
Clinical Briefs in **Primary Care**™

The essential monthly primary care update

By Louis Kuritzky, MD

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Barrett's Esophagus: What's the Risk?

Source: Hvid-Jensen F, et al. Incidence of adenocarcinoma among patients with Barrett's esophagus. *N Engl J Med* 2011;365:1375-1383.

FOR UNKNOWN REASONS, ADENOCARCINOMA of the esophagus (E-ca) is experiencing the most rapid increase of any known cancer in the United States. Although the absolute incidence of E-ca pales next to lung, prostate, or breast cancer, the inexplicable proliferation of this cancer has spurred increased scrutiny of at-risk individuals. Barrett's esophagus, which is felt to represent an attempt at protective epithelial remodeling in response to the trauma of acid exposure, occurs in as many as 10% of individuals undergoing endoscopy for symptoms of GERD. Once Barrett's is identified, consensus group guidelines suggest ongoing surveillance, despite the absence of outcomes trials indicating that such surveillance improves survival.

The Danish Pathology Registry and Cancer Registry provide an opportunity to review data accrued for the entire population of Denmark. Follow-up of persons with Barrett's esophagus (n = 11,029) over a median of 5.2 years of observation identified 197 cases of E-ca, for an annual incidence of 0.12%. Likelihood of developing E-ca was increased in persons with higher degrees of dysplasia. Based on these data, the authors suggest that ongoing surveillance of Barrett's esophagus might wisely be limited to those with demonstrated dysplasia, since the incidence of E-ca in persons without dysplasia was so very low. ■

Life Expectancy: The Japanese Are #1

Source: Murray CJ. Why is Japanese life expectancy so high? *Lancet* 2011; 378:1124-1125.

EVEN THOUGH JAPAN SPENDS ESSENTIALLY half of what the United States spends on health care (8.5% of their gross domestic product vs 16.4% of ours), they have ranked No. 1 in life expectancy for 30 years. To what might we attribute their success?

That Japan provides universal health coverage can certainly be responsible for a portion of their favorable outcomes, but other factors are also at play. For instance, Japanese public health programs to reduce salt intake and become more aggressive about blood pressure control are credited with substantial reductions in stroke. Indeed, such Japanese hypertension programs have evoked a substantial decline in blood pressure among the population as a whole, especially in women (the gender in which successful blood pressure control is conspicuously less prominent in the United States).

Although it is difficult to measure the direct impact of one additional factor — educational attainment — on health, epidemiologic surveys do consistently indicate a linear relationship between education and positive health outcomes. The generally high educational attainment among Japanese may be a critically important factor.

Current health trends suggest that Japan may not stay in the No. 1 slot: Inadequate tobacco control and a rising BMI among the population, unless

counteracted, may incur similar health decrements as have been seen in other nations. ■

The Calcium/Cardiovascular Disease Link

Source: Sabanayagam C, Shankar A. Serum calcium levels and hypertension among U.S. adults. *J Clin Hypertens* 2011;13:716-721.

THE RELATIONSHIP BETWEEN CALCIUM intake — through diet and/or supplements — and vascular health is complex. Some recent epidemiologic surveys have found a positive association between calcium supplements and adverse cardiovascular (CV) outcomes, as well as vascular calcification (i.e., more CV disease and calcification with calcium supplementation than without). Because hypertension (HTN) is the most common vascular antecedent to adverse CV events, investigation of the relationship of calcium to blood pressure (BP) is pertinent.

The National Health and Nutrition Examination Survey (NHANES) has published cross-sectional data from diverse populations throughout the United States for more than 30 years. The authors obtained data from the NHANES population (n = 12,403) of adults over age 20 seeking to examine the relationship between serum calcium levels and BP.

Persons in the highest quartile of serum calcium were 1½ times more likely to have HTN than those in the lowest quartile. Even when adjusted for age, race, alcohol, body mass index, cholesterol, C-reactive protein, glomerular filtration rate, serum albumin, vitamin D,

and phosphorus, the relationship between calcium and BP remained.

Several mechanisms through which calcium might incur increased risk of HTN have been offered, including a direct vascular effect, parathyroid activity, and renal vasoconstriction. Before concluding that calcium is simply a “bad guy,” it is important to recognize that several reports have shown that *dietary* calcium is *inversely* related to HTN. ■

What Factors Lead to Acquisition of *Clostridium difficile*?

