news&views

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NYU Langone MEDICAL CENTER

In the Cobble Hill Section of Brooklyn, Emergency Medical Care at Its Best

For the First Time, the Ronald O. Perelman Department of Emergency Medicine Extends Its Expertise Beyond Manhattan

In the Emergency Department of NYU Langone Cobble Hill, Dr. David Barlas, chief of service (center), confers with Lauren Feltington, RN, and Dr. Amitabh Chandra.

Joshua Bright

Brooklyn residents account for over 25% of NYU Langone Medical Center's inpatient admissions and nearly 20% of its ambulatory care visits, and now those who live and work in the most populous borough can benefit from our expertise in emergency medicine on their own turf. NYU Langone Cobble Hill, a freestanding emergency department located at the site of the former Long Island College Hospital, opened in November. Staffed by an experienced, multidisciplinary team of physicians, nurses, and support personnel, the refurbished interim facility will provide full-service emergency care 24 hours a day, seven days a week. In addition, NYU Langone's experts in various specialties will be available for consultation through high-definition telemedicine capabilities.

If, after receiving initial treatment, inpatient admission is required, two ambulances are available on-site to transfer patients to one of several receiving hospitals in Brooklyn, including Lutheran Medical Center, an NYU Langone affiliate with Level 1 trauma service, or NYU Langone. The Medical Center recently obtained approval from the New York State Department of Health and the New York City Fire Department to arrange for NYU Langone Cobble Hill to receive ambulances via 911 calls.

The Medical Center also plans to bring a wide range of ambulatory services to Cobble Hill and its neighboring communities. A four-story, 125,000-square-foot outpatient facility, owned and operated by NYU Langone, is scheduled for completion by early 2018. Once fully operational, it will be staffed by more than 400 clinicians and support personnel, including some 70 physicians. NYU Langone Cobble Hill will include a new state-of-the-art emergency department; a surgical suite for outpatient procedures; a broad spectrum of primary and specialty care practices; a full-service satellite of the Laura and Isaac Perlmutter Cancer Center, including an infusion center and a clinical pharmacy; an on-site clinical laboratory and pathology team; and comprehensive imaging services.

A Close Call

NYU Langone Creates a Multidisciplinary Center to Diagnose and Treat Dangerous Blood Clots

Two years ago, Robert Temple, then 73, awoke one morning with a sharp pain behind his left knee. Dismissing it as a cramp, he climbed out of bed, but when he tried to walk, the pain shot through him with blinding intensity. He could hardly stand, let alone walk. "It was enough to make me want to jump out the window," recalls Temple, a retired office manager for New York City's Department of Social Services. He promptly called 911 and was rushed by ambulance to a nearby emergency room in Brooklyn.

An ultrasound revealed a blood clot lodged in a vein deep inside his left leg, a condition known as deep vein thrombosis (DVT), which claims the lives of an estimated 100,000 Americans annually. In about 50% of all cases, there are no symptoms, or symptoms so seemingly innocuous that they're dismissed or ignored until the clot suddenly becomes life threatening. Temple was referred to vascular surgeon Thomas Maldonado, MD. Dr.

Bud Glick

Dr. Thomas Maldonado, Robert Temple's vascular surgeon, displays the fine-mesh filter he implanted in Temple's vena cava to trap fragments of blood clots. Dr. Maldonado is director of the new Venous Thromboembolic Disease Center.

Maldonado is the newly appointed director of the Venous Thromboembolic Disease Center (VTEC), which sets a new standard of care to screen, detect, treat, and manage DVT.

(continued on page 4)

Trimming Hypertension

An Innovative Community Outreach Program at Barbershops Owned by African-Americans throughout New York City Targets a High-Risk Population for Blood Pressure Screening

Ismail Traore eases into a chair at Denny Moe's Superstar Barbershop on Frederick Douglass Boulevard in Harlem. Tall, lanky, in his early 30s, Ish, as he's known in the neighborhood, owns a popular clothing boutique just up the block, and he usually comes to Denny Moe's to get his hair cut. Today, though, he's here for a different kind of procedure. He's having his blood pressure checked.

Denny Moe's is one of more than 90 barbershops owned by African-Americans throughout New York City that provide free blood pressure screenings under the auspices of the Men's Health Initiative, a venture of NYU Langone's Center for Healthful Behavioral Change. The initiative, one of several community outreach programs sponsored by the Medical Center to screen high-risk populations, was launched in 2010 by hypertension specialist Joseph Ravenell, MD. Dr. Ravenell was dismayed by studies showing that 52 out of 100,000 adult black males in the US die of complications stemming from high blood pressure—triple the rate of white men.

One reason, he knew, is that men from this group are less likely to visit a physician regularly and have their blood pressure checked, for a variety of reasons—not the least of which is that many of them lack health insurance. But most go for a trim every few weeks, and conversations about personal issues are often part of the ritual. "It's often said that black men trust their barbers more than their doctors," notes Dr. Ravenell. "I thought that by partnering with these respected members of the community, we could help a population that's disproportionately impacted by a deadly but very treatable disease."

The Men's Health Initiative holds screening events at selected barbershops, where outreach workers measure blood pressure, offer advice on healthy lifestyles, and counsel those with high readings on how to find proper care. "If a patient doesn't have his own physician, he's referred to me," Dr. Ravenell explains. (A separate program at the Center for Healthful Behavioral Change offers similar events at New York City's predominantly black churches.)

Joshua Bright

Dr. Joseph Ravenell, a hypertension expert, shows Harlem barbershop owner Denny Moe how to properly take a blood pressure reading. Denny Moe's establishment is one of more than 90 barbershops throughout New York City that provide free blood pressure screenings to African-American men at high risk.

So far, more than 8,000 men have been tested for hypertension through the initiative. The outreach team also shares information on colorectal cancer, another disease that strikes black men more than any other group. Men age 50 or over with hypertension can sign up to receive six months of telephone-based counseling aimed at lowering their blood pressure, as well as guidance through the colon cancer screening process. By tracking the results of these interventions, researchers hope to fine-tune future programs.

