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INSIDE

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Finally an Optimal Strategy for Diagnosing Deep Vein Thrombosis

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Professor, University of California, San Diego

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

Synopsis: *A medical research unit in the United Kingdom analyzed 18 different strategies for managing patients with suspected deep vein thrombosis (DVT). Using systematic review, meta-analysis and cost effectiveness analysis, they settled on an algorithm based on clinical risk. The initial screen for all patients is a latex D-dimer test. If the D-dimer test is negative and the patient is low or intermediate risk (Wells rule), DVT is ruled out. If the clinical risk is high, and the D-dimer test is negative, an above-the-knee ultrasound is ordered, and, if positive, the patient is treated. If the D-dimer test is positive, an ultrasound is ordered regardless of risk. If the ultrasound is negative and the patient is high risk, it is repeated before a treatment or discharge decision is made.*

Source: Goodacre S, et al. How should we diagnose suspected deep-vein thrombosis? *QJM*. 2006;99:377-388.

DEEP VEIN THROMBOSIS OF THE PROXIMAL LOWER EXTREMITY IS one of the most important and challenging diagnoses to make. The treatment requires inpatient care and is potentially life saving. Multiple evolving diagnosis and treatment algorithms are available which make clinical decision making difficult. Variations in the management of patients with suspected DVT are an important quality issue. Credit the United Kingdom and its National Health Service to commission a meticulous detailed analysis of multiple strategies to come up with an approach which is both highly accurate and cost effective.

After a systematic review and meta-analysis of 18 different strategies, a hypothetical group of 1000 patients were managed using each algorithm. A mean survival of 11.6 quality adjusted life years (QALYs) was used after a diagnosis of DVT at age 60. Clinical risk was assigned using the Wells Clinical Prediction Rule using 9 fac-

VOLUME 28 • NUMBER 18 • SEPTEMBER 29, 2006 • PAGES 137-144

tors to score the risk of DVT. A recent analysis of the *Annals of Internal Medicine* questioned the reliability of the Wells rule in ruling out DVT.[1] However, in the British analysis, the Wells rule was mostly used to identify patients at high risk of DVT for further analysis even if the D-dimer test is negative.

The latex D-dimer test is a major advance in screening for DVT and other hypercoagulation states. The D-dimer reflects fibrin degradation products which indicate thrombus formation, and is positive in a number of conditions besides DVT, such as disseminated intravascular coagulation (DIC). The test is sensitive for DVT but not specific, and may rise in the elderly, with false positives in patients with rheumatoid arthritis, high triglycerides, and elevated bilirubin. The test is not diagnostic for DVT and should be followed up by more specific testing such as venous ultrasound.

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Please call **Robert Kimball**, Managing Editor, at (404) 262-5413 (e-mail: robert.kimball@thomson.com) between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Using the algorithms in this study, the percentage of patients with proximal DVT who would be treated appropriately ranged from 90.1% to 99.5%, and the patients without DVT treated inappropriately ranged from 0.6% to 6.0%. The final recommendations for the most accurate and cost effective algorithm are quite simple. The initial screen for all patients is a latex D-dimer test. If the D-dimer test is negative and the patient is low or intermediate risk (Wells rule), DVT is ruled out. If the clinical risk is high, and the D-dimer test is negative, an above the knee ultrasound is ordered and if positive the patient is treated. If the D-dimer test is positive, an ultrasound is ordered regardless of risk. If the ultrasound is negative and the patient is high risk, it is repeated before a treatment or discharge decision is made.

COMMENTARY

Even though this study is based on hypothetical patients, the analysis is quite rigorous, and uses the best available evidence. No combination of tests is perfect and there is always a risk of a missed diagnosis. A main contribution of this analysis is that not all patients require ultrasound, which may be difficult to obtain acutely in the primary care setting. As the study in the *Annals of Internal Medicine* points out, some patients (2.9% in their analysis) will have a low Wells score and a negative D-dimer test and will be found on ultrasound to have DVT. Maybe clinical judgment here should also include the "thin slicing" of rapid clinical intuition described by Malcolm Gladwell in *Blink*.[2] If our initial assessment makes one think of DVT, we should be quite certain it is not present before accepting that it is ruled out.

