UPDATE

Abstracts and news from the medical literature of interest to the primary-care physician

Does CRP Predict Inducible Ischemia?

- **The Findings:** New data suggests a strong relation between C-reactive protein (CRP) levels and inducible ischemia in patients with coronary atherosclerosis.
- **The Study:** California researchers determined CRP levels in 118 subjects with inducible ischemia by stress echo, and in 111 subjects without such ischemia.
- **The Results:** Overall, patients in the highest quintile of CRP levels (> 0.38 mg/dL), were significantly more likely to exhibit inducible ischemia than patients with lower CRP levels (75% versus 45%). This association was strongest in subgroup analyses of patients who did not receive beta blockers (93% versus 42%), or statins (94% versus 44%), and was not significant in subgroup analyses of patients who did receive either or both of these medications.

Beattie MS, Shlipak MG, Liu H, et al: C-reactive protein and ischemia in users and non-users of ß-blockers and statins: Data from the Heart and Soul Study. Circulation 2003; 107(2):245-50.

Is Carvedilol Safe for Patients With Severe CHF?

Beta blockers are now recommended for patients with chronic congestive heart failure (CHF), but clinicians are reluctant because they worry these drugs might initially cause acute decompensation of CHF.

- **The Study:** Researchers examined the early effects of carvedilol in patients with severe CHF. Data were drawn from a previously published, industry-sponsored, randomised trial in which carvedilol was compared with placebo in 2,289 patients with ejection fractions lower than 25%. Carvedilol was titrated upward from 3.125 mg to 25 mg twice daily, if tolerated, during a six-week period.
- **The Results:** During the first eight weeks of treatment, rates of CHF were not higher in the carvedilol group than in the placebo group. Dizziness, hypotension, edema, and bradycardia were more common with carvedilol than with placebo. These side effects rarely led to withdrawal from the trial, presumably because the investigators reduced doses when necessary. Carvedilol and placebo recipients withdrew from the trial with equal frequency during the first eight weeks.

Krum H, Roecker EB, Mohacsi P, et al: Effects of initiating carvedilol in patients with severe chronic heart failure: Results from COPERNICUS study. JAMA 2003; 289:712-8.

What's the Deal With Vertebroplasty & Kyphoplasty?

Percutaneous vertebroplasty and balloon kyphoplasty are increasingly popular new interventions for painful vertebral compression fractures.

- **What is vertebroplasty?** Trocar is inserted into the vertebral body, and polymethylmethacrylate cement is injected.
- **What is kyphoplasty?** A balloon is inflated inside the compressed vertebral body to restore height before cement is injected.
- **Study 1:** A retrospective, multicentre, U.S. study included 245 patients who underwent vertebroplasty. Mean self-reported pain scores decreased from 8.9 (on a 10 point scale) before vertebroplasty, to 3.4 after vertebroplasty. The proportion of patients who were able to perform activities of daily living with no pain or only mild pain, increased from 7% to 62%.
- **Study 2:** A retrospective study from a U.S. neurosurgical practice included 96 patients who underwent kyphoplasty. A manufacturer of kyphoplasty equipment sponsored this study. Mean pain scores fell from 8.6 before the procedure to 2.1 one month afterwards. The proportion of patients who were fully ambulatory increased from 35% to 84%. In a subset of patients with serial X-rays, mean height of compressed vertebrae increased from 65% to 90% of predicted.

Evans AJ, Jensen ME, Kip KE, et al: Vertebral compression fractures: Pain reduction and improvement in functional mobility after percutaneous polymethylmethacrylate vertebroplasty-A retrospective report of 245 cases. Radiology 2003; 226:366-72.

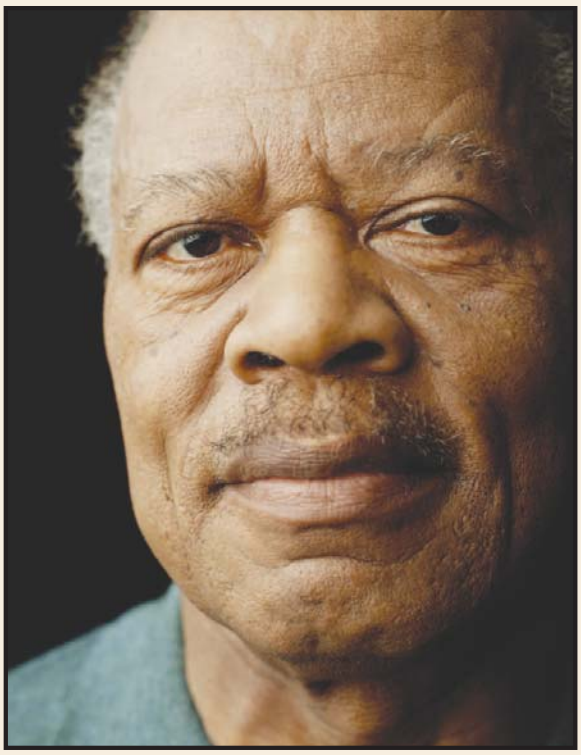
Ledlie JT, Renfro M: Balloon kyphoplasty: One-year outcomes in vertebral body height restoration, chronic pain, and activity levels. J Neurosurg 2003; 98:36-42.

Ear Infections be Gone!

