By David C. Tong, MD

Is FASTER Always Better?

A new study explores early combination antiplatelet therapy in TIA patients.

In our last column ("Transient Ischemic Attack: New Studies, New Questions," March 2008), we reviewed data indicating a substantially increased risk of subsequent stroke in TIA patients. What can be done to ameliorate that risk? Recently, several new studies have begun to address this important issue. In this month's column, we will discuss the use of combination antiplatelet treatment to reduce early recurrent stroke risk in these patients.

The "Fast Assessment of Stroke and Transient ischemic attack to prevent Early Recurrence" (FASTER) study was a pilot clinical trial that studied the use of clopidogrel and simvastatin in patients with symptoms <24h after symptom onset. The rationale for this trial was that in the acute phase following TIA or minor stroke, there is a high risk of recurrent ischemia (for more, see the March column, available at avondalemedical.com/PN_archive.htm), and perhaps in this situation the benefit of combination therapy would be more pronounced. Moreover, it was hypothesized that the risk of hemorrhagic complications might be lower, given the transient nature of the symptoms. It was also an exploratory analysis to determine the feasibility of a trial of this type.

In past columns we have discussed the clear lack of effectiveness of aspirin and clopidogrel in long term stroke prevention (the reader may wish to download the June and July 2006 columns, also available at avondalemedical.com/PN_archive.htm). In fact, in the MATCH trial, this combination was associated with harm; namely, increased intracranial hemorrhage. Has this trial changed our view on the use of this combination for acute stroke management?

In the FASTER study, patients >40 years old with a minor stroke (NIHSS <3) or symptoms <24h after onset were eligible. Only patients with weakness, or speech disturbance, dyarthria or dysphasia of >5 minutes duration were eligible for enrollment. Patients with pure sensory loss vertigo or dizziness, ataxia or visual disturbance without speech disturbance or weakness were excluded.

The study used a double-blind 2x2 factorial design with clopidogrel and simvastatin as the study treatments. All patients received aspirin therapy (162mg load if ASA-naive, then 81mg/d). Clopidogrel-treated patients received a 300mg loading dose, then 75mg/d. Simvastatin patients received 40mg immediately followed by 40mg/daily. Final follow up was at 90 days. A total of 3101 patients were screened, and 396 enrolled (~90/group). The most common reasons for exclusion were prior treatment with a statin, antiplatelet agent (other than aspirin) or anticoagulant (27% of excluded patients), or an alternative cause for symptoms (18%).

Although understandably underpowered due to the small sample size, the trial had some puzzling results. Patients receiving clopidogrel plus aspirin had a non-significantly lower risk of the primary outcome (90d risk of stroke), compared with the aspirin monotherapy group (7.1% vs. 10.8%; p= NS). However, there was an increased risk of stroke in patients receiving simvastatin versus those that did not (10.6% vs. 7.3%. p=NS). This was rather surprising and puzzling, given the quite strong indirect evidence of a protective effect of statins described in prior cardiac and stroke studies. Nevertheless, the 3.3% absolute difference in recurrent stroke risk could be important, and might justify more aggressive treatment with this combination. No significant differences were observed by stroke subtype, but this is not unexpected with such a small study.

Unfortunately, the only statistically significant difference in outcome between the two groups was in the symptomatic hemorrhage rate (3.0% vs 0% p=0.03) and asymptomatic hemorrhage rate (30.8% vs 13.9%, p=.0001). These findings are disturbing, and also a bit surprising, given the minor nature of the symptoms which had been hypothesized to reduce bleeding rates. However, they are consistent with prior trials of the aspirin-clopidogrel combination (around 30,000 patients studied), which have shown a clear increased clinically significant hemorrhage risk. Moreover, consistent with prior studies, the bleeding risk associated with clopidogrel aspirin combination appears to mitigate the potential reduction in recurrent ischemic events.

