the fetal period has become the critical entry point for children's healthcare in a way it never was before," explains Michele Lloyd, vice president

Maternal-fetal specialist Ashley Roman, MD (below), and pediatric surgeon Jason Fisher, MD (opposite), collaborated closely on Joey Doell's case through NYU Langone's Fetal Diagnosis and Treatment Program.

for children's services at NYU Langone. Lloyd and her colleagues are overseeing plans for the new inpatient and perioperative facility at Hassenfeld Children's Hospital of New York, which is slated to open in 2018 within the new Helen L. and Martin S. Kimmel Pavilion.

The newest generation of ultrasound machines produce moving images that are almost as crisp as photographs; doppler ultrasounds measure fetal blood flow so precisely that they can expose conditions as subtle as anemia; fetal echocardiograms help cardiologists detect anomalies as early as eight weeks of gestation. Unsurprisingly, this flood of new tools to see fetal anomalies is inspiring new ways to treat them.

Mara Rosner, MD, assistant professor of obstetrics and gynecology, is among a very small cadre of physicians nationwide trained to diagnose and treat fetal conditions, thanks to fellowship training in both maternal-fetal medicine and fetal therapy. With Dr. Rosner's help, the Fetal Diagnosis and Treatment Program aims to establish a prenatal laser-surgery program within the next two years to treat, among other things, twin-to-twin transfusion syndrome, a condition in which twins sharing a single placenta develop connected blood vessels that deliver too much blood to one baby and not enough to the other. A tiny laser guided by a periscope-like instrument inserted into the uterus is used to occlude problematic blood vessels.

Clinical capabilities aside, Dr. Rosner believes that perhaps the most important part of her job is helping mothers cope with devastating diagnoses. "We're guiding patients through one of the most distressing times in their lives," says Dr. Rosner. "It's so important to get to know them and their families, to understand their wishes and their plans for the future. My patients have my cell phone number, and we talk frequently."

With the worst behind him, Joey recovered well in the NICU. Not that it was easy for his parents to return home each night without him or understand what his progress meant for the future. "There was so much uncertainty," his mother recalls. "Would he come home with oxygen? Would he need a feeding tube? Would he be able to run around in the backyard someday? Nick was good at saying, 'Okay, let's take it day by day.' "

With his lung capacity growing, Joey was off the ventilator within weeks. "The nursing team was very good at challenging him to do more without tiring him out," says Jaclyn. Typically, a baby recovering from CDH remains hospitalized for six months, but Joey went home after two—near the original due date—with no monitors or tubes. "There is a lot of morbidity associated with CDH that he thankfully escaped," says Dr. Fisher. "He should live a normal life. Maybe he runs a 10-minute mile instead of an 8-minute mile."

Being home, at last, during her husband's paternity leave in May was among the most satisfying days of their marriage, says Jaclyn. The family of three spent every minute together, even 4:00 a.m. feedings, and friends made up for the missed baby shower by quietly leaving gifts at the front door. "Every time I look at Joey, I'm just in awe," says his mother. "He has the best spirit. You would never know he was critically ill. He looks like any healthy six-month-old."

Because he is. ●

A Medical Center Reimagined, Redefined, and Reinvented

DR. ANDREW BROTMAN, CHIEF CLINICAL OFFICER, ON A STRATEGY FOR GROWTH THAT PUTS PATIENTS FIRST

As medical advances improve recovery times, and policy changes encourage shorter hospital stays, more and more patients now receive care in an ambulatory setting, away from a hospital. Anticipating this trend nearly a decade ago, NYU Langone Medical Center adopted a bold new growth strategy to stay ahead of the curve. Today, its widespread network of some 140 ambulatory care sites serve neighborhoods throughout the New York metropolitan area, contributing largely to the Medical Center's record total of more than 5 million patient visits in 2016.

"NYU Langone is really an ambulatory care network with some hospitals rather than the other way around," explains Andrew W. Brotman, MD, senior vice president and vice dean for clinical affairs and strategy. As chief clinical officer, Dr. Brotman is responsible for program development, ambulatory care, faculty practice, and affiliations. Prior to joining NYU Langone in 1999, he was senior vice president and chief operating officer for physician practice management and network development for CareGroup in Boston. Dr. Brotman also served as chief of psychiatry at Beth Israel Deaconess Medical Center. Here, he shares his insights and perspectives on NYU Langone's institutional strategy to meet the ongoing challenges of healthcare.