Source: Loo VG, et al. Host and pathogen factors for *Clostridium difficile* infection and colonization. *N Engl J Med* 2011;365:1693-1703.

THE TOXICITY ASSOCIATED WITH INTESTINAL habitation by *Clostridium difficile* ranges from asymptomatic colonization to life-threatening infection. In the United States, *C. difficile* is the most common cause of health care-associated diarrhea. Although the association of *C. difficile* with use of antibiotics and/or hospitalization is clear and well established, why certain individuals fall prey to infection/colonization — whereas most do not — remains ill-defined.

Loo et al performed a prospective study of patients admitted to Canadian

hospitals over 15 months (n = 4143). Subsequent to hospital admission, *C. difficile* infection was identified in 2.8% (n = 117) and colonization in 3% (n = 123); excluded from these numbers were the 4.4% of individuals who were already *C. difficile* colonized upon admission.

As has been noted in previous observational studies, older age, antibiotic use, and use of proton pump inhibitors (PPI) or histamine-type 2-receptor antagonists (H2RA) were each associated with *C. difficile* colonization and infection. The mechanism by which PPI/H2RA use is associated with *C. difficile* remains speculative, but is attributed to disturbance of bacterial flora. Whether more restraint in use of antibiotics, PPI, or H2RA medications will reduce the incidence of serious *C. difficile* infections remains to be determined. ■

The Relationship Between Sleep and Hypertension

Source: Bansil P, et al. Associations between sleep disorders, sleep duration, quality of sleep, and hypertension: Results from the National Health and Nutrition Examination Survey, 2005 to 2008. *J Clin Hypertens* 2011;13:739-743.

IT IS PROBABLY OBSTRUCTIVE SLEEP APNEA (OSA) with which clinicians most familiarly associate hypertension (HTN). Indeed, some recent trials have found a remarkably high prevalence of previously unsuspected OSA in persons with resistant HTN. What about other sleep variances, such as persons with sleep movement disorders (e.g., restless legs, sleep apnea), short sleep (< 7 hrs/night), or poor sleep? The authors report on data obtained through the most recent National Health and Nutrition Examination Survey obtained through direct interview with 10,308 adults.

Overall, persons with HTN were statistically significantly more likely to have a sleep disorder than normotensive individuals (11% vs 6%). “Poor sleep” did not appear to be a relevant factor, but less than 7 hours of sleep nightly was. No gender or ethnicity differences were detected.

In contrast to prior data sets, this study did not find a consistent relationship specifically with sleep disorders and HTN. Rather, it was in persons who reported both a sleep disorder *and* short sleep that risk of HTN rose steeply: this combination was associated with more than a doubling of risk. Finally, the authors also note that more than two-thirds of persons with sleep problems had not discussed their issues with a health professional. ■

DPP4 Inhibitors are Associated with Reduced Risk of Hip Fracture

Source: Monami M, et al. Dipeptidyl peptidase-4 inhibitors and bone fractures: A meta-analysis of randomized clinical trials. *Diabetes Care* 2011;34:2474-2476.

IN AN ERA WHERE CONCERN ABOUT ADVERSE consequences of pharmacotherapy on bone health are prominent — proton pump inhibitors associated with increased risk of hip fracture, bisphosphonates associated with an increased risk of spiral femoral fractures, and even thiazolidinediones noted to increase fracture risk — a more sanguine headline is certainly welcome.

The dipeptidyl peptidase-4 inhibitors (DPP-4) currently include three agents: sitagliptin, saxagliptin, and linagliptin, each of which provides a fairly similar degree of glucose reduction. The physiologic activity of GLP-1 (the primary pathway through which DPP-4 treatment enhances glucose control) includes activation of osteoblasts and inhibition of osteoclasts. Animal studies have shown that DPP-4 agents actually increase bone density, but no large, long-term clinical trial has confirmed a relationship between DPP-4 and fractures in humans.

Monami et al performed a meta-analysis on trials of DPP-4 inhibitors lasting 6 months or longer from which data on fractures was able to be extracted. Based on 28 trials of DPP-4 treatment (n = 11,880) vs comparator (n = 9175), the odds ratio for fracture was 40% less in persons receiving DPP-4 than in comparator. DPP-4 appear to have a protective effect on bone. ■

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Executive Editor: Leslie Coplin.

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Customer Service: 1-800-688-2421

E-Mail Address: neill.kimball@ahcmedia.com

World Wide Web: www.ahcmedia.com

Address Correspondence to: AHC Media, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305.

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