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INSIDE

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Is Polypharmacy Harming Your Patients?

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Clinical Professor, University of California, San Diego

Dr. Scherger reports no financial relationship to this field of study.

Synopsis: *One in 25 older Americans, and almost 10% of older men, are at risk for serious health problems such as bleeding and muscle weakness because they take an unwise combination of medications; half the time a non-prescription medication is involved.*

Source: Qato DM, et al. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. *JAMA* 2008;300:2867-2878.

A RESEARCH GROUP FROM THE UNIVERSITY OF CHICAGO CONDUCTED in-home surveys of medication use among a representative sample of 3005 Americans aged 57-85 years. These older Americans were on about 15,000 different medications! Overall, 4% were on potentially risky combinations of medications for harmful drug-drug interactions and half of these involved the use of non-prescription medications. Men in the older age group (75-85 years) had the greatest risk, about 10%, and nearly half of that involved the use of anticoagulants. The actual risk of harm may be greater than this survey suggests since only the top 20 prescription and non-prescription medications were studied.

The most common potentially harmful drug-drug interactions were: lisinopril and potassium increasing the risk of hyperkalemia; aspirin and warfarin increasing the risk of bleeding; aspirin and ginkgo increasing the risk of bleeding; and simvastatin and warfarin increasing the risk of bleeding and rhabdomyolysis. Some combinations decreased the effectiveness of both drugs, such as albuterol with atenolol or metoprolol.

The authors conclude with emphasis on the importance of physicians and pharmacists asking about all the medications a person is taking, including prescription and non-prescription medications,

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and educating patients about appropriate and inappropriate combinations.

■ **COMMENTARY**

Polypharmacy has made a comeback from a recent time when taking many medications was considered a risk factor for harm. A single common chronic disease like diabetes usually results in our patients taking 4 or 5 medications. Add hypertension, lipid disorder, heart disease, and arthritis and you have a recipe for potentially harmful medication interactions. Add to that the multibillion dollar supplement industry and it is no wonder than many of our patients are harmed from risky medication combinations.

Memorizing all drug-drug interactions is not possible and information support is necessary for us and our patients. Good computerized drug-drug interaction programs are available and we should use them liberally at the point of care. Increasingly, patients will have drug-drug interaction programs on their home computers.

More important is open and complete information about what our patients are taking. Computerized personal health records kept by our patients and shared with providers will help with medication disclosure. We should encourage our patients to use them. Applications such as Google Health and Microsoft Healthvault may play an increasingly important role in medication safety.

Most important, in my opinion, is to have a philosophy about medication use that less is better. When I hear that older patients are on more than 10 medications, I cannot help but believe that all these may be doing more harm than good. Getting patients off medications should be a goal as much as or more than prescribing them. Lifestyle improvements such as exercise and weight loss may allow us to reduce the number of medications our patients are taking.

The dietary supplement industry, which is protected from needing to give accurate health information, is a duplicate therapy system that many of our patients believe is harmless and may be helpful. When we have patients on a therapeutic regimen of multiple medications, we need to be proactive in talking about supplements and know exactly what our patients are taking, and caution them to avoid adding to the regimen with non-prescription products.

The Institute of Medicine estimates that there are 1.5 million adverse drug events in the United States every year.[1] These occur in office practices, hospitals, and long-term care facilities. It may be that the patient's home is the riskiest place for harmful medication use. Only by getting patients actively involved with reporting and managing their medication use will we get a handle on the pervasive problem of harm from medications. ■

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Questions & Comments

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Peppermint Sticks It to IBS

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

Residency Program Director, Associate Professor of Family Medicine, University of Alabama at Birmingham School of Medicine—Huntsville Regional Medical Campus, Huntsville

Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *Peppermint oil, psyllium, and antispasmodics are all effective in the treatment of IBS.*

Source: Ford AC, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: Systematic review and meta-analysis. *BMJ* 2008;337:a2313.

THE AUTHORS OF THIS META-ANALYSIS SEARCHED MEDline, Embase, and the Cochrane Controlled Trials Register for randomized controlled studies of treatment

of irritable bowel syndrome (IBS) with fiber, antispasmodic drugs, or oil of peppermint. Treatment had to last at least a week to allow the plasma concentrations of the medications to reach steady state. They found 615 citations, of which only 101 were deemed potentially relevant. Of these, only 35 remained after exclusion. They were scored on the Jadad scale, which measures the quality of studies, and those studies that scored 4 or more, indicating good quality, were analyzed separately. The primary outcome was the percentage of subjects with "persistent or unimproved symptoms after treatment" (P/USAT), a lower percentage indicating a better result. The relative risk (RR) and the number-needed-to-treat (NNT) were calculated.

