Synapse
a clinical resource
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The ABCs of Secondary Stroke Prevention

Peter T. Skaff, MD and Stacie Crain, FNP-BC

Thanks to advances in stroke treatment, stroke mortality has dropped from the third to fifth leading cause of death in the United States in the last five years. However, due to our aging population, stroke incidence is rising, increasing the likelihood that non-neurologists will be seeing stroke patients for secondary prevention management. Stroke prevention guidelines were updated by the American Heart Association/ American Stroke Association (AHA/ASA) in 2014. Key recommendations can be easily recalled using the ABCs.

A = Antiplatelet Agents or Anticoagulation. For patients with noncardioembolic stroke or transient ischemic attack (TIA), daily antiplatelet therapy with aspirin 50-325 mg/d, clopidogrel (Plavix) 75 mg/d, or combination aspirin/dipyridamole (Aggrenox) 25/200 mg twice daily is recommended for recurrent stroke prevention. Dual antiplatelet therapy with aspirin and clopidogrel is generally not recommended for stroke prevention, but may be considered for initiation within 24 hours of TIA or minor stroke and continued for up to 21 days. This may be extended to 90 days in cases of intracranial stenosis. The most effective anti-platelet therapy regime should be based upon patient characteristics including other disease processes, safety, and practicality (including side effect tolerance and cost). Anticoagulation with either warfarin or a newer oral anticoagulant is recommended for the prevention of recurrent stroke in non-valvular atrial fibrillation, whether paroxysmal or permanent.

B = Blood Pressure. Outside of the immediate, post-stroke period, when blood pressure is allowed to run high in order to promote cerebral perfusion, normalization of blood pressure is the long-term goal for stroke prevention. In general, average readings of less than 140/90 are recommended. In diabetics, or for patients who have had a recent, lacunar stroke, a stricter goal for average systolic BP < 130 is reasonable.

C = Cholesterol and Carotids. Unless contraindicated, statin therapy is recommended to reduce stroke risk for all patients with LDL ≥ 70 who have had a cardiovascular or cerebrovascular event presumed to be of atherosclerotic origin. The American Heart Association recommends initiating high intensity statin therapy if the patient is under 75 years old and has no other "conditions, drug-drug interactions influencing statin safety, or a history of statin intolerance" (AHA/ASA 2013 Guidelines on the Treatment of Blood Cholesterol to Reduce ASCVD Risk).

When internal carotid artery stenosis of 70-99% is detected ipsilateral to TIA or non-disabling stroke, Carotid Endarterectomy (CEA) is recommended within two weeks of the incident event if perioperative morbidity and mortality risk is estimated to be <6%. For moderate stenosis (50-69%), the benefit of CEA over medical management is marginal and is recommended in carefully selected patients. CEA is not recommended for asymptomatic patients or when symptomatic carotid stenosis is <50%.

D = Diabetes and Diet. Patients who have had an ischemic stroke or TIA should be screened for diabetes, preferably with HbA1c. Diabetic patients should be treated according to ADA guidelines. With regard to diet, recent studies have linked the Mediterranean diet to a lower stroke risk. This diet emphasizes eating plant-based foods, such as fruits and vegetables, whole grains, legumes, and nuts, and use of healthy fats such as olive oil.


Peter T. Skaff, MD

E = Exercise. For patients who are physically capable of moderate- to vigorous-intensity exercise (considered

continued on page 2

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The ABCs of Secondary Stroke Prevention—continued from page 1

"break a sweat" exercise), three to four sessions per week averaging 40 minutes each are recommended. All patients who are willing and able to continue or begin physical activity should be encouraged to do so. If a patient cannot complete a lengthy duration of activity, have him/her set a goal and foster the desire to increase activity as tolerable. Stroke support groups, where available, often include encouragement and reinforcement of this practice.

F = Follow-Up. In preventing a second cerebrovascular event after an initial TIA or ischemic stroke, there is an opportunity to re-address a patient's risk factors, act as a health coach, and provide evidence-based medicinal care. Among lifestyle factors, smoking cessation provides the most dramatic risk reduction, but physical activity, diet, and weight management are also factors which are patient-controlled. Patients are often committed to lifestyle changes while in the hospital, but enthusiasm can wane after discharge. This is an area where follow-up and health coaching can make a substantial impact on wellness and prevention.

The Mercy Medical Group San Juan neurology clinic, located on the campus of the region's only certified Comprehensive Stroke Center, are pleased to offer a stroke clinic. The clinic is staffed by a vascular neurologist and board certified nurse practitioner and is ready to assist you with any clients you feel may benefit. Please call 916.536.3670 for more information or for appointment availability.

