Clinical Briefs in Primary Care™

The essential monthly primary care update

By Louis Kuritzky, MD

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Dark Chocolate and Arterial Function

Source: Vlachopoulos C, et al. *Am J Hypertens*. 2005;18:785-791.

Chocolate enthusiasts, take heart! Evidence that dark chocolate benefits more than just the palate is presented in this study from Greece.

Vlachopoulos et al studied 17 healthy non-smoking adults (mean age 29), who were free from vasculopathies such as diabetes, hyperlipidemia, or family history of premature vascular disease. Subjects were asked to abstain from caffeine, alcohol and flavonoid-containing foods for 24 hours or more prior to testing. Endothelial function was measured by means of forearm flow-mediated dilation, which is dependent primarily on nitric oxide derived from the endothelium. Subjects received either active intervention (dark chocolate) or sham-procedure (chewing without chocolate), both followed by 8 ounces of water. Endothelial function was measured at 30, 60, 90, 120, and 150 minutes after intervention.

Brachial artery diameter and arterial flow were significantly increased by dark chocolate. Normally, as arteries dilate their vasodilator response to stimulation decreases. In this trial, vasodilator responses increased even in the face of arterial dilation.

They comment that the salutary effects of chocolate could be attributable to improved nitric oxide bioavailability, prostacyclin increase, a direct effect of chocolate upon sooth muscle cells, or some central mechanism. And for the ultra-scientists amongst us, the 'bar of choice' (the study bar, that is) was Noir Intense, a 100 g dark chocolate bar manufactured by Nestle of Vevey, Switzerland. ■

Tetanus, Diphtheria, and 5-Component Pertussis Vaccine

Source: Pichichero ME, et al. *JAMA*. 2005;293:3003-3011.

Many clinicians still think of pertussis as a disorder limited to childhood. In 2004, more than 18,000 cases of adolescent or adult pertussis were reported to the CDC, and it is likely that this number is only a fraction of the actual number of cases, since pertussis is often not recognized, or presents in an atypical fashion. In the current vaccination schema, there is no provision for enhancing the waning pertussis immunity that appears to allow adolescent and adult pertussis to occur after appropriate childhood vaccination.

A new vaccine containing pertussis, tetanus, and diphtheria suitable for administration as a booster for adults has been recently developed. This trial examined the tolerability and efficacy in mounting a booster antibody response to pertussis. End points with the new vaccine were compared with the already established tetanus-diphtheria vaccine alone, and with pertussis antibody levels achieved in children after a complete immunization series.

The study population consisted of healthy adults and adolescents (n ³ 4,000) who were randomized to either the new pertussis-containing vaccine, or traditional tetanus-diphtheria vaccine.

These data suggest that providing an added component of pertussis may meaningfully reduce the incidence and consequences of adolescent and adult pertussis. ■

Lung Cancer Screening

Source: Mulshine JL, et al. *Engl J Med*. 2005;352:2714-2720.

Lung cancer (LCA) is currently responsible for 30% of cancer deaths in the United States. The majority of LCA cases have metastasized at the time of diagnosis, resulting in a 15% survival rate at 5 years. Recent studies have applied screening with increasingly sophisticated and sensitive tools amongst high-risk individuals (current and former smokers), and do indeed discover LCA at an overall earlier stage than by traditional clinical means: more than 50% are stage 1 at the time of screening diagnosis. Lead-time bias (the apparent lengthening of life seen in persons diagnosed by screening rather than by onset of symptoms simply due to natural history), length bias (slow-growing tumors, less like to cause symptoms may be preferentially discerned by screening), and overdiagnosis bias (some small tumors would be destined to never impact life, yet if discovered on screening would artificially inflate the benefit of screening) can contribute to an overly sanguine appraisal of screening benefits.

Because no randomized controlled trials of screening with a mortality end point have been completed (some are in process), there remains the possibility that screening may improve, be neutral towards, or even may worsen LCA outcome (ie, harms of intervention to complete the diagnostic process such as transthoracic needle biopsy increases morbidity and mortality). Until such data are in evidence, clinicians should convey to their interested patients the as-yet indefinite risk-to-benefit ratio of screening. ■

Staphylococcal Toxins, Psoriasis, Atopic Dermatitis, Erythroderma in Healthy Control Subjects

Source: Tomi NS, et al. *J Am Acad Dermatol*. 2005;53:67-72.