As Denny Moe—his real name is Dennis Mitchell—puts the cuff on Ish, Dr. Ravenell looks on. The reading is 133/71. Dr. Ravenell explains that this indicates a prehypertensive condition, controllable through diet, exercise, and possibly medication. Ish listens closely and takes the doctor's card before leaving. "Folks around here don't get checkups, and they don't like taking pills," says Denny Moe. "We haven't been taking care of ourselves. But now we are."

Protecting Your Child from a Peanut Allergy

A Pediatric Allergist Offers Strategies for Prevention and Guidelines for Treatment

Among the 4.1 million children in America with reported food allergies (as of 2012), peanut is the most common allergen. Adverse reactions range in severity, at their worst resulting in anaphylaxis, a potentially life-threatening response marked by respiratory distress, a steep drop in blood pressure, and loss of consciousness. Parents are understandably fearful. Controlling food at home and insisting on new rules for school cafeterias are not enough to quell the anxiety that a child could be exposed to peanuts, or even traces of peanuts, with traumatic results.

But awareness and action are the antidotes to fear. "Parents can protect their children from an adverse reaction by taking a few important precautions," insists Paul Ehrlich, MD, a pediatric allergist and immunologist at NYU Langone Medical Center. With an expertise informed by nearly four decades in practice, Dr. Ehrlich equips parents with strategies for prevention and guidelines for treatment.

Wes Bedrosian

1. Test high-risk children. Special blood testing is recommended when obvious symptoms (skin reactions, shortness of breath, digestive discomfort) have been exhibited or when there's a family history of peanut or legume allergy. Children with other food allergies should also be tested. There's rarely a need to test infants fed exclusively on breast milk or formula.

2. Monitor your child's diet. To limit the risk of exposure, learn whether your child's school has a peanut-free policy and how it's enforced. When dining out, even if the waiter says that a dish doesn't contain peanuts or peanut oil, check with the chef. At an early age (as young as three years old), teach your children to ask whether the food they're being served contains peanuts.

3. Read food labels. All packaged food products sold in the US that contain peanuts as an ingredient are required by federal law to list the word "peanut" on the label. However, food packagers are not required to include a warning or to indicate whether the product was prepared in a facility that processes nuts. When in doubt, contact the manufacturer.

4. Keep an over-the-counter antihistamine containing diphenhydramine on hand. For minor reactions, this can provide relief against irritating symptoms, such as itching and hives.

5. For severe attacks involving respiratory distress, use an epinephrine auto-injector, and take your child to the emergency department. Epinephrine, a naturally occurring form of adrenaline, can slow or even reverse anaphylaxis when properly injected by a caretaker. Allergists commonly prescribe the portable EpiPen® or Auvi-Q® injector (the latter provides audiovisual cues).

Therapy in Motion

New Early Mobilization Program Finds That Even Critically Ill Patients Can Move About Safely and Far Sooner Than Was Previously Believed

Getty Images

A new program known as ICU Early Mobilization helps get patients moving—to the extent they can, and as soon as their condition allows—in the clinical area of Tisch Hospital where some of the most acutely ill patients can be found: the medical and surgical intensive care units (ICUs). "Nearly every system in the body is negatively affected by immobilization," explains John Corcoran, DPT, site director for rehabilitation therapy services. "For example, muscle atrophy occurs rapidly, blood vessels thicken, and delirium may set in."

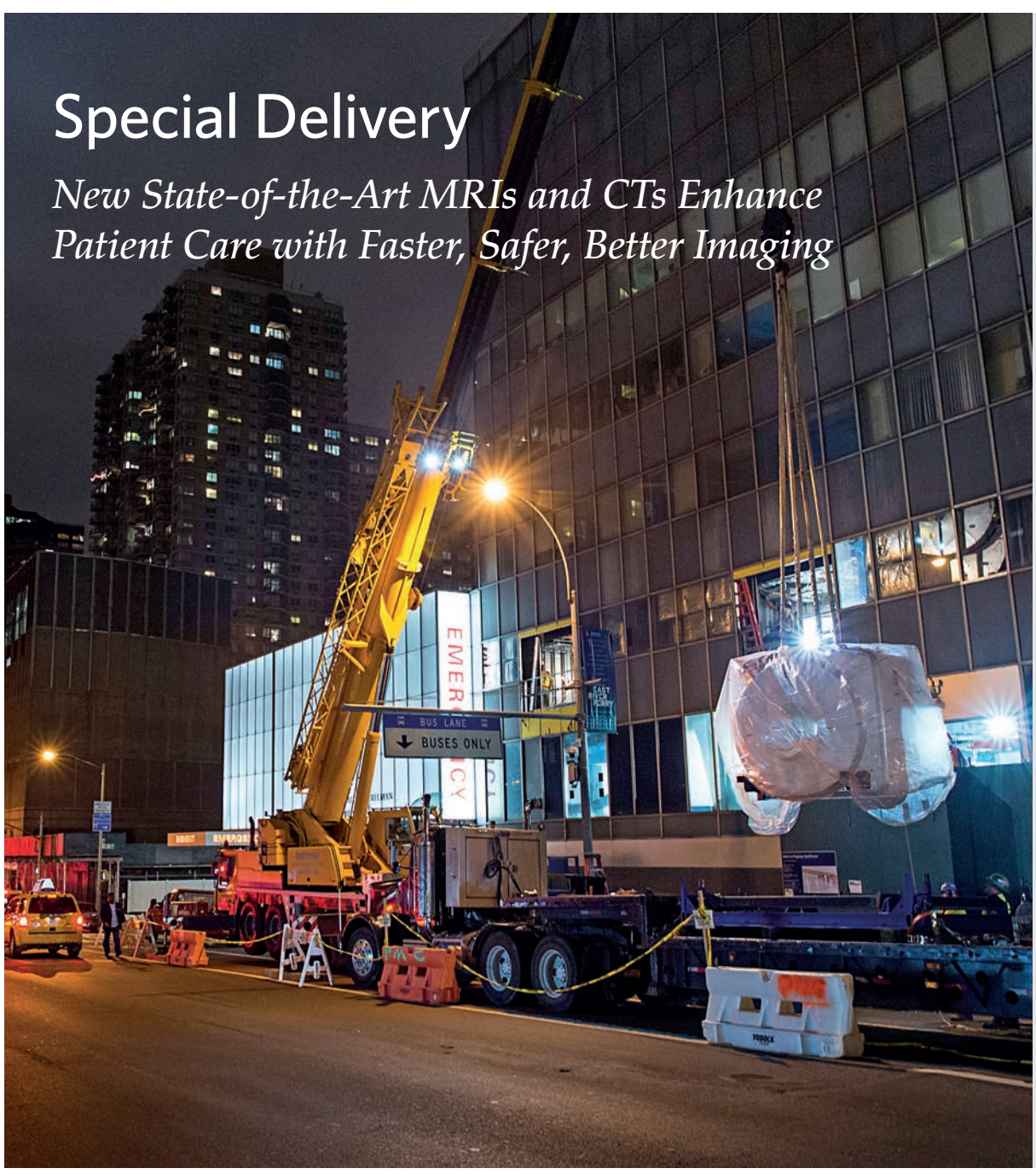
Tethered to machines that monitor their bodies and keep them functioning, critical care patients face many obstacles to mobility. Over the past few years, however, a growing body of research has shown that they can move about safely and far sooner than was previously believed. An NYU Langone Medical Center study comparing 160 ICU Early Mobilization patients to 123 preprogram patients found that the average length of stay in the ICU fell by 20%, or nearly a full day. What's more, these patients spent 30% less time in the hospital after being moved to other units, and they also required fewer follow-up services, such as treatment in other inpatient facilities, after discharge. "In many cases, each day that a critically ill patient is bedridden translates into two or three days of rehabilitation that will be required as a result of lost muscle mass and deconditioning," notes Spiros Frangos, MD, chief of the Division of Trauma, Emergency Surgery, and Surgical Critical Care. "Early mobilization—performed on the right patients with safety as a priority—accelerates the rate at which our patients reestablish their functional independence."