Stacie Crain, FNP-BC

Disease Modifying Therapies in Multiple Sclerosis

Sabeen Lulu, MD

Multiple Sclerosis (MS) is a chronic, immune-mediated disease that results in inflammation, demyelination, and neurodegeneration of neurons in the central nervous system. MS is characterized by relapses and remissions earlier in the disease course. If untreated, MS has a high potential for disability and progression. About 15% of patients with MS have a progressive course from disease onset.

Until the early 1990s, there were no treatments available to prevent new attacks for people with MS. In 1993, Betaseron (interferonß-1b), the first injectable therapy was approved for prevention of relapses in MS. By the year 2000, four other injectable therapies were available. Currently, there are thirteen FDA approved therapies for relapsing types of MS. Despite numerous trials and agents tested, none were found to be effective in preventing progression in primary progressive MS. This emphasizes the important role of initiating early and effective therapy in MS.

There continues to be rapid development and evolution of MS therapies. Ocrelizumab and Daclizumab will undergo FDA review in 2016 for approval for MS.

Injectable therapies (Avonex (interferonß-1a); Copaxone (glatiramer acetate); Betaseron (interferonß-1b); and Rebif (interferonß-1a)) have been prescribed longer and in clinical trials decreased relapses by about 30%. Safety data suggest no safety concerns to their use. Mitoxantrone (Novantrone)

continued on page 3

Disease Modifying Therapies in Multiple Sclerosis—continued from page 2

approved for progressive forms of MS is considered highly toxic and very rarely used. All except Copaxone require monitoring of liver enzymes. Plegridy (peginterferonß-1a) a longer acting form of interferon is also available.

Due to its efficacy in reducing relapses by about 70%; Natalizumab (Tysabri) monthly infusions received accelerated FDA approval in 2004. It was, however, withdrawn within a few months after three cases of progressive multifocal leukoencephalopathy (PML) (caused by the JC Virus) were reported. In 2006, it was released again with more stringent monitoring and testing requirements. Those who are negative to JC virus antibodies were found to have minimal risk of developing PML on Tysabri, but did require repeated testing.

Oral therapies; Gilenya (Fingolimod), (Aubagio (teriflunomide); and Tecfidera (dimethylfumarate) were approved in 2010, 2012, and 2013 respectively. Both Gilenya and tecfidera decreased relapses by about 50%. Aubagio is thought to be comparable to injectables at about 30% relapse reduction. With the slightly improved relapse reduction comes more side effects and monitoring requirements, as well as unclear long term safety data. More recently, both Gilenya and Tecfidera have been associated with PML but at much lower rates than Tysabri.

Lemtrada (Alemtuzumab) infusions became available in 2014. Lemtrada was found to prevent 65-70% of relapses compared to Rebif. With its very high efficacy come mostly immune-related adverse events, and increased risk of malignancy. Lemtrada is therefore reserved for those who have failed at least two other therapies or with very aggressive disease.

There continues to be rapid development and evolution of MS therapies. Ocrelizumab and Daclizumab will undergo FDA review in 2016 for approval for MS. Ocrelizumab is thought to carry high efficacy with a favorable safety profile for relapsing remitting MS and is the only agent to-date which has shown benefit in primary progressive MS. Ongoing research into remyelination therapy to repair the damage in MS offers the potential for better outcomes from relapses in MS.

Sabine Lulu, MD

Chronic Migraine: Is Botox an Option for Treatment?

Kellie Zumot, PA-C, MSCS

Kellie Zumot, PA-C, MSCS

Migraine is defined by the National Institute of Health (NIH) as throbbing, pulsating, or dull head pain that can often be associated with nausea, vomiting, sensitivity to light, noise, or sound. This pain can last hours to days without treatment. Migraines are defined as chronic when the pain occurs for at least 15 days out of the month for at least three months and with associated symptoms of migraine on at least eight of those days.

Unfortunately, migraines are a very common ailment in the United States. One out of seven Americans suffer from migraine and 3.2 million Americans have chronic migraines. This diagnosis can come at a cost. It is estimated that one out of six outpatient visits for migraine occurs in the emergency department. While urgent or emergent treatment can be helpful to treat acute pain, this type of treatment is not adequate for long-term management. Emergency visits can increase health care costs for the patient and providers. Better preventative and abortive care can prevent this.

What does this diagnosis mean for our patients? It is estimated that patients with chronic migraine average 63 days of missed work, school, and time with family or friends over a three-month period. This increases stress, strain on relationships, and insomnia. As a result, patients are sent to additional specialists and started on medications for the consequences of this disease.

