

FALL/WINTER 2015

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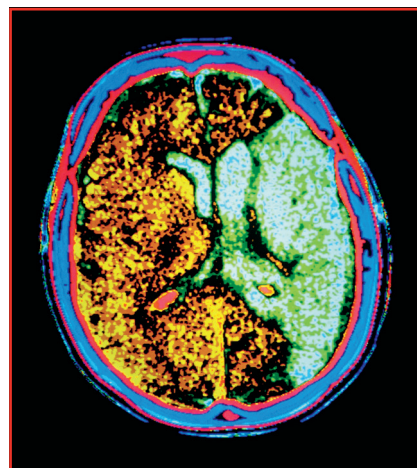
NewYork-Presbyterian Advances the Management and Treatment of Complex Stroke

Over the past few years, NewYork-Presbyterian Hospital has aligned its emergency, medical, interventional, and surgical expertise and capabilities to advance the diagnosis and treatment of acute stroke – the fifth leading cause of death in the United States.

“NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center were among the earliest programs designated through New York State as primary stroke centers,” says Babak Navi, MD, MS, Director of the Stroke Center at NewYork-Presbyterian/Weill Cornell. “Combined, we have one of the largest stroke centers in the country, treating more than 2,000 patients a year with acute stroke. Besides having the systems in place to administer tPA quickly and to perform endovascular therapy, we also have access to many exciting clinical trials that other centers do not – benefitting patients who are not eligible for the more standard approaches.”

Over the past several years, the Hospital has seen dramatic changes on several fronts: a sharp increase in total patient volume both through the Emergency Departments and via patient transfers; a growing number of patients who come in for acute treatment with intravenous tissue plasminogen activator (tPA); and advanced care with interventional approaches.

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CT scan showing cerebral infarction

care program offers specially trained medical staff, round-the-clock surveillance, state-of-the-art brain monitoring, and specialized medical and surgical treatments to minimize immediate and delayed brain damage and maximize each patient’s chance for a full recovery.

Acute Stroke Teams at the Ready

The stroke centers at Weill Cornell and Columbia draw on the expertise of multidisciplinary teams to evaluate and treat patients brought in with ischemic and hemorrhagic stroke. “Patients are evaluated by intensivists, neurosurgeons, and interventional neuroradiologists, and all decisions are made as a team with expert advice and ideas given simultaneously,” says Jared Knopman, MD, a neurosurgeon and interventional neuroradiologist at NewYork-Presbyterian/Weill Cornell, who is one of the few neurosurgeons in New York City with dual expertise in both open neurosurgical and minimally invasive endovascular techniques for the treatment of neurologic disease. “When a patient presents with stroke in the emergency room, the neurology stroke team is first on the scene to assess the patient. It is a streamlined process from ER triage to interventional techniques to postoperative ICU care.”

(continued on page 2)



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NewYork-Presbyterian Advances the Management and Treatment of Complex Stroke (continued from page 1)



“In the 2000s, nationally only about 3 to 5 percent of patients with ischemic stroke were being treated with tPA, which was the only FDA-approved treatment at the time. But now major stroke centers like NewYork-Presbyterian are giving it to 15 to 20 percent of ischemic stroke patients.”

— Dr. Babak Navi

“Great strides have been made in stroke care in recent years,” adds Dr. Navi. “We have become better at identifying stroke sooner and treating patients sooner, more often with tPA,” he says. “In the 2000s, nationally only about 3 to 5 percent of patients with ischemic stroke were being treated with tPA, which was the only FDA-approved treatment at the time. But now major stroke centers like NewYork-Presbyterian are giving it to 15 to 20 percent of ischemic stroke patients. Our systems have also improved, so we are giving tPA faster. In a typical stroke, with every minute that passes patients on average will lose about two million brain cells, so each minute is crucial.”

At NewYork-Presbyterian the median time from emergency room arrival to initiation of tPA – the door-to-needle time – was about 40 minutes in 2014. “That is significantly faster than it was five years ago,” says Dr. Navi. “A new target recommended by the American Heart Association is that in 50 percent or more of patients treated with tPA the door-to-needle time should be less than 45 minutes. However, tPA can only be given within four and a half hours after onset, while studies have shown that endovascular therapy can be effective within six hours, particularly for severe strokes.”