NYU Langone has changed a lot since you came here in 1999. How would you describe its transformation?

We've always had outstanding doctors. What's different now is that we've moved from individual excellence to programmatic excellence. In other words, our doctors are now working within high-quality, multidisciplinary programs. So if you're being treated for a serious condition, you're not just going to Dr. So-and-So. You're benefiting from the expertise of numerous specialists who work as a team. When I came here, there were virtually no programs with multiple specialists. Once we shifted from an individual model of care to a programmatic one, we were able to take on cases that are much more complex. What hasn't changed, of course, is the basic doctor-patient relationship, which we hold as sacred.

Your province is large and diverse. How do all the pieces fit together?

My job is mostly to look outward—to

JONATHAN KOZOWYK

From atop Tisch Hospital, Andrew Brotman, MD, who has directed NYU Langone's growth initiatives over the last decade.

meet the needs of our patients, keep pace with healthcare reform, and compete effectively. I read half a dozen newspapers every morning to find out what our competitors are doing, what hospitals in other states are doing—their needs and innovations. We now employ nearly 2,000 doctors, with an additional 700 or so in private practice who are aligned with us. We have ambulatory care sites throughout the five boroughs and Long Island, and some in Westchester.

How does NYU Langone ensure that new participants and practices measure up?

We try to recruit people who have a similar viewpoint, come from a compatible culture, and who are interested in a long-term commitment. We carefully evaluate their credentials, records, training, etc. Then there are the softer factors, like reputation. We practice due diligence and do the best we can.

What distinguishes our network of ambulatory care sites from that of other institutions?

Ours are primarily physician-driven, multidisciplinary group practices that combine primary and specialty care. They provide about 95 percent of the patient's care and refer patients to a hospital or hospital-based program if the disease is complex or acute. We haven't expanded our ambulatory network to fill beds. We don't have that many beds. We've built these programs to deliver high-quality care to our patients in their

"NYU Langone is really an ambulatory care network with some hospitals rather than the other way around."

own neighborhoods.

How have the evolving needs and expectations of patients shaped our overall strategy?

More than ever, patients expect and demand more access, better customer service, and higher-quality care. Two decades ago, if it took six months to get an appointment with a doctor and the patient had to wait an hour and a half to see him, many doctors thought that was terrific because it meant they were in demand. Today, that means that we're not doing our job. One of our greatest assets is that we are truly patient centered. A perfect example is our electronic medical record system, Epic, which serves and empowers patients in so many practical ways.

How does NYU Lutheran fit into our long-range plan?

