

SYNAPSE

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Anticoagulation for Atrial Fibrillation in the Elderly: Are We Being Too Cautious?

Peter Skaff, MD

Atrial fibrillation (AF) is a common cause of ischemic stroke in patients over the age of 60 and increases the risk of stroke five-fold. Strokes due to AF are also deadlier and cause greater disability than other ischemic strokes. The risk of AF increases with age, as does the risk of stroke due to AF. By the ninth decade of life, the prevalence of AF is approximately 10%, and for these individuals the incidence of stroke can exceed 20% without anticoagulation. Paradoxically, those who are at the greatest risk of stroke from AF are also the least likely to be treated with anticoagulation. A common reason for the lack of treatment is concern about the risk of falls.

Contrary to common assumptions, the benefits of anticoagulation may strongly outweigh the risks of hemorrhage due to falls. The efficacy of anticoagulation at reducing stroke risk in AF has been repeatedly demonstrated. Relative risk reduction with anticoagulation is approximately 70% vs. placebo and 50–80% vs. aspirin. Conversely, aspirin has not been consistently shown to reduce stroke risk in AF, particularly for patients at highest risk; i.e. those who are elderly (age > 75 years old) and who have multiple vascular risk factors.



Peter Skaff, MD

All-cause mortality is also significantly reduced with anticoagulation vs. either aspirin or placebo, particularly in elderly individuals. As such, the American College of Chest Physicians (ACCP) and the American Heart Association/American Stroke Association (AHA/ASA) recommend anticoagulation for prevention of stroke in AF patients over age 75.

Despite the demonstrated superiority of anticoagulation over aspirin or placebo at preventing strokes in AF,

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The New Anticoagulant— What You Need to Know

Patty Montgomery, PharmD

Dabigatran is the first oral direct thrombin inhibitor to be approved by the FDA. Dabigatran was approved to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. It has also been studied for prevention of venous thromboembolism and, in combination with parenteral anticoagulants, for treatment of venous thromboembolism.

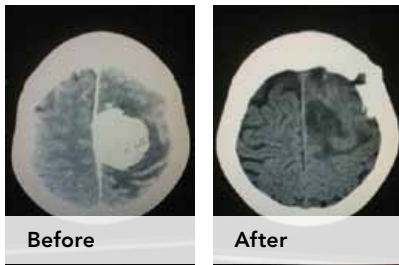
Dabigatran inhibits both clot-bound and fluid-phase thrombin and thrombin-induced platelet aggregation. The anticoagulant effects from dabigatran are seen within hours of the first dose and reach steady state in two to five days. Absorption is not decreased by taking it with food. However, opening the capsules causes an increase in absorption of up to 75% and it is not recommended.

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Man Finds Hope for His Mother at Mercy

Virginia McCollum’s family first noticed a problem more than a year ago when she began to lose function in her right arm and developed pain in her right shoulder. Her doctors thought the problem was a rotator cuff disorder or arthritis. Fast forward to March 2011—72-year-old Virginia had suffered a perforated bowel a few months earlier and was back in her hometown hospital in Red Bluff to have a colostomy removed. As she recovered from that procedure, her children noticed she was suffering from facial droop, had a blank stare and she was aphasic.

“It was scary,” remembers her son, Ramon Hernandez. A paramedic in Sacramento, he knew something was wrong. “I immediately asked for a CT scan. I assumed she had suffered a stroke during surgery. When the results came back, I was shocked.”



The CT scan showed no signs of a stroke. Instead, it showed two benign tumors growing on Virginia’s brain.

The first, a calcified tumor, was small and located between the frontal lobes, posing no threat. However, the other tumor was large—measuring roughly 6 cm, located in the left hemisphere, near the crown of her head. That tumor was pressing on the speech and motor function areas of

Virginia’s brain. The general surgeon treating Virginia was not optimistic. “He told us he wasn’t sure what it was, but no solutions were offered,” recalls Ramon.

Ramon was determined to pursue treatment options for his mother. He sought out the best care he could find and was referred to Dr. Kavian Shahi, a medical director with the Mercy Neurological Institute. Ramon and his parents met with Dr. Shahi a couple weeks later. “That was truly one of the best medical appointments I have ever been a part of,” Ramon says. “Dr. Shahi was patient, kind and informative. He sat down and spoke to my elderly parents on their level, explaining things two, three, four times—whatever they needed to get all their questions answered. I left that meeting feeling completely confident that my mother was in great hands.”