The Bottom Line

What are we to conclude from these results? Should we be using aspirin plus clopidogrel in TIA/minor stroke patients <12h after symptom onset? Clearly, these results do not warrant such an approach. Aside from the small size of the study, there are the puzzling results of the simvastatin-treated groups, as well as the substantial concerns over bleeding risk. Moreover, the study only evaluated patients with specific TIA symptoms (dysphasia, motor weakness), and so the vast majority of individu-

(Continued on p. 47)

David Tong, MD is Medical Director of the California Pacific Medical Center Stroke Institute in San Francisco.

Considering the Use of Statins to Lower Stroke Risk

Q ***How can statins help reduce the risk of stroke or cardiovascular event? How long was it before you saw measurable reductions?***

A A new study[1] found that statins may not only reduce blood cholesterol levels but may also lower blood pressure, allowing "these modest effects [to] contribute to the reduced risk of stroke and cardiovascular events reported on statin." Researchers conducted a randomized, double-blind, placebo-controlled trial with equal allocation to 20mg simvastatin, 40mg pravastatin or placebo for six months to 937 patients without known cardiovascular disease or diabetes. They found that participants who took the statins had an average decrease of 2.2 mmHg in systolic blood pressure and an average decrease of 2.4 mmHg in diastolic pressure.

"The trends toward lower blood pressure than in the placebo group were beginning to be evident for both statins at month one, but were not significant," says Beatrice Golomb, MD, PhD, the study's lead author. However, there was an effect following six months of treatment, and the effect decreased two months after the treatment was finished.

Q ***Is it reasonable to use the possibility of reduced risk of stroke or cardiovascular event to start a patient on a statin treatment? What factors would influence your decision to start the therapy?***

A Dr. Golomb believes the patient should be the unit of analysis for determinations of which groups should receive preventive treatments, through objective outcomes of importance that equitably assess risks and benefits across causes. "Such as all-cause mortality and all-cause morbidity—indexed by serious adverse effects," she says. Groups that receive benefit using these metrics are her targets for preventive treatments.

"But the norm is to consider cause-specific indices that receive benefit," she says. Combined cardiovascular endpoints—including stroke—are often examined and often show benefit with statin therapy, particularly in high-risk subjects with cardiovascular risk factors. "I'm not sure I would modify my decisions about whom to treat, necessarily; but the information may modify my thinking about how benefits are reaped," Dr. Golomb says. "In subjects already close to a blood pressure target who are being considered in any case for statin therapy, I might see whether they could be spared the addition of another med, based on blood pressure response, when statins have been initiated."

Q ***What precautions are needed when adding a statin to stroke therapy? What side effects would you be most concerned about and how can you minimize them? Is there any need to monitor liver enzymes?***

A The precautions regarding statin use in patients at risk for stroke are not necessarily different than those in other settings. The side effects of statins most often reported by patients are muscle/fatigue, cognitive difficulty and neuropathy, with a range of other adverse effects reported, Dr. Golomb advises. "We have a paper accepted for publication in the Am J Cardiovasc Drugs that will be the first comprehensive review of statin adverse effects, mechanisms, and risk factors," she says, adding it's not expected to go to press until later this summer.

Dr. Golomb reminds readers that physicians should be vigilant about the potential risks as well as benefits. Side effects are more common with concurrent use of medications known to affect statin metabolism in certain clinical settings, combining statins with other lipid-lowering agents, and with higher-potency lipid drug use. "While a limited literature indicates that coenzyme Q10 supplementation may reduce the average severity of symptoms in those who experience them," Dr. Golomb points out, "there is no literature combining statins with Q10 versus placebo and examining the hard endpoints statins seek to protect against, limiting ability to make recommendations for use with statins generally."

Liver enzyme monitoring is readily available and is advised, though serious adverse effects to the liver are not common, she says.