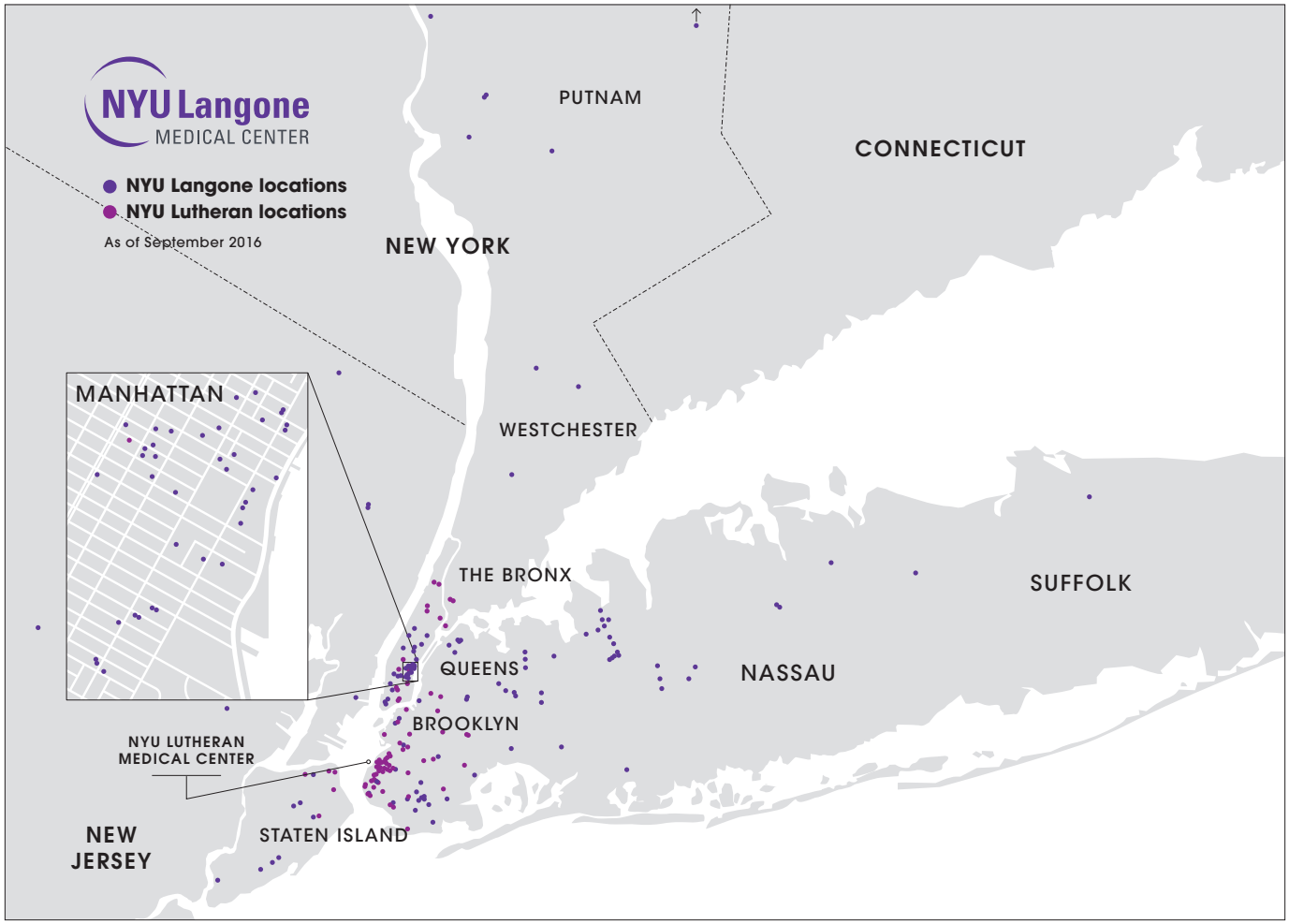
Because NYU Lutheran is a full asset merger, and not a strategic partnership, we're under the same governance. This allows us to serve Brooklyn's more than 2.5 million residents in closer proximity to where they live and work. About 90 percent of the care provided to our Brooklyn patients is within that borough, so only about 10 percent requires travel to our main campus for subspecialty care. Like most of our alliances, the goal is to bring excellent care closer to home.

A large part of strategic planning is adapting to trends, correct? How do we stay ahead of the curve?

By monitoring the Center for Medicare and Medicaid Services and other governmental agencies for things like changes in reimbursement policies. We developed an ambitious ambulatory strategy in response to a growing trend: from inpatient care to outpatient care. We anticipated that we were going to need a different payer framework, and that bet has come true. Increasingly, hospitals will provide high-end care for acute illnesses, while most other kinds of care will be offered in the ambulatory sphere.

Healthcare is undergoing so many changes so fast. Which reforms pose the biggest challenges for NYU Langone?

Broad initiatives like the Affordable Care Act and bundled care are the most sweeping in scope. But the development of new



pharmaceuticals, medical devices, and other technology continually requires us to measure and assess projected costs versus desired outcomes.

Which healthcare reforms do you wish for the most?

I think we are always going to have to balance cost and care. But I wish that there were better policies established by the insurance companies, the pharmaceutical companies, and the federal government so that it isn't left to practicing clinicians to explain to patients what the restrictions are on the cost side. Other countries have clear policies relating to cost versus availability of services, but in this country we have no integrated guidelines, so it's left to those on the front line to try to adjudicate all this.

Inpatient stays are shorter, yet the acuity of illness is higher. What does that new equation mean for us?

It means that when a patient is discharged from our hospital, they're not out of our care. They are in our care in another segment, and we're responsible for them. If we have shorter lengths of stay that result in higher rates of readmission, then we'll be penalized. The daily judgment calls are very difficult. Our philosophy is that hospitals are necessary when they're necessary.

As health insurers cover less, what does the future hold for patients?