The program brings together a multidisciplinary team of intensivists, physiatrists, nurses, physical therapists, occupational therapists, speech-language pathologists, and respiratory therapists to design a mobility plan for each patient, based on their needs and abilities. "Our goal is to get every patient walking," says Corcoran, "though several steps may be necessary before that can happen." Assisted by a nurse or physical therapist, a patient may begin by simply sitting on the edge of the bed, then moving to a chair, and then standing—with some rest periods in between to allow the patient's heart rate and oxygen levels to recover. An occupational therapist may help the patient relearn simple tasks, such as brushing teeth and getting dressed, which are key to practicing motor skills, as well as to maintaining mental clarity and morale. To encourage such activity, caregivers use an array of portable life-support equipment and keep sedatives to a minimum.

"When we first ask patients to get out of bed, some of them just look at us as if to say, 'Are you kidding?' " says Corcoran. "But after they've worked with us for a bit, they're usually able to go home healthier and with fewer complications."

Special Delivery

New State-of-the-Art MRIs and CTs Enhance Patient Care with Faster, Safer, Better Imaging



Joshua Bright

The kind of delivery that takes place in the middle of the night at NYU Langone Medical Center is usually that of a newborn, but in the wee hours one night several months ago, the arrivals were considerably larger. Over several hours, a crane hoisted two new magnetic resonance imaging (MRI) scanners—one weighing 11,000 pounds, the other 17,000 pounds—onto the second floor of Tisch Hospital, where they were installed in a new MRI suite. Positioning the massive machines was a monumental task requiring an entire window facade to be dismantled for the rigging. Previously, the Medical Center performed inpatient MRI scans on a single system. The additional unit will increase capacity, allowing inpatient imaging to be performed earlier in the day, as well as availability for pediatric patients and those requiring general anesthesia. It will also increase the capacity for sophisticated interventional procedures in urology and neurosurgery.

One of two next-generation CT scanners has also arrived—the first of their kind in New York City and two of only seven such systems in the US. The first scanner is located in the faculty practice radiology unit on the second floor of the Schwartz Health Care Center, while its twin will occupy dedicated space in the new Ronald O. Perelman Center for Emergency Services. The new scanners—equipped with more powerful technology—offer sharper, more vivid images. Moreover, they expose patients to significantly less radiation than their predecessors. Scans of the chest and abdomen take less than a second, enabling radiologists to make speedy diagnoses. In many cases, this speed eliminates the need for uncomfortable breath holds and enhances visual clarity because images can be captured between heartbeats.

Getty Images

When Names Hurt Even More Than Sticks and Stones

Q&A on Bullying with Dr. Lori Evans

Bullying can actually be deadly, but even at its least harmful, it's damaging. For insight and perspective on this complex social phenomenon, news & views recently spoke to Lori Evans, PhD, a psychologist at NYU Langone Medical Center's Child Study Center, who counsels children and parents who are struggling with bullying, and advises schools on bullying policies in the New York City metropolitan area.

When does teasing cross the line and become bullying?
Teasing is not characterized by a repeated pattern. It's a repartee between two people on equal footing. Bullying, on the other hand, is intended to hurt. Bullying is the intentional infliction of injury or discomfort, either physical or verbal, onto another person, repeated over time. It exploits weaknesses, and it's done in a way that makes the victim feel bad about himself or herself. Moreover, it's often covert. Bullying doesn't necessarily take place in a classroom. It takes place in the stairwells, in the cafeteria, at recess, and on the way to school. In other words, it's often not seen. A key component is the power differential—the bully has power, either social or physical, over the victim. Generally speaking, football players don't get picked on.

Are bullies born or made?
People will sometimes say: "Oh, these kids feel bad about themselves, and that's why they do it." That can certainly be the case. But sometimes the opposite is true. Some bullies have an overinflated sense of self. What changes bad behavior is understanding what leads to it and giving the bully other things to do that fulfill that need. If they're bullying because they feel inadequate, they need to be helped to feel adequate. If they have an overinflated sense of self, they need to be taught to be more realistic about what their competencies are. No matter what the behavior stems from, bullying must have consequences, or it will simply persist.