- **The Findings:** Prevnar (heptavalent pneumococcal conjugate vaccine [PCV]), a vaccine to protect young children from invasive pneumococcal disease, has a secondary benefit; the reduction in the occurrence of otitis media (OM).
- **The Study:** A double-blind, manufacturer-sponsored study conducted in a Northern California health maintenance organisation from 1995 through 1998, randomised 38,000 infants to receive either PCV or control vaccines, and were followed for as long as 3.5 years.
- **The Results:** At all ages, children who received PCV had significantly fewer office visits for OM than those who received control vaccines (*e.g.*, a 7% reduction in office visits during the first year of life). The reduction was not sustained unless infants received their second and third PCV doses by the age of six months. PCV was most effective in children prone to OM. PCV recipients were 10% less likely to have three or more office visits for OM within six months and were 26% less likely to have ten office visits within six months than were controls. Compared with the control vaccine, PCV reduced tympanostomytube placement by 24% and there were 35 fewer antibiotic prescriptions per 100 children in the PCV group.

Fireman B, Black SB, Shinefield HR, et al: Impact of the pneumococcal conjugate vaccine on otitis media. Pediatr Infect Dis J 2003; 22:10-6.

Nondiabetic Renal Disease and Combination Therapy



- **The Study:** A Japanese randomised controlled trial, Combination Treatment of Angiotensin-II Receptor Blocker and Angiotensin-Converting-Enzyme (ACE) Inhibitor in Non-Diabetic Renal Disease (COOPERATE), was designed to evaluate the efficacy of maximum-dose ACE inhibitors, maximum angiotensin-II-receptor blockers (ARBs) or both, for patients with nondiabetic renal disease. A total of 263 outpatients (18 to 70 years) with nondiabetic renal disease (serum creatinine concentration, 1.5 mg/dL to 4.5 mg/dL; or glomerular filtration rate 20 mL/min/1.73 m^2 to 70 mL/min/1.73 m^2) were allocated to an ACE inhibitor (trandolapril, 3 mg daily), and ARB (losartan, 100 mg daily), or both. Nearly all participants had treated hypertension, with a mean baseline blood pressure of 130/75 mmHg on drug therapies (other than ARBs and ACE inhibitors). Median followup was 2.9 years.
- **The Results:** The proportion of patients who reached the primary combined endpoint (doubling of serum creatinine concentration or end stage renal disease) was significantly lower in the combination-therapy group (11%) than in the ACE-inhibitor and ARB groups (23% in each). In addition to combination therapy, factors that were associated independently with lower incidence of the primary endpoint were larger reductions in proteinuria and use of diuretics. All three groups had the same average decreases in blood pressure (5 mm systolic and 3 mm diastolic). There were no significant differences in side effects between combination therapy and monotherapy.

Nakao N, Yoshimura A, Morita H, et al: Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in nondiabetic renal disease (COOPERATE): A randomised controlled trial. Lancet 2003; 361:117-24.

Reducing Morbity in Type 2 Diabetes: A Multifactorial Intervention

- **The Study:** Danish researchers randomly assigned 160 patients (mean age 55) with Type 2 diabetes and microalbuminuria to receive one of two interventions, starting in 1992.
- **Group 1:** This group received intensive treatment, which included diet and exercise programs, smoking cessation courses, acetylsalicylic acid, angiotensin-converting enzyme inhibitors or angiotensin-II-receptor blockers, and algorithms with specified treatment goals for glycosylated hemoglobin, blood pressure, and lipid levels. These patients were offered individual consultations with a multidisciplinary team every three months on average.
- **Group 2:** The other group received conventional therapy with less stringent treatment goals, according to 1988 Danish guidelines.
- **The Results:** During an average followup of eight years, a composite endpoint (cardiovascular death, nonfatal myocardial infarction, invasive coronary intervention, nonfatal stroke, amputation, or peripheral vascular surgery) occured in 24% of intensively treated patients and 44% of conventionally treated patients. The intensive treatment group also experienced significantly lower rates of nephropathy, retinopathy, and autonomic neuropathy.

Gaede P, Vedel P, Larsen N, et al: Multifactorial intervention and cardiovascular disease in patients with Type 2 diabetes. N Engl J Med 2003; 348:383-93.

Difficulties Diagnosing the Flu in Vaccinated Adults

- **The Study:** During the 1998-1999 flu season, a large Veterans Affairs study was carried out in 2,215 veterans with chronic obstructive pulmonary disease. Investigators compared the efficacy of combined intranasal and standard intradermal vaccination with intradermal vaccination alone. A substudy was conducted to evaluate the clinical presentation of participants who developed the flu or other respiratory illnesses despite vaccination.
- **The Results:** Vaccinated participants developed 715 episodes of respiratory illnesses including 109 cases of laboratory-confirmed influenza (breakthrough rate, 5% [109 of 2,215]). When symptoms in 94 patients with the flu were compared with symptoms in 491 people with other respiratory infections, only documented fever and myalgia were associated with the flu. The positive predictive values of these variables were quite low (21% to 26%), singly or in combination, but their absence excluded flu in about 90% of patients. Dx

Neuzil KM, O'Connor TZ, Gorse GJ, et al: Recognizing influenza in older patients with chronic obstructive pulmonary disease who have received influenza vaccine. Clin Infect Dis 2003; 36:169-74.