Table

Summary of results by treatment and quality of study

Treatment	All Studies (n)	% P/USAT vs placebo	RR	NNT	Quality Studies (n)	RR
Fiber	12	52 vs 57	0.87	11	7	0.90*
Bran	5	54 vs 54	1.02	N/A	1	
Psyllium	6	52 vs 64	0.78	6	5	0.86*
"Concentrated fiber"	1	40 vs 29	1.37	N/A		
Antispasmodics	22	39 vs 56	0.68	5	12	0.65
Scopolamine	3	29 vs 46	0.63	3.5		
Dicyclomine	1	44 vs 67	0.65	4.2		
Peppermint oil	4	26 vs 65	0.43	2.5	3	0.40

* Not statistically significant

Twelve studies looked at fiber compared to placebo, 5 with bran, 6 with ispaghula husk (psyllium), and 1 with "concentrated" fiber. Seven of them were judged good quality. Although fiber significantly improved symptoms compared to placebo when all studies were analyzed, that disappeared when only the quality studies were examined. Bran had no effect on symptoms. Psyllium (Metamucil® and a host of others) was effective when all studies were included, but not when the analysis was limited to quality studies. The "concentrated" fiber was ineffective. The percentage of adverse events for fiber and placebo was the same, about 1%-2%.

Antispasmodics accounted for 22 studies, 12 of which were quality ones. The drugs studied were alverine, cimetropium, dicycloverine (dicyclomine), hyoscine (scopolamine), mebeverine, otilonium, pinaverium, pirenzipine, prifinium, propinox, rociverine, and trimebutine. Only dicyclomine (Bentyl® and others) and scopolamine (Scopace®, Transderm Scop®, and others) are available in the United States. A closely related drug, hyoscyamine (Anaspaz®, Levsin®, Levbid®, and others) is also available. When all 22 trials were considered, antispasmodics were significantly better than placebo, and this did not change when the analysis was restricted to quality studies. Patients receiving antispasmodics were more likely to experience adverse side effects, 14% vs. 9%, when compared to patients receiving placebo.

Oil of peppermint was the subject of 4 studies with 3 studies considered quality ones. It was significantly better than placebo, whether considering all studies or only the quality ones. Five of 174 (3%) subjects suffered adverse side effects from peppermint; no adverse effects were reported for the 171 placebo subjects.

The table *(above)* summarizes the data for the active ingredients available in the United States.

■ COMMENTARY

IBS "is a disorder characterized most commonly by cramping, abdominal pain, bloating, constipation, and diarrhea" that afflicts as many as 1 in 5 Americans.[1] That puts it right up there with obesity and makes it more common than diabetes mellitus and heart disease. I find that disturbing, because when I think of my patient population, I can name a lot of patients with obesity, diabetes, or heart disease, but only a couple with IBS. That says much about my diligence in searching for the syndrome and my patients' willingness to disclose their symptoms. Its etiology is "multifactorial," code word for "we're not really sure." This is not surprising since the symptom complex includes both diarrhea and constipation. There is a concise primer on IBS available on the *British Medical Journal* web site (www.bmj.com).[2] The American College of Gastroenterology recently updated its 2002 monograph on IBS.[3] It was not impressed by the quality of the evidence for fiber, antispasmodics, and peppermint oil, but supported their use. Among its new recommendations is routine screening of patients with celiac sprue serology.

It wasn't too long ago that medications were marketed in the United States specifically for IBS. In particular, the serotonin receptor antagonists, Type 3 (alosetron [Lotronex®]) and Type 4 (tegaserod [Zelnorm®]), were sold to combat diarrhea- or constipation-predominant IBS, respectively, but now are on restricted access or withdrawn from the U.S. market, respectively. Other medications and modalities have been evaluated for IBS, including antidepressants[4] and acupuncture,[5] and were not found to be effective.

Of the 3 agents in this meta-analysis, peppermint oil provides the best combination of effectiveness and a low rate of adverse effects, and is available over the counter.