We now have coherence in the diagnosis of suspect DVT. The three-part assessment is easy to remember, D-dimer testing, the Wells rule and venous ultrasound. Combined with the clinical judgment of an experienced clinician, we have sound and consistent strategies for the diagnosis of DVT. ■

References

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2. Gladwell M. *Blink*. Little, Brown and Company. New York, NY: Time Warner Book Group, 2005.

Esomeprazole 40 mg Once a Day in Patients with Functional Dyspepsia

ABSTRACT & COMMENTARY

By Malcolm Robinson MD, FACP, FACG

Emeritus Clinical Professor of Medicine, University of Oklahoma College of Medicine, Oklahoma City

Dr. Robinson serves as a consultant for TAP, Pfizer, Janssen, Eisai, J&J-Merck, and Procter & Gamble, is on the speaker's bureau of Janssen, Eli Lilly, Solvay, TAP, and Aventis, and does research for Forest Labs, Wyeth-Ayerst, AstraZeneca, and Centocor.

Synopsis: *Functional dyspepsia cannot reliably be diagnosed using symptoms alone. Esomeprazole therapy is not effective vs placebo in an 8-week study of endoscopy-negative patients with histories thought to be diagnostic of FD.*

Source: Sander Veldhuyzen van Zanten, et al. *Am J Gastroenterol*. 2006. Epub ahead of print.

FUNCTIONAL DYSPEPSIA (FD) HAS BEEN DEFINED AS persistent or recurrent upper abdominal pain in the absence of organic disease by upper endoscopy and other appropriate investigations. Pathophysiology probably has many variations, but some patients seem to respond to acid suppression. It has been assumed that many patients with FD relieved by acid inhibition have unrecognized GERD despite the fact that FD is supposed to exclude patients with dominant heartburn or regurgitation. In previous FD studies, esomeprazole treatment (ESO) has resulted in better outcomes than omeprazole, ranitidine, or cisapride. The present study was designed to test efficacy of ESO vs placebo one half hour before breakfast. FD patients were from primary care settings and specifically did not have dominant GERD symptoms.

Forty nine primary care centers in Canada were involved in the trial, and 109 patients were randomized to ESO and 115 received placebo. All patients had normal pre-study endoscopies. Exclusions included IBS, previous history of mucosal acid peptic disease, and maintenance acid suppressive therapy within 6 months of study entry. Urea breath testing for *H. pylori* was done at baseline, but results were not disclosed to investigators during the study. Data on daily symptoms were gathered. 'Symptom relief' was defined as minimal or no symptoms during the 2 days prior to 4 and 8 week evaluations. Sample size was calculated prior to initiating the trial; 41% of prospective enrollees were disqualified at screening endoscopy with 23.6% having erosive esophagitis, 1.5% gastric ulcer, 4.2% duodenal ulcer, 12.3% gastric erosions, and 5.3% duodenal erosions. Thirty nine patients were eliminated because symptoms at study entry 7-10 days post-endoscopy were no longer moderate or greater in intensity. A wide range of symptoms were present in those accepted for the study: 26.8% bloating, 25% epigastric pain, 10.7% postprandial fullness. Overall prevalence of *H. pylori* was 22.8%, matched between recipients of ESO and placebo. Symptom relief as defined at 8 weeks did not differ between ESO and placebo although the 4-week data were significantly different (relief in 50.5% on ESO vs 32.2% on placebo; $P = 0.009$).

COMMENTARY

The study was commissioned and supported by AstraZeneca Canada (marketer of esomeprazole). Obviously disappointed with the results of the study, the authors extensively speculated regarding the possible explanations for the lack of efficacy of ESO vs placebo at the conclusion of this 8-week study. However, at least for this reviewer, the bottom line here is the absence of long-term efficacy of aggressive acid suppression in functional dyspepsia. The study did do a good job of showing that the clinical diagnosis of FD is highly imprecise in that many of the patients with this 'diagnosis' were found on screening endoscopy to have a wide range of pathologies. It has long been clear that acid suppressive therapy is grossly over prescribed, and this study is further evidence that the chronic use of PPIs in functional dyspepsia cannot be scientifically justified. ■

Oral Anticoagulation for Stroke Prevention in AF

ABSTRACT & COMMENTARY

By Matthew E. Fink, MD

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Dr. Fink reports no financial relationship relevant to this field of study.