Rethinking Endovascular Techniques for Treatment of Complex Stroke

Developments in endovascular techniques and neuroimaging are expanding the arsenal of treatments available for the management of acute stroke. “While most emergency rooms can administer tPA, it is important for physicians to be aware of all the treatment options now available for stroke patients, and also the capabilities of their particular institution in treating patients with varying complexities,” says Olajide A. Williams, MD, Director of Acute Stroke Services, Department of Neurology, NewYork-Presbyterian/Columbia University Medical Center.

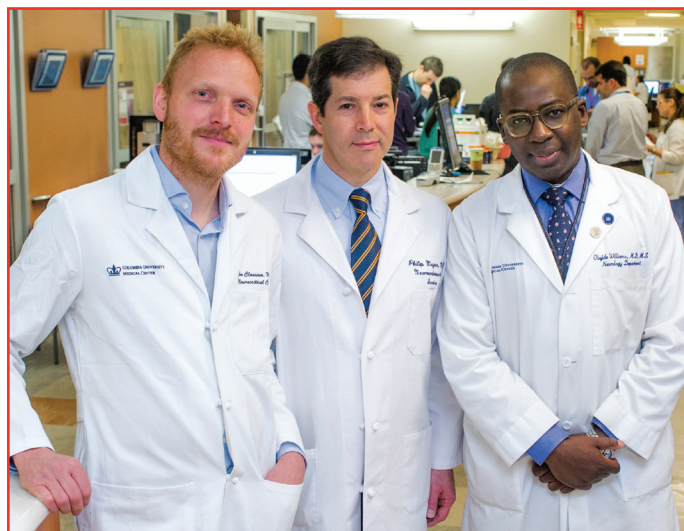
According to Dr. Williams, endovascular techniques for stroke treatment, including clot retrieval, had been utilized for some years, but began to fall out of favor a few years back. “The use of certain endovascular treatments began to dwindle due to some negative clinical trials that were published in *The New England Journal of Medicine*,” notes Dr. Williams. “However, there is new

excitement on the horizon for revisiting endovascular techniques for acute stroke treatment.”

The renewed attention has been stimulated by study results presented in the MR CLEAN study (Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands) at the World Stroke Congress meeting in Istanbul in October 2014, and the study’s subsequent publication in the January 1, 2015 issue of *The New England Journal of Medicine*.

“The researchers reported that for patients with acute ischemic stroke caused by an intracranial arterial anterior circulation occlusion, intraarterial treatment is highly effective and safe for emergency revascularization when given within six hours of stroke onset,” says Dr. Williams. “This was a well-designed trial involving 500 patients across 16 medical centers in the Netherlands, with 233 patients assigned to the intraarterial treatment group and 267 to the group treated with intravenous thrombolysis – the current standard of care. There was a significant difference in the rate of functional independence that favored endovascular therapy – 32 percent in the endovascular cohort versus 19 percent in the standard of care cohort. Despite the three previous negative trials, this particular trial showed positive results and generated great interest across the stroke world in thromboendovascular intervention for acute stroke.”

“For the treatment of acute stroke, endovascular techniques to restore brain blood flow have now been proven effective. I’ve worked on stroke treatment for my entire career, and the role for neurointerventional procedures has all come to fruition just within the last year,” says Philip M. Meyers, MD, Clinical Co-Director, Neuroendovascular Services at NewYork-Presbyterian/Columbia, whose expertise is in the treatment of vascular disorders of the brain and spinal cord using minimally invasive, image-guided techniques. “MR CLEAN was the first of a series of next generation endovascular stroke trials where the tools used were different, the pace at which we were doing these procedures was faster, and the ability to select appropriate stroke patients had improved. Suddenly, these trials showed the benefit of mechanical revascularization.”



Dr. Jan Claassen, Dr. Philip M. Meyers, and Dr. Olajide A. Williams

Dr. Meyers notes that not every patient with acute stroke who receives intravenous tPA improves, particularly when a large blood vessel is blocked. “In fact, the data showed that patients with large artery blockages are the least likely to get better with IV tPA alone,” says Dr. Meyers. “So the focus of these new endovascular procedures is to remove the clot immediately to restore blood flow to the brain. Using a special form of brain scan called CT angiography [CTA] to see a large blood vessel blockage, these are the patients that we rush to the angiography suite.”