Its mechanism of action appears to be reduction of colonic contractility by blocking calcium channels in smooth muscle. It should be taken as an enteric-coated capsule containing 0.2 or 0.4 mL of oil. Psyllium is only marginally effective, and the antispasmodics have a higher rate of adverse side effects (cholinergic, such as dry mouth or blurred vision). That particular order (peppermint oil, psyllium, antispasmodic) seems to be the best escalation of medications for IBS. ■

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The View from the Right Side: Effectiveness of Colonoscopy

ABSTRACT & COMMENTARY

By Malcolm Robinson, MD, FACP, FACG, AGAF

Synopsis: *Although colonoscopy is associated with reduced deaths from colorectal cancer, its effect seems to be limited to deaths from cancer developing in the left colon.*

Source: Baxter NN, et al. Association of colonoscopy and death from colorectal cancer: A population-based, case-control study. *Ann Intern Med* 2009;150:1-8.

COLORECTAL CANCER (CRC) IS OFTEN DEADLY, AND IT remains the second most frequent cause for cancer-related death in North America. Although its utility for this purpose has never been validated in randomized clinical trials, colonoscopy has been strongly recommended by various medical societies as the preferred screening method for CRC. Some indirect evidence for efficacy of colonoscopy comes from randomized trials of fecal occult blood testing (with colonoscopy for positive tests) that seem to indicate a reduction in CRC mortality. Previous case-control studies have suggested that colonoscopy might reduce CRC incidence by 50% and CRC deaths by 60%. However, these studies largely excluded women and they primarily evaluated sigmoidoscopy rather than complete colonoscopy. This exceptionally large and statistically complicated Canadian study attempted to evaluate the association between colonoscopy and subsequent CRC deaths. Ontario provincial patients aged 52-90 who were diagnosed with CRC between January 1996 and December 2001 and died of CRC by December 2003 were each matched with 5 controls that did not die of CRC. There were 10,292 case patients (with CRC) and 51,460 controls identified. A total of 719 case patients (7%) and 5031 controls (9.8%) had undergone colonoscopy. Complete colonoscopy was strongly associated with fewer deaths from left-side CRC (odds ratio [OR], 0.33; confidence interval [CI], 0.28-0.39), but there was not a positive association with death from right-side CRC (OR, 0.99; CI, 0.86-1.14). In this retrospective provincial data analysis, screening colonoscopy could not be differentiated from colon exams designed to evaluate signs or symptoms. The authors hypothesized that colonoscopy might not be effective in the right colon due to the greater likelihood of poor right colon bowel cleansing, the presence of non-pedunculated or even flat or depressed polyps or cancers, or other causes of inadequate colonic mucosal evaluation.

■ COMMENTARY

In an accompanying editorial by David Ransohoff, MD, of the University of North Carolina, some potential defects of the study are elaborated. Included is the fact that this was not a randomized controlled trial, that most colonoscopies (70%) were performed by internal medicine physicians and surgeons and family physicians rather than gastroenterologists, and that rapid colonoscope withdrawal could have led to missed lesions (a recently documented phenomenon not necessarily known at the time of this study). It was also noted that any significant symptoms prior to colonoscopy might have preferentially associated the procedure with CRC and death, thus obscuring any favorable effect of colonoscopy on cancer development and mortality. However, this possibility may have been countered by the exclusion of patients who developed cancer within 6 months of the colonoscopy. There seems to be some literature suggesting that right colon cancers may grow more rapidly than those in the left colon, and this could make routine colonoscopy less effective in right-side

CRC prevention. The bottom line seems to be that the precise utility of colonoscopy for CRC and CRC death prevention will remain uncertain until large randomized controlled studies are completed. The previous hope that 90% of CRC could be prevented by colonoscopic screening seems quite unrealistic, and patients should be told that the actual reduction of risk is closer to 60% or 70%. As Dr. Ransohoff comments, this reduction in risk is still quite respectable. For example, there is no proven cancer mortality reduction with screening for prostate cancer. Likewise, breast cancer screening reduces cancer mortality by 25% or less. The American Society for Gastrointestinal Endoscopy (ASGE) was quite alarmed by the release of this article. As might have been expected, the ASGE response was that patients should only have colonoscopies done by highly experienced and qualified gastroenterologists and that colonoscopies almost certainly have dramatically improved since the era of the Canadian data acquisition. One hopes that this is true, but only data will answer this question. ■

Is CKD in Your Future?

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

Synopsis: *These investigators derived and validated a risk score that predicts incident kidney disease.*

Source: Kshirsagar AV, et al. A simple algorithm to predict incident kidney disease. *Arch Intern Med* 2008;168:2466-2473.