By the time Virginia underwent surgery to remove the large meningioma on April 16, her condition had deteriorated to the point where she could no longer get out of a chair on her own, go to the bathroom independently or communicate with her family. The procedure lasted nearly five hours and involved crossing the midline of the brain, a sometimes challenging task. “Here at Mercy, we do a higher proportion of complex cranial cases,” explains Dr. Shahi. “And the higher volumes lead to decreased mortality and improved outcomes.”

That level of experience is exactly what led Ramon to Mercy for his mother’s care. He saw the results of that choice immediately. “Within 12 hours of waking up from surgery, her facial droop was gone,” recalls Ramon. “She began

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Nearly 150 physicians and healthcare professionals attended the Mercy Neurological Institute's "Insights and Innovations" CME event on May 18 at the Sheraton Grand.

INSIGHTS & INNOVATIONS 2011



Prior to the program beginning, attendees crowded into the reception area to network and check out vendors.



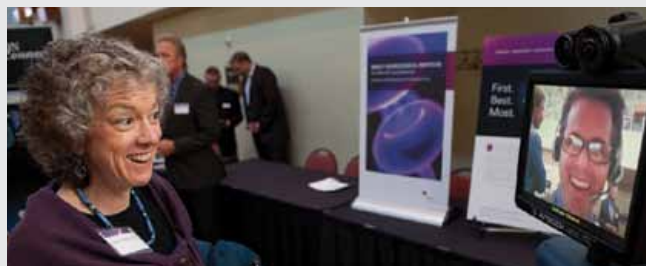
Neurologist John Schafer, MD, (right) helps field questions from the audience during the case study portion of the CME event.



George Luh, MD, the Institute Medical Director of Interventional Neuroradiology, discusses the "New Frontiers in Brain Aneurysm Treatment."



The presentation team and medical directors for the May 18 Insights & Innovations CME event included Alex Nee, MD; Marc Lenaerts, MD; Alan Shatzel, DO; John Schafer, MD; Kavian Shahi, MD; and George Luh, MD.



Physician Assistant Kathy Robinson gets first-hand experience of what patients encounter when they meet up with the Mercy Telehealth Network. Mathew Williams from Intouch is on the other end of this high-tech conversation.

Man Finds Hope for His Mother at Mercy, continued from page 2

standing on her own and regained strength in her right arm. Two days later, she was walking around with minimal help. Since then, her mobility has returned to what it was before and her speech is almost back to normal. It is a huge turnaround."

Dr. Shahi expects Virginia to make a complete recovery. He credits the entire Mercy neuro team with that success. "My work in the OR wouldn't be as effective if it wasn't for the exceptional nursing care Mrs. McCollum received

in the dedicated neuro ICU and the step-down unit," Dr. Shahi explains. "It is a spectrum of care that begins with the referral and continues all the way through follow-up care." Ramon extends his gratitude to everyone who cared for his mother. "I have nothing but praise for the whole Mercy team... I just want to thank everyone who helped our family through this ordeal."

If you have questions or comments, please e-mail us at mercyneuro@chw.edu. 🏥

The Diagnosis and Treatment of Carpal Tunnel Syndrome

Richard A. Beyer, MD

Carpal Tunnel Syndrome (CTS), caused by compression of the median nerve, is the most common and the most treatable of the entrapment neuropathies. The estimated prevalence in the general population is in the range of 1 to 5%.

Standard Symptoms:	Hand paresthesia Dull ache in hand /arm Hand weakness Numbness in Median nerve territory
Provocative Factors:	Sleep Sustained hand /arm positions Repetitive actions of the hand/wrist
Mitigating Factors:	Changes in hand/arm posture Shaking hand

The sensory and motor portions of the median nerve arise from the C6 to T1 roots. The nerve travels with the brachial artery through the antecubital fossa, gives off the anterior interosseous nerve in the forearm, the palmar cutaneous sensory branch just before it enters the carpal tunnel, and within the tunnel the recurrent motor branch to the thenar muscles. Another branch exits the tunnel and innervates the first and second lumbricals and provides sensation to the palmar thumb, index, middle, and lateral side of the ring finger.

The carpal tunnel is formed by the carpal bones of the wrist and the transverse carpal ligament and is filled by the nine flexor tendons of the fingers, the median nerve, and connective tissue. Causes of compression of the nerve within the carpal tunnel include fibrosis of the connective tissue surrounding the flexor tendons, congenitally small space, mass lesions (ganglion) and medications (e.g., aromatase inhibitors). Flexion and extension of the wrist increase pressure within the carpal tunnel. Repetitive use has been suspected of causing CTS, but studies have shown conflicting results.