Is bullying on the rise?
There's no indication of this. This kind of misbehavior has been known about and reported for a long time. What has increased is our awareness of bullying and the negative effects of it, due to the reach and rapidity of how children can communicate in our modern world.

Are you referring to cyberbullying?
Yes. We have found that even children who might not bully at school are easily tempted to bully online because of the anonymity it affords, and the impact, of course, can be more devastating. In cyberspace, a rumor spreads faster than word of mouth, and its presence is permanent. You can crumple a note or erase what's scribbled on a bathroom wall. But social media posts and texts don't go away. Although we don't have research on this because the technology is relatively new, my guess is that the more public the bullying is, the more shame and humiliation it brings. Suicide is the third leading cause of death in children and adolescents, and when we look into the reasons, we see that bullying, including cyberbullying, is one of them.

On a less tragic level, what are the negative effects of bullying?
There's social rejection and personal pain, but we also know from research that kids who are bullied are more at risk for developing depression and anxiety. Bullying causes chronic stress, and we know how harmful that can be, both physically and cognitively, to the development process. When we talk about bullying, we often think we're talking about physical abuse. But verbal abuse can be just as harmful. The old saying "Sticks and stones can break my bones, but words can never hurt me" is just silly. Yes, they can.

How much bullying goes unreported?
The majority of victims—as many as 60%—do not report bullying to adults. Only about 20% of bystanders who witness bullying report it to an adult, and only 5% of kids say they would tell a parent about it.

Why is that?
Because kids are afraid, especially with cyberbullying, that parents will freak out and create additional restrictions for them. They also feel that parents or other adults won't do anything to help.

Does hiding the problem make it even worse?
Absolutely. Schools need to make it safe for kids to tell without having it seem like tattling. Parents also have to have a way to let their kids know they can tell them what's going on. Without parents knowing what's going on, children suffer in silence way too long.

What are the best strategies to combat bullying?
It's very hard to work on just an individual level—working with the bully or the victim. Often, we're asking parents to be the agent for systemic change in the school. So if your child is a victim, you can work with him or her, individually or in therapy, on how to respond assertively and how to report the behavior. But that's only going to help minimally if the school isn't on board. Schools need to take this problem very seriously and make it clear that all reports of bullying will be addressed promptly and fully. Some of the comprehensive antibullying programs that schools have put into place have helped decrease this kind of behavior by as much as 50%. Bystanders can also be taught to help—not by confronting the bully but by supporting the victim, by saying something like "Come on, Sarah, hang out with us." Kindness goes a long way.

A Close Call *(continued from page 1)*

Whenever a patient at NYU Langone Medical Center is diagnosed with a blood clot, the VTEC team is alerted. With expertise in hematology, vascular surgery, cardiology, radiology, emergency medicine, and other disciplines that treat embolisms (sudden obstructions of blood vessels), the team determines the best course of action. A core component of VTEC is research led by cardiologist Jeffrey Berger, MD, who specializes in complex thrombotic disorders of the cardiovascular system. "The holy grail," says Dr. Berger, "is to figure out what predisposes some people to blood clots and identify them as early as possible."

Risk factors for DVT include long periods of immobility, trauma or surgery, smoking, obesity, cancer, birth control pills, and a family history of blood clots. The most common treatment for DVT is a blood thinner. Clots in the leg are particularly dangerous because fragments can break off and travel through the inferior vena cava, a large vein that returns deoxygenated blood from the lower body, up through the abdomen, and to the heart and lungs. If a clot blocks one or more of the pulmonary arteries in the lungs—a condition known as a pulmonary embolism—it can be fatal. On Dr. Maldonado's recommendation, Temple had an umbrella-like filter implanted in his vena cava to trap such fragments. He was not a candidate for a blood thinner because he had recently had surgery for kidney stones and was at risk for bleeding.

Temple felt fine until February 2014, when the same kind of excruciating pain recurred, this time with shortness of breath and severe swelling in his leg. A blood clot had surrounded the filter, a rare complication. Recognizing the situation as a medical emergency, Dr. Maldonado ordered a CT scan, which revealed clots in Temple's lungs. "Prompt diagnosis and treatment can mean the difference between life and death," says Dr. Maldonado. In the OR, Dr. Maldonado used a special catheter to break up and extract most of the clot from the vena cava, which had become completely occluded, and other veins in his leg. Within 24 hours, Temple's swollen legs had returned to normal size. More important, he was no longer in danger.

Temple had a close call, but not everyone is so fortunate. VTEC was established in November with a gift from Medical Center Trustee Bernard Schwartz and his late wife, Irene. Our goal, explains Dr. Maldonado, is "to ensure that diagnosis and treatment are never delayed for anyone."

The Fine Line Between Safe and Sorry

Diagnosing Heart Attacks in Women

Women are the subtler sex, goes the saying, and apparently that holds true even when it comes to heart attacks. "The signs can be so subtle that not only women but even physicians often mistake what's happening, attributing the symptoms to some other problem," says cardiologist Harmony Reynolds, MD, the Saul J. Farber Assistant Professor of Medicine. Although women and men can suffer chest discomfort, the crushing, squeezing "elephant sitting on my chest" pain—the classic symptom—is frequently missing in women. Instead, women may experience mild pressure in their back, abdomen, or shoulder, or no pressure at all. They may feel short of breath, lightheaded and dizzy, extremely fatigued, or have a sense of impending doom—vague symptoms that can be easily attributed to acid reflux, muscle strain, the flu, or anxiety. They are also more likely to be in the grip of a strong emotion. "A man may suffer a heart attack while out running," notes Dr. Reynolds, "while a woman may have one in the middle of an argument."