Synopsis: *Warfarin remains superior to antiplatelet agents for stroke prevention in patients with AF.*

Source: Connolly S, et al. Clopidogrel Plus Aspirin versus Oral Anticoagulation for Atrial Fibrillation in the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE W): A Randomized Controlled Trial. *Lancet*. 2006;367:1903-1912.

IN THE 1980S, PRIMARILY FROM THE FRAMINGHAM Study, atrial fibrillation (AF) was a clearly established

major risk factor for stroke and other cardioembolic vascular events. In the 1990s, several randomized clinical trials established the efficacy of vitamin K-dependent oral anticoagulants (warfarin and other coumarins) in preventing stroke from AF, and also demonstrated its superiority over aspirin. However, because of the difficulty in managing patients who are taking oral anticoagulants (OA), and the reluctance of many patients to undergo frequent blood tests and physician visits, there is a continuing desire to find a simple and safe regimen as an alternative to OA.

Connolly and colleagues compared the effectiveness of aspirin (75-100 mg per day) plus clopidogrel (75 mg per day) versus OA with a coumarin agent. Patients were enrolled if they had AF plus one or more risk factors for stroke—age 75 years or older, treatment for hypertension, previous stroke, TIA, non-CNS embolus, decreased left ventricular ejection fraction, peripheral arterial disease, diabetes mellitus, or coronary artery disease. They were randomly allocated to receive OA (target INR, 2.0-3.0; n = 3371) or clopidogrel plus aspirin (n = 3335). Primary outcome was the first occurrence of stroke, non-CNS systemic embolism, myocardial infarction, or vascular death.

The study was stopped early because of clear evidence for superiority of OA over combined antiplatelet therapy. There were 165 primary events in the OA group (annual risk = 3.93%) and 234 in the aspirin/clopidogrel group (annual risk = 5.6%), with an increased relative risk of 1.44 (1.18-1.76; P = 0.0003). In addition, there was no significant difference in overall bleeding complication rates between the 2 groups. Patients who were already on OA therapy, and were maintained on OA, had the best overall therapeutic response, with the lowest rate of primary events, and the lowest rate of bleeding complications.

COMMENTARY

In the quest for a safer and better oral antithrombotic treatment to prevent stroke in patients with AF, warfarin and its relatives still come out on top when compared to combination therapy with aspirin and clopidogrel. It is projected that the number of people with AF will double by the year 2050 and, therefore, physicians will be treating more patients who have stroke and TIA with some form of OA. The good news from the ACTIVE study is that the annual rate of stroke in the aspirin/clopidogrel group was 2.4%; much lower than in other studies that looked at aspirin alone. It is likely that better management of all risk factors has resulted in an overall reduction in stroke rates in patients with AF, and this finding should give us hope and optimism for the future. ■

Does HCV Really Go Away?

ABSTRACT & COMMENTARY

By Carol A. Kemper, MD, FACP

Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center

Dr. Kemper reports no financial relationships to this field of study.

Synopsis: *HCV may persist and replicate in the liver and PBMCs of healthy, anti-HCV antibody-positive, serum HCV RNA-negative patients who have persistently normal ALT levels. These patients should be followed up, because they have an ongoing viral infection.*

Source: Carreño V, et al. Detection of Hepatitis C Virus (HCV) RNA in the Liver of Healthy, Anti-HCV Antibody-Positive, Serum HCV RNA-Negative Patients with Normal Alanine Aminotransferase Levels. *J Infect Dis*. 2006:194:53-60.

A small number (5% to 15%) of fortunate people who become acutely infected with HCV appear to clear their infection with no residual evidence of HCV viremia and normal transaminases. Suspicions are, however, being cast on whether HCV can ever be, in fact, completely cleared from the body. Studies have shown that patients successfully treated with antiviral therapy who achieve sustained undetectable levels of plasma HCV RNA may still harbor occult intrahepatic virus. Other investigators have identified HCV RNA in the peripheral blood mononuclear cells (PBMC) of a few patients who apparently cleared their viremia and developed anti-HCV antibodies, either naturally or in response to antiviral treatment.

Carreño and colleagues in Madrid, Spain, examined liver biopsies from 12 patients with anti-HCV antibodies by recombinant immunoblot assay and negative serum HCV RNA (Amplicor HCV, version 2.0, Roche Diagnostics). Two of the patients had a remote history of blood transfusion more than 25 years earlier. The remaining patients had no history of hepatitis and no risk factor for HCV. During a mean follow-up of 29 ± 20 months, none of the patients developed clinical or laboratory evidence of HCV infection. Serum transaminases remained normal; they continued to have undetectable plasma HCV RNA, and all 12 remained HCV antibody positive.