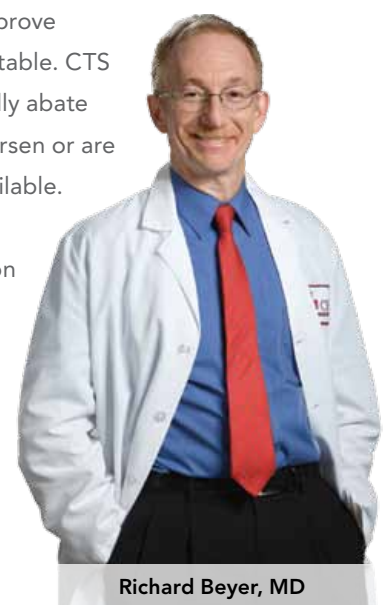
Symptoms of CTS include painful paresthesias and/or numbness in the median nerve territory of the hand

(though many patients describe symptoms in the entire hand). A dull ache may extend into the forearm and even as high as the shoulder. Because flexion and extension of the wrist increase the pressure within the carpal tunnel, certain sustained postures, as in sleeping, and repetitive use typically aggravate the symptoms. Many will complain of “weakness,” manifest by dropping heavier objects out of their hand, which likely represents loss of proprioceptive input rather than frank muscle weakness. Actual weakness of some movements of the thumb occurs with more severe cases. [See table 1]

Physical exam is often unhelpful because sensory loss and motor weakness or atrophy of the thenar muscles are usually late findings. Bedside provocative signs are helpful, but sensitivity and specificity average 50–75% for each.

Electrodiagnostic Testing (ET) may confirm the diagnosis of CTS but is not necessary if symptoms are early, typical and respond to conservative treatment. ET should be performed if symptoms are not typical or if the patient is being considered for surgical treatment. ET consists of Nerve Conduction Velocity (NCV) and Electromyography (EMG). NCV can help document severity and can exclude confounding factors such as other types of peripheral neuropathy. NCV testing is highly specific but only 75 to 85% sensitive, so a negative test does not exclude the diagnosis. EMG is not always necessary if the NCV shows characteristic changes but can detect mimics of CTS such as a C6–7 radiculopathy and may help to estimate duration of the compression.

About 20% of cases of CTS will improve spontaneously, and many remain stable. CTS that starts in pregnancy will typically abate following delivery. If symptoms worsen or are unbearable, good treatment is available. Splinting of the wrist is first-line treatment and reduces compression of the nerve caused by flexion and extension. There is no agreement as to whether custom splints are better than mass produced or whether it is better to wear them



Richard Beyer, MD

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Ten Key Facts for the Pregnant Woman with Epilepsy

Edwin Cruz, MD

1) More than 90% of babies born to epileptic mothers are normal. In the U.S., there are about one million women of child-bearing age with epilepsy. With careful treatment, most will have normal pregnancies and delivery.

2) Importance of pre-pregnancy counseling should be emphasized. Any woman with a preexisting medical condition should be counseled as to possible risks of her disease and teratogenic effects of medications. Seizure management should be optimized before pregnancy. Pre-conception Folate supplementation 0.4–1 mg per day may prevent major congenital malformation.

3) During pregnancy, close follow-up is needed. Patients should be counseled against use of tobacco, alcohol and illicit drugs. Women who smoke have increased risk for premature labor and delivery.

Seizure control before pregnancy correlates with seizure recurrence during pregnancy. A guideline from the American Academy of Neurology states that patients who have been seizure free for at least nine months have high likelihood of remaining seizure-free during pregnancy. About one-fourth of patients may have increased seizures. Patients who have been seizure-free for two to five years may consider complete withdrawal of all antiepilepsy drugs (AEDs) under medical supervision.

Because epilepsy medications may interfere with vitamin K metabolism, vitamin K 10–20 mg per day in the last month of pregnancy, and 1 mg IM at birth should be given to reduce risk of hemorrhagic disorder of the newborn.

4) Risk of fetal malformation is 3–6% in babies of epileptic mothers compared to 1–3% in the general population. However, studies show that the risk is also increased in babies of untreated epileptics, indicating that this is not medication effect alone, and genetic predisposition also plays a role. Patients may be advised that although the risk of birth defects is increased

three-fold, it is not as high as most patients fear. Risks include facial clefts, neural tube defects and cardiac anomalies.

Because these risks are increased by polypharmacy, Antiepileptic Drug (AED) therapy should be simplified before pregnancy.

5) Do not stop AED therapy, because risk for breakthrough seizures would be harmful to the mom and the fetus. Also, by the time patients realize they are pregnant the critical period of organogenesis (first four weeks of gestation) is almost over.