"Women and physicians have a knowledge gap that needs to be closed," says cardiologist Nieca Goldberg, MD, medical director of NYU Langone Medical Center's Women's Heart Program and of the Joan H. Tisch Center for Women's Health. Only in the past 25 years have women been studied for cardiovascular disease, notes Dr. Goldberg. Cardiac disease was previously thought of as primarily a man's disease, and the misperception lingers. Women are still not treated as aggressively as men, even when they have the same high risk profile: obesity, diabetes, smoking, high cholesterol, and family history. Moreover, they receive fewer referrals for corrective angioplasty and coronary bypass surgery. As a result, more women than men die of cardiovascular illness each year—400,000 women in 2010, for example, compared to fewer than 350,000 men.

"Where we have made progress," says Dr. Goldberg, "is in understanding the differences between men and women in terms of cardiovascular disease." For one thing, women frequently have a different pattern of plaque formation that doesn't get detected by an angiogram, a routine diagnostic test. In women, a blockage may be evenly distributed along coronary arteries instead of concentrated in one spot. But that information has not reached enough doctors. "As physicians," says Dr. Goldberg, "we need to do better with prevention and treatment." She notes that women need to be alert to the subtle signals that their heart is being attacked, especially if they have risk factors. Dr. Reynolds adds, "If you have any of the signs, get checked immediately. It may prove to be nothing serious—but you're better off safe than sorry."

Sandra Dionisi

PERLMUTTER CANCER CENTER GALA

NYU Langone Medical Center raised over $1.7 million at the Perlmutter Cancer Center Gala, held on October 22 at The Plaza Hotel. Some 400 guests honored Medical Center Trustees Isaac and Laura Perlmutter for their generous leadership commitment and John Golfinos, MD, chair of the Department of Neurosurgery, for his exceptional care of patients. Those celebrating the honorees included former patient Amy Novogratz; her brother, Medical Center Trustee Michael Novogratz; Medical Center Trustee and Perlmutter Cancer Center Advisory Board Chair Lori Fink; and Dean and CEO Robert I. Grossman, MD.

John Abbott

Dr. Benjamin Neel, new director of the Laura and Isaac Perlmutter Cancer Center, and Medical Center Board Chair Kenneth G. Langone.

Jay Brady

Dr. John Golfinos, Laura Perlmutter, Lori Fink, and the Saul J. Farber Dean and CEO Robert I. Grossman, MD.

THE MUSCULOSKELETAL BALL

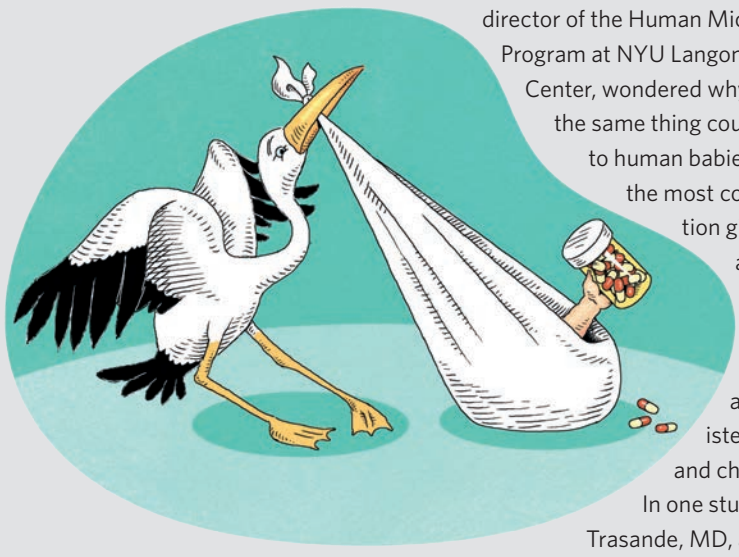
NYU Langone Medical Center hosted its annual Musculoskeletal Ball at the American Museum of Natural History on November 12, raising more than $2 million to support research, education, and patient care in orthopaedics, rehabilitation medicine, and rheumatology. Honorees Mindy Nam Dehnert and Mark Dehnert were recognized for their commitment to pediatric integrative health at Rusk Rehabilitation. The Dehnerts introduced the gala's physician honoree, Steven Flanagan, MD, the Howard A. Rusk Professor of Rehabilitation Medicine, chair of the Department of Rehabilitation Medicine, and medical director of Rusk Rehabilitation. The event also celebrated the 25th anniversary of the Harkness Center for Dance Injuries. Medical Center Trustee and Musculoskeletal Advisory Board Chair Gary Cohn teamed up with Joseph Zuckerman, MD, the Walter A. L. Thompson Professor of Orthopaedic Surgery and chair of the Department of Orthopaedic Surgery, for a live auction that saw many hands go up among the 430 guests.

Clockwise from top left: The staff of the Harkness Center for Dance Injuries. Dean and CEO Robert I. Grossman, MD; Elaine Langone; Dr. Steven Flanagan; Medical Center Board Chair Kenneth G. Langone; and Medical Center Trustee and Musculoskeletal Advisory Board Chair Gary Cohn. Mark Dehnert and Mindy Nam Dehnert. Dr. Joseph Zuckerman.

All photos: John Abbott

Study Suggests That Infants Exposed to Antibiotics May Be at Higher Risk for Obesity

Newborn farm animals given antibiotics gain weight quickly. Years ago, Martin Blaser, MD, the Muriel G. and George W. Singer Professor of Translational Medicine and director of the Human Microbiome Program at NYU Langone Medical Center, wondered why—and whether the same thing could be happening to human babies. Antibiotics are the most common medication given to newborns, and public health scientists had already found a link between antibiotics administered in infancy and childhood obesity. In one study, Leonardo Trasande, MD, and colleagues at the Medical Center examined data from more than 11,000 babies in Great Britain. They found that infants who had received antibiotics in the first six months of life had a greater risk of being obese when they were about one to three years old.