Q ***IWhat is the take home message for practicing neurologists?***

A "Blood pressure reduction may occur with statins," says Dr. Golomb. While the average effect is small, there is variability in the magnitude of effect and in some cases it may be clinically material. "This should be borne in mind particularly if modification of treatment for both lipids and blood pressure is occurring in tandem," she says. **PN**

1. Golomb BA, Dimsdale JE, White HL, Ritchie JB, Criqui MH. Reduction in blood pressure with statins: results from the UCSD Statin Study, a randomized trial. Arch Intern Med. 2008 Apr 14;168(7):721-7.

Beatrice A. Golomb, MD, PhD is an Associate Professor of Medicine in the Division of General Internal Medicine at the University of California, San Diego School of Medicine.

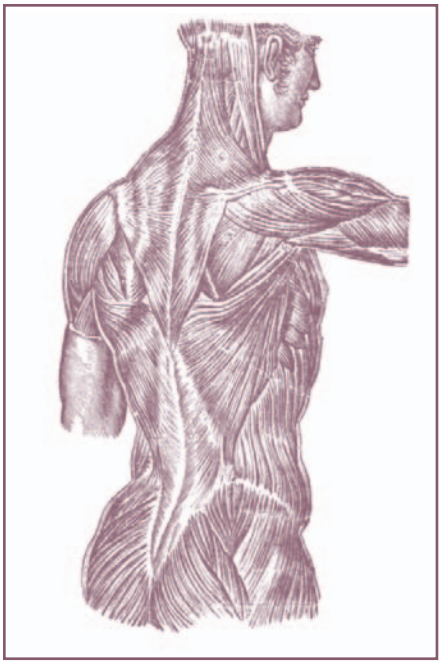
By Charles Argoff, MD

Muscle Relaxants: An Update on Their Role in Clinical Practice

As new questions are being raised about long-term use of these agents, here's a look at the efficacy and side effect profile of the most commonly used options.

As practicing neurologists, we are often faced with the need to advise a patient regarding the symptomatic control of painful muscle spasm, a condition associated with many disorders. Recent changes in Europe have prompted me to review in this month's column the currently available skeletal muscle relaxants in the United States.

In November 2007, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) concluded that the benefits of medicines containing carisoprodol no longer outweigh their risks and that all marketing authorizations for such products be suspended throughout Europe. What was the basis for this review? In March 2007, new information regarding the potential risk of altered mental status and psychomotor impairment of carisoprodol as well as an increased risk of abuse and addiction in Norwegian patients was noted by Norwegian authorities. According to a November 2007 communication from the EMEA, the company marketing carisoprodol-containing medications in Norway has agreed to withdraw these products from the Norwegian market. As a consequence of this action by Norwegian authorities, the CHMP of the EMEA was notified so that it could review carisoprodol data separately in order to prepare its own opinion regarding whether or not the marketing of all products containing carisoprodol in the European Union should be continued, changed, suspended or withdrawn (EMEA Document ref. EMEA/520140/2007 London, 15 November 2007).



The class of medications commonly termed "skeletal muscle relaxants" remains confusing to many clinicians and scientists alike. Historically and at present, skeletal muscle relaxants have been prescribed for both acute and chronic conditions associated with muscle-related pain. Agents in this medication class include carisoprodol, chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol and orphenadrine. These agents are indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions. Baclofen and tizanidine are indicated for the treatment of spasticity due to multiple sclerosis, as well as spinal cord disease or injury, but are sometimes prescribed in my experience for the relief of painful muscle spasm. Benzodiazepines, principally diazepam, are also commonly used and indicated for adjunctive relief of skeletal muscle spasm. These acute pain presentations may include local pain and tenderness, muscle spasm and limited range of motion; however, the concept of the painful muscle spasm is often difficult to define and has been the subject of some controversy. It is likely that both peripheral and central factors may play a role in the pathophysiology of painful muscle spasm. Even though data from various animal models are available, the exact mechanism of action for these various agents is not known. Below is a brief review of many of the available agents.