Dr. Meyers emphasizes that the use of IV tPA in the emergency room is complementary to the subsequent endovascular procedure. “The speed at which treatment is initiated – any treatment including IV tPA – is very important,” he says. “The clot busting drug is started as soon as possible if the patient is eligible. There are, however, several contraindications to tPA administration, for example, a propensity to bleeding. The endovascular approach seems to work just as well in patients who do not meet the criteria for tPA.”

“The clot retrieval technology and the devices that we use now are superior and have largely replaced some of the devices that we used in earlier trials,” adds Dr. Williams. “In earlier trials there was limited use of third generation mechanical thrombectomy devices, such as retrieval stents, and a relatively long interval before intraarterial treatment commenced. And we know that time is brain. Lastly, there was an absence of pretreatment vascular imaging to confirm the presence of a proximal intracranial occlusion. The combination of these factors, which has since been addressed, in my opinion led to the failure of the earlier trials.”

“Opening up the artery plus tPA is better than just tPA alone,” says Dr. Navi. “We have been doing this for years, but not until five major trials came out this year that put to rest the argument of whether pulling a clot out makes a difference in stroke did we really know for sure that it was a proven, beneficial treatment. So I suspect that in the next year or so the FDA will approve endovascular therapy as a treatment for acute ischemic stroke within the first few hours in patients who have proximal arterial occlusion.”

The Sooner, the Better

“By the time the patient reaches us, we’re incredibly fast having the scans taken and read and getting the embolectomy done if necessary,” says Dr. Knopman. “Where we lose time is before the patient gets to us. It is crucial that patients be taken directly to an institution that can perform advanced therapies, including the capability of doing an embolectomy.”

“Certain patients need to be triaged as soon as possible to highly specialized centers like ours,” says **Jan Claassen, MD, PhD, FNCS**, Medical Director of the Neurological ICU and Director of Critical Care Neurology at NewYork-Presbyterian/Columbia. Dr. Claassen is a nationally and internationally recognized expert in neurological intensive care with particular expertise in brain hemorrhages. “We’re 24/7 ready and willing for them to be transferred here where we can make a difference.”

Drs. Williams, Meyers, and Claassen emphasize the importance of early communication with the referring physician or transferring institution and the availability of patient care related data. “It is very important to know if a patient is suspected of having a large vessel syndrome or clot occluding the anterior circulation; these are the clots that often are not recanalized by intravenous tPA,” says Dr. Williams. “They can be visualized with a simple

CT angiograph. Patients with these clots would benefit from the type of endovascular treatment that we provide.

“If the hospital does not have the CT imaging technology to diagnose the patient, but the neurologist there feels that this is most likely a large vessel syndrome where the patient is not improving, or if the patient is deteriorating despite thrombolytic therapy, these are the patients that we can help,” says Dr. Williams. “The sooner all of the information is made available to us, the more efficient the transfer process will be so that we can treat the patient in a timely manner. Even if a patient is presenting outside of that six-hour window, we can still offer them some lifesaving measure here at NewYork-Presbyterian.”



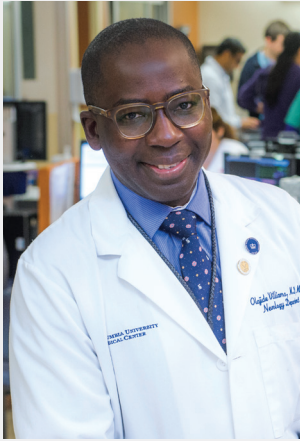
Dr. Babak Navi, Dr. Jared Knopman, and Dr. Halinder S. Mangat

Going forward, Dr. Meyers notes that there are still questions to be answered. “Is endovascular treatment of stroke the right thing to do in emergencies when people have large artery blockages in the brain? The answer is definitely yes,” he says. “Then the question becomes, what if this is someone who wakes up with a stroke and the time of stroke onset is unclear? What happens if that individual didn’t get in as quickly as we would like? Are there still people who are salvageable? The answer is probably yes. Research will focus on the use of advanced imaging to identify those patients whose brain function hangs in the balance, waiting to have the blood vessel reopened, versus those who can’t be helped with treatment or might even be harmed if we intervene. That is going to be the next big challenge in our science.”

