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The essential monthly primary care update

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Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin

Source: Knowler WC, et al. *N Engl J Med*. 2002;346:393-403.

PERSONS WHO ARE AT HIGH RISK FOR developing type 2 diabetes (DM2) include persons with elevated fasting and 2-hour postprandial glucose levels (ie, above normal but not qualifying as frank diabetes). Whether interventions such as weight loss, exercise, or pharmacotherapy can reduce the incidence of development of DM2 has been little studied, with the exception of recent information pertinent to reduction in new onset DM2 among vasculopathic recipients of ramipril.

Knowler and colleagues randomly assigned nondiabetic persons (n = 3234) with an elevated glucose (fasting and postprandial) to either placebo, metformin (850 mg b.i.d.) or lifestyle modification (at least 150 minutes of physical activity such as brisk walking per week), and weight reduction to maintain at least a 7% loss of initial body weight. Subjects were followed for an average of 2.8 years.

Only about half of the subjects intended for 7% weight loss were able to do so; similarly, between half and two-thirds of subjects maintained assigned levels of physical activity. Nonetheless, subjects assigned to lifestyle modification demonstrated a 58% reduction in incidence of DM2. Metformin treatment also reduced the incidence of new onset DM2 by 31%.

Lifestyle intervention can prevent the onset of DM2 in high-risk individuals. Pharmacotherapy with metformin also substantially reduces risk. Whether combining the interventions would have an even greater effect is unknown. ■

Eradication of *Helicobacter pylori* and Risk of Peptic Ulcers in Patients Starting Long-Term Treatment with NSAIDs

Source: Chan FK, et al. *Lancet*. 2002;359:9-13.

THERE ARE A VARIETY OF PATIENT groups that require long-term therapy with NSAIDs, such as arthritis sufferers. That traditional NSAIDs can produce an increased risk of significant GI bleeding has been well demonstrated. It is also known that, independent of NSAIDs, the presence of *Helicobacter pylori* (HEL) infection in the GI tract is a primary risk factor for development of GI bleeding. Whether pre-emptive eradication of HEL in persons embarking upon a long-term course of NSAID treatment will reduce occurrence of ulcers has not been previously determined.

Chan et al studied 128 patients with arthritis who were HEL-positive by breath testing, randomized to receive either an active treatment (omeprazole 20 mg + amoxicillin 1 g + clarithromycin 500 mg b.i.d. × 1 week) or placebo. All patients began a course of diclofenac slow-release 100 mg QD for 6 months. Frequency of ulcer and complicated ulcer (ie, associated with bleeding) was assessed endoscopically.

Over 6 months time, almost 3 times as many persons in the control group (34.4%) demonstrated any ulcers than in the HEL-eradication group (12.1%). Complicated ulcers were even more skewed in favor of active treatment (4.2% vs 27.1%). Based upon this data, clinicians may wish to screen persons in whom long-term NSAID treatment is planned. ■

Physiotherapy for Patients with Mobility Problems More than 1 Year After Stroke: A Randomized Controlled Trial

Source: Green J, et al. *Lancet*. 2002;359:199-203.

FOR STROKE VICTIMS WHO SUFFER A subsequent decrement in mobility (ie, falls, difficulty in walking, problems getting out of a chair), consequences of such disability are potentially substantial. Typically, primary care clinicians may refer such persons for treatment by physiotherapists (PT), though there is a paucity of data confirming the benefits of such intervention. Green et al identified a population of stroke patients (n = 359) with persistent

dysmobility at least 1 year later. Intervention by a community PT was supplied and compared with no treatment (patients were randomized).

The PTs treatment consisted of traditional physical therapy interventions, applied at least 3 times over 13 weeks. Primary outcome was assessed by the Rivermead mobility index.

Although PT did result in a statistically significant different change in Rivermead mobility index at 3 months, the difference was not a clinically relevant one. Unfortunately, by 6 months and 9 months, no difference was discerned. Additionally, PT did not reduce the number of falls. Whether other forms of PT will provide meaningful benefit to stroke victims with persistent dysmobility remains to be determined. ■

BV Antibodies and Risk of MS

Source: Ascherio A, et al. *JAMA*. 2001;286:3083-3088.

Current theories dominantly support an autoimmune etiologic basis for multiple sclerosis (MS). An epidemiologic phenomenon peculiar to Epstein-Barr virus (EBV) is its pattern of asymptomatic infection in childhood, but commonly symptomatic presentation in adults and adolescents. Since MS presents usually in young adults, and bolstered by the observation that MS risk is increased following an episode of EBV, a relationship between EBV and MS has been hypothesized.

The study population was the participants of the Nurses' Health Study (n = 62,439), of whom 144 developed MS. Antibody titers to EBV and cytomegalovirus (CMV) were compared between MS patients and age-matched controls. Of the 144 women with MS, 18 had blood samples collected before disease onset, and hence were able to be analyzed for antibody titers to EBV.

Prediagnosis mean antibody titers to EBV were significantly higher in MS patients than in matched controls. For the EBNA-2 antibody, a 4-fold difference in titers was associated with a marked increase in relative risk of MS (RR = 3.9). No association between CMV antibodies and MS was discernible. Ascherio and colleagues conclude that this study supports the hypothesis that EBV plays an etiologic role in MS. ■

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Coronary Magnetic Resonance Angiography for the Detection of Coronary Stenoses

Source: Kim WY, et al. *N Engl J Med*. 2001;345:1863-1869.

Coronary angiography (cANG) is the current gold standard for diagnosis of clinically significant coronary artery disease (CAD), which is generally designated as greater than 50% reduction in luminal diameter. Despite its widespread use and utility, cANG is invasive, costly, and associated with some not-insubstantial risks. Hence, noninvasive modalities for diagnosis of CAD are an attractive alternative.

This report examined a direct comparison of cANG and coronary magnetic resonance angiography (cMRA), in 109 persons who underwent both methods of evaluation during the same diagnostic encounter. Within less than 2 weeks after cMRA, all patients underwent cANG. Most of the subjects were male, with a history of chest pain.

The sensitivity of cMRA in identifying clinically significant CAD was 93%. "Missed" CAD was comprised of isolated single-vessel disease, half of which was left circumflex artery involvement. Isolated left circumflex CAD, however, was seen in only 4% of subjects.

Advantages of cMRA include that absence of radiation and contrast dye, and its previously demonstrated superiority to cANG in persons with anomalous coronary vessels. ■

Vitamin A Intake and Hip Fractures Among Postmenopausal Women

Source: Feskanich D, et al. *JAMA*. 2002;287:47-54.

Vitamin A and its analogues (VitA) have been shown to produce changes in bone metabolism and structure that would logically increase risk of fracture. In animals, retinoic acid decreases osteoblast activity and activates osteoclasts, as well as inhibiting vitamin D activity. Yet, recent studies have been inconclusive about the potentially toxic effect of VitA intake on bone health in humans. This report involves an 18-year prospective analysis of participants in the Nurses' Health Study studying the relationship between hip fracture and VitA intake, including foods and supplement ingestion.

During the period of observation, there were 603 hip fractures. Risk of fracture in the highest quintile of VitA (which includes food and supplements) was 1½ times greater than the risk in the lowest quintile. This adverse association may possibly underestimate the potential bone toxicity of high VitA intake because women with higher intake also tended to smoke less and exercise more! Feskanich and colleagues conclude that chronic intake of high amounts of VitA increases risk of hip fractures in women. Since the study population was dominantly populated with white women, whether other ethnicities experience the same effects remains unknown. ■