Carisoprodol. It is important to recognize that carisoprodol is converted in the liver to meprobamate, a schedule IV controlled substance. It is known that meprobamate may produce phenomena that result in physical and psychological dependence. As the result of concerns regarding substance abuse with the use of carisoprodol (possibly in part due to the process of meprobamate formation), in recent years, several states have begun listing carisoprodol as a controlled substance within their state formularies. It must be clarified that carisoprodol is not considered a controlled substance at the federal level. As a consequence of its potential for physical dependence, carisoprodol should be carefully tapered as opposed to immediately discontinued following long-term use.

Chlorzoxazone. Chlorzoxazone does not have any significant drug interactions, but does have a significant adverse effect profile that includes a rare idiosyncratic hepatocellular reaction. It is unclear what role this agent has in practice, considering its lack of superior efficacy and especially

Table 1. Pharmacotherapies Commonly Used for Muscle Spasm

Drug	Onset	Duration	Common Dosing
Sedative			
Carisoprodol (Soma)	30 min	4-6 hours	350 PO QID 250 PO QID
Chlorzoxazone (Parafon Forte)	~ 1 hour	3-4 hours	250-750mg PO TID-QID
Metaxalone (Skelaxin)	1 hour	4-6 hours	400-800mg PO TID
Methocarbamol (Robaxin)	30 min (PO)	N/A	750-1000mg PO QID
TCA Like			
Cyclobenzaprine (Flexeril)	~ 1 hour	12-24 hours	5-10mg PO TID
Antihistamine			
Orphenadrine (Norflex)	1 hour (PO)	4-6 hours	100mg PO BID
GABA Type			
Diazepam (Valium)	30 minutes (PO)	Variable	2-10mg PO TID
Baclofen (Lioresal)	3-4 days (PO)	Variable	5mg PO TID titrated up to 40–80mg/day
Central Alpha 2 Agonists			
Tizanidine (Tizanidine)	Up to 2 weeks	Variable	2-8mg PO TID-QID

given its significant toxicity profile.

Metaxalone. FDA-approved over 30 years ago, several double blind, placebo-controlled trials have demonstrated superiority of metaxalone over placebo in helping to bring rapid relief from symptoms and signs of acute musculoskeletal conditions including pain, tenderness and limitation of normal motion, palpable spasm and interference with daily activities.

Metaxalone does not have any significant drug interactions and appears to have a fairly benign side effect profile. Patients taking metaxalone have uncommonly experienced hemolytic anemia and impaired liver function. Metaxalone is contraindicated in patients who have severe renal or hepatic impairment.

Methocarbamol. Methocarbamol is available in oral and parenteral preparations. However, many complications have arisen with the injectable form, including pain, dermatologic reactions and thrombophlebitis. The published placebo-controlled studies comparing methocarbamol to placebo suggest a role for this agent in the treatment of musculoskeletal pain.

Orphenadrine Citrate. Orphenadrine is directly related to diphenhydramine, and thus exhibits antihistaminic and anticholinergic properties. Like methocarbamol, orphenadrine is available in a parenteral dosage formulation. There have been reports of severe adverse reactions with parenteral use, including an anaphylactoid reaction, complicating the use of this formulation. Orphenadrine when coprescribed and used with propoxyphene may cause confusion, anxiety and tremors. Orphenadrine's anticholinergic actions have been noted to produce significant adverse effects including tachycardia, palpitations, urinary retention and blurred vision.

Cyclobenzaprine. Cyclobenzaprine is structurally and pharmacologically related to the tricyclic antidepressants and in fact has a chemical structure strikingly similar to amitriptyline's. As with the other skeletal muscle relaxants, cyclobenzaprine does not have activity directly on muscle tissue. Animal data suggest cyclobenzaprine acts primarily at the level of brain stem. It is interesting and worthwhile to note that the newer 5mg dose has yielded similar clinical efficacy with less sedation than the 10mg dose.

