## **September 24 Highlights**

#### Mitoxantrone-induced heart failure in MS

Ghalie et al. reviewed records of 1,378 patients who received mitoxantrone in MS clinical trials. At median cumulative dose 62.5 mg/m<sup>2</sup> and follow-up 29 months, 2 of 1,378 patients (<0.20%) experienced congestive heart failure (CHF). Whether the incidence of CHF in MS patients will prove to be higher with greater cumulative mitoxantrone doses is not yet established.

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#### Fatal leukemia with mitoxantrone treatment of MS

Brassat et al. report acute leukemia in a mitoxantrone-treated patient with severe MS—the first case among 802 French mitoxantrone-treated MS patients.

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### Mitoxantrone-related toxicity in multiple sclerosis

Commentary by John W. Rose, MD

Mitoxantrone is an important new therapy recently approved by the FDA for treatment of severe relapsing and secondary progressive multiple sclerosis. In this issue of Neurology, two articles discuss potential side effects of the drug. The article by Ghalie et al. examines the cardiotoxicity of the drug in multiple sclerosis patients demonstrating a low incidence of clinical congestive heart failure across several studies. The result of a 0.2% incidence for heart failure is much lower than the incidence in patients treated for neoplasias, a group frequently treated with other cardiotoxic

therapies prior to mitoxantrone administration. It is clear, however, that careful monitoring of cardiac function is important in the evaluation of patients treated even with low-dose mitoxantrone.1

Of concern is the report by Brassat et al. of chemotherapy-related acute mveloblastic leukemia following mitoxantrone therapy. While leukemia occurred in only one patient of over 800 patients receiving a full course of mitoxantrone in the study, this is the second case of leukemia reported in a multiple sclerosis patient treated with the drug.2 These manuscripts on mitoxantrone-related toxicity underscore the requirement of appropriate patient selection and monitoring.

#### References

- 1. Strotman J, Spindler M, Weilbach F, Gold R, Ertl G, Wolfram V. Myocardial function in patients with multiple sclerosis treated with low-dose mitoxantrone. Am J Cardiol 2002;89:1222-1225.
- 2. Vicari A, Ciceri F, Folli F, Lanzi R, Colombo B, Comi G, Camba L. Acute promyelocytic leukemia following mitoxantrone as single agent for the treatment of multiple sclerosis. Leukemia 1998;12:441-442.

## Diffusion MR imaging of neonates with brain injury

McKinstry et al. prospectively characterized changes in