Meeting the Critical Care Needs in Complex Stroke

“Our Neuro ICU is one of the first of its kind in the country to provide neurosurgical and neurological expertise for the sickest of patients, and is equipped to treat patients with intraarterial therapy within six hours of stroke onset,” says Dr. Claassen. “There are disease processes and vascular problems with stroke that are not frequently seen in other centers, but that we treat here at a high rate.”

The Neurological Intensive Care Units at NewYork-Presbyterian/Columbia and NewYork-Presbyterian/Weill Cornell have well established and proven track records of turning the sickest patients around and saving lives that have been deemed irretrievable.



“While most emergency rooms can administer tPA, it is important for physicians to be aware of all the treatment options now available for stroke patients, and also the capabilities of their particular institution in treating patients with varying complexities.”
— Dr. Olajide A. Williams

“We feel it is important for local physicians and local emergency rooms to know that we have a team capable of supporting their complex stroke patients through the more advanced care that we offer,” says Dr. Claassen.

“Not all hospitals have the ability to administer endovascular therapy,” adds Dr. Williams. “It requires a much more sophisticated level of care that includes an angiography suite, along with an interventional radiologist, an interventional neurosurgeon, or even an interventional neurologist. And it requires the ability to cope with the complications that may arise from the treatment itself.”

In addition to acute endovascular treatment, the Hospital’s neuro teams provide decompressive hemicraniectomy for malignant middle cerebral artery (MCA) occlusion, a condition that occurs in 10 percent of ischemic strokes. An estimated 13 percent of all proximal MCA occlusions develop severe brain swelling and herniation.

“Hemicraniectomy involves removing half of the skull to allow the swelling to move in the outward direction rather than in the inward direction and compress the rest of the brain structure that leads to death,” says Dr. Williams. “The use of hemicraniectomy has been demonstrated in three clinical trials, all of which showed a survival benefit, as well as some functional benefit when the data of all three trials were pooled.”

In addition, the Hospital’s Neuro ICUs provide multimodality monitoring with MRI or multichannel CT on site. “A lot of the care that we provide is aimed at minimizing secondary worsenings,” says Dr. Claassen. “A patient in a coma might have a storm going on in their brain, but you don’t see it. They’re just lying there peacefully as if nothing is happening. A lot of what we do is try to detect what is happening as soon as possible. For example, if you have a hemorrhagic stroke patient with a subarachnoid hemorrhage, they may get a vasospasm. You often can’t detect this in a poor-grade patient. So we have devised a number of monitoring techniques, noninvasive as well as invasive, to detect this in real time in order to intervene and prevent damage from occurring.”

Patients also undergo stringent neurological monitoring. “Our nurses check patients every hour, monitoring their level of consciousness,” says **Halinder S. Mangat, MD**, a neurointensivist with Weill Cornell whose training includes advanced clinical neurovascular physiology monitoring techniques using

invasive devices such as cerebral microdialysis and cerebral oximetry. “If the patient is unconscious and ventilated, other neurological assessments are done that help us determine if the patient’s clinical condition is changing. Monitoring for a patient in a deep coma includes placing probes in the patient’s brain to check cerebral blood flow, intracranial pressure, oxygen levels, and importantly, to look at the brain metabolism in real time.”

Neurocritical care is a relatively young and dynamic field, notes Dr. Mangat. “The perception has always been that we’re neurologists first and then perhaps intensivists. I think the paradigm has changed and neurointensivists are intensivists first. Any patient who needs to be in an ICU and is suffering from a neurological or brain injury needs to be in a neurocritical care unit. Scientific evidence shows that these patients have better outcomes when they are cared for in specialized units that are trained to look after brain injury patients. It doesn’t matter the nature of the brain injury.”