BUILDING ON THEIR PREVIOUS WORK, THIS GROUP OF investigators from the University of North Carolina's Kidney Center combined two data sets, the Atherosclerosis Risk in Communities (ARIC) Study and the Cardiovascular Health Study (CHS) to derive a risk score that would predict future chronic kidney disease (CKD) in the general population. ARIC enrolled 15,732 participants and followed them for a maximum of 9 years. CHS enrolled 5888 participants and followed them for a maximum of 10 years. The participants had the usual demographic information, clinical findings, and health history recorded. Some common laboratory tests, including hemoglobin, lipid profile, and serum creatinine were obtained. The subjects' glomerular filtration rate (GFR) was estimated with the formula from the Modification of Diet in Renal Disease Study, which uses as variables creatinine, age, race, and gender. CKD was defined as a GFR < 60 mL/min/1.73 m^2.

After proper exclusion, which included missing data and baseline renal insufficiency, 14,094 participants were left in the combined data set. A total of 9470 were randomly assigned to the development data set and 4624 to the validation data set. A little more than 11% of the combined data set developed CKD during follow-up. Performing multiple logistic regressions on the development data set, age, diabetes mellitus, peripheral vascular disease, anemia, female sex, white race/ethnicity, systolic blood pressure, history of coronary vascular disease, history of heart failure, and low HDL-cholesterol concentration (≤ 40 mg/dL) were identified as predictors of CKD. The investigators looked at two models, one which used all 10 of the identified predictors and the other which dropped white race/ethnicity and low HDL-cholesterol level. Each identifier, except age, was assigned a risk score of 1. Age was divided into three intervals, 50-59, 68-69, and ≥ 70 years, and assigned 1, 2, and 3 points, respectively. When both models were applied to the validation data set, they performed similarly. The authors recommend using cut points of 5 for the full model and a cutoff of 3 for the simplified model. These cut points would identify 20% and 13% of participants progressing to CKD in the next 10 years, respectively.

■ COMMENTARY

Back in 2007, Bang[1] published (and *Internal Medicine Alert*[2] reviewed) this team's development of a risk score for predicting CKD. So why are we looking at this again? Partly, it's my fascination with risk scoring tools, but more importantly, SCORED looks at prevalence and predicts who has CKD. SCORED also used a different set of variables, including the presence of proteinuria. The current algorithm tries to predict who will develop CKD. Presumably, this knowledge would allow patients to make lifestyle changes and physicians to intervene to address risk factors. The authors liken these risk score models to the Framingham risk score for predicting cardiovascular disease in the next 10 years. Interventions are based on a patient's risk score and those patients scoring > 20% are recommended for pharmaceutical and lifestyle interventions. The authors envision their CKD risk scores being used in physician offices, on medical web sites, and at health fairs to identify patients at risk.

In this combined data set, body mass index (BMI) was 27 kg/m^2 in participants without CKD and 28 kg/m^2 in those with CKD. In a recent study, researchers from Tufts University, using the same data sets as these authors, showed that waist-to-hip ratio (WHR), but not BMI, was associated with progression to CKD and mortality.[3] Perhaps future refinements of these risk scores will incorporate WHR.

Of the risk factors listed, only anemia, hypertension, diabetes, and low HDL are modifiable and of these, only treatment of hypertension and diabetes has been shown to slow the progression to CKD. Anemia is more likely the result of CKD than a cause. Age is the most potent risk factor, and in the simplified model, being 70 years or older garners enough points by itself to identify a patient at risk. This suggests that we skip the simplified model and use the full one for our elderly patients. Of course, more than half of our elderly patients would get another point by virtue of being female, but in the full model that combination is still not enough to reach the cut point of 5. An elderly patient who has no other risk factors is likely to be healthy in general and unlikely to develop CKD in the next 10 years.

Family physicians and primary care internists are expected to manage chronic diseases, but we cannot manage what we do not detect. Risk scores like this one help us identify patients who may need our attention. ■

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Pharmacology Update

Lacosamide Tablets and Injection (Vimpat®)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Clinical Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Chan and Elliott report no financial relationship to this field of study.

A NEW ANTIEPILEPTIC DRUG WITH A NOVEL MECHANISM of action has been approved for the treatment of partial seizures. Lacosamide is a new chemical entity, which potentially has a dual mechanism of action. It will be marketed by UCB, Inc., as Vimpat®.

