

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

The essential monthly primary care update

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## Botulinum Toxin for Treatment of Hyperhidrosis

Lowe NJ, et al. *J Am Acad Dermatol.* 2007;56:604-611.

PERSONS WHO DO NOT SUFFER hyperhidrosis (HID) may be surprised to learn that it has been associated with both occupational and physical impairment, as well as limitations in social interaction. Some success in managing primary axillary hyperhidrosis may be achieved with topical agents, systemic pharmacotherapies, and/or surgical intervention, but many patients continue to have inadequately controlled symptoms, or are dissatisfied with available methods.

The release of sweat from eccrine glands is mediated by acetylcholine through cholinergic neurons. Injected botulinum toxin type A (BTX) produces transient blockade of the cholinergic nerves that supply sweat glands.

Patients with primary axillary HID were randomized in a double-blind placebo-controlled trial of treatment with BTX. Each subject received BTX or placebo and was followed for symptom control at weeks 1, 4, 8, and monthly thereafter. Subjects could elect an additional BTX injection, but not sooner than 8 weeks after the last injection.

Most of the BTX subjects (75%) reported a major improvement in HID symptoms (at least a 50% improvement in the Hyperhidrosis Disease Severity Scale). The median duration of positive effect was greater than 6 months. There

were no significant adverse effects that differed between BTX and placebo (placebo was an injection of sterile saline). BTX has a favorable efficacy and tolerability profile, and should be useful in management of HID. ■

## A Fish Story

Yokoyama M, et al. *Lancet.* 2007;369:1062-1063.

TWO MAJOR INTERVENTION TRIALS have shown that consumption of fish (either in the diet, or by means of fish-oil supplement) is effective in secondary prevention of coronary events post-MI. Long-chain fatty acids in fish—specifically eicosapentanoic (EPA) and docosahexanoic acid (DHA)—have been shown to be inversely related to CAD mortality.

The population of Japan has a diet high in fish. Whether the addition of EPA to this diet would impact coronary events in dyslipidemic patients was the clinical question addressed by JELIS: The Japan EPA Lipid Intervention Study.

JELIS was a prospective randomized placebo-controlled trial in hypercholesterolemic men and women (n = 18,645), all of whom were already receiving statin treatment (specifically, pravastatin or simvastatin). Subjects were assigned to either EPA (1,800 mg/d) or placebo for 5 years. The primary endpoint was any major coronary event.

After a mean followup of 4.6 years, there was a statistically significant 19% relative risk reduction in the primary endpoint for persons on EPA compared to placebo. When the population was separat-

ed to look at effects in those with pre-existing CAD vs without, it was discerned that only the former group had a statistically significant benefit, although the trend for event reduction even in the primary prevention group looked promising (18% relative risk reduction). EPA/DHA supplements offer benefit even in persons with diets commonly high in fish, and already on a statin. ■

## Diabetes Control: It's More Than Just A1c Control

Vinik AI, Ahang Q. *Diabetes Care.* 2007;30(4):795-800.

IN OUR ZEAL TO REFINE GLUCOSE control in diabetes to attain microvascular risk reduction, we sometimes overlook an equally relevant attribute: better glucose control helps patients feel better! Quality of life (QOL) studies have generally demonstrated QOL improvements with better glucose control. Does it make a difference how you get better control? That question was addressed by Vinik and Zhang in their randomized trial of glargine (GLAR) vs Rosiglitazone (ROSI).

Subjects with uncontrolled type 2 diabetes despite full therapeutic doses of metformin and a sulfonylurea were randomized to add either GLAR or ROSI, and followed for 6 months. In addition to monitoring changes in control of diabetes (A1c) a health-related quality of life instrument was used to measure out-

comes.

GLAR and ROSI provided similar improvements in A1c (1.5%-1.66% reduction). Numerous differences in QOL were evident however, favoring GLAR: total symptom distress score, mood symptoms, ophthalmologic symptoms, fatigue, and perception of general health.

Clinicians have been sometimes reluctant to initiate insulin therapy for persons with uncontrolled diabetes. These data suggest that insulin treatment not only provides substantial A1c improvements, but—with comparable glucose control—resulted in better QOL improvements than ROSI. How we gain control of type 2 diabetes may make a difference. ■

## MI: Try to have it Monday Thru Friday

Kostis WJ, et al. *N Engl J Med.* 2007;356:1099-1109.

**H**OSPITAL LEGENDS ABOUT THE relative availability (or unavailability) of services/personnel on weekends vs weekdays often lead to jocularity about the wisdom of choosing one's day to be admitted to the hospital careful-

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ly! Yet, whether such issues as calendar timing (being admitted on the weekend, vs weekday) really make a difference is largely unknown.

Using a database comprised of more than 59,000 patients admitted to New Jersey hospitals for an acute MI between 1999-2002, an appraisal of the relationship between day of admission and outcomes was performed.

The relative risk of 30-day mortality was 8% greater for persons admitted on a weekend than during the week (12.9% vs 12.0%). Similarly, utilization of services such as cardiac catheterization within 48 hours was remarkably lower if admitted on a weekend (odds ratio for catheterization by day 2 = 0.51). The authors reflect that “our study suggests that a hospital workweek of Monday through Friday is not optimal for the care of patients with acute MI.” ■

## Can MRI Provide Better Clarity About Contralateral Breast Cancer?

Lehman CD, et al. *N Engl J Med.* 2007;356:1295-1303.

**A**MONGST THE POPULATION OF women who are diagnosed with and treated for breast cancer (BCA), an additional cancer is detected in the contralateral breast in as many as 10% of cases (identified by clinical examination, mammography, or both). Mammography has generally been considered the “gold standard” in this regard.

MRI is more sensitive than mammography for detection of primary BCA. The American College of Radiology Imaging Network conducted a trial of women diagnosed with BCA who had already been examined with negative mammography of the contralateral breast (n = 969). MRI diagnosed thirty of these women (3.1%) to have biopsy-confirmed BCA that had been missed by both mammography and clinical examination.

More than half of the occult cancers were invasive, and (fortunately), all were node-negative at the time of discovery.

Although current costs of MRI do not favor its utilization for routine screening, in the higher-risk group of women with known BCA, it has superior performance in diagnosing disease in the contralateral breast than mammography. ■

## Dapsone Gel 5% for Acne

Draelos ZD, et al. *J Am Acad Dermatol.* 2007;56:439-447.

**D**APSONE (DAP) IS A SULFONE that possesses both antimicrobial and anti-inflammatory activity, but its use systemically is limited by substantial toxicity, including methemoglobinemia and hemolysis. In the recent past, consideration of DAP as a topical agent was limited by the poor solubility of DAP in traditional vehicles. Recently, a gel formulation with adequate DAP delivery has been developed.

DAP 5% gel was studied in persons greater than age 12 with acne (n = 3,010). Two identical placebo-controlled, double-blind trials were performed using DAP 5% twice daily vs placebo gel.

DAP produced statistically significant and clinically relevant improvements in acne at the 12 week endpoint of the study; a divergence between placebo and DAP was visible beginning as early as two weeks into the study. Subjects with G-6-PD deficiency (who are particularly sensitive to hemolysis) were proactively included in the trial and monitored for hemolysis.

DAP was well tolerated with no evidence of serious adverse effects. The overall adverse effect profile was not statistically different from placebo.

In an era of increasing Propionibacterium acnes (the primary causative bacterium for acne) resistance to many of the antibacterial agents commonly used for acne treatment, DAP may offer a new therapeutic alternative. ■