

# Clinical Briefs in **Primary Care**<sup>TM</sup>

The essential monthly primary care update

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## Erectile Dysfunction and Subsequent Cardiovascular Disease

**Source:** Thompson IM, et al. *JAMA*. 2005;294:2996-3002.

**T**HE PRESENCE OF ERECTILE DYSFUNCTION (ED) has recently been recognized to commonly be a consequence of endothelial dysfunction. Indeed, some have suggested that ED may be an indicator of existing vasculopathy in the same way angina, intermittent claudication, or TIA reflect vascular compromise.

The Prostate Cancer Prevention Trial population (n = 18,882) was designed to investigate the impact of finasteride upon incidence of prostate cancer in healthy men. As part of the data accrual, assessment of sexual function at baseline and on followup was performed. Because finasteride can affect sexual function, only the placebo group data (n = 9,457) were used for analysis. In this group, 85% were free of cardiovascular disease at baseline.

Although approximately half of the men were free of ED at baseline, by the 5-year mark of the study, 57% of these had developed it. Amongst these men (incident ED), there was a 25% increased hazard ratio for new cardiovascular events. Amongst all men with ED (incident plus present at study initiation), the hazard ratio for a new cardiovascular event was increased by 45%.

ED predicts increased risk of new cardiovascular events. The magnitude of association is as strong as that of cigarette smoking or family history. Men with ED should be encouraged to have close scrutiny and appropriate modification of their cardiovascular risk factors. ■

## Oseltamivir for Influenza A Infection

**Source:** de jong MD, et al. *N Engl J Med*. 2005;353:2667-2672.

**N**O ONE DOUBTS THAT INFLUENZA CAN extract dread consequences on a grand scale. Some degree of complacency may have been fostered by the development of highly effective oral agents for the treatment of influenza A and B, such as the neuraminidase inhibitors oseltamivir (OTV) and zanamivir. Clinicians share a great respect for the capacity of bacteria to develop resistance to antibiotics; there is little corresponding awareness of the role of viral resistance in antiviral therapeutics.

The H5N1 influenza virus (FLU-H5N1) is particularly ominous in its adverse outcomes and potential for pandemic spread. There has been great hope that agents like OTV might provide adequate treatment or prophylaxis for FLU. Unfortunately, resistance to antivirals, including OTV, might become problematic.

De jong et al provide data from Vietnam about 8 cases of FLU-H5N1. In 2 of the patients, neuraminidase amino acid substitution resulted in OTV resistance; both of these patients died. Amongst the other 6 patients, prompt reductions in FLU-H5N1 viral load was correlated with survival: 2 of 6 patients (without resistance) who failed to evidence a prompt reduction in viral load succumbed.

These sobering data suggest that OTV alone may be insufficient to ensure successful treatment of some evolving strains influenza virus. It may be that a 2-drug regimen will be required to grapple with the potential for emergence of resistant strains, or when failure of monotherapy to promptly reduce viral load occurs. ■

## Dietary Intake of Antioxidants and AMD

**Source:** van Leeuwen R, et al. *JAMA*. 2005;294:3101-3107.

**A**GE-RELATED MACULAR DEGENERATION (AMD) is the most prevalent cause of blindness in first-world nations. Although vitamin and antioxidant supplementation has not fulfilled its blush of initial promise for cardiovascular endpoints, data on supplements of beta carotene, vitamin C, vitamin E, and zinc indicate a beneficial slowing of AMD progression. Whether dietary intake (apart from supplements) is associated with AMD was the subject of this study.

Rotterdam, the Netherlands was the source of this population-based study (n = 10,725) of socioeconomically middle-class adults older than age 55 (mean age, 68). Early AMD was defined by the presence of drusen (white retinal deposits). All study subjects underwent photographic evaluation of their fundi. All subjects completed food diaries. Follow up was 8 years.