6) There is no safe AED in pregnancy. Most AEDs are FDA Category C (risk to humans has not been excluded). Some are Category D (+evidence of risk to humans). The AAN guideline states that valproate (VPA) is associated with neural tube defects. Phenobarbital can cause cardiac problems. Carbamazepine (CBZ) and phenytoin (PHT) can cause cleft palate. Lamictal (LTG) should be limited in the first trimester but only under medical supervision. There is limited data about the other second-generation AEDs.

7) Best AED during pregnancy is the appropriate drug for the seizure type. The drug that is most effective to control the patient's seizures should be used, and changing a well tolerated and effective drug is generally not recommended.

Avoid polypharmacy and aim for lowest possible dose. Be aware of changes in drug metabolism during pregnancy. This includes decreased drug absorption, increased renal and hepatic elimination, and increased volume of distribution. Changes in protein binding will also increase the amount of unbound AED that may cause toxic side effects. Consider checking AED levels and adjusting doses accordingly. Changing to a lower dose given more frequently (TID- QID), or an XR preparation to assure lower and more consistent levels should also be considered.

8) Allow breast-feeding. Highly protein bound AEDs such as PHT, PHB, VPA and CBZ have lower levels in breast milk.

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Edwin Cruz, MD

Anticoagulation for Atrial Fibrillation in the Elderly, continued from page 1

approximately half of elderly patients with AF are not receiving anticoagulation. This may be due to an overestimation of the risk of intracranial hemorrhage (ICH) in patients on anticoagulation. Degree of anticoagulation, increasing age and uncontrolled hypertension are all risk factors for ICH. However, when hypertension is controlled and warfarin anticoagulation is maintained under an INR of 3.5, the risk of ICH in clinical trials has been similar to, or only marginally higher than in patients taking aspirin. It is important to keep in mind that neither “low-dose” warfarin regimens (INR < 1.7) nor aspirin effectively reduce stroke risk in elderly individuals with AF. Moreover, elderly individuals taking aspirin or low-dose warfarin have similar ICH rates when compared to patients treated with standard-dose warfarin with a target INR of 2.0–3.0. Thus, withholding anticoagulation markedly increases the risk of stroke while, at best, only marginally reduces the risk of ICH. An article by Man-Son-Hing, et. al. published in Archives of Internal Medicine in 1999 concluded that

when annual stroke risk exceeds 2%, patients “must fall approximately 300 times in one year for warfarin to not be the optimal therapy.”

Given these findings, the best approach to treating elderly patients with AF is to focus on reducing the risks associated with anticoagulation. This can be accomplished through measures such as proper and more frequent anticoagulation monitoring, control of co-morbid hypertension, improved patient/caregiver education, and assessment and modification of fall risk. Because elderly individuals are at the highest risk of stroke from AF, they have the most to gain from anticoagulation, and while medical treatment decisions should be individualized, neither age nor gait impairment should disqualify a patient with AF from receiving anticoagulation therapy.

For references for this article, please e-mail us at mercyneuro@chw.edu. 🏥

The Diagnosis and Treatment of Carpal Tunnel Syndrome, continued from page 4

just at night or 24/7. Benefit is usually obtained by four weeks, and the success rate for improvement of symptoms is over 50%. The best candidates for this treatment are patients with duration of symptoms less than one year, no permanent sensory loss, and less severe or predominantly nocturnal, symptoms.

Glucocorticoid injection into the carpal tunnel can be tried if wrist splints fail. Risks are miniscule, though the injection can be painful. Onset of relief is within days and lasts for one to three months or even longer if combined with wrist splinting.

Surgical carpal tunnel release is the most effective and durable of treatments, with a success rate in pooled studies of about 75%. Surgery consists of incising the transverse carpal ligament, which decompresses the carpal tunnel, and can be conducted either with an open or an endoscopic technique under local anesthesia. Critics

say that the endoscopic approach may have a higher rate of complications.

Therapies without proven effectiveness include NSAIDs, diuretics and pyridoxine (vitamin B6). Nerve gliding, carpal bone mobilization and ultrasound treatment have been proposed, though results of studies are conflicting.

In summary, carpal tunnel syndrome can usually be diagnosed by history and by exam. Confirmatory testing by ET is indicated for atypical cases or if surgical treatment is being considered. Treatment starts with splinting and may extend to surgical release. ET is generally performed by neurologists or physiatrists and surgical treatment by neurosurgeons, orthopedists, hand surgeons or plastic surgeons, all of which are available through the Mercy Neurological Institute or through Mercy-affiliated physicians.