Patients will need to be better informed than ever. With an ever-increasing amount of responsibility for their own coinsurance, copays, etc., patients need to be savvy consumers and careful decision makers. They must look for medical

services and providers that give them real value for their contribution. Hopefully, they won't just look for the lowest cost, but rather the most durable, long-term solution. The patient should be asking himself, "Given the fact that I'm responsible for a fair amount of this cost, is this the place I should go to? Is this the doctor I should see?"

We hear so much bad news about healthcare. Tell us some good news.

The survival rates for various forms of cancer have increased dramatically. Hepatitis C, which used to be fatal, is now essentially curable. Operations that once required 10-day hospital stays now enable the patient to go home after 10 hours—and with better results. These are remarkable advances.

Do you miss practicing psychiatry?

One of my mentors used to say that management is a subspecialty of psychiatry. There's a lot of conflict resolution. You try to synthesize different points of view. Management is about removing boulders from people's paths so that they can do their work. I use the skill sets of psychiatry every day.

You seem to enjoy making people laugh.

I do. It's critically important. In my psychiatry training, I had supervisors who spent a lot of time focusing on how we needed to keep ourselves even-keeled in the midst of suffering. Part of that is humor, and patients actually appreciate it. It has to be appropriate, of course, but caregivers must maintain a sense of optimism because what they do is very serious business. There needs to be a counter-balance.

What's the future of NYU Langone?

This year, *U.S. News & World Report* ranked us as one of the country's top 10 hospitals and one of its top 15 medical schools. In both categories, we want to be in the top 5—and ultimately first. ●

"Once we shifted from an individual model of care to a programmatic one, we were able to take on cases that are much more complex. What hasn't changed, of course, is the basic doctor-patient relationship, which we hold as sacred."

FACULTY BULLETIN

Bret J. Rudy, MD, at the Helm of NYU Lutheran, Aims to Reshape Healthcare in Brooklyn

In September, Bret J. Rudy, MD, was named executive hospital director and senior vice president of NYU Lutheran, a 450-bed acute care teaching hospital in southwest Brooklyn. The announcement comes just three months after Dr. Rudy was appointed the institution's chief medical officer.

A longtime faculty member and board-certified adolescent medicine physician at NYU Langone, Dr. Rudy had previously served as vice chair of the Department of Pediatrics. Prior to his leadership posts at NYU Lutheran, he helped lay the groundwork for establishing pediatric subspecialty services there, including pediatric gastroenterology, pulmonology, cardiology, and a pediatric hospitalist program. In his new role as hospital director, Dr. Rudy is responsible for improving operational efficiencies and enhancing the scope and quality of care and services at NYU Lutheran.


Bret J. Rudy, MD

Drawing upon the deep resources and expertise of NYU Langone, NYU Lutheran aims to redefine healthcare in Brooklyn. "Our vision is to become the hospital of choice in Brooklyn," says Dr. Rudy. As other hospitals in the area close or expect to close, the need for high-quality medical services in the city's most populous borough, particularly urgent care, is growing steadily. NYU Lutheran, home to a Level 1 Trauma Center and a nationally recognized Comprehensive Stroke Center, has enlarged its staff in emergency medicine. Plans call for the opening of a cancer treatment facility, an expansion of the network of family health centers, the addition of an ambulatory surgery center, and an increase in the number of inpatient beds.

NYU Lutheran, founded in 1883, serves as the hub of the NYU Lutheran system, which encompasses the Lutheran Family Health Centers (65 sites, which include the largest school-based clinic system in the state), Lutheran Augustana (a comprehensive extended care and rehabilitation center), the Lutheran Community Care Organization (a licensed home-care agency), and three subsidized senior housing developments.

Nationally recognized for providing culturally competent care to one of New York City's most diverse communities, NYU Lutheran has more than 5,000 physicians and staff. In September, it marked a major milestone with the launch of Epic, NYU Langone's electronic medical records system. Epic enables caregivers to share patient information efficiently and confidentially across various sites and providers, and gives patients access to a host of clinical information through a secure online portal. ●

"Our vision is to become the hospital of choice in Brooklyn."

