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Teleneurology Update:
Growing a Telemedicine Program for In-Hospital General Neurology Services

More than 10 years ago, the UPMC Department of Neurology introduced an innovative telemedicine program for the evaluation and care of patients experiencing a stroke. This "tele-stroke" program allows neurologists in Pittsburgh to rapidly evaluate patients at remote hospitals and order tissue plasminogen activator (tPA), which must be given within 4.5 hours of the appearance of stroke symptoms.

Since that time, UPMC has been at the forefront of telemedicine and remote patient care and has developed an array of telemedicine programs in diverse fields including psychiatry, maternal-fetal medicine, dermatology, radiology, and wound care. About a year ago, UPMC began offering general neurology in-hospital services via telemedicine. **Neil Busis, MD**, a clinical professor in the Department of Neurology and chief of the UPMC Shadyside Department of Neurology, has overseen the development of this telemedicine program with **Lawrence Wechsler, MD**, the chairman of the UPMC Department of Neurology. The in-hospital teleneurology program is now providing many benefits to patients, their physicians, and hospitals utilizing the service.

The relatively new teleneurology program currently provides access to a neurologist using a real-time, audio-visual interface to all UPMC-affiliated hospitals and to non-UPMC hospitals with sufficient proximity to UPMC Presbyterian in Pittsburgh, Pa., UPMC Altoona in Altoona, Pa., or UPMC Hamot in Erie, Pa., to allow patient transfer if needed. The hospitals range greatly in size and are located in a number of different healthcare systems. Currently, the location furthest from Pittsburgh receiving services is UPMC Susquehanna Health System in north-central and central Pennsylvania. The support provided by the teleneurology program depends on the needs of the local hospital. At some hospitals, a neurologist is not available for in-patient care, and UPMC Neurology provides coverage via telemedicine 24 hours a day, 7 days a week. At other hospitals, the teleneurology program provides only partial or emergency coverage.

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As technology has become more affordable, telemedicine has reaped the benefits. The neurologist can use any computer or device. At the hospital receiving teleneurology services, a high-resolution camera that can be controlled by the remote physician to zoom and pan is ideal. Sufficient internet bandwidth is needed for both the hospital and the remote neurologist. Fortunately, bandwidth is getting better nationwide. Some expertise is needed at both sites to establish the connection and run the HIPAA-complaint software that maintains a virtual room for the telemedicine interaction.

Dr. Busis has found that the patient history that the neurologist obtains during a telemedicine conference tends to be more complete than the history collected during an in-person visit to the hospital ward.

When performing a teleneurology in-hospital evaluation the neurologist has immediate access to the patient's medical records including the results of laboratory or imaging tests. This helps streamline care. UPMC was one of the first adopters of electronic medical records (EMRs) nationally and has capitalized on the advantages of EMRs. More than a dozen UPMC hospitals are at the highest levels of EMR use as measured by the Healthcare Information and Management Systems Society Analytics. This is a great asset for all the UPMC telemedicine programs. Improvements are also being made toward a unified messaging platform for telemedicine, which will streamline communication between providers.

Nurses often assist as telepresenters at the remote site. The telepresenters must become competent in working with remote physicians. They must know how to perform key elements of the neurological exam, such as testing strength and reflexes, as directed by the neurologist. If the patient has difficulty interacting with neurologist on the screen, the telepresenter needs to assist. Additionally, the telepresenter often needs to represent the remote neurologist when conveying results and recommendations to the referring physician.

Dr. Busis has identified many advantages of in-hospital teleneurology since the UPMC program started approximately one year ago. He has found that the patient history that the neurologist obtains during a telemedicine conference tends to be more complete than the history collected during an in-person visit to the hospital ward. Because the teleneurology visit occurs at a preset time, the patient's family participates more often than during in-person neurology consults on the hospital ward, and the patient, when able, and their family have more time to prepare for the conference with the neurologist. Because the process of care is streamlined, the physician can spend more time with each patient. Although some may be leery at first, patients and their families seem very happy with teleneurology care. "Patient satisfaction surveys are always through the roof," says Dr. Busis. Informal surveys of cognitively intact patients have also yielded uniformly positive feedback.

