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 13, NUMBER 2 PAGES 3-4 FEBRUARY 2008

# Resilient Medical Myths: Disproven Precepts that Refuse to Die

**Source:** Tatsioni A, et al. *JAMA.* 2007;298(21):2517-2526.

Probably every clinician has more than one medical "belief" to which he clings, despite the preponderance of evidence to the contrary. Sometimes, clinical thinking contrary to science persists because of conflicting bodies of evidence, or, as was the subject of this communication, because powerful initial data sets—especially when they fit comfortably with our common-sense judgment—are hard to relinquish even in the face of newer, better science. The recent shock of disillusionment subsequent to the Women's Health Initiative, which did NOT confirm the essentially "assumed" cardiovascular benefits in menopausal women, was a prime example of the disparate information obtainable from observational data (which said that HRT uniformly reduces cardiovascular risk) to interventional data (which said that no demonstrable CHD benefit was seen with HRT).

In the 1990s, common wisdom held that vitamin E—purportedly through its antioxidant activity—should be beneficial for reducing vascular events. Indeed, some early reports supported this concept. The HOPE trial, a large randomized interventional trial that included a vitamin E arm, not only failed to show benefit, but trended towards HARM from vitamin E. Subsequently, two meta-analyses conclude that vitamin E is associated with INCREASED mortality.

Tatsioni, et al compared the support stance of authors for utilization of vitamin E in the period immediately after publication of the initial positive trials, and compared this with publications after large data sets had essentially refuted vitamin E benefits. Even 5 years after the best data had refuted vitamin E benefits, a majority of articles addressing the topic still supported the opposite conclusion, although trends in support did decrease over time. Apparently, the progress of science is often difficult for some proponents of opposing ideas to accept. Clinicians will have to be vigilant that outdated or observational data sets not cloud their perceptions of established scientific fact. ■

# NSAID, Manipulation or Both for LBP

**Source:** Hancock MJ, et al. *Lancet.* 2007;370:1638-1643.

Current knowledge on management of acute low back pain (LBP) suggests that best outcomes are obtained when patients anticipate a favorable outcome, remain active, avoid bed rest, and use acetaminophen for analgesia. NSAIDs used to be considered appropriate first line therapy, but recent heightened awareness of NSAID potential toxicities (GI bleeding, electrolyte disarray, renal dysfunction, BP elevation, and CHD events) mandates that their continued utilization provide meaningful benefits that outweigh such adversity.

Hancock et al studied 240 patients who were randomized to receive—in addition to the advice/acetaminophen—either NSAID (diclofenac), spinal manipulation, both, or placebo. Diclofenac was administered 50 mg b.i.d., and spinal manipulation was provided by trained physiotherapists diplomated in manipulative therapy. All subjects were followed for 12 weeks, looking at the number of days until recovery, defined as the first pain-free day, and the first 7 consecutive 7-day period in which the patient reported pain 0-1/10 every day.

Neither diclofenac, spinal manipulation, nor the combination of both was superior to simple first-line advice. Predictable adverse effects of NSAIDs were seen (none serious). Simple first-line tools for management of LBP are not improved by the addition of diclofenac, but adverse events are increased. ■

# Pomegranate Juice for Erectile Dysfunction

**Source:** Forest CP, et al. *Int J Impot Res.* 2007;19:564-567.

Pomegranate juice (POM) has attributes that might benefit men with erectile dysfunction (ED), including potent antioxidant activity and enhanced endothelial nitric oxide production. Forest, et al studied the effects of POM when administered as 8 ounces of POM daily vs placebo in men with ED.

Men with mild-moderate ED (n=53) were randomly assigned in a crossover fashion to two 4-week periods of POM or placebo. The primary outcomes assessed at 10 weeks were improvements on the International Index of Erectile Function (IIEF)

score and the Global Assessment Questionnaire (GAQ) for sexual dysfunction.

Although there was a trend towards improvement in both GAQ and IIEF in persons receiving POM, it did not achieve statistical significance ($p$ = 0.58). The mean age of the subjects in this pilot study population, 46 years, was younger than usually selected in studies of ED; additionally, the overall ED severity (mild-moderate) was low. The authors consider that perhaps with a larger study population, and longer duration of evaluation, the effects of POM might achieve statistical significance. ■

## Fenofibrate for Diabetic Retinopathy

Keech AC, et al. *Lancet.* 2007;370:1687-1697.