DR. BRET J. RUDY, EXECUTIVE HOSPITAL DIRECTOR OF NYU LUTHERAN


Feza Remzi, MD

Feza Remzi, MD, Pioneering Colorectal Surgeon, Joins NYU Langone

Feza Remzi, MD, a renowned colorectal surgeon, has been appointed director of NYU Langone 's Inflammatory Bowel Disease Center. Dr. Remzi is a pioneer in the surgical treatment of inflammatory bowel disease (IBD) and other complex colorectal conditions, employing minimally invasive techniques. He specializes in rectal operations that spare the sphincter, reoperative abdominopelvic surgery, and procedures involving J-pouches—an alternative way to store and pass stool in patients who have had their colons and rectums removed due to colitis or cancer.

"The recruitment of Dr. Remzi is a game-changer for the care of our patients with complex inflammatory bowel disease," says H. Leon Pachter, MD, the George David Stewart Professor of Surgery and chair of the Department of Surgery.

Dr. Remzi joins NYU Langone from the Cleveland Clinic, where he served as chair of the Department of Colorectal Surgery. A native of Turkey, he earned his MD from Hacettepe University School of Medicine in Ankara, and completed his general surgery residency and a fellowship in colon and rectal surgery at the Cleveland Clinic. The author of more than 320 peer-reviewed articles and book chapters, Dr. Remzi has held leadership positions in several surgical societies and serves on the executive council of the American Society of Colon and Rectal Surgeons. ●

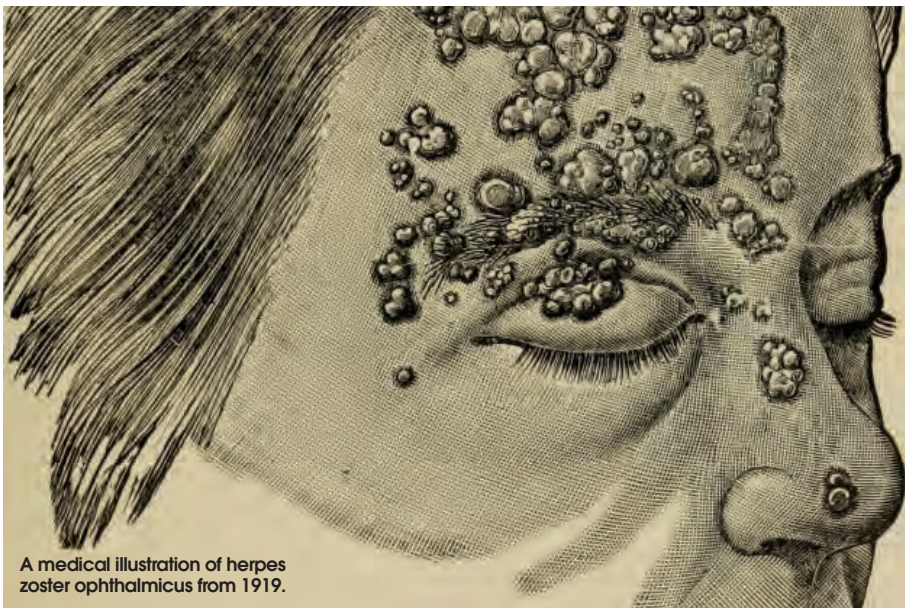
NEW PARTNERSHIPS

NYU LANGONE FORMS A STRATEGIC ALLIANCE WITH WINTHROP-UNIVERSITY HOSPITAL ON LONG ISLAND

NYU Langone and Winthrop-University Hospital, a 591-bed medical center in Mineola on Long Island, have approved an affiliation agreement that will bring the two organizations together to expand, enhance, and integrate their respective healthcare networks. The affiliation will help Winthrop increase its capacity to meet the growing demand for its services while bolstering NYU Langone's presence on Long Island.

NYU Langone has identified several key commonalities with Winthrop that make it an appealing partner, including a commitment to medical excellence, improving quality and safety standards, and compatible cultures. The affiliation relationship would begin after regulatory approval is obtained from federal and state agencies. After five years, both institutions would transition to a full asset merger.

Winthrop, founded in 1896 as Long Island's first voluntary hospital, is a New York State–designated Regional Trauma Center, a New York State–designated Stroke Center, and a New York State–designated Regional Perinatal Center. It has numerous ambulatory care centers that serve the surrounding community, including sites in Garden City and Deer Park. A Magnet-designated hospital recognized for the quality of its nursing, Winthrop has been named one of the best hospitals in the New York metropolitan area, and its Children's Hospital has been named one of the best in the nation by *U.S. News & World Report* for 2016–17. ⬢



A medical illustration of herpes zoster ophthalmicus from 1919.