The core medical fundamentals of good neurology are not changed by telemedicine. When Dr. Busis has compared diagnoses obtained by remote assessment with diagnoses obtained after a local assessment in patients who were initially evaluated remotely and were later transferred to UPMC Shadyside, the diagnoses remained the same. Teleneurology is just a different way of connecting people. Based on his personal experience, Dr. Busis thinks that teleneurology, and perhaps all telemedicine, may be best suited to senior clinicians.

Successful teleneurology relies on the established clinical expertise of the doctor doing the telemedicine consult. Senior clinicians have the experience to make most of their diagnoses from the information available in a telemedicine conference — how a patient looks, how they respond during standard neurological tests, conversations with the patient and their family, followed by confirmation with laboratory findings, and imaging results. Senior clinicians are also more confident in identifying patients who need to be transferred.

Expanding Care Options

Like all telemedicine, teleneurology offers patients expanded options to access world-class clinical care, while maximizing efficiency, overcoming provider shortages, and decreasing the overall cost of care. Although Dr. Busis, Dr. Wechsler, and other telemedicine specialists at UPMC continue to analyze the outcomes of telehealth, the positive impact for patients is evident. Hospital systems can use teleneurology to overcome staffing difficulties due to a shortage of neurologists, especially in rural areas, and to provide hospital coverage when local neurologists may be particularly busy with their clinical practices or require time off. This leads to shorter wait times for outpatient services as well and higher patient satisfaction. Dr. Busis has explored physician burnout extensively as a member of the American Academy of Neurology Wellness Task Force and National Academy of Medicine Action Collaborative on Clinician Well-being and Resilience and suspects that telemedicine will reduce burnout among neurologists. Dr Busis thinks that "a lot of the friction that causes burnout is minimized by telemedicine." For example, both pre-service time, such as travel between hospitals, and post-service time, such as clinical documentation, are greatly reduced by the current teleneurology program.

A Growing Program

The UPMC teleneurology program has significant room to expand. Dr. Busis and his colleagues are actively recruiting additional remote hospitals for the in-hospital teleneurology service and identifying UPMC hospitals that could benefit from a greater neurology presence. Currently, the teleneurology program provides in-hospital evaluation and care. Opportunities for service at other locations are currently untapped. Many patients with neurological disorders are cared for at home or in nursing homes. Although there are barriers to overcome, establishing a teleneurology presence to evaluate patients in these locations could be highly beneficial for the patients and their caregivers.

UPMC currently offers over 35 clinical specialties via telemedicine, and more than 25,000 patients have accessed on-demand clinical care via the UPMC AnywhereCare platform. Few academic medical centers currently provide general neurology services via telemedicine. As was the case with tele-stroke care, the physicians at UPMC are leading the way, researching best practices in telemedicine and pioneering new methods for care delivery.

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Improving Care for Patients Experiencing Stroke

The UPMC Stroke Institute played a key role in establishing mechanical endovascular thrombectomy as the current standard of care for treating patients with an ischemic stroke. Now, **Ashutosh Jadhav, MD, PhD**, director of the Comprehensive Stroke Center at UPMC Mercy and UPMC Presbyterian and an associate professor in the Department of Neurology, and his colleagues are performing evidence-based research to expand the indications for the procedure and improve patient care.

The UPMC Stroke Institute is an assembly of brain specialists who have access to cutting-edge technology, including six faculty members from the UPMC Department of Neurology who specialize in stroke, three stroke fellows, and an NIH-funded Stroke Trial Network fellow, **Shashvat Desai, MD**. Additionally, the UPMC Center for Neuroendovascular Therapy within the Cerebrovascular Neurosurgery Center is staffed by two neurologists and two neurosurgeons who are interventional-trained and stroke-trained, along with four fellows — two neurology fellows and two neurosurgery fellows.

The UPMC Stroke Institute provides care via a hub-and-spoke model. Primary Stroke Centers are found throughout western Pennsylvania. Through the innovative use of telemedicine, 30 peripheral hospitals, both within the UPMC system and non-UPMC hospitals, are linked with Comprehensive Stroke Centers in Pittsburgh, Erie (UPMC Hamot), and Altoona (UPMC Altoona) that can perform mechanical endovascular thrombectomy and always have experts on call. Additionally, clinical trial access is increased by this UPMC telemedicine network, giving our patients access to new treatments. Experts from the UPMC Stroke Institute also perform telephone consultations as needed and field more than 5,000 phone calls per year. Last year, more than 2,000 patients were discharged after a stroke from the Comprehensive Stroke Centers at UPMC Presbyterian and UPMC Mercy. These two stroke centers were the first in western Pennsylvania certified by the Joint Commission of the American Stroke Association and the American Heart Association. Approximately 350 mechanical thrombectomies were performed at this central UPMC center, the highest single-center volume in the United States.