There was an inverse relationship between vitamin E and zinc intake and AMD. Each 1-standard deviation increase in dietary intake was associated with an 8-9% decrease in AMD. Overall intake of vitamin C, E, beta carotene, and zinc above the median was associated with approximately one-third less risk of new AMD. Interestingly, among those in the highest quintile of dietary intake, adding supplements did not appear to affect risk reduction. This observational data suggests that diet may have a meaningful impact upon risk of AMD. ■

# High-Dose Acyclovir in Pityriasis Rosea

**Source:** Drago F, et al. *J Am Acad Dermatol.* 2006;54:82-85.

**A**LTHOUGH IT HAS BEEN LONG SUSPECTED that pityriasis rosea (PTR) is of viral origin, proof of that remains lacking. Recent evidence suggests that herpes virus 6 (HSV 6) and herpes virus 7 (HSV7) are etiologic in PTR. Antiviral therapy such as acyclovir (ACV) has proven effective for management of other HSV infections, but it is not clear whether PTR is treatment-responsive. Indeed, PTR is often treated with watchful waiting or antipruritic medication, on the basis that it is usually self limited. Nonetheless, because HSV6 has been associated with increased risk for abortion, were antiviral treatment effective for PTR, treatment might be worth considering on this basis coupled with potential symptom reduction.

Consecutive patients (n = 82) with typical dermatologic findings of PTR underwent serologic evaluation for HSV6 and HSV7. Other bacterial and viral agents which might produce similar dermatologic findings were included in serologic analysis (eg, Borellia, toxoplasmosis). Patients were

alternately assigned to either ACV treatment (800 mg five times daily for one week), or placebo in a single-blind fashion.

On day 7, regression of PTR skin lesions was seen in 90.5% of the ACV treatment group vs 26.7% in the placebo group. New lesions appearing beyond one week were seen in none of the treatment group, and 40.5% of the placebo group. By 2 weeks, complete lesion regression was seen in 78.6% in the ACV group, but only 4.4% in the placebo group.

PTR-associated symptoms, eg, fatigue, headache, sore throat, irritability, insomnia, and nausea, followed a similar course: by day 7, none of the placebo recipients were fully symptomatically resolved compared with 36.8% in the ACV group. These data suggest that ACV treatment may be helpful in PTR. ■

## Rimonabant and Weight and Risk Factors in Obese Patients

**Source:** Pi-Sunyer FX, et al. *JAMA.* 2006;295:761-775.

**D**ESPITE A GROWING PUBLIC AND professional awareness of the health consequences of overweight, there is little in the way of pharmacologic management to provide a meaningful impact on excess body weight. Recently, interest has been expressed in capturing the influence of the endocannabinoid system, which has receptors in the CNS, adipose tissue, muscles, GI tract, and liver. Stimulation of the cannabinoid-1 receptor results in increased eating, decreased muscle mass, and lipogenesis. Rimonabant (RIM) is a cannabinoid-1 receptor blocker, and has shown favorable effects upon both body weight and some of the metabolic consequences of overweight. The RIO-North America study is a randomized, controlled trial of RIM in adult overweight or obese individuals.

Through 2002, subjects were enrolled and randomly assigned to either RIM 5 mg/d, RIM 20 mg/d, or placebo. After 1 year, subjects who had received RIM were rerandomized to drug or placebo; the original placebo group continued on placebo. All subjects were also placed on a diet.

RIM 20 mg/d produced favorable results at 1 year which were statistically

significantly different from placebo: a reduction of body weight 6.3 kg, reduced waist circumference, increase in HDL, and reduction in triglycerides. Subjects who were switched from RIM to placebo in year 2 lost much of the favorable weight and metabolic changes attained in year 1, but those who remained on RIM 20 maintained these positive effects. Rimonabant is a promising method of modulating excess weight and attendant metabolic derangements. ■

## Watchful Waiting vs Repair of Inguinal Hernia in Minimally Symptomatic Men

**Source:** Fitzgibbons RJ, et al. *JAMA.* 2006;295:285-292.

**I**NGUINAL HERNIA (ING) IN MEN IS rarely associated with serious adverse outcomes. Nonetheless, because ING can result in bowel incarceration and strangulation, there is some uncertainty about the propriety of watchful waiting (WW). Some men are motivated to intervene surgically because of pain or cosmetic effects; but the study by Fitzgibbons et al suggests that a conservative approach for men with minimal symptoms is appropriate.

The randomized trial included adults with ING (n = 720) who were randomized to surgical repair or WW. Subjects were followed for 2-4.5 years. Among those assigned to WW, 23% ultimately elected surgical repair during the study, most commonly due to increased pain; a similar percentage (17%) in the group originally randomized to surgery chose instead to use WW.

At 2 years, the primary end point (pain interfering with activity) was the same in the WW as the surgical group. Only 2 patients in the WW group who were followed for up to 4 years sustained incarceration.

The authors conclude that WW is a reasonable strategy for managing ING because serious adverse events are rare, and other clinical outcomes are similar with either approach. ■

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