Muscle relaxant monotherapy remains of uncertain benefit, and it has been recommended that these agents may be best used as an adjunct to other therapies. On a clinical note, it is extremely important to recognize that cyclobenzaprine is pharmacologically similar to the tricyclic antidepressants, and that it also has a similar adverse event profile. Thus, one might want to strongly consider this and avoid prescribing both cyclobenzaprine and another tricyclic antidepressant concurrently unless truly clinically indicated. One should keep in mind as well that one of the proposed mechanisms of action of the analgesic tramadol is similar to the tricyclic antidepressants, *e.g.*, blockade of the reuptake of norepinephrine and serotonin. Cyclobenzaprine labeling suggests that concomitant use with tramadol may place patients at higher risk for developing seizures. Because of the structural relationship to TCAs, clinicians must be cognizant of the anticholinergic side effects like dry mouth, urinary retention and constipation seen with cyclobenzaprine.

Use of cyclobenzaprine is contraindicated in the setting of arrhythmias, congestive heart failure, hyperthyroidism, or during the acute recovery phase of a myocardial infarction. Recently it has been reported that co-administration of cyclobenzaprine with serotonergic agents such as selective serotonin reuptake inhibitors may predispose patients to life-threatening serotonin syndrome.

Concomitant use of cyclobenzaprine with monoamine oxidase inhibitors or use within 14 days after their discontinuation is contraindicated. Cyclobenzaprine can enhance the effects of agents with CNS depressant activity and older patients should be carefully moni-

tored for CNS related adverse reactions, *e.g.*, hallucinations and confusion, when using cyclobenzaprine. Withdrawal symptoms have been noted with the discontinuation of chronic cyclobenzaprine use; therefore, a medication taper may be warranted for patients with chronic use of this medication.

Diazepam. This is the most commonly prescribed and referenced benzodiazepine in the treatment of muscle spasms. Diazepam demonstrates hypnotic, anxiolytic, antiepileptic and antispasmodic properties. Sedation and abuse potential are the main concerns with this agent and class in general. It is important to slowly taper this agent after long-term use to avoid any withdrawal symptoms.

Baclofen. Baclofen is unique in that it can be administered intrathecally in cases of severe spasticity and for patients who do not tolerate or have failed oral therapy. Baclofen should be tapered slowly after long-term use to avoid a withdrawal reaction and rebound phenomena. Baclofen should be used with caution in the elderly and for patients with renal impairment.

Tizanidine. Tizanidine is related chemically to clonidine, but has significantly lower antihypertensive effects. The main adverse effect for most patients with this agent is profound sedation. Currently tizanidine is FDA approved only for the management of increased muscle tone associated with spasticity resulting from central nervous system disorders, such as multiple sclerosis or spinal cord injury. There are currently two published studies on the use of tizanidine in the setting of back pain or muscle spasm either alone or in combination with ibuprofen, as well as one report of effective use in myofascial pain.

Clinical Notes

Available clinical data indicate that skeletal muscle relaxants are more effective than placebo with respect to relieving acute low back pain. Unfortunately, most of these data are based upon studies that would be considered methodologically flawed if conducted today. In general terms, there are no data that support a claim that any one agent is more efficacious than another; however, one should keep in mind the various adverse effect profiles, ease of use and potential for abuse when prescribing an agent. New relevant guidelines do exist. For example, the current American College of Physicians and the American Pain Society guidelines for the diagnosis and treatment of low back pain, published in 2007, recommend the following:

1. That clinicians conduct a focused history (including assessment of psychosocial risk factors, which predict risk for chronic disabling back pain) and physical exam to categorize patients with low back pain as follows: nonspecific low back pain, back pain potentially associated with radiculopathy or spinal stenosis, or back pain potentially associated with another specific spinal cause.