But why would early exposure to antibiotics cause newborns to pack on the pounds? Dr. Blaser's research in mice suggests that the answer has a lot to do with the trillions of microbes that inhabit our intestines, helping us digest food, produce vitamins, and bolster the immune system, among other things. Two years ago, his lab showed that lifelong exposure to low doses of antibiotics altered the intestinal bacteria of mice, causing the rodents to gain 10 to 15% more fat than untreated mice. The findings were the first to prove a causal link between altered intestinal microbes and obesity, but there was still the question of newborn exposure. Did it matter when the medication was administered?

The newest study from Dr. Blaser's lab, published in August in the journal *Cell*, suggests that timing indeed matters. Recent experiments show that mice exposed to the same low doses of antibiotics in the womb and during nursing pack on even more fat in adulthood than mice exposed later in life. Antibiotics in early life, the scientists conclude, can disrupt a critical window of development for gut bacteria, setting off permanent, lifelong metabolic changes.

In one experiment, the researchers administered penicillin-treated water to two groups of mice. One group received antibiotics in the womb during the last week of pregnancy and continued the medication throughout life. Another received antibiotics after weaning and, like the first group, continued the medication throughout life. A third group, which served as the control, received no antibiotics. "While we saw increased fat mass in both penicillin groups, mice treated in the womb were the fattest," reports lead author Laura Cox, PhD, a postdoctoral fellow in Dr. Blaser's lab.

Intriguingly, the unhealthy metabolic changes that accompanied the fat gain persisted even when the antibiotics were stopped, and the gut bacteria rebounded. "The effects on the microbes are transient," explains Dr. Blaser, "but the effects on host metabolism are permanent. This supports the idea of a developmental window in which microbes participate. It's a novel concept, and we're providing direct evidence for it."

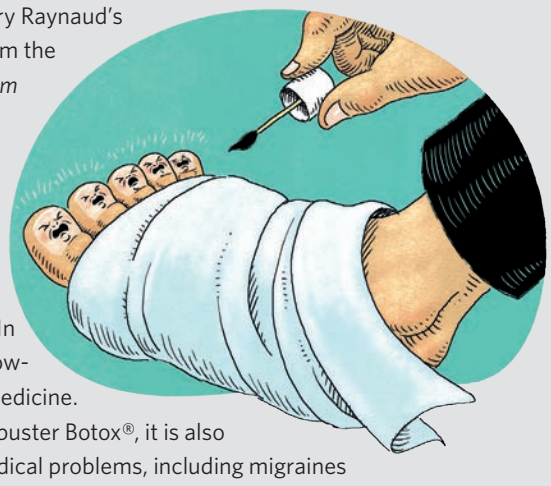
A New Wrinkle for the Medicinal Use of Botox

For Caroline Boynton, last winter's deep freeze wasn't just uncomfortable—it nearly cost her a toe. Boynton, a 66-year-old Episcopal deacon, suffers from a severe form of Raynaud's phenomenon, a condition in which cold temperatures set off spasms within the blood vessels, cutting off blood flow to the extremities. Most people with Raynaud's have the primary type and experience only mild discomfort. Boynton, however, suffers from the secondary type, associated with more serious symptoms, and her condition is exacerbated by scleroderma, an autoimmune disease in which scar tissue builds up in the skin.

Her fingers and toes were so starved of blood at times that they turned an icy patchwork of blue and white. "The nerves were screaming out in pain," recalls Boynton. The pain in her toes was particularly excruciating. Sometimes she could barely stand. She took medications to expand the blood vessels and relax the nerves, but nothing worked for long. Then, the second toe of her left foot developed an ulcer, a common occurrence among patients with severe Raynaud's, due to a lack of circulation. When the ulcer became infected, her suffering hit a new, unthinkable intensity. Desperate for relief, Boynton begged, "Please cut off my toe."

"It's not uncommon for patients with severe Raynaud's to come into my office and ask for amputations," says Andrew Franks, Jr., MD, director of the Skin Lupus & Autoimmune Connective Tissue Disease Service in the Ronald O. Perelman Department of Dermatology. "They just can't deal with the pain any longer."

Fortunately, Dr. Franks had a better solution. Since 2011, he has treated about a dozen extreme cases of secondary Raynaud's with botulinum toxin. Derived from the soil-dwelling bacterium *Clostridium botulinum*, this neurotoxin blocks nerve signals to muscles and glands. If leached into food or water, the naturally occurring toxin can cause botulism, a potentially lethal illness that can paralyze the respiratory system. In extremely low concentrations, however, it can serve as a powerful medicine.



Best known as the wrinkle buster Botox®, it is also used to treat a growing list of medical problems, including migraines and excessively sweaty palms. More recently, it has been used to increase the circulation and reduce the debilitating pain of severe secondary Raynaud's. "Botox releases the strangulation of the vessels," explains Dr. Franks. "It has a direct vasodilation effect and also diminishes pain transmission, resulting in pain relief that is nearly immediate, as well as an increase in the vital circulation of blood to the tissue."

Last February, after treating the infection in Boynton's toe with antibiotics, Dr. Franks injected Botox into the webbing between her toes, targeting nearby blood vessels and nerve bundles. The results were dramatic. "Within an hour, the nerves stopped screaming," Boynton recalls. While the pain relief from Botox can last up to a year, the infection in Boynton's toe returned, necessitating another round of antibiotics, followed by a second round of Botox injections. Again, the pain relief was dramatic. "Once I got an adequate blood supply, the nerves really shut up," says Boynton. "It's an incredible drug."

Dr. Franks is encouraged by his patient's success, but he cautions that botulinum toxin is still reserved only for severe cases where conventional treatment has failed. "It's not a magic bullet," he says. Nor is it a substitute for quitting smoking and reducing caffeine consumption, both of which he recommends to his patients as ways to improve circulation.

Two Studies Reveal New Clues about a Master "On" Switch That Triggers a Form of Childhood Leukemia

Over the past two decades, researchers have made great strides in treating the most common childhood cancer, an aggressive blood-borne disease known as acute lymphoblastic leukemia, or ALL. Of the 6,000 cases diagnosed annually among children and adults in the US, some 85% can now be cured. Not all subtypes respond equally well, however. One, known as T cell acute lymphoblastic leukemia, or T-ALL, accounts for only 15 to 20% of all cases, but it has a considerably higher rate of treatment failures and deaths.