Indication

Lacosamide is indicated for adjunctive treatment of partial seizures in patients 17 years of age and older.[1]

Dosage

The initial dose is 50 mg twice daily (oral or intravenous administration). Depending on response and tolerability, the dose may be increased at weekly intervals by 100 mg (2 divided doses) up to 400 mg daily.[1] The injection should be administered at the same daily dose and frequency. The infusion should be over 30-60 minutes. Oral tablets may be taken without regard to meals. No dose adjustment is necessary for patients with mild-to-moderate renal impairment. For patients with impaired hepatic function, titration should be done with caution and the daily dose should not exceed 300 mg in patients with mild or moderate hepatic impairment.

Lacosamide is available as 50 mg, 100 mg, 150 mg, and 200 mg tablets, and a single-use vial (200 mg/20 mL).

Potential Advantages

Lacosamide has been shown to improve seizure control in patients with uncontrolled partial-onset seizures taking up to 3 antiepileptic drugs.[1-3] The drug has high oral bioavailability and its pharmacokinetics have low intrapatient and interpatient variability. Lacosamide does not appear to have any significant drug-drug interaction with common antiepileptic drugs.[1,2]

Potential Disadvantages

As with other antiepileptics, there is potential for increased risk of suicidal thoughts or behavior. Patients should be monitored for signs of worsening depression, suicidal ideation, and/or other mood or behavior changes.[1] Albeit rare (0.4%-0.5%), lacosamide may prolong PR interval and predispose patients to atrial arrhythmias. Common adverse events for the 400 mg daily dose include dizziness (30%), headache (14%), nausea (11%), and diplopia (10%). Ataxia (7%) and syncope (1.2%) have also been reported. Safety and effectiveness have not been established in patients younger than 17 years of age.

Comments

Lacosamide is an antiepileptic that is chemically and mechanistically different from currently marketed agents. Its proposed mechanism of action is selective enhancement of the slow inactivation of voltage-gated sodium channels and binding to collapsin response protein-2 (CRMP-2), a phosphoprotein mainly expressed in the nervous system.[1] These actions may result in controlling neuronal hyperexcitability and neuroprotective effects.[2] The efficacy of lacosamide was established in

three 12-week, randomized, placebo-controlled studies (n = 1294).[1,2] Study participants had partial-onset seizures with or without generalization and were not adequately controlled with up to 3 concomitant antiepileptics. They had an average of 4 or more seizures per 28 days and no seizure-free period greater than 21 days. Across these studies, subjects were randomized to 200 mg, 400 mg, and 600 mg daily or placebo. These studies included 3 phases: 8-week baseline phase, 6-week titration phase, and a 12-week maintenance phase. The primary endpoints were reduction in the seizure frequency per 28 days and percent of subjects with at least a 50% reduction in frequency from baseline to maintenance phase (50% responder rates). Median reduction in seizure episodes ranged from 26%-35% for 200 mg, 39%-37% for 400 mg, and 10%-21% for placebo. The 600 mg dose showed essentially the same efficacy as the 400 mg, but with a higher frequency of adverse events. Forty percent (40%) of patients had a 50% or greater reduction in seizure frequency at 400 mg daily compared to 23% for placebo. Discontinuation rates were 5%, 11%, 19%, and 30% for placebo, 200 mg, 400 mg, and 600 mg, respectively.[2] Dizziness is the most common adverse event resulting in discontinuation. Lacosamide has also shown antinociceptive activity and is being studied for the treatment of diabetic neuropathic pain.[4]

Clinical Implications

The new antiepileptic lacosamide provides an alternative to patients with partial-onset seizures who are not adequately controlled on multiple antiepileptics. ■

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CME Questions

4. **Which of the following medication interactions is *not* true?**
   a. Taking lisinopril and potassium increases the risk of hyperkalemia.
   b. Taking ginkgo and aspirin increases the risk of bleeding.
   c. Taking albuterol and metoprolol increases the effect of both medications.
   d. Taking warfarin and simvastatin increases the risk of rhabdomyolysis.

5. **Choose the *incorrect* answer. In the meta-analysis of treatment of irritable bowel syndrome:**
   a. peppermint had the lowest number-needed-to-treat.
   b. bran was superior to psyllium.
   c. fiber had the lowest rate of adverse side effects.
   d. antispasmodics had the highest rate of adverse effects.
   e. antispasmodics were more effective than fiber.

6. **Using either of the multivariate models for chronic kidney disease, a 68-year-old male with hypertension would have which of the following risk scores?**
   a. 1
   b. 2
   c. 3
   d. 4

Answers: 4. c, 5. b, 6. c.

CME Objectives

The objectives of *Internal Medicine Alert* are:
- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances;
- to describe cost-effective treatment regimens;
- to describe the pros and cons of new screening procedures.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville
Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Which is better for hypertension?