Clinicians may recall that the FIELD trial (Fenofibrate Intervention and Event Lowering in Diabetes) failed to achieve its primary endpoint: reduction of fatal + nonfatal MI. A substudy of the FIELD trial was comprised of subjects (n = 1,012) who underwent standardized retinal photography at baseline and during followup to determine the incidence of new diabetic retinopathy. Subjects were treated with micronized fenofibrate 200 mg QD (or placebo) for 5 years. This substudy trial endpoint was needed for laser treatment of diabetic retinopathy.

A statistically significant relative risk reduction of 31% in the need for first laser retina treatment was seen in the treatment group vs placebo (3.4% vs 4.9%, absolute risk reduction = 1.5%). In the group of patients with pre-existing retinopathy at baseline, there was a marked reduction in need for second laser treatment (3.1% vs 14.6%).

The retinal benefits seen in FIELD were in patients most of whom were already receiving standard-of-care interventions such as statins, glucose control, and blood pressure control. The mechanisms by which Fibrates provide reductions in progression of diabetic retinopathy are uncertain, although potential effects on apoptosis, inflammation, and oxidation are postulated. The authors suggest that fenofibrate should be considered in the treatment regimen of diabetic eye disease. ■

***Clinical Briefs in Primary Care*** is published monthly by AHC Media LLC.

**Senior Vice President/Group Publisher:** Brenda Mooney. **Associate Publisher:** Lee Landenberger. **Editor:** Stephen Brunton, MD. **Managing Editor:** Iris Young.
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:** iris.young@ahcmedia.com
**World Wide Web:** www.ahcmedia.com
**Address Correspondence to:** AHC Media LLC
3525 Piedmont Road, Building Six, Suite 400
Atlanta, GA 30305.

AHC Media LLC

## Does Obesity Cause A Delay in Diagnosis of Prostate Cancer?

**Source:** Banez LL, et al. *JAMA.* 2007;298(19):2275-2280.

It has been demonstrated in more than one population that obese men have a lower PSA than nonobese men. One explanation of this was that obese men have lower androgens, resulting in lower PSA. However, it has been recently hypothesized that the larger plasma volume seen in obese men might artifactually lower PSA levels by simple hemodilution.

To examine the relationship between obesity and PSA, as well as with PSA corrected for plasma volume, three different populations of men (total n = 13,534) who were post-prostatectomy for prostate CA were studied.

There was an inverse association between BMI and PSA level. For instance, men with a BMI over 35 had a PSA that was 11-21% lower than normal weight men; in the Duke population, as an example, the mean PSA at a BMI < 25 was 6.64, vs a PSA of 5.27 for men with BMI > 35. These effects are felt to be due to hemodilution.

Even though the relationship between BMI and PSA has been clarified, these data are retrospective, and represent information from men proven to have prostate cancer. Whether the hemodilution effects on PSA screening are meaningful remains to be prospectively studied. ■

## Protecting Bone During Glucocorticoid Treatment

**Source:** Saag KG, et al. *N Engl J Med.* 2007;357:2028-2039.

Current guidelines suggest that if patients are receiving long-term Glucocorticoid treatment (ie, 5 mg/d of prednisone for 90 days or longer), they should be considered for preventive interventions to forestall the anticipated bone loss, and reduce fracture risk.

Teriperatide (TPT) is a parenteral recombinant parathyroid hormone that has been shown to stimulate osteoblasts, increase bone mass, and reduce fracture risk. The relative efficacy of TPT vs bisphosphonate for prevention of glucocorticoid-induced bone mineral density (BMD) loss has not been previously studied.

Adults with osteoporosis who were receiving glucocorticoid therapy for at least 3 months (n = 428) were randomized to TPT or the oral bisphosphonate alendronate (ALN), 10 mg qd orally The study is intended to extend for 36 months, but this initial report provides interim outcome data at 18 months.

BMD at the lumbar spine increased in both groups, but TPT surpassed ALN (7.2% vs 3.4%). Similarly, fewer new vertebral fractures were seen in the TPT group (0.6% vs 6.1%). There were no serious drug-attributable adverse events in either group, however hypercalcemia was seen substantially more commonly in TPT recipients. Based upon this data, TPT emerges as an equally, if not more effective intervention for prevention of glucocorticoid induced osteoporosis and fracture than ALN. ■