HERPES ZOSTER, THE VIRUS THAT CAUSES SHINGLES, STRIKES AN ESTIMATED 1 MILLION AMERICANS EACH YEAR, WITH HERPES ZOSTER OPHTHALMICUS ACCOUNTING FOR UP TO 20 PERCENT OF ALL CASES.

NEW FUNDING

Medical Center to Lead $15 Million Study of Therapies for Shingles Infections in the Eye

One day in 2008, Elisabeth J. Cohen, MD, noticed a small bump near her hairline and dismissed it as a mosquito bite. But a few hours later, when a cluster of blisters had arisen, she diagnosed herself with herpes zoster ophthalmicus (HZO), a form of shingles that can cause chronic pain, permanent eye damage, and even stroke. Dr. Cohen—then the director of the Corneal Department of the renowned Wills Eye Institute in Philadelphia—immediately started on antiviral medication, hoping it would ward off the ravages of the disease. But within a year, she had lost so much vision in her right eye that she could no longer perform surgery. Ultimately, she required four operations. "I thought zoster ended my career," she recalls, "but the truth is, it reenergized it in new directions."

Dr. Cohen, now professor of ophthalmology at NYU Langone, has been researching antiviral treatment to reduce the complications of HZO ever since. Thanks to these efforts, the National Eye Institute has awarded the Medical Center a five-year, $15 million grant as the lead institution among 60 medical centers nationwide to participate in the Zoster Eye Disease Study (ZEDS). Judith Hochman, MD, the Harold Snyder Family Professor of Cardiology, and Judith Goldberg, ScD, professor of biostatistics, will lead the coordinating center at NYU Langone.

The standard treatment for HZO involves the short-term use of a high dose of the antiviral valacyclovir. The ZEDS study, enrolling 1,050 patients, will test the efficacy of a lower dose over one year, a treatment that has proven to be successful for eye disease caused by herpes simplex virus.

Shingles strikes an estimated 1 million Americans each year, with HZO accounting for up to 20 percent of all cases. It is caused by localized reactivation of the varicella zoster virus in people who have had chicken pox. The shingles vaccine, shown to decrease herpes zoster by 50

percent, was approved by the Food and Drug Administration in 2006 and is recommended by the Centers for Disease Control and Prevention for people age 60 and older with a healthy immune system. In 2011, it was approved for immunocompetent people age 50 and older. As of 2014, only 28 percent of eligible people age 60 and older in the U.S. have received the vaccine, which is now available without a prescription at most pharmacies. Dr. Cohen encourages doctors to strongly recommend the vaccine to immunocompetent people age 50 and older. ●

"No matter what happens during the day in my administrative life, the last thing I think about before I go to sleep is an intriguing set of data I saw during the day. And the first thing that I think about when I get up in the morning is what's going to happen in the lab today."

DR. DAFNA BAR-SAGI (BELOW), VICE DEAN FOR SCIENCE AND CHIEF SCIENTIFIC OFFICER AT NYU LANGONE, AND PANCREATIC-CANCER RESEARCHER

Dafna Bar-Sagi, PhD, Receives National Cancer Institute's Prestigious Outstanding Investigator Award

As vice dean for science and chief scientific officer of NYU Langone Medical Center, Dafna Bar-Sagi, PhD, is the principal strategist for the institution's research enterprise, which last year received $328 million in grant revenue.

But her passion for scientific investigation extends beyond the boardroom. "No matter what happens during the day in my administrative life," Dr. Bar-Sagi says, "the last thing I think about before I go to sleep is an intriguing set of data I saw during the day. And the first thing that I think about when I get up in the morning is what's going to happen in the lab today."

In October, the National Cancer Institute recognized Dr. Bar-Sagi—a senior member of NYU Langone's Perlmutter Cancer Center—for her devotion to science and contributions to cancer research, honoring her with its Outstanding Investigator Award. The prestigious award supports scientists with esteemed records of productivity, encouraging them to continue or embark on research projects with high potential. By providing extended financial support, the award empowers investigators to take greater risks and follow more adventurous paths.

