

Clinical Briefs in **Primary Care**

The essential monthly primary care update

By Louis Kuritzky, MD

Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports.*

VOLUME 11, NUMBER 7

PAGES 13-14

JULY 2006

Does Aspirin Work Differently in Women than Men?

Source: Becker DM, et al. *JAMA*. 2006;295:1420-1427.

ALTHOUGH ASPIRIN (ASA), PARTICULARLY low-dose ASA 81 mg/d (LD-ASA), is well established as an appropriate agent for secondary prevention of cardiovascular disease, recent results from the Women's Health Study (WHS) about the impact of ASA in primary prevention came as a surprise: LD-ASA provided a 24% reduction in stroke, but no reduction in MI. Theorists suggested that perhaps, since MI impact has been demonstrated to be much more favorable in men than in women, there is a difference in responsiveness of platelet reactivity to LD-ASA between the sexes. To investigate this hypothesis, the platelet reactivity of at-risk men and women (n = 1,282) was measured 14 days after daily LD-ASA treatment. The at-risk group was selected from a pool of healthy individuals who had siblings with documented early CHD endpoints, but had no manifest coronary artery disease themselves. Presumably, this is a higher risk group, in whom it would be wise to be able to better define the benefits of primary prevention.

After 14 days, platelet aggregation in response to arachidonic acid stimulation (the blockade of which is the proposed mechanism by which LD-ASA prevents CVD) was equally affected in men and women. The reason(s) for the apparent differential effects of LD-ASA on CVD in men versus women remain uncertain: it is apparently not due to a diminished responsiveness of women's platelets to the antiaggregation effects of LD-ASA. ■

Is There Something About Air Travel Besides Immobilization that Increases Risk of DVT?

Source: Schreijer AJ, et al. *Lancet*. 2006;367:832-838.

THAT DEEP VEIN THROMBOSIS (DVT) can occur after air flight is not a new observation, having been first reported in the 1950s. Recent data have singled out very long flights (8 hours or greater) as being remarkably more important for DVT risk than shorter flights. Generally, risk for DVT with air flight has been simply attributed to only one of the 3 characteristics of Virchow's Triad: stasis (due to immobility). Schreijer et al studied the impact of clotting factor activation associated with air flight.

To differentiate simple immobilization 'on the ground,' from immobilization with air flight, study subjects were divided into 3 groups: a real 8-hour plane flight, an 8-hour period of immobilization while watching successive movies, or the control of 8 hours of normal daily activities. The 71 men and women participated in 2 cross-over periods, so that all subjects experienced all 3 group activities.

Several coagulation factors were monitored. After flight, thrombin-antithrombin complex was elevated (indicating increased thrombotic activation), but not after 8 hours of movie immobilization or daily activities. Coagulation activation was most marked in women on oral contraceptives who had known factor V Leiden at baseline. The

authors postulate that the hypobaric hypoxia encountered in flight explains the coagulation activation. Advice to avoid protracted immobility on long flights can be helpful, but may not be fully protective, since other mechanisms in addition to immobility appear to be etiologic. ■

The Dermatologic Nikolskiy Sign: How Good is it?

Source: Uzun S, Durdu M. *J Am Acad Dermatol*. 2006;54:411-415.

PV NIKOLSKIY WAS A RUSSIAN DERMATOLOGIST who published information about pemphigus foliaceus in 1896. He was the first to describe an altered structural integrity of the epidermis in pemphigus. The Nikolskiy Sign (also commonly spelled 'Nikolsky') is performed by placing pressure upon skin adjacent to tissue involved with bullae. In pemphigus, because the attachments of the intraepidermal intercellular bridges are damaged, skin pressure will allow the bulla to dissect further within the epidermis, as the layers separate due to IgG-mediated attachment defects. Although at one time considered specific to pemphigus, Nikolsky Sign has been sometimes reported in association with other skin disorders, such as toxic epidermal necrolysis, mycosis fungoides, and epidermolysis bullosa.

To study the sensitivity and specificity of the Nikolsky Sign, patients (n = 127) with a variety of bullous lesions were tested. The sensitivity for diagnosis of pemphigus by Nikolsky sign was only 38%. Disor-

ders other than pemphigus also manifest Nikolsky sign. A positive Nikolsky sign is useful to support the diagnosis of pemphigus, but is also seen in other disorders. ■

Smoking: If at First You Don't Succeed. . .

Source: Fu SS, et al. *Am J Manag Care.* 2006;12:235-243.

