

Clinical Briefs in Primary Care[™]

The essential monthly primary care update

By Louis Kuritzky, MD

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Risk of Adenocarcinoma in Barrett's Esophagus

Source: Murray L, et al. *BMJ(USA)*. 2003;3:534-535

ALTHOUGH SURVEILLANCE OF Barrett's esophagus (BES) for early detection of esophageal adenocarcinoma (E-CA) has become routine, the cost efficacy of this intervention is only scantily described.

Population data from Northern Ireland include all incident cancers. Murray and colleagues identified all subjects who had undergone esophageal biopsies with a diagnosis of BES between 1993 and 1999 and followed them up until 2000 identifying the number of subjects who were ultimately diagnosed with E-CA. Subjects who were diagnosed with E-CA within 6 months of the initial biopsy were not included in the data analysis.

Of 15,670 esophageal biopsies, almost 3000 met criteria for BES. In a follow-up period of 3.7 years (range, 1-8 years) 29 E-CA cases were identified. The mean yearly rate for E-CA was 0.26%, and 2.5 times higher in men than women. Risk was greatest in men older than 70 with specialized intestinal metaplasia found at esophageal biopsy, in whom the annual incidence was > 1%. Murray et al comment that when E-CA annual risk is 1%, surveillance may be cost-effective but that based upon these data, restricting surveillance to only the "high-risk" population would miss two-thirds of the incident cases of cancer. Our knowledge about the optimum schedule for BES surveillance remains incomplete. ■

Long-Term Effect of Doxazosin, Finasteride, and Combination for BPH

Source: McConnell JD, et al. *N Engl J Med*. 2003;349:2387-2398.

BENIGN PROSTATIC HYPERPLASIA (BPH) is commonly treated with alpha blockers such as doxazosin (DOX), alpha reductase inhibitors such as finasteride (FIN), or both. Long-term trials of DOX and FIN in combination have not been previously available to allow clinicians to compare the effect of alpha blockers, alpha reductase inhibitors, or both upon BPH symptoms. In addition to the value of symptom control, long-term treatments that reduce the need for surgical intervention are desired by clinicians and patients alike. Previous trials of alpha reductase inhibitors alone have indicated success in reducing the need for surgical intervention and the frequency of acute urinary retention.

Approximately 3000 men with symptomatic BPH who had not previously undergone surgical intervention, and whose PSA was < 10, were randomized to placebo, DOX, FIN, or DOX + FIN. The primary outcome was the first occurrence of a meaningful increase in the AUA symptom score (4 points or greater on a scale of 30).

Compared to placebo, both FIN and DOX had a statistically significant effect on the AUA symptom score (34-39% risk reduction). For this same end point, the benefit of combination therapy (DOX + FIN) was significantly greater than either agent alone. The risk of required surgical intervention or acute urinary retention was

significantly reduced by FIN and DOX + FIN, but not DOX alone. Clinicians now have multiple logical options for long-term treatment of BPH. ■

Once Daily Valacyclovir to Reduce Herpes Transmission

Source: Corey L, et al. *N Engl J Med*. 2004;350(1):11-20.

AMONG GENITAL HERPES VIRUS (HSV-2) discordant couples, couples in whom one partner is HSV-2 infected and the other has not been, several strategies have been used to reduce likelihood of transmission to the uninfected partner. None of the strategies, save abstinence, can provide perfect assurance that HSV-2 transmission will not occur.

Asymptomatic persons shed HSV-2 and place their sexual partners at risk of transmission even during asymptomatic periods. It has been reported that subclinical viral shedding is the primary source of HSV-2 transmission. Antiviral treatment can reduce both the amount of time subclinical viral shedding occurs and the intensity with which virus is shed.

HSV-2 discordant monogamous couples (n = 743) were randomized to 500 mg valacyclovir QD (VAL) vs placebo for 8 months.

Only 4 of 743 susceptible partners on VAL developed symptomatic infection during the study period, compared with 16 placebo recipients (hazard ratio = 0.25). Similarly, seroconversion was found in 14 of 743 VAL-treated susceptibles, vs 27 of 741

on placebo. Placebo-treated patients excreted HSV-2 on 10.8% of days, compared with 2.9% of days with VAL treatment.