Dafna Bar-Sagi, PhD

Dr. Bar-Sagi will receive $1 million per year for seven years to fund her research on understanding the mechanisms that drive pancreatic cancer. The Bar-Sagi laboratory, widely known for elucidating cellular pathways involved in controlling cell growth, has helped shape a finer understanding of how *Ras* oncogenes, a well-studied family of cancer genes, regulate cell proliferation and survival, tumor immunity, metabolism, and cell-to-cell signaling. Her lab is currently exploring a novel nutrient-delivery system in tumor cells. Previously unobserved in mammalian cells, this system involves the scavenging of extracellular protein by macropinocytosis. It has broad implications for understanding the metabolic vulnerabilities of *Ras*-driven tumors, which Dr. Bar-Sagi and team hope to exploit in an effort to develop more effective therapies against pancreatic cancer—among the most difficult malignancies to treat. The life expectancy for most people diagnosed with pancreatic cancer is less than a year.

Prior to joining NYU Langone in 2006 as chair of the Department of Biochemistry, Dr. Bar-Sagi headed the Department of Molecular Genetics and Microbiology at the State University of New York at Stony Brook. ●

Epidemiologist Leonardo Trasande, MD, Receives Nearly $9 Million to Study the Health Impact of Air Pollution in Early Childhood

"Every baby should have the best opportunity to remain healthy and thrive throughout childhood." So declared Francis S. Collins, MD, PhD, director of the National Institutes of Health, when he announced in September that his agency would award $157 million in research grants to launch a seven-year initiative called Environmental Influences on Child Health Outcomes (ECHO). The ECHO program investigates how exposure to a range of environmental factors in early development—from conception through early childhood—affects the health of children and adolescents. "ECHO will help us better understand the factors that contribute to optimal health in children," Dr. Collins explained.

This fall, Leonardo Trasande, MD, a pediatrician, epidemiologist, and expert in environmental medicine at NYU Langone, received one of those grants. The award, totaling $8.9 million over two years, will significantly expand his research on the short- and long-term risks of environmental hazards. Dr. Trasande is striving to better understand the mechanisms by which phthalates, bisphenols, pesticides, and other chemical contaminants contribute to disease and disability.

Environmental exposures during developmental windows—around the time of conception, later in pregnancy, and during infancy and early childhood—can have long-lasting effects on health. Dr. Trasande seeks to identify the role of such exposures in childhood obesity and cardiovascular risks, and document the economic costs of failing to prevent diseases in children proactively. In 2012, he published an article in the *Journal of the American Medical Association* associating bisphenol A exposure in children and adolescents with obesity, and in 2011 reported in *Health Affairs* that children's exposures to chemical contaminants cost the U.S. $340 billion in 2008.

Dr. Trasande's research will combine data from two studies. The NYU Children's Environmental Health Study (CHES) will monitor the health of nearly 1,000 pregnant mothers and their offspring—all patients at NYU Langone, NYU Lutheran Medical Center, and Bellevue Hospital (NYU Langone's primary teaching affiliate)—to determine how early-life exposure to contaminants impacts the children's early growth and development through age two. Another study—the Infant Development and Environment Study II (TIDES)—is monitoring the health of 717 mothers and their children in four cities: San Francisco, Seattle, Minneapolis, and Rochester in upstate New York. All children participating in TIDES have been closely monitored since before birth, and the new funding will extend their monitoring through age nine. ●

IN MEMORIAM

Martin S. Begun, 1931–2016

Martin S. Begun, who served as senior associate dean and vice president for external affairs at NYU Langone Medical Center for 34 years, from 1963 to 1997, and whose distinguished career spanned the fields of medicine, public service, and community relations, died on May 21 following complications from pneumonia. He was 85 years old.

Begun devoted the prime of his career to NYU Langone, presiding over the offices of Public Relations, Development, and Government Affairs. A passionate champion of the Medical Center, he worked tirelessly to raise its standards and profile at a time when medical training and healthcare underwent dramatic changes. As the institution's chief liaison with government officials on federal, state, city, and local levels, he forged close relationships with New York's governors, senators, mayors, and other public officials, enabling NYU Langone to advance strategic initiatives designed to better serve patients, faculty, staff, and students. He also cultivated strong ties with the community, ensuring that the Medical Center's rapid expansion supported, rather than disrupted, its surrounding neighborhoods, and laid the foundation for decades of ongoing growth.