COMMENTARY

Surprisingly, despite this lack of evidence for residual HCV infection, 10 of 12 (83%) liver biopsies were posi-

tive for genomic HCV RNA. All 10 of these specimens also demonstrated positive antigenomic HCV RNA strands, indicating occult replication. All 10 individuals had genotype 1b, raising concerns about possible cross-contamination in the lab, but nucleotide sequencing revealed distinct clones.

Genomic HCV RNA was also detected in the PBMCs of 6 of 12 patients (50%) (all of whom had positive liver biopsies); anti-genomic RNA was identified in 5 of these.

Despite a lack of clinical or other laboratory evidence of infection, histopathology in one patient revealed chronic active hepatitis and stage 1 fibrosis. Other potential causes of liver disease were ruled-out in this individual. Three patients had steatohepatitis or steatosis (2 were overweight and one was diabetic). The remaining 6 patients with positive intrahepatic HCV RNA had normal or minimal histologic changes. ■

Antibiotics for Acute Purulent Rhinitis? 'S not a Good Idea

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

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

Synopsis: *Antibiotics may improve acute purulent rhinitis at the cost of gastrointestinal upset and rash.*

Source: Arroll B, Kenealy T. Are antibiotics effective for acute purulent rhinitis? Systematic review and meta-analysis of placebo controlled randomised trials. *BMJ*. 2006;333: 279-282.

Purulent nasal discharge is a common sign in the common cold and acute sinusitis. It is also a key trigger for prescription of antibiotics.[1,2] Arroll and Kenealy report their systemic review and meta-analysis of studies of the use of antibiotics in acute purulent rhinitis. They searched Medline, EMBASE, and the Cochrane controlled trials register and included controlled trials that studied purulent rhinitis, nasopharyngitis, common cold, and sinusitis where the study groups received an antibiotic and the control groups received a placebo. "Acute" was defined as less than 10 days. They found 5 papers which examined purulent rhinitis and 2 that examined rhinitis, but did not specify whether it was clear or cloudy. Several different antibiotics were studied: demethylchlortetracycline (demeclocycline, Declomycin® and others), amoxicillin (Amoxil® and others), co-trimoxazole (trimethoprim/ sulfamethoxazole, Bactrim® and others), and cephalexin (Keflex® and others).

Pooling the data, there was a significant benefit from antibiotics with a relative risk of 1.21 (95% confidence interval, 1.09-1.34, number-needed-to-treat [NNT] 8.) Looking at adverse effects (primarily vomiting, diarrhea, abdominal pain, and rash), the pooled relative risk was 1.46 (95% CI, 1.10-1.94). The number-needed-to-harm was seven.

COMMENTARY

Eight guys walk into a physician's office with green-yellow gunk coming out of their noses. We could treat all of them and, statistically, one of them might get better. On the other hand, at least one might suffer from an adverse side effect. What's a prudent physician to do?

Last year these authors published a systemic review of antibiotics for the common cold and acute purulent rhinitis.[3] In it they concluded that the evidence of benefit with use of antibiotics for upper respiratory tract infections is too weak to recommend it, but the evidence in acute rhinitis, purulent or clear, was stronger. Since antibiotics can cause significant adverse effects, they did not recommend their routine use. A Cochrane Review of chronic (10 days or greater) purulent nasal discharge in children[4] concluded that when there was radiographic evidence of sinusitis, antibiotics provided modest short-term help. NNT was eight.

Back to our prudent physician. The first step should be a discussion with the patient about the probable efficacy and the probable harm associated with use of antibiotics. Watchful waiting is appropriate. If "something" must be done, consideration should be given to nasal hypertonic saline irrigation. It is effective in acute sinusitis[5] and well tolerated.[6] ■

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2. Gonzales R, et al. The relation between purulent mani-

festations and antibiotic treatment of upper respiratory tract infections. *J Gen Intern Med*. 1999;14:151-156.
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4. Morris P, Leach A. Antibiotics for persistent nasal discharge (rhinosinusitis) in children. *Cochrane Database Syst Rev*. 2002;(4):CD001094. Review.
5. Rabago D, et al. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: a randomized controlled trial. *J Fam Pract*. 2002;51: 1049-1055.
6. Rabago D, et al. Qualitative aspects of nasal irrigation use by patients with chronic sinus disease in a multimethod study. *Ann Fam Med*. 2006;4:295-301.