A major research focus of Dr. Jadhav and Dr. Desai is determining which patients can benefit from mechanical endovascular thrombectomy. There are approximately 800,000 strokes per year in the United States; 87 percent are ischemic. Of these, approximately 25 percent are caused by a large vessel occlusion (LVO) and could potentially be treated with endovascular thrombectomy. This is notable because strokes caused by LVOs account for 90 percent of the mortality and 60 percent of the morbidity caused by all strokes. Current treatment guidelines for mechanical endovascular thrombectomy apply to 7 percent of all strokes, 30 percent of strokes with a vessel occlusion, and 50 percent of strokes with a major occlusion.

When mechanical endovascular thrombectomy was first introduced, the ESCAPE and SWIFT-Prime clinical trials, which included UPMC patients and physicians, provided significant evidence that the procedure was safe and beneficial, but those trials only proved a benefit within the first six hours after detection of an ischemic stroke. The DAWN trial, spearheaded at UPMC by Tudor Jovin, MD, who recently left UPMC and served as the global principal investigator of more than 30 sites, was the first study to show that mechanical thrombectomy can still be beneficial when performed up to 24 hours after stroke onset. In the DAWN trial, Dr. Jadhav, Dr. Jovin, and their colleagues found that if patients were selected for mechanical thrombectomy based on MRI or perfusion imaging, looking for a mismatch between clinical deficit and infarct size that indicates brain tissue that is at risk but not permanently damaged (penumbra), patients could be identified who would benefit from thrombus removal, even though more than six hours had passed.

The guidelines of the American Stroke Association (ASA) changed because of this trial, in which UPMC enrolled the highest number of patients worldwide.

Most recently, Dr. Jadhav and Dr. Desai have found that 24 hours is not a hard deadline. In select patients, mechanical endovascular thrombectomy is beneficial and safe even when performed more than 24 hours after symptom onset. In a retrospective review of patients treated with mechanical endovascular thrombectomy at three comprehensive stroke centers at greater than 24 hours from the time they were last known to be well, Dr. Desai and Dr. Jadhav found that patients could still benefit from clot removal after more than 24 hours, particularly if they had a small stroke. Most of the patients were treated at UPMC, and the benefit was measured primarily by functional independence 90 days after the stroke but also by early therapeutic response. They also found that the risks of the endovascular thrombectomy procedure did not increase after the 24-hour time point. This study supports using physiology-based patient selection using imaging to assess clinical core mismatch rather than strictly time-based patient selection, and Dr. Jadhav advocates this approach.

Stroke neurologists are now recognizing that they may be underutilizing mechanical endovascular thrombectomy. More stroke patients than indicated by current guidelines may benefit from endovascular thrombectomy, but clinical trials have not addressed other populations, so evidence to justify expansion of endovascular thrombectomy as the standard of care is currently lacking.

Dr. Jadhav and Dr. Desai are beginning to explore the utility of endovascular thrombectomy in patients with a large stroke volume (> 70 cc), a small occlusion, or minimal symptoms. Maximizing the potential of endovascular thrombectomy is essential to improve patient outcomes.

In addition to their pioneering work on mechanical endovascular thrombectomy, the members of the UPMC Stroke Institute are exploring ways to improve the entire continuum of patient care — from actions taken when a patient first experiences symptoms of stroke through hospital admission and treatment to rehabilitation and discharge. Dr. Jadhav and his colleagues have examined emergency department procedures to determine where a patient should be admitted after the decision is made to transfer them from a Primary Stroke Center to a Comprehensive Stroke Center. They found that if they admit the patient straight to the angiography suite, rather than through the emergency department, they save up to an hour of potential delays. Because research suggests that every 20-minute reduction in time to reperfusion increases disability-free lifespan by three months, this may translate into significantly improved patient outcomes. When a patient stays at a local hospital staffed with a general neurologist and not a stroke neurologist, telemedicine is increasingly an option. A pilot study at UPMC Passavant has shown that hospital stays can be cut in half with telemedicine involvement by experts from the UPMC Comprehensive Stroke Center. This allows the specialists to provide longitudinal care and is being expanded to other hospitals.

