# **August 28 Highlights**

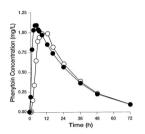
### Generic vs brand-name drugs

"When taking phenytoin sodium with food, product switches may result in either side effects or loss of seizure control."

Wilder et al. examined food-associated differences in drug concentrations between two phenytoin products in 24 healthy subjects and simulated the impact of switching products with data from epileptic patients. Results suggest product switches may have the adverse effect of causing seizures if phenytoin is taken with food.

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### Does food affect the bioavailability of Dilantin Kapseals?



Plasma concentration of phenytoin: fed (open circles) and fasted (filled circles)

Cook et al. reported that a high-fat meal does not alter phenytoin bioavailability from Dilantin Kapseals. Thus, patients may be instructed to take Dilantin Kapseals without regard to meals.

The editorial by Lesser and Krauss notes that these articles point to problems with the generic equivalency policies of the US Food and Drug Administration (FDA). While providing cheaper drugs for patients is laudable, FDA standards do not include the effect of food studied here (or many other issues that could change drug levels and patient tolerability of a drug).

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## Duchenne dystrophy (DD): Diagnosis by blood test vs muscle biopsy

"This study is excellent news for genetic counseling of Duchenne dystrophy families."

Mendell et al. studied 93 typical DD patients who had been negative on previous genetic blood testing. Using a highly sensitive single-strand conformational polymorphism method they found small dystrophin gene mutations in 68/73 patients (73%). The increased rate of defection is a major advance in carrier detection and antenatal diagnosis.

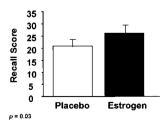
In the accompanying editorial, Muntoni reviews the issue of whether a muscle biopsy is still needed in suspected DD patients. Since all 73 Mendell et al. patients had a biopsy confirmation of DD by dystrophin absence (and the clinical phenotype of DD), this study does not necessarily speak to the issue of unselected patients who might receive genetic testing. Muntoni asserts that biopsy is still needed. see page 574

# Memory risk and bilateral hippocampal atrophy

Martin et al. studied the incidence of memory loss following anterior temporal lobectomy (ATL) in patients with MRI evidence of bilateral hippocampal atrophy. The highest proportion of patients experiencing memory loss following surgery were left ATL patients with preoperative evidence of bilateral hippocampal atrophy.

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# Alzheimer's disease (AD): Therapeutic potential of estradiol



Treatment-related benefits in cognitive performance

Asthana et al. evaluated the cognition-enhancing potential and neuroendocrine response to treatment with a high dose of transdermal estradiol for postmenopausal women with AD. They found that estradiol improved verbal memory and selective attention, and suppressed the activity of the insulinlike growth factor system in plasma. These findings support a continued systematic evaluation of the of estradiol for women with AD.

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#### Donepezil in moderate to severe Alzheimer's disease

Feldman et al. report on the efficacy and safety of donepezil in a randomized placebo controlled clinical trial in more advanced Alzheimer's disease (AD). In moderate to severe AD, they found that donepezil treatment benefited the spectrum of global function, cognition, activities of daily living, and behavior, while being very well tolerated.

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### Screening for PS1 mutations in a referral-based series of AD cases

The Rogaeva et al. study revealed a high frequency of PS1 mutations in a series of 414 consecutive patients referred for AD diagnostic testing: 48 independent AD cases could be explained by coding sequence PS1 mutations (21 of which have not been previously described).

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### Cortical disconnection in aging

The mechanisms of cognitive decline with age remain unclear. Using diffusion-tensor MRI, O'Sullivan et al. provide evidence for white matter tract damage in elderly subjects with normal conventional MRI scans. These changes correlated with cognitive performance, suggesting that cortical disconnection may play a role in age-related decline.

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### Parkinson's disease: Cost-effectiveness of deep brain stimulation

Tomaszewski et al. performed a cost-effectiveness analysis of deep brain stimulation (DBS) compared with best medical management in late-stage PD patients. Since the long-term effectiveness of DBS is not established, they developed a theoretical decision model over patients' remaining lifetime. Results suggest that, under certain conditions, DBS may be considered a cost-effective strategy.

see page 663

## Fatigue in multiple sclerosis

Fatigue is common in MS and its pathogenesis is poorly understood. Giovannoni et al. investigated the role of systemic markers of inflammation in fatigue: no correlation was found. Interestingly, patients with primary-progressive MS had less fatigue than patients with relapse-onset disease. The two independent fatigue rating scales used, the Fatigue Questionnaire Score and the Krupp's Fatigue Severity Score, failed to correlate with each other. Better fatigue rating scales are needed.

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## CSF 14-3-3 protein: Prognostic of early conversion to clinically definite MS?

Martínez–Yélamos et al. found that five of the 38 patients with a first neurologic event suggestive of MS had 14-3-3 protein in their CSF. This finding was an independent predictor for early relapse and disability in the short term.

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