What causes migraine? The cause of migraine is not completely established but is considered to be multifactorial. Genetics and environmental factors play a role in stimulating a chain reaction of pain through the central nervous system and cranial nerves. This in turn can increase inflammation of the cerebral vessels. This sequence of events can have many triggers: foods, alcohol, stress, sleep disorders, medications (especially abortive medications taken regularly, including Excedrin, Fiorinal, Imitrex, and opioids; taken more than two days a week can cause rebound pain), nutritional deficiencies, dehydration, lack of physical activity, elevated blood pressure, trauma, etc.

How can we help? If a patient is experiencing chronic migraine, it is best to discuss prevention with a daily oral medication. The typical types of medications given are: anti-hypertensives (beta-blockers, calcium-channel blockers, ACE-inhibitors), anti-epileptics, and anti-depressants. It is best to discuss the patient's overall medical status to see if any of these medications would be mutually beneficial for other health conditions. When two or more categories of medications fail, Botox (Onabotulinumtoxin A) should be considered.

What is Botox? BOTOX blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine, which results in muscle weakness. For this reason it is widely used to treat dystonia, spasticity, and other disorders caused by muscle overactivity. BOTOX is believed to also block release of pain mediating neuropeptides, which may account for its benefit in migraine and other pain disorders.

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What does the treatment look like? Botox is a 15-20 minute office procedure in which the toxin is distributed throughout 31 sites of the forehead, temples, neck and shoulders. This procedure may be repeated every 12 weeks. The patient experiences a slight pinch and burn at each site during the procedure causing some discomfort, but it is not considered "painful." Improvement with treatment usually occurs within 1-2 weeks of injections and lasts 10-12 weeks. Possible side effects include: bruising at injection sites, tenderness of injected muscles, eyebrow lift, stiffness of forehead muscles, and neck/shoulder tenderness. Rare reactions include: allergic reaction, infection at injection site, difficulty swallowing, bruising of nerves near injection, and vasovagal reactions.

What are the results? The anticipated result is a 50% reduction in pain severity or the number of pain days. This can be life changing for patients. Typically, it may take 2-3 rounds of injections to experience best benefit. If the patient does not see typical relief with the first round but does not experience any significant side

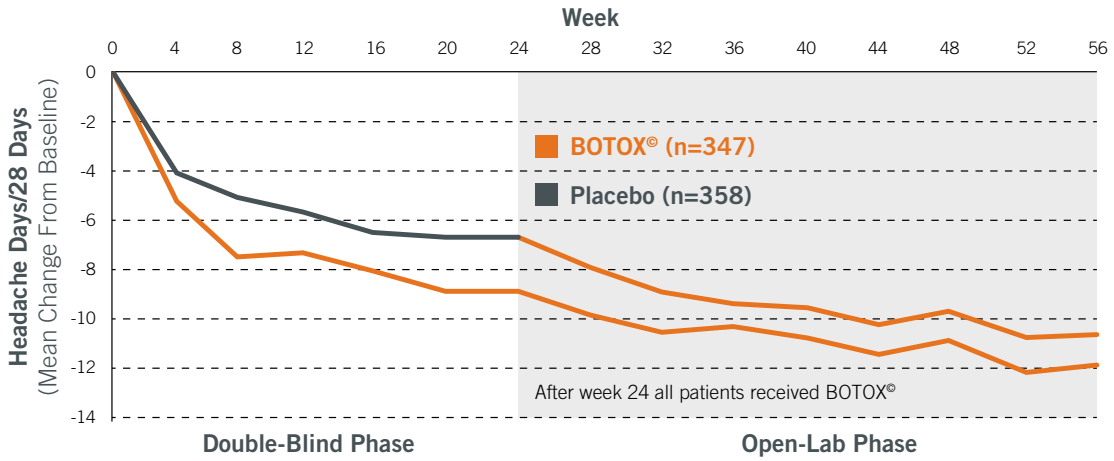
continued on page 5

Chronic Migraine; Is Botox an option for treatment?—continued from page 4

effect, it is recommended that they try future rounds of injections. With the reduction in pain, the result is: more days of attended work or school, less impact on relationship with family or friends, less abortive medications taken, and ultimately less health care cost due to decreased outpatient or Emergency department visits.

Even though combination therapy has not been studied, when patients' pain improves, lifestyle modifications are easier to obtain. It is suggested that patients work on their sleep hygiene, nutrition, and exercise, and eliminate medications that are no longer needed, especially daily use of NSAIDs or opioids. When such changes in lifestyle are made, quality of life improves.