2. That clinicians consider the use of medications with proven benefits in conjunction with back care information and self-care. Clinicians should assess severity of baseline pain and functional deficits, potential benefits, risks and relative lack of long-term efficacy and safety data before initiating therapy.

Most clinical guidelines list skeletal muscle relaxants as optional agents for use individually or in combination with a nonsteroidal anti-inflammatory agent (NSAID). Skeletal muscle relaxants have been shown to be more effective than placebo for patients with acute low back pain (LBP) with respect to outcomes such as short-term pain relief, global efficacy and improvement of physical outcomes. Most clinicians and researchers agree that skeletal muscle relaxants may be of benefit to patients with acute low back pain by reducing the duration of their discomfort and accelerating recovery. It is probably best to consider the use of skeletal muscle relaxants as an adjunct or alternative to NSAIDs, especially in cases where NSAID toxicity is a concern or when NSAID monotherapy proves suboptimal. In this setting, it is important for the prescriber to choose a muscle relaxant that has a favorable safety profile, as well as one that is less likely to be abused in addition to being one that has evidence for its efficacy.

Despite the common use of skeletal muscle relaxants, relatively little data exist to elucidate their role in the treatment of chronic back pain. None of the skeletal muscle relaxants has an indication for use in the setting of chronic back pain. Despite this lack of evidence, muscle relaxants are often prescribed on a long-term basis. In general the skeletal muscle relaxants, excluding baclofen and tizanidine, maintain FDA labeling as adjuncts to treatment of short term acute LBP. As previously mentioned, baclofen and tizanidine have FDA indications for spasticity. When used in an acute back pain paradigm, skeletal muscle relaxants are used to treat muscle spasms and associated pain during the normal recovery period of one to three weeks. Since this correlates with the time course that most patients recover from their acute injury, it is difficult to discern the exact nature of the utility for these medications. As a group these agents may provide some global palliative quality, but probably do not effect the time course per se.

Skeletal muscle relaxants have CNS depressant effects and should be used with caution, particularly for patients with concomitant use of alcohol, anxiolytics, opioid analgesics, or other sedating agents. There is strong evidence that skeletal muscle relaxants are associated with higher risks of total adverse effects, especially those related to the central nervous system. Given the choice of many muscle relaxants, the prescriber is again advised to consider efficacy but also routine and serious side effects as well as the risk for abuse and misuse of each of these when treating patients. **PN**

Charles Argoff, MD is Professor of Neurology at Albany Medical College and Director of the Comprehensive Pain Program at Albany Medical Center.

EDUCATIONAL OPPORTUNITIES

• JUNE 1-4, *Whistler, BC*
2008 Annual Meeting of the Neurological Society of America
Phone: (507) 284-2254
E-Mail: atkinson.john@mayo.edu

• JUNE 15-19, *Sitges, Spain*
Ninth Eilat Conference on New Antiepileptic Drugs
Phone: +972 3 5175150
Fax: +972 3 5175155
E-mail: eilatIX@targetconf.com
http://www.eilat-aeds.com/

• JUNE 17-20, *Victoria, BC*
42nd Canadian Neurological Sciences Federation
Phone (403) 229-9544
E-mail: info@cnsfederation.org

• JUNE 17-22, *St. Thomas, VI*
2008 Annual Meeting of the International Behavioral Neuroscience Society
Phone: 830-796-9393
E-Mail: ibns@ibnshomepage.org

• JUNE 22-26, *Chicago*
12th International Congress of Parkinson's Disease and Movement Disorders
Phone: (414) 276-2145
www.movementdisorders.org/congress/

• JUNE 26-29, *Boston*
50th Annual Scientific Meeting of the American Headache Society
Phone: (856) 423-0043
ahsmtgs@talley.com
americanheadachesociety.org

• AUG. 6-9, *Hot Springs*
Parkinson's Disease and Movement Disorders
Phone: (800) 462-9633 / (904) 953-7114
Fax: (904) 953-2954
E-Mail: cme-jax@mayo.edu