Pharmacology Update

Efavirenz/Emtricitabine/ Tenofovir Tablets (Atripla™)

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

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; 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 relationships to this field of study.

THE FDA HAS APPROVED THE FIRST, ONE TABLET, ONCE-daily, three-drug combination for the treatment of HIV-1 infections. This fixed-dose combination contains efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg (EET). It was approved in less than 3 months under the FDA's fast track program. EET was developed as a joint venture between Bristol-Myers Squibb and Gilead Sciences and will be marketed as Atripla™.

Indications

EET is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.[1]

Dosage

The recommended dose is one tablet daily on an empty stomach and at bedtime to reduce adverse events.[1]

Potential Advantages

EET is the first one-tablet once-daily complete regimen for treatment of HIV-1. The combination significantly reduces pill burden and may improve medication adherence. This three-drug regimen appears to have synergistic antiviral activity.[1]

Potential Disadvantages

The most common adverse events include headache, dizziness, abdominal pain, nausea, vomiting and rash.

Comments

The approval of EET was based on a 48-week randomized open-label, active control, trial. The active control was efavirenz, zidovudine and lamivudine (EZL).[1] The study participants were 511 antiretroviral naïve patients with a mean baseline CD4 count of 245 cells/mm^3 and a median baseline plasma HIV-1 RNA of 5.01 $\log_{10}$ copies/mL. Percentage of patients achieving HIV-1 RNA < 400 copies/mL through week 48 were 84% for EET and 73% for EZL. HIV-1 RNA < 50 copies/mL were 80% for EET and 70% for EZL. The mean increase in CD4 was 190 cells/mm^3 and 158 cell/mm^3 and discontinuation rate for adverse events was 4% and to 9% respectively. Combining three drugs in one does not affect their pharmacokinetics as one EET tablet is bioequivalent to each component administered individually.[1] According to the manufacturers, Atripla will cost $1,150.88 for a 30-day supply.

Clinical Implications

The approval of EET reduces pill burden to the minimum of one tablet once a day. This should increase convenience and improve adherence. Currently efavirenz + (zidovudine or tenofovir) + lamivudine or emtricitabine are the preferred NNRTI-based regimens for initial treatment of treatment-naïve patients.[2] Findings from a recently published randomized controlled trial in treatment-naïve patients concluded that there was no significant difference in efficacy or safety with a 3-drug regimen (zidovudine, lamivudine, and efavirenz) compared to a 4-drug regimen (zidovudine, lamivudine, efavirenz, and abacavir).[3] ■

References

1. Atripla Product Information. Bristol-Myers Squibb and Gilead. July 2006.
2. Guideline for use of antiretroviral agents in HIV-1 infected adults and adolescents. www.aidsinfo.nih.gov/ContentFiles/AboutHIVTreatmentGuidelines_FS_en.pdf. Accessed September 13, 2006.

3. Gulick RM, et al. Three- vs four-drug antiretroviral regimens for the initial treatment of HIV-1 infection: a randomized controlled trial. *JAMA*. 2006;296:769-778.

CME Questions

16. Choose the one correct answer. When considering the use of antibiotics for acute purulent rhinitis, the physician should be aware that

a. the probability of helping a patient is equivalent to the probability of harming him.
b. more patients receive benefit than not.
c. more patients are harmed than not.
d. adverse side effects include headache and visual disturbance.

17. Functional dyspepsia may be anticipated to have what clinical response to esomeprazole 40 mg given once daily?

a. Symptoms of FD will disappear promptly and continue to respond to ESO over the course of an 8 week study.
b. Patients with symptoms classical for FD may have significant mucosal pathology at endoscopy.
c. FD clearly has a unique and consistent pathophysiology.
d. Symptom relief in this study was defined as 4 continuous weeks without significant symptoms.
e. All of the patients entered into this study had abdominal bloating and early satiety.

18. Which of the following strategies is the most cost effective for diagnosing deep vein thrombosis in a 60-year-old patient?

a. Observe the patient with a low clinical risk, and order a venous ultrasound if the clinical exam becomes more suggestive.
b Order a D-dimer test and if negative, observe the patient.
c. Order a D-dimer test and if positive, order an ultrasound.
d. If a D-dimer test is negative in a high-risk patient, order an ultrasound and discharge the patient if it is negative.