Patients lose, on average, two million neurons per minute during an ischemic stroke with LVO. With Marcelo Rocha, MD, PhD, an assistant professor in the UPMC Department of Neurology, Dr. Desai and Dr. Jadhav have been dissecting this "time is brain" mantra. They discovered that there is a great deal of heterogeneity to neuronal loss during a stroke. Some patients lose more than 35,000 neurons per minute, while others lose up to 27 million neurons per minute. The fast progressors have failing collateral circulation and quickly develop a large ischemic core, while the slow progressors have good collateral circulation and slow infarct growth over time. The underlying pathophysiology is poorly defined but depends on blood flow above a certain threshold, baseline tissue oxygen demand, and each patient's tolerance to focal cerebral ischemia. The differences between fast progressors and slow progressors are not distinguishable by EMS providers or upon initial triage in the emergency department, so improving the speed of triage, possibly by initially limiting advanced imaging studies in some patients, is the only way to improve care for fast progressors. Conversely, slow progressors with late-presenting stroke may still benefit from interventional therapies because they may still have substantial areas of salvageable brain.

By determining the best triage and treatment methods for patients in the greater Pittsburgh area, Dr. Jadhav, Dr. Desai, and the faculty of the UPMC Stroke Institute are elucidating best practice principles that may be applicable nationwide and advancing life-changing medicine for patients with stroke.

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New Therapies for Migraine Prevention

In spring 2018, the first of four monoclonal antibody therapies for migraine prevention was approved by the United States Food and Drug Administration (FDA) and became widely available for clinical use. These drugs provide migraine-specific preventive therapy and are a landmark improvement in the care of patients with migraine.

Migraine is a neurological disease that significantly reduces quality of life, and patients with chronic migraine suffer 15 days a month or more. In any given year, 18 percent of women and 6 percent of men experience migraine with throbbing headaches often accompanied by nausea, vomiting, sensitivity to light, and sensitivity to sound. **Robert Kaniecki, MD**, director of the UPMC Headache Center and an associate professor in the Department of Neurology, has 27 years of experience as a neurologist specializing in migraine. In that time, there have been two major developments in migraine treatment. The first was the introduction of triptans (e.g., Imitrex) in 1992, which revolutionized care of acute migraine. Now 25 years later, there has been a second pivotal development in migraine care. With the introduction in May 2018 of monoclonal antibody-based therapies targeting calcitonin gene-related peptide (CGRP) and the CGRP receptor, headache specialists such as Dr. Kaniecki and his colleagues now have effective drugs that are specific for migraine prevention.

A regimented lifestyle, including regular sleep patterns, regular eating to avoid hypoglycemia, hydration, regular exercise, and regular school or work, if symptoms allow, can improve migraine symptoms in some patients and do not harm the patient. Avoiding nicotine and common food triggers and reducing caffeine and food additive consumption also can be helpful. When lifestyle changes are insufficient, and a patient still has greater than five days with migraine per month, medical therapy is initiated. This standard medical therapy is not specific to migraine. Blood pressure medications, antiseizure medications, antidepressants, and BOTOX® are tested and titrated to see if migraine frequency or severity decreases. Adverse side effects of these drugs can include weight gain, memory loss, sexual dysfunction, and fatigue, and the patient and physician must balance the benefits of continuing therapy with the side effects. Patient adherence to these treatment regimens is low. Additionally, some patients cannot receive standard medical therapies because of comorbid conditions and drug interactions, especially cardiovascular complications.

Since late-May 2018, four drugs have been introduced to the market. These are specific for migraine prevention and have far fewer adverse side effects and contraindications for their use.