Source: Jamerson K, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high risk patients. *N Engl J Med* 2008;359:2417-2428.

JNC 7 IS PROBABLY THE CONSENSUS document most utilized by U.S. clinicians to make decisions about HTN. The ALLHAT trial was instrumental in establishing the equal efficacy of chlorthalidone, amlodipine, and lisinopril in reference to mortality, with some subgroups (CHF, stroke) showing superiority of chlorthalidone. These results led to the suggestion that diuretic therapy be a foundation of HTN treatment.

Clinical trials have consistently demonstrated that only a minority of patients are able to have their HTN controlled on monotherapy, and little direction has been available to guide therapy about which combination of agents provides best outcomes. The ACCOMPLISH trial was designed to compare outcomes in HTN patients (n = 11,506) considered to be high-risk because of substantial comorbidity (e.g., PAD, LVH, MI, stroke, CKD). The two regimens compared were ACE/CCB (benazepril/amlodipine) and ACE/HCTZ (benazepril/hydrochlorothiazide). The primary endpoint was a composite of CV death, nonfatal MI/stroke, hospitalization for angina, sudden death resuscitation, and revascularization.

The trial was stopped early at 36 months when the clear advantage of ACE/CCB was seen: a 20% relative risk reduction for the primary endpoint. In situations where clinicians are choosing combination therapy, ACE/CCB has been superior to ACE/HCTZ. Because HCTZ and chlorthalidone are not identical, there is some controversy over whether results would have been the same had chlorthalidone (the agent used in ALLHAT) been used instead. At the current time, since the vast majority of prescriptions for an antihypertensive diuretic in the United States employ HCTZ, these results should be generalizable to most practice situations. ■

Putting sunscreen to the test

Source: Sang SQ, et al. In vitro assessments of UVA protection by popular sunscreens available in the United States. *J Am Acad Dermatol* 2008; 59:934-942.

SPF STANDS FOR "SUN PROTECTION factor," but if FDA recommendations change, the name will soon stand for "Sunburn Protection Factor" because of the recognition that current SPF testing reflects erythema effects of UVA light in the 320-340 nm and UVB light in the 290-320 nm wavelengths, but does not necessarily reflect efficacy for other photodamaging wavelengths. UVA light in the 340-400 nm range is also dermotoxic, but impact of sunscreen on this light component has not previously been included in labeling. In August 2007, the FDA suggested a new rating scale that includes a ratio of UVA 340-400 nm (termed UVA1) to total UV light absorption. Agents that have low efficacy for absorbing UVA1, even though they have good efficacy for other wavelengths, would be rated lower in overall efficacy.

An analysis of 13 OTC sunscreen products using the new FDA criteria found 8 to provide medium protection and 5 to provide high protection. All but one of the selected products had an SPF of at least 30. If the proposed FDA metric becomes widely accepted, consumers will have an opportunity to better appraise the overall efficacy of sunscreen products. ■

Triglycerides and risk of stroke

Source: Freiberg JJ, et al. Nonfasting triglycerides and risk of ischemic stroke in the general population. *JAMA* 2008;300:2142-2152.

THE CONSISTENT AND STRONG RELAtionship between LDL and adverse CV events, coupled with widely replicated risk reduction achieved with statins, leaves little doubt about the risk-benefit ratio of such intervention. On the other hand, the relationship between triglycerides (TRGs) and CV events, and the benefits of lowering elevated TRGs, is much less well established.

The Copenhagen City Heart Study has been following approximately 14,000 men and women since 1976. Although TRGs are typically measured fasting, the authors of this paper measured non-fasting TRG (nf-TRG) to gain insight into associated CV risk.

An analysis was performed comparing 6 incremental levels of nf-TRG. The reference level was nf-TRG < 89 mg/dL. Risk for stroke was assessed for men and women, at increments of 89 mg/dL, from an nf-TRG level of 89 mg/dL to > 443 mg/dL. For both men and women, ischemic stroke increased with increasing levels of nf-TRG. For instance, individuals with nf-TRG > 443 mg/dL had a hazard ratio 2.5-3.8 times greater than persons with nf-TRG < 89 mg/dL.

These intriguing findings suggest that nf-TRG might be useful, in concert with LDL, as a target for CV risk reduction. Of course, whether intervention to modulate nf-TRG is appropriate will depend on future interventional trials documenting that reduction of nf-TRG is beneficial. ■