For another subtype, called B-ALL, investigators have developed a promising therapy that recruits the body's immune cells to attack the disease. "But there are no such treatments, not even on the horizon, for T-ALL," explains cancer biologist Ionnis Aifantis, PhD, chair of the Department of Pathology at NYU Langone Medical Center and an early career scientist at the Howard Hughes Medical Institute.

Yet, two recent studies by Dr. Aifantis and his colleagues may help to expand other treatment options for T-ALL. Together, they have revealed new clues about how a protein called Notch1 acts like a master "on" switch, triggering a majority of T-ALL cases. The research also has enlarged the pool of Notch1-related therapeutic targets that may be blocked to halt the advance of the leukemia.

For one study, published in *Nature*, the researchers investigated the roles of two enzymes that activate specific genes by binding and altering chromosomal DNA, a process known as epigenetic modification. To their surprise, Dr. Aifantis and his collaborators found that an enzyme called UTX suppresses T-ALL, while another, called JMJD3, does just the opposite, promoting tumors. JMJD3, they learned, helps to turn on Notch1, allowing it to activate a host of genes that promote the leukemia's growth. Intriguingly, the study showed that an investigational drug called GSKJ4 inhibits the enzyme's binding activity. "By targeting JMJD3, you switch off the Notch1 pathway and kill the leukemic cells," Dr. Aifantis explains. "It doesn't kill normal cells, and it doesn't kill other types of leukemia. It's specific for this particular tumor."

In a separate study, published in *Cell*, the researchers scrutinized part of the human genome formerly likened to "a desert or trash bin," notes Dr. Aifantis. Less than 3% of our DNA encodes proteins, and researchers once called the remainder "junk DNA." More recent studies, however, have shown that about 70% of genomic DNA can still be converted into its chemical cousin, RNA. Dr. Aifantis and his team identified thousands of long noncoding RNA pieces that were more abundant in T-ALL cells than in their healthy counterparts, and zeroed in on one they named LUNAR1. "When we silenced LUNAR1, the leukemic cells would actually die or stop growing," Dr. Aifantis explains. Through experiments with tumor cells and mice, the researchers showed that the RNA belongs to the same Notch1 signaling pathway as the JMJD3 enzyme.

Based on the converging evidence, Dr. Aifantis says compounds that gum up the epigenetic machinery needed to activate tumor-promoting genes may provide a new option for T-ALL therapeutics. In addition, what was once considered a genomic desert may actually be an unexplored jungle teeming with useful RNA drug targets.

Illustrations by Wes Bedrosian

What's Past Is Prologue

Doris Fontanilla Pareja, RN, Had Always Aspired to Become a Nurse. But after the Care She Received as a Patient at Tisch Hospital, She Was Inspired to Become One

Doris Fontanilla Pareja, RN, 35, always thought she'd make a great nurse. She was detail oriented, upbeat, and very caring. She even took a few prerequisite courses for nursing school. But it wasn't until the medical profession saved her life that she found the inspiration and drive to pursue a career in nursing.

Her transformation began in November 2010 with a frightening symptom: numbness in the right side of her face. An MRI revealed a vestibular schwannoma, a slow-growing, benign tumor that sits on the nerves leading from the inner ear to the brain stem. The mass, a little bigger than a grape, was operable, she was told, but the delicate task of untangling it from the nerves was risky. The surgery might leave her face partially paralyzed and cause permanent hearing loss.

Fontanilla researched neurosurgeons methodically, seeking opinions from several of them, including one in Germany. Ultimately, she chose Chandranath Sen, MD, professor of neurosurgery and director of the Benign Brain Tumor and Cranial Nerve Disorders Programs at NYU Langone Medical Center. While Fontanilla was impressed by Dr. Sen's technical expertise—even the German neurosurgeon knew of his reputation—it was his compassion that really put her at ease. "He encouraged me to spend time with my family for the holidays," she recalls. Her younger son was only five weeks old when she was diagnosed. Dr. Sen met with Fontanilla several times before the operation, not only to prepare her for what might come, but also to build trust. "I treat these relationships as very special," says Dr. Sen. "Patients are entrusting me to open up their heads."

In March 2011, after an operation that took eight hours, Fontanilla awoke in the neurosurgical intensive care unit. The good news was that Dr. Sen had successfully removed the tumor. The bad news was that to do so, he had to sacrifice the hearing in her right ear. "It was kind of expected," she says. "So I decided to focus on the positives—the tumor was gone."

Fontanilla's nine days in the ICU were tough to endure, but despite her many challenges, she found herself deeply moved by the extraordinary care she received, particularly from the nurses. "They were so attentive," she recalls. "Not only to me, but to my whole family." One nurse, who also had two young boys, would chat with Fontanilla to distract her from the unpleasantness, even when she wasn't assigned to care for her.

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Fontanilla felt inspired. "In the ICU, you're so dependent," she says, "and the care they give is so crucial. Experiencing that, I knew I wanted to go to nursing school." Fontanilla spent six months in rehabilitation to overcome the facial paralysis that developed later, but she didn't put nursing on the back burner. "From the first time I saw her, she was very stoic and strong," notes Dr. Sen. "I've been doing this for more than 25 years, and she totally stands out in my mind."

Fontanilla enrolled in an accelerated program at NYU College of Nursing—the only nursing school she applied to. "In many, many instances, I was sitting in class and seeing things from a patient's perspective," she says. "I hope to never lose that." After graduating summa cum laude in 2013, Fontanilla was accepted by NYU Langone's nurse residency program. She was assigned to 12 East in Tisch Hospital, just across from the neurology unit on 12 West. When she first stepped off the elevator, she looked to the left and saw the entrance to the neurosurgical ICU. "That's my past," she thought. Then, looking to the right, she thought, "And that's my future."

Joshua Bright

Doris Fontanilla Pareja, RN.

Joshua Bright

Susan Agliato shoots hoops with her granddaughter just several days after having brain surgery performed with NYU Langone's new Gamma Knife.