CURRENT TOOLS TO ASSIST IN SMOKING cessation are successful in only a minority of persons. Clinical trials are generally based upon a single cessation attempt, usually measured over 6-12 months to assess long-term abstinence. Given the fact that most smokers (70%) indicate that they would like to quit, it is surprising that so little evidence has been assembled about 'next step management:' what to do when the patient fails an initial cessation attempt or relapses.

Fu et al collected data on almost 1,000 smokers at a VA Hospital who had recently attempted smoking cessation. Subjects received a phone call 6 months after their prescription for a smoking cessation intervention. As predicted from previous trials,

approximately two thirds of respondents had already relapsed.

One might intuitively conclude that a recently relapsed smoker would have little interest in trying again, but au contraire, 65% stated that they wished to make another attempt within the next 30 days. The majority of relapsed smokers wanted to have a combination of behavioral and pharmacologic treatments, but only a tiny fraction (2%) were interested solely in behavioral treatment.

On average, those who ultimately permanently quit smoking over the long term require about 4 attempts at cessation before they are successful. These data suggest that relapsed subjects feel positive about attempting cessation again promptly. Perhaps a rapid cycling approach by clinicians, by encouraging relapsed patients who are willing to try again quickly to do so, will facilitate a greater degree of success. ■

Can Hypertension be Prevented by Pharmacotherapy?

Source: Julius S, et al. *N Engl J Med.* 2006;354:1685-1697.

PREHYPERTENSION (pHTN), DEFINED as either a systolic blood pressure of 135-139, a diastolic BP of 85-89, or both, evolves into frank hypertension (HTN) in most individuals. Although treatment tools for established HTN are well defined, whether treatment of pHTN is both feasible and tolerable has only been the subject of limited study.

Subjects with pHTN (n = 809) were randomly assigned to the angiotensin receptor blocker (ARB) candesartan 16 mg/d or placebo, and followed for four years. For the first 2 years of the trial, subjects received either candesartan or placebo; for the next 2 years, both groups received placebo.

At 2 years, 40.4% of placebo recipients developed HTN, as compared with 13.6% in the candesartan group. At the 4-year measurement (remember that the candesartan group had been off medication for 2 years at this point), those who had

received ARB treatment for the first 2 years still enjoyed a 16% relative risk reduction for HTN compared to placebo-only treated patients. Adverse effects were LESS frequent in the treatment group than placebo.

Even though this study confirms that treatment of pHTN prevents HTN, the authors close their discussion with a note of caution that until further confirmatory research of the benefits of pHTN treatment are at hand, the time is not yet right to advocate for universal treatment of pHTN patients. ■

Does an Impaired Gastric Acid Environment Reduce Absorption of Thyroxine?

Source: Centanni M, et al. *N Engl J Med.* 2006;354:1787-1795.

THE TREATMENT OF HYPOTHYROIDISM with levothyroxine is generally straightforward. Nonetheless, simple missteps in treatment can compromise success. For instance, co-administration of calcium salts or iron interferes with thyroxine absorption. Maintenance of gastric acid pH may also play a role.

Centanni et al studied patients receiving levothyroxine (n = 248) who had one of several possible etiologies for a less acidic gastric environment: Helicobacter gastritis, atrophic gastritis, or treatment with a proton pump inhibitor (omeprazole). Thyroxine doses necessary to maintain a therapeutic TSH were compared in subjects with one of these three reasons for an increased gastric pH, compared with a group of matched controls.

On average, the amount of levothyroxine needed to appropriately suppress TSH was 22-34% higher in subjects with elevated gastric pH than in controls. Supportive of the fact that gastric acidity was the critical element, thyroxine doses after cessation of PPI treatment reverted to the levels required prior to PPI treatment. The authors conclude that gastric acidity ultimately affects the effectiveness of levothyroxine absorption. ■

Clinical Briefs in Primary Care™ is published monthly by American Health Consultants. Copyright © 2006 Thomson American Health Consultants. **Vice President/Group Publisher:** Brenda Mooney. **Editorial Group Head:** Lee Landenberg. **Editor:** Stephen Brunton, MD. **Managing Editor:** Rob Kimball. **Associate Managing Editor:** Leslie Hamlin. This is an educational publication designed to present scientific information and opinion to health professionals, stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for the layman.

Subscriber Information

Customer Service: 1-800-688-2421

E-Mail Address: robert.kimball@thomson.com

World Wide Web: www.ahcpub.com

Address Correspondence to: American Health Consultants 3525 Piedmont Road, Building Six, Suite 400 Atlanta, GA 30305.

THOMSON
★
AMERICAN HEALTH CONSULTANTS