Answers: 16 (a); 17 (b) 18 (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; and
- to describe cost-effective treatment regimens.

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.

Does Glucose Monitoring Really Help Type 2 Diabetics?

TIGHT GLUCOSE CONTROL HAS BEEN shown to provide improved outcomes in both Type 1 and Type 2 diabetes (DM2). Although intuitively one would assume that self-monitoring of blood glucose (SMBG) in DM2 would improve glucose control, 5 randomized controlled trials have failed to conclusively confirm this notion. Since SMBG requires substantial time, energy and resources, we would like to have an evidence base which confirms benefits to the patient.

Study subjects (n = 1,286) comprised participants in the Fremantle Diabetes Study of western Australia. At baseline, 70% of subjects utilized SMBG, allowing a substantial comparison group of 'non-users.' The median frequency of SMBG was 4 tests weekly. Data were compiled based upon 5 years of observation.

A1c control was not found to be superior in persons utilizing SMBG versus persons who did not perform SMBG. In Australia, SMBG per patient costs an average of $123/yr (United States dollars), without considering the actual price of the glucometer. Although SMBG can be useful for confirming hypoglycemia, convincing evidence of meaningful benefit in improving A1c control remains to be presented. ■

Davis WA, et al. Is self-monitoring of blood glucose appropriate for all type 2 diabetic patients? The Fremantle Diabetes Study. Diabetes Care. 2006;29: 1764-1770.

CV Risk in Migraineurs

SEVERAL STUDIES HAVE SUGGESTED that migraine (MIG), particularly MIG with aura (MIG/a), is associated with increased risk of ischemic stroke. Less data have accrued to study the relationship between MIG and other ischemic vascular end points, such as myocardial infarction (MI). Since the prevalence of MIG in women is three times that of men (18% vs 6%), the Women's Health Study (WHS) provides an appropriate population of healthy women (n = 27,840) in whom we may observe the cardiovascular outcomes of migraineurs over time.

In concordance with established prevalence data, 18.4% of WHS participants reported MIG, of which 40% had MIG/a. In an earlier report from the WHS, a six-year followup did not detect any relationship between MI and migraine. The 10-year followup looks distinctly different.

The hazard ratio for major cardiovascular disease among women with MIG/a was more than double that of women without MIG. Specifically looking at MI, the hazard ratio was also doubled (HR = 2.08; $P = .002$).

The population of women with MIG but no aura was *not* demonstrated to be at increased cardiovascular risk in this population. The factors that place persons with MIG/a (as opposed to simple MIG) at greater ischemic CV risk remain to be elucidated. ■

Kurth T, et al. Migraine and risk of cardiovascular disease in women.JAMA. 2006;296:283-291. Erratum in: JAMA. 2006;296:654; JAMA. 2006;296:1 p following 291.

Motorcycling and ED

NUMEROUS REPORTS HAVE indicated a relationship between bicycling and erectile dysfunction (ED). Even when overt sexual dysfunction is not apparent, bicycling has been shown to alter penile sensation in some subjects. Such findings have been attributed to ischemic neuropathy secondary to mechanical compression. Motorcycling involves similar postural events, albeit with different saddle design; additional vibration forces occur with motorcycling that are not seen with bicycling, which could also impact development of neuropathic sequelae. There have not been any studies previously of the relationship between motorcycling and ED.

Members of an amateur motorcycle club in Japan (n = 244) form the data base for this study. Erectile function was measured by means of the IIEF, a 5-item questionnaire validated for identification and monitoring of ED. On the IIEF, a normal point score ≥ 26; in this trial, ED was defined as a score < 22.

Compared to prevalence data generated by the Massachusetts Male Aging Study, the prevalence of ED in the motorcycle club was surprising: 58% (age, 20-29), 63% (age, 30-39), 76% (age, 40-49), and 93% (age, 50-59). The majority of ED was mild-moderate degree. For men with ED, clinicians may wish to inquire about motorcycling activity. ■

Ochiai A, et al. Do motorcyclists have erectile dysfunction? A preliminary study. Int J Impot Research. 2006;18:396-399.

In Future Issues: The Estrogen Controversy