The role that microbes play in some dermatoses is not always immediately evident. For instance, the yeast *Pityrosporum orbiculare* is etiologic in some cases of seborrheic dermatitis; hence, even though topical steroid treatment can control symptoms by reducing inflammation, antifungal treatment may also resolve seborrheic dermatitis.

Staphylococcus aureus (SA) is found on the skin or nares of up to 30% of healthy individuals. In skin lesions of atopic dermatitis (AD) or psoriasis (PSO), colonization with SA is found even more often (46-93%). Additionally, SA is cultured disproportionately more frequently in active skin lesions of AD and PSO than in uninvolved skin, giving credence to a potential etiologic role.

Patients (n = 75) with AD, PSO, and controls were evaluated for the presence of SA; additionally, SA subtyping was performed to determine the presence of Staphylococcal enterotoxin. More AD patients (88%) than PSO (60%) were lesion-positive for SA. In both disorders, there was a correlation between the presence of SA enterotoxin and disease severity. The authors posit that SA enterotoxin may induce or aggravate skin lesions of psoriasis and atopic dermatitis, and that methods to reduce SA colonization might be beneficial in both disorders. ■

Insulin Resistance and Risk of Congestive Heart Failure

Source: Ingelsson E, et al. *JAMA*. 2005;294:334-341.

Heart failure (CHF) is most commonly caused by hypertension and coronary artery disease. Framingham data from as far back as 1974 have shown an association between diabetes and CHF. Only recently has a relationship between obesity and CHF been described. A variety of mechanisms by which diabetes or obesity might increase risk for CHF has been offered, but the insulin resistance (IR) shared by both maladies appears a likely culprit.

The Uppsala Longitudinal Study of Adult Men is a prospective observational study intended to investigate metabolic risk factors for cardiovascular disease in Uppsala, Sweden; between 1970-1974, all men age 50 were invited to participate (n = 2322), and the population was re-investigated in 1990-1995; these data provide the baseline information for this study. Baseline data included BP, smoking status, waist circumference, BMI, oral glucose tolerance test, insulin resistance (by euglycemic insulin clamp method), plasma insulin, plasma proinsulin, and lipids.

The population selected for study was free of CHF or valvular disease at baseline. During a mean follow-up of 8.9 years, 104 men developed CHF.

The presence of IR was found to be a predictor of CHF, independent of diabetes, and other known CHF risk factors. The association between obesity and CHF, which held true whether waist circumference or BMI was used as the metric, was mitigated when IR was included in the multivariate analysis, suggesting that IR is, to some degree, causal in the relationship. ■

Ciprofloxacin Interacts with Thyroid Replacement Therapy

Source: Cooper JG, et al. *BMJ*. 2005; 330:1002.

A number of commonplace medications have been shown to interfere with absorption of orally administered thyroid hormone (levothyroxine), including aluminum-containing antacids, iron, cholestyramine, sucralfate, and calcium carbonate. Such interactions can be problematic on a large epidemiologic scale since, for instance, many of the middle-aged women who are taking thyroid hormone replacement (TH) are also taking calcium carbonate for bone health.

Two case reports highlight the potential of ciprofloxacin (CIP) to impede TH absorption. In Case 1, an 80-year-old woman who had been stable on 125 mg/d TH reported fatigue after 4 weeks treatment with CIP for osteomyelitis. Lab evaluation showed marked decreases in T4 and T3, with corresponding elevation in TSH (up to 44 mIU/L). Increasing the TH had no effect.

Case 2 was a 79-year-old woman treated with CIP (500 mg b.i.d. ´ 3 weeks) for a wound infection. Thyroid function tests and symptoms been previously stable on 150 mg/d of levothyroxine. Testing after 3 weeks of CIP indicated a decline in free T4 (from 22 to 13 picomoles/L) and an elevation in TSH (from 1.6 to 19 mIU/L). Providing an interval of 6 hours between CIP and TH produced normalization of thyroid function tests.

Other data have shown that providing a gap between calcium carbonate administration and TH resolves the medication competition. For patients who take TH, administration of CIP should be separated by at least several hours. ■

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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.

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