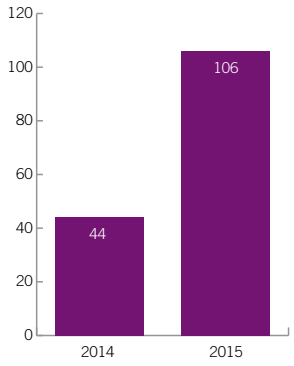
For references, please e-mail us at dignityhealthneuro@dignityhealth.org.



Mercy San Juan Medical Center Comprehensive Stroke Center Update

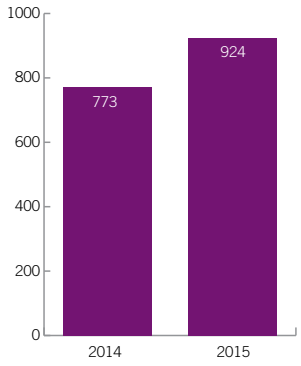
As a Comprehensive Stroke Center (CSTK), Mercy San Juan Medical Center (MSJMC) provides the highest level of services, with its clinical teams and technology available 24/7/365. Hospitals large and small throughout Northern California have relied on Dignity Health for years. The charts below show that our clinical team not only treats a growing number of strokes, but that Dignity Health Neurological Institute also provide the most rapid treatment compared to Comprehensive Stroke Centers across the nation. With the recent data proving the effectiveness of mechanical thrombectomy, the numbers of referrals and treatments have more than doubled since 2014.

Mechanical Thrombectomy



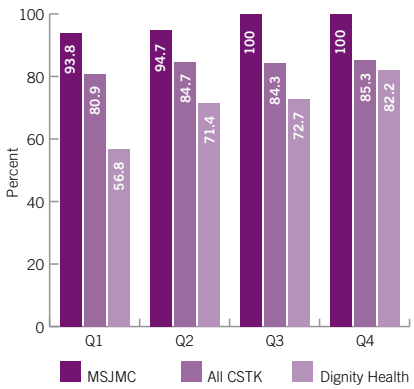
In the past year, six positive trials of endovascular thrombectomy for ischemic stroke have provided level 1 evidence for improved patient outcome compared with standard care

Inpatient Strokes



Includes acute ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage

Time to Intravenous Thrombolitic Therapy—Percent Under 60 Minutes



Percent of acute ischemic stroke patients receiving intravenous tissue plasminogen activator (tPA) therapy during the hospital stay who have a time from hospital arrival to initiation of thrombolytic therapy administration (door to needle) of 60 minutes or less

Full Time at 5000 Feet

Stacie Crain, FNP-BC

Prior to a career in neurology, I spent many years in emergency care, some of that time as a flight nurse. What the air medical crew does and how they care for critically ill people in a patient care area the size of the backseat of a Volkswagen is mysterious to those who do not practice in this environment.

The helicopter acts as a portable intensive care unit/emergency department moving at a speed of 100-120 mph. Whether in a rural ICU, at 10,000 feet in snow in the Sierras, or in the middle of an interstate, the crew must be able to perform the same assessment and interventions.

The primary job of a flight crew is to ensure all who are flying go home at night. Safety takes precedence over time… every time. Regardless of how emergent the situation is, the goal of the flight crew is to make sure that the risks of flight medicine are minimized. The medical staff checks every detail on the inside, down to how many syringes of each size are onboard, and the pilot is responsible for operational inspection. During shift briefing the weather, events in the area, construction that surrounds any hospitals in range, and any other concerns that may impact safety are discussed.

There is a tremendous amount of autonomy as a flight nurse, so communication skills, accurate patient assessment, and planning and initiating appropriate treatment is paramount to optimize patient outcomes. Capabilities include airway control including rapid sequence intubation (cricothyrotomy if indicated), initiating or maintaining ventilator therapy, starting peripheral or central lines, initiating vasopressors, cardiac procedures including needle thoracostomy or mini chest tube insertion, pacing, and maintaining intra-aortic balloon pumps.

Most flight crews work a 12- or 24-hour shift. In most programs, when the pager goes off the goal is to be in the air in eight minutes or less. Often, details of the flight request are unknown—sometimes just a location (latitude and longitude). Procedure is designed that way because efficiency is the top priority, not second guessing the actual need for a flight crew or worrying about whose life has just changed forever. More details are received en route so supplies can be prepared. "Should I flood lines? Get the ventilator circuit prepared? Prep Dopamine? Ready pediatric airway equipment?"