Born in the Washington Heights section of Manhattan, Begun earned a BA from the University of Wisconsin and an MA in public law and government from Columbia University. He served as a sergeant in the Army National Guard from 1955 to 1960. During the 1960s and 1970s, Begun was a Democratic district leader on Manhattan's East Side, the beginning of a lifelong career in public service. Over the years, he led or was a member of many boards and civic organizations, serving as board chair of CUNY's Baruch School of Public and International Affairs and, as a board member of the Parks Council of New York City, the New York City Economic Development Corporation, the American Red Cross of Greater New York, and the New York State Hospital Review and Planning Council, among other organizations. A deeply committed advocate for mental health issues, he served as chair of the Community Services Board of the New York City Department of Mental Health and Mental Retardation.

Begun was a senior fellow at the Taub Urban Research Center of NYU's Robert F. Wagner Graduate School of Public Administration. He remained active until his illness—as a partner at Reiter/Begun, a marketing and management consulting firm for governmental and community relations, and as founder and president of MSB Strategies, a public policy planning consulting firm. He is survived by his wife of nearly 20 years, Louise Sunshine, three step-children, and three step-grandchildren. ●

LIFE LESSONS FROM ROBERT I. GROSSMAN, MD, DEAN & CEO

THIS FALL, Dr. Grossman shared his insights on life and leadership as part of NYU School of Medicine's Leaders & Teams lecture series for first-year medical students. Here, a few highlights.

I'm a fan of the underdog. My early years were quite difficult. My mother was an illegal immigrant. My father and his family were from a coal mining town in Pennsylvania. I grew up sharing a room with my uncle in a four-story walkup in the Bronx. Money was tight, so I started working when I was seven years old. I babysat, delivered papers, stocked shelves, washed dishes, scraped paint—I was always working.

You are what your experiences are. For me, what I've experienced has made me a more sensitive person, because I know what it means to come from difficult circumstances. I don't use that as an excuse. Rather, I try to use it in a positive way—to understand the needs of others and help people fulfill their aspirations. It's also given me much thicker skin, because when you're contending with significant issues, it doesn't really matter when somebody says something stupid to you.

Leadership requires emotional intelligence. If you can't understand the needs and aspirations of others—if it's just about you—you will never lead successfully.

Be authentic. Know who you are, and be proud of who you are. Know your strengths and weaknesses. People have good B.S. detectors. When you're pretending, people can tell, and ultimately that will have a negative impact on how they perceive you as a leader.

Don't ask someone to do something you wouldn't do yourself. Effective leaders lead from the front, not from behind.

And healthcare needs more effective leaders. If you look at successful businesses, they invest heavily in leadership training. That hasn't been the case in medicine. Historically, leadership rarely gets discussed. We've never actively trained leaders. But that's changing, and now there are tremendous opportunities for physicians aspiring to leadership roles. Healthcare is one of the fastest-growing segments of the United States economy.

A successful business is agile and accountable. In 2001, when I became chair of Radiology, our institution was well run and it had greatness. But some of the facilities were suboptimal, and the culture was somewhat depressed. One day I was sitting in my office thinking, "Oh, I'm chair of Radiology, this is a big deal," when a pipe burst in the wall. All of the plaster came down. The office was a mess, and I was trying to recruit people. They would walk in and say, "Hey, what's all this about?" I called the appropriate people, and nothing happened. It took six weeks for the hospital and the school to settle on who owned the wall and who owned the pipes. It's a prime example of why I wanted to combine the school and the hospitals and serve as both dean and CEO.

JOHN ABBOTT

Everything is important, so you should work really hard. Medicine is an exacting profession. You really have to have a breadth of knowledge—it's more than just googling. Eventually you have to apply the seat of your pants to the seat of the chair.

I disregard organizational charts and titles—sometimes to my detriment, because it can drive people crazy. I get the paradox. People say, "Well, it's easy for you to say, Bob, because you're the dean!" But I try to behave as if we don't have hierarchies.

Try to be open-minded. I have an institutional perspective and people may not always agree with it.

A leader, in my mind, is a team builder, someone who is passionate, someone who sees things differently. They express themselves clearly. And they're nice. I don't want jerks, no matter how smart.

Not everybody needs to be a leader. Get to know who you are and what maximizes your happiness. ●

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