Call 1-800-NYP-STAT

The NewYork-Presbyterian Physician Access Transfer Center coordinates patient transfer to the advanced neurological and neurosurgical services available at NewYork-Presbyterian Hospital. NYP STAT – available 24/7 – connects the referring physician to either an attending neurologist or an attending neurointensivist who will immediately begin the process of accepting the patient.

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Clinical Trials Update: NeuroNEXT

The Network for Excellence in Neuroscience Clinical Trials, NeuroNEXT, was created to conduct studies of treatments for neurological diseases through partnerships with academia, private foundations, and industry. The network is designed to expand the capability of the National Institute of Neurological Disorders and Stroke to test potential new therapies, increase the efficiency of clinical trials, and respond quickly as new opportunities arise to test promising treatments. Karen Marder, MD, MPH, and Claudia Chiriboga, MD, MPH, are co-principal investigators, and Claire Henchcliffe, MD, DPhil, is site PI at Weill Cornell. Joyce Moran, CCRC, is NeuroNEXT Project Manager.

NN103: A Phase 2 Trial of Rituximab in Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune disorder of neuromuscular transmission with an estimated annual incidence of about 1 to 2 per 100,000. Common symptoms include a drooping eyelid, double vision, slurred speech, difficulty chewing and swallowing, weakness in the arms and legs, chronic muscle fatigue, and difficulty breathing. Despite current therapies a subset of patients remains medically refractory or have intolerable medication adverse effects. The purpose of the study is to find out the effect and safety of a new use of the drug rituximab in MG patients who are on prednisone.

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NN104: A Multicenter, Phase 2 Study of 3K3A-APC with tPA in Ischemic Stroke

Currently, the only approved treatment in the U.S. for ischemic stroke is a drug called recombinant tissue plasminogen activator (rtPA or tPA), indicated for intravenous administration within three hours of onset of the stroke. The drug is designed to break down blood clots to restore blood flow to the brain. In some patients, however, tPA can cause internal bleeding and other complications.

This multicenter, Phase 2 study uses a continual reassessment method to determine the safety, tolerability, and activity of 3K3A-APC, a recombinant variant of human activated protein C (APC), in combination with tissue plasminogen activator (tPA), in subjects with moderately severe acute hemispheric ischemic stroke. The cytoprotective properties of 3K3A-APC may be useful in protecting ischemic brain tissue from further damage, while avoiding an increase in the chance of treatment-related bleeding. The study intervention will be administered as a 15-minute infusion every 12 hours for up to 5 infusions. Four dose levels will be considered for this trial. Approximately 100 participants, ages 18 to 80 years old, will be enrolled and followed for 90 days.

For More Information

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New Neurology Division to Track Outcomes

As a fledgling neurologist in the early 1990s, Mitchell Elkind, MD, had few treatment options to offer patients once he made a diagnosis. Nothing for dementia or stroke and just one drug for multiple sclerosis. Over the past few decades, new treatment options have emerged giving rise to the need to track outcomes. "There's a lot more available," says Dr. Elkind, "so the question has become, 'Which is the best treatment and what's going to give the patient the best quality of life when you consider side effects and benefits and even the financial cost?'"

In October, in a joint effort with the Gertrude H. Sergievsky Center, the Department of Neurology at NewYork-Presbyterian/Columbia formed a new research division to answer those questions. Dr. Elkind is founding Director of the Division of Clinical Outcomes Research and Population Sciences (Neuro CORPS), one of the nation's first such divisions.

In September, Dr. Elkind, a member of the Stroke Division in the Department of Neurology, submitted a proposal for funding the first Neuro CORPS investigation, to weigh the relative merits of inpatient and outpatient evaluation of patients with transient ischemic attacks and minor strokes. "At present, patients are managed in a variety of ways and settings, including outpatient, inpatient, and often during prolonged emergency department stays," says Dr. Elkind, who seeks to test a protocol based on rapid assessment in an outpatient setting.

"Defining optimal evaluation and treatment for these patients, including risk stratification and referral to urgent outpatient specialty clinics, would have the benefits of preventing stroke, improving patient outcomes and satisfaction, reducing emergency department and hospital length of stay, optimizing resource utilization, and reducing costs," he says.

Advances in Neurology and Neurosurgery

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