• AUG. 17-22, *Glasgow*
12th World Congress on Pain
Phone: (206) 547-6409
Email: iaspdesk@iasp.pain.org
www.iasp-pain.org

• AUG. 23-26, *Madrid*
12th Congress of the European Federation of Neurological Societies
Phone: +41 22 908 0488
Fax: +41 22 732 2850
E-mail: efns08@kenes.com
http://www.kenes.com/efns/

• AUG. 24-27, *Garden Grove, CA*
Alzheimer's Association Dementia Care Conference
Phone: 312-335-5833
E-mail: careconference@alz.org
www.alz.org/careconference

• SEPT. 5-6, *Toronto*
9th Annual Interventional Neuroradiology Symposium
Phone: 416-978-2719
Fax: 416-946-7028
help-MIM0804@cmetoronto.ca

• SEPT. 17-20. *Providence*
American Association of Neuromuscular & Electrodiagnostic Medicine Meeting
Phone: (507) 288-0100
E-mail: aanem@aanem.org
www.aanem.org

• SEPT. 17-20, *Montreal*
ACTRIMS-ECTRIMS-LACTRIMS Joint Meeting
Phone: 212-476-0452
Fax: 212-499-0741
E-mail: actrims@nmss.org
Online: www.actrims.org

• SEPT. 19-20, *Halifax*
5th Atlantic Canada Stroke Conference
Phone: (902) 494-2061
Fax: (902) 494-1479
E-Mail: cme@dal.ca

• SEPT. 21-24, *Salt Lake City*
American Neurological Association 133rd Annual Meeting
Phone: (952) 545-6284
E-mail: ana@llmsi.com
www.aneuroa.org

• SEPT. 24-27, *Vienna*
6th World Stroke Congress
Phone: 41-229-080-488
Fax: 41-227-322-850
E-Mail: stroke2008@kenes.com

• OCT. 17, *Orlando*
Society of Neurosurgical Anesthesia and Critical Care Annual Meeting
Phone: (847) 825-5586
Fax: (847) 825-5658
E-Mail: snacc@asahq.org

• OCT. 18-25, *Woods Hole, MA*
2008 Research Update in Neuroscience for Neurosurgeons
dempsey@neurosurg.wisc.edu

• NOV. 5-8, *Santa Clara, CA*
Child Neurology Society (CNS) 37th Annual Meeting
Phone: (651) 486-9447
Fax: (651) 486-9436
E-Mail: nationaloffice@childneurologysociety.org

• NOV. 7-9, *Scottsdale*
Scottsdale Headache Symposium
Phone: (856) 423-0043
ahsmtgs@talley.com
www.americanheadachesociety.org

• NOV 15-19, *Washington, DC*
Society for Neuroscience 38th Annual Meeting
Phone: (202) 462-6688
Email: info@sfn.org
www.sfn.org

Vascular Clinic *(Continued from p. 42)*

als with TIA-like symptoms have not been adequately studied.

In addition, given the established superiority of aspirin-dypyridamole combination compared with aspirin for stroke prevention, it seems premature to use the aspirin-clopidogrel combination, especially given the suggestion that aspirin-dypyridamole does not substantially increase bleeding risk and has at least a similar if not lower bleeding risk than aspirin alone (see the June and July 2006 columns). Moreover, we will soon have the results of the PROFESS (Prevention Regimen For Effectively avoiding Second Strokes) study, which is comparing clopidogrel vs. dypyridamole-aspirin in over 20,000 minor stroke/TIA patients. This study may provide better information upon which to make treatment decisions in these commonly encountered patients.

What other interventions can reduce stroke risk in TIA/minor stroke patients? In next month's column, we will discuss the results of several new studies that suggest that early management may substantially reduce recurrent event rates. Stay tuned. **PN**