Erenumab-aooe (Aimovig™), fremanezumab-vfrm (Ajovy™), galcanezumab-gnlm (Emgality™), and eptinezumab are migraine-specific preventive therapies that target CGRP signaling with monoclonal antibodies. CGRP is a neurotransmitter that creates a state of neuroinflammation and is a potent vasodilator. CGRP pathways have been a target for migraine therapies for more than a decade, but CGRP-receptor antagonists had significant hepatic toxicity. Because the liver does not metabolize monoclonal antibodies, they do not result in hepatic toxicity. Additionally, there are no concerns about cardiac toxicity, nephro-toxicity, or damage to any other organ. Erenumab is specific to the CGRP receptor, and the other three antibodies target the CGRP ligand. Erenumab, fremanezumab, and galcanezumab are currently FDA-approved and on the market. These therapeutics are administered subcutaneously either once a month or once every three months. Eptinezumab, which is administered intra-venously, is likely to become available in 2020.

In pivotal, phase III clinical trials, erenumab, fremanezumab, galcanezumab, and eptinezumab reduced monthly headache days in patients with chronic migraine (> 15 headache days per month) and episodic migraine (< 15 days per month). Patients with chronic migraine treated with the monoclonal antibody therapies had, on average, two fewer days with migraine per month than patients given a placebo. The antibodies reduced consumption of triptans for acute migraine relief and resulted in better scores on patient-reported outcome measures, such as the Headache Impact Test (HIT-6) and the Migraine Disability Assessment (MIDAS) score. The therapeutic effects were seen within seven to 14 days of injection, indicating an early onset of action. The participants in the treatment and placebo groups reported similar side effects, with no adverse cardiovascular or cerebrovascular effects. The major therapy-specific adverse event was pain and swelling or redness at the injection site. Additionally, there was good adherence of patients to treatment because of the infrequency of delivery and adverse effects. In short, migraine specialists like Dr. Kaniecki and his colleagues at the UPMC Headache Center are finding that these monoclonal antibody therapies are the most effective and best-tolerated drugs they have ever seen in migraine prevention.

Integrating these revolutionary monoclonal antibody therapies into current care protocols is critically important. Dr. Kaniecki currently is focusing on working with pharmaceutical companies and health insurance plans to get these drugs to the patients who will benefit from them. All of the monoclonal antibody therapies are more expensive than the nonspecific drugs used to treat migraine, but at approximately $575 per month, they are reasonably priced when compared with other monoclonal antibody therapies. The therapies do not need to be titrated and typically are started without discontinuing other antimigraine medications. If the antibody therapies are effective, the patient and his or her doctor can then begin testing which medications and supplements previously taken for migraine prevention can be discontinued. The risks of long-term inhibition of CGRP signaling are unknown, and safety if taken during pregnancy is unclear and of concern,

so patients taking the CGRP-targeted therapies must be closely monitored moving forward. Patients on standard migraine therapies with good results, good adherence, and few adverse side effects are unlikely to switch to the new monoclonal antibody therapeutics.

The UPMC Headache Center is one of the busiest headache centers in the country and maintains extensive electronic records. Approximately 90 percent of the 1,200 patients cared for by the physicians at the center each month experience migraine. Although the monoclonal antibody therapies have been widely available for less than a year, six months of clinical experience at UPMC is significantly different from six months of experience at a less busy center. Dr. Kaniecki and his colleagues eventually hope to compare the CGRP-targeting antibody therapies and gain insight into whether there is a best drug for each patient. They have administered erenumab, fremanezumab, and galcanezumab to hundreds of patients. Once they have experience with thousands of patients, these comparisons will be feasible. Dr. Kaniecki also is moving forward with plans to research the effectiveness of the monoclonal antibody therapeutics in patients with chronic migraine (> 15 a month) but with medication overuse headaches as a result of using pain-relieving medication for > 10 days a month. Care of these patients is very challenging, and they have been excluded from most clinical trials of the drugs.

Targeting the CGRP pathway for treatment of acute migraine, rather than migraine prevention, also is an area of active investigation. Although triptans are the well-established standard-of-care for the relief of acute migraine, they can lead to vascular complications, such as heart disease and stroke. The monoclonal antibody therapies can be used in patients with vascular problems, so migraine specialists are hopeful that the new drugs might provide relief for acute migraine.

The introduction of migraine-specific preventive therapies with few side effects that can be used in a wide range of patients is a revolutionary advancement in migraine care.

"It is impressive to see people who had failed multiple other treatment options do extraordinarily well with these products," says Dr. Kaniecki. "It is a game changer."

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