Going under the Beam

Thanks to the Gamma Knife, Some Types of Brain Surgery Have Become Low-Risk Outpatient Procedures

To watch Susan Agliato shoot baskets with her granddaughter, you would never know she had brain surgery just a few days earlier. The bloodless, painless procedure was performed at NYU Langone Medical Center with a Gamma Knife, a noninvasive alternative to open surgery. "I wasn't even aware that surgery was being done," says the 58-year-old homemaker, who recently underwent a 37-minute procedure to treat two small benign meningiomas, the most common type of primary brain tumor.

Some 450 patients will be treated this year at the new Gamma Knife suite in Tisch Hospital. Opened in February to replace the facility that was destroyed by Hurricane Sandy, the new unit boasts the most sophisticated model available: the Leksell Gamma Knife® Perfexion. It is not a knife at all, but many small beams of precisely focused gamma radiation. This device is used to treat a variety of small- to medium-size tumors and lesions, particularly when the target is deep within the brain. The radiation distorts or destroys the DNA of target cells, rendering them unable to reproduce. Over time, the tumor simply shrinks in size until it disappears.

First, a lightweight, box-shaped metal frame is fastened to the patient's skull to serve as a guiding device during treatment. Then, the brain is imaged, and the data is fed into a computer. This information enables the Gamma Knife team to tailor the angle and intensity of the beams, depending on the characteristics of the tumor. NYU Langone's team—consisting of a neurosurgeon, radiation oncologist, and medical physicist—is one of the most highly experienced in the world. Finally, the patient lies on a table that locks the head frame in place to ensure stability, and the table slides head-first into the Gamma Knife. Depending on the number of tumors being treated, the procedure can take from 20 minutes to two hours.

"What used to be a highly invasive operation taking many hours and requiring one to two weeks in the hospital, perhaps months out of work, and sometimes permanent neurologic damage is now a low-risk outpatient procedure with a rapid return to normal function," explains neurosurgeon Douglas Kondziolka, MD, director of NYU Langone's Center for Advanced Radiosurgery. "That's what I call progress."

news & views

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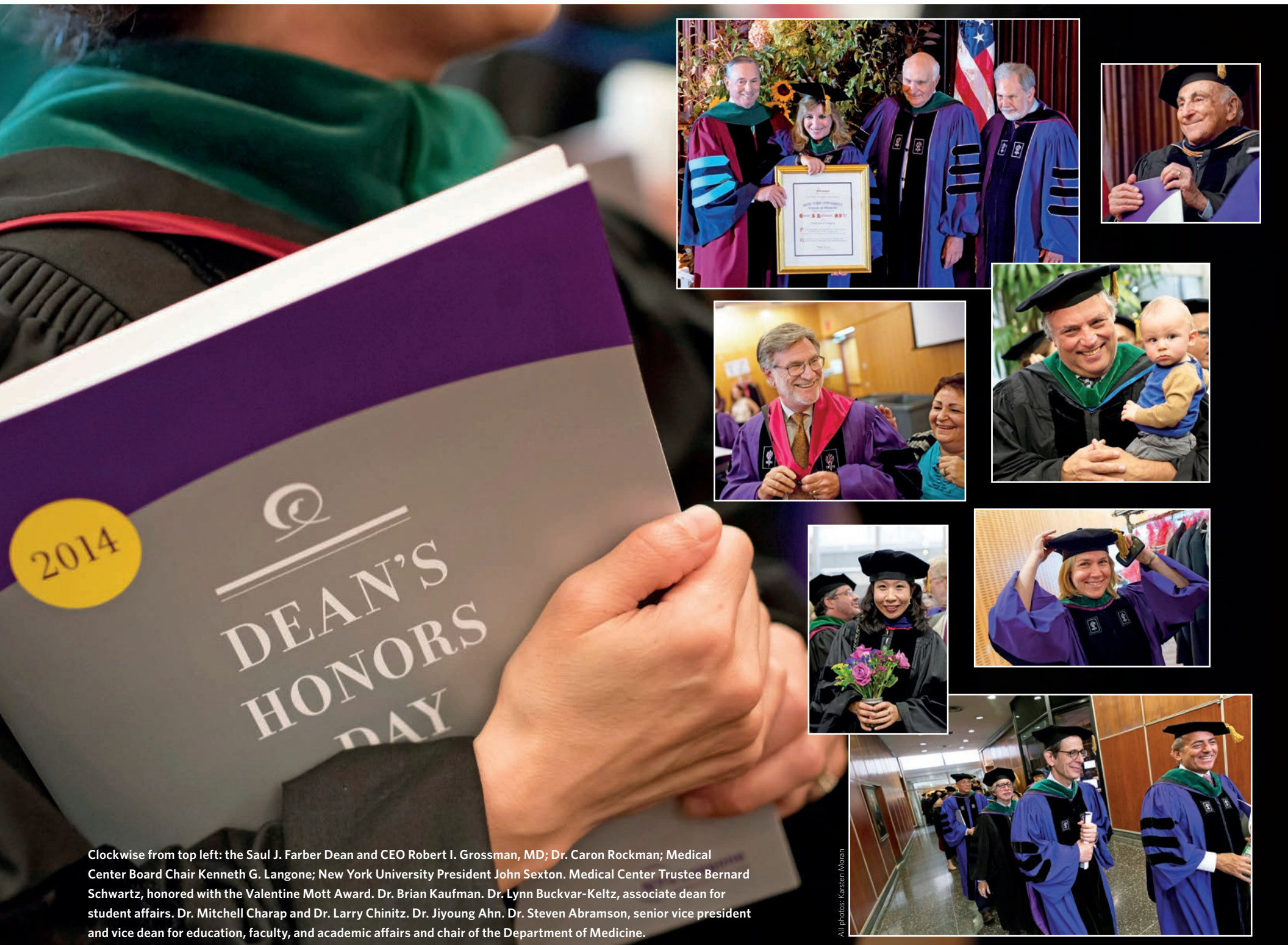

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