Flight crews have a mix of cases. In some calls the helicopter is first to arrive, and the crew provides all the initial medical assessment and treatment for a patient. In contrast, for an inter-facility transport, the patient's condition requires a transfer to a facility with more expansive capabilities. Interventions which were initiated at the first facility are continued during transport with critical care monitoring and treatment adjustments performed during flight. Flight nurses work with one medically trained partner and a pilot. There is no opportunity to request a second opinion or page a physician for a consult. The only back-up is a radio where an emergency department physician can weigh in on decisions if needed. If the patient requires a life-saving treatment, the flight nurse is authorized by protocol to initiate these procedures. Therefore, one needs to be comfortable and confident in providing technical medical skills and directing patient care.

Critical emergencies that may require air transport include trauma, medical and neonatal care, and acute stroke. Mercy San Juan Medical Center is the only Joint Commission-certified Comprehensive Stroke Center in the Sacramento region and one of a few in northern California. Our team is ready to receive neurologic emergencies 24/7.


Stacie Crain, FNP-BC

The Transfer Center Line for Dignity Health is 1.888.637.2941.

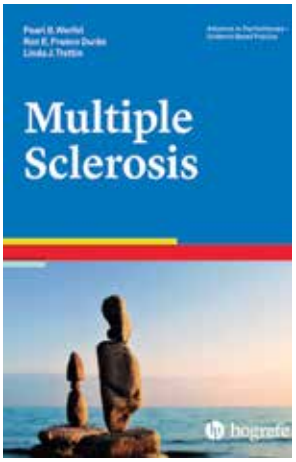
Brain Waves

Dignity Health Welcomes New Neurosurgery Talent

Kevin Hsieh, MD, a graduate of Vanderbilt University School of Medicine, is board certified in neurological surgery. He was chief resident at New York University's Bellevue Hospital and the Manhattan VA Hospital. He completed his internship at New York University. Following his training, Dr. Hsieh spent six years in Atlanta in private practice, primarily performing degenerative and complex spine surgery. Dr. Hsieh earned a bachelor's degree in neurobiology and a minor in music performance from the University of California, Berkeley. In his spare time, Dr. Hsieh enjoys playing classical violin and piano, having performed throughout the United States and Europe. Today, Dr. Hsieh is proud to be serving the Greater Sacramento community as a new addition to Capital Neurological Surgeons and the team of renowned specialists comprising Dignity Health Neurological Institute of Northern California.

Dignity Health Neuropsychologist Co-authors Guide to MS Treatment

Dignity Health clinical neuropsychologist and Multiple Sclerosis Certified Specialist Linda J. Trettin, PhD, recently co-authored Multiple Sclerosis, a new volume in Hogrefe Publishing's series "Advances in Psychotherapy — Evidence-Based Practice."



Trettin contends that the less visible symptoms of MS such as cognitive weaknesses and mood changes, if unattended, can leave individuals feeling isolated and confused. This innovative book is designed to help both mental health and medical professionals empower MS patients to improve their quality of life. It is a practical, culturally relevant guide to the most effective current medical, psychological, and neuropsychological diagnostic methods and interventions. The book was released February 5, 2016. You can order it at hogrefe.com or by calling 800.228.3749.

DHNI Cycling at Waves to Wine

On September 26 and 27, 2015, the Dignity Health Neurological Institute Cycling Team (DHNI Cycling) made its 6th consecutive appearance and joined over 2,200 other cyclists at the National Multiple Sclerosis Society's annual "Bike MS 150: Waves to Wine" charity cycling event. This year, our team (pictured below) rode distances of up to 180 miles from San Francisco to Rohnert Park during the two-day event and raised over $43,000. The contributions from our generous donors help serve those affected by MS throughout our community, including at the Dignity Health Mercy MS Achievement Center. If you would like to join DHNI Cycling, either on the road or as a virtual cyclist, please contact team captain, Dr. Peter Skaff, at peter.skaff@dignityhealth.org.

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CONTINUING MEDICAL EDUCATION 2016

Monthly Neuro Grand Rounds
Mercy San Juan Medical Center
Conference Rooms 2, 3 and 4
First Friday of each month at 12:30 p.m.

Stroke & Vascular Neurology Conference
Mercy San Juan Medical Center
CC4
2nd Wednesday of the month at 7 a.m.

Epilepsy & Subspecialty Neurology Case Conference
Mercy General Hospital
East West Auditorium
4th Tuesday of the month at 6 p.m.

Neurointerventional Radiology, Neurocritical Care, & Neurosurgery Conference
Mercy San Juan Medical Center
CC3
1st Thursday of the month at 12:30 p.m.—beginning in March

Neuro-Oncology Tumor Board
Mercy Cancer Center, C Street
3rd Thursday of the month at 7:30 a.m.

If you have any questions about upcoming opportunities, contact DignityHealthNeuro@DignityHealth.org or call 916.962.8751.