Once-daily VAL can reduce, but not eliminate, HSV-2 transmission. ■

Use of B-Type Natriuretic Peptide in the Evaluation and Management of Acute Dyspnea

Source: Mueller C, et al. *N Eng J Med.* 2004;350:647-654.

THE ETIOLOGY OF ACUTE DYSPNEA (DSP) can be diverse, and it is often especially difficult to separate pulmonary from cardiac causes. Recently, brain natriuretic peptide (BNP)—so called because of its original identification in porcine brain—has become recognized as a valuable diagnostic tool because it promptly rises in response to pathologic cardiac ventricular wall stress (eg, heart failure), and its levels are proportional to the degree of cardiac dysfunction. BNP is not affected by pulmonary conditions such as COPD, unless

COPD has been of sufficient severity to result in right ventricular failure.

Whether standard clinical evaluation or BNP-based diagnosis provides more effective management for acute DSP was studied in this trial (n = 452). Primary end points were time to discharge and cost, both of which would be presumed to be adversely affected by inaccurate initial diagnosis.

Evaluation for all patients in the emergency department included an initial history and physical, EKG, oximetry, blood chemistry, chest X-ray and (for half of the group) point-of-contact BNP testing (15 minute on-site results). A BNP level > 100 pg/mL was considered sufficiently elevated to be consistent with heart failure.

Use of BNP testing provided an advantage for time-to-discharge from the ED (63 minutes vs 90 minutes), need for hospitalization (75% vs 85%), time to hospital discharge (8 days vs 11 days), and intensive care costs (\$874 vs \$1516)

Use of BNP testing, in concert with traditional diagnostic tools, shortens the time to initiation of specific and appropriate treatment, and hospitalizations. Overall, use of the BNP test reduced total treatment cost by more than 25%. ■

Association Between C-reactive Protein and Age-related Macular Degeneration

Source: Seddon JM, et al. *JAMA.* 2004;291:704-710.

AGE-RELATED MACULAR DEGENERATION (AMD) is an important cause of loss of visual acuity, and because there are few effective treatments, enhanced prevention is paramount. The association between some cardiovascular risk factors (eg, smoking, dyslipidemia, obesity) and AMD has not gone unnoticed. Since C-reactive protein (CRP) has been associated with cardiovascular risk, it has become an item of interest whether CRP is similarly associated with AMD.

Study subjects (n = 4757) comprised persons with mild (n = 1063), intermediate (n = 1621), and advanced (n = 956) AMD, and controls (n = 1117). Subjects were followed every 6 months with tests of visual

acuity and funduscopy.

CRP levels were particularly discordant in persons with advanced AMD compared to those with no AMD. Even after statistical adjustment for age, sex, smoking, and obesity, CRP levels maintained a relationship with AMD. Persons in the 90th percentile for CRP had almost a 2-fold increased odds ratio for AMD. Seddon and colleagues suggest that CRP elevation is an independent risk factor for AMD. Since this is the first evidence to implicate inflammation (as manifest by CRP) etiologically in AMD, it remains to be shown whether modulation of CRP might have favorable effects on this end point. ■

VZV Reactivation in Astronauts

By Carol Kemper, MD, FACP

Source: Mehta SM, et al. *J Med Virol.* 2004;72:174-179.

STRESS IS A KNOWN TRIGGER FOR reactivation of herpes viruses. Just the physical and psychological trauma of swapping alpha-male mice between 2 mouse colonies and the resultant battle for new alpha-male-dom has been shown to trigger reactivation of HSV in about half the mice. Herpes zoster can also reactivate after stress, including the stress of surgery.

After a 47-year-old healthy astronaut developed herpes zoster 2 days before a space flight, Mehta and associates decided to examine whether the stress of space flight can result in the reactivation of VZV. A total of 312 saliva samples, obtained from 8 astronauts before, during, and after space flight were examined by PCR. Amazingly, 61 of 200 (30%) specimens obtained during and after space flight were positive, compared with 1 of 112 (< 1%) obtained in a 234-265 day period before flying. No VZV was detected in 88 samples from 10 control subjects, who did not fly. Seven of 8 astronauts had at least 1 positive specimen during flight (2-12 days), while all 8 had anywhere from 1-8 positive specimens within 15 days of returning to earth. ■

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