If you have questions for Dr. Beyer or would like to see a longer version of this article, please e-mail us at mercyneuro@chw.edu. 🏥

The New Anticoagulant—What You Need to Know, continued from page 1

The drug should be eliminated within three days after discontinuation in patients with normal renal function. In patients with renal disease, rate of elimination is decreased.

A large study compared dabigatran doses of 110 mg or 150 mg twice daily to warfarin in 18,113 patients with atrial fibrillation. Outcomes included stroke or systemic embolism and major hemorrhage. The 150 mg dose of dabigatran was more effective than warfarin at preventing stroke or systemic embolism and less likely to cause hemorrhagic stroke or life-threatening bleeding, but it was more likely to cause gastrointestinal bleeding. The 110 mg dose had efficacy similar to warfarin and caused less bleeding. Other adverse effects with dabigatran include gastrointestinal upset and dizziness.

Unlike warfarin, there is no laboratory test that can be used in clinical practice to measure the degree of anticoagulation produced by dabigatran. It does cause increases in several measurements of anticoagulation including activated partial thromboplastin time (aPTT), international normalized ratio (INR), and ecarin clotting time (ECT). The manufacturer of Pradaxa is working on development of tests that would be useful to monitor anticoagulation in patients on dabigatran. In addition, there is no agent available to reverse anticoagulation with dabigatran. Consequently, when patients on dabigatran present with a stroke, the inability to define or reverse the degree of anticoagulation complicates decisions concerning use of tissue plasminogen activator (tPA).

The other critical safety concern with dabigatran is renal function. Patients on dabigatran must have renal function monitored regularly and the dose adjusted accordingly. In patients with severe renal disease it should not be used. In addition, patient profiles should be assessed for significant drug interactions, although interactions are less common than with warfarin.

Dabigatran was approved with a medication guide that should be given to all patients being initiated on dabigatran.

Currently, the direct cost of dabigatran is over \$6 per day, as opposed to warfarin, which costs pennies per day. The cost of monitoring warfarin is expected to be higher than for dabigatran.

In summary, dabigatran has a faster onset of action than warfarin and causes less overall bleeding in appropriate patients. Significant concerns include inability to monitor or reverse anticoagulation, a potential increase in gastrointestinal bleeding and accumulation in patients who have impaired renal function.

While dabigatran is the first oral thrombin inhibitor to be approved by the FDA, other agents are under review.

For references for this article, please e-mail us at mercyneuro@chw.edu 🇺🇸

**Ten Key Facts for the Pregnant Woman with Epilepsy**, continued from page 5

Primidone and Levetiracetam transfer in amounts that may be clinically significant. Data on newer AEDs are limited. In general, breast-feeding need not be discouraged because the potential benefits outweigh the risk. In most instances breast-feeding does not cause any difficulties. If the baby becomes irritable or sedated then breast-feeding should be stopped.

9) Enroll patient in National AED Pregnancy Registry, 1.888.233.2334.

10) Epileptic patients who are pregnant or who want to be pregnant should be referred to a neurologist.

If you have comments or questions for Dr. Cruz, please e-mail us at mercyneuro@chw.edu. 🇺🇸

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UPCOMING EVENTS

Monthly Neuro Grand Rounds

Mercy General Hospital

First Thursday of each month at 12:30 p.m.

Mercy San Juan Medical Center

First Friday of each month at 12:30 p.m.

*Questions can be directed to Candy Collins,
CHW CME Office, at 916.733.6334.*

MS Lecture Finale Oct. 24

The final lecture of the Mercy MS Center/National Multiple Sclerosis Society quarterly series will take place on Monday, Oct. 24., in the Lukens Auditorium of the Mercy Plaza building at 6555 Coyle Avenue in Carmichael. 6:30 to 8 p.m. The topic is Family Dynamics and Communications.

Please register by calling the MS Society office at 1.800.344.4867 two weeks prior to the event.

Free CME Opportunity

You can earn free CME and find out more about the advantages of Group Visits/Shared Medical Visits by registering for the PRIME Education, Inc. online Virtual Symposium, which is based on a group visit session of the Mercy MS Clinic.

*The sessions will be held Aug. 17 and Aug. 30.
For specific times and to register, go to
www.primeinc.org/sma.*

Open House at MGH

Mercy General Hospital's CARF-accredited Acute Rehabilitation Unit is celebrating 25 years of service:

Thursday, Sept. 22

Mercy General Hospital, 4001 J Street
Acute Rehabilitation Unit Dining Room and Gym
Open House: 3 p.m. to 6 p.m.; Program: 4 p.m.

Please RSVP by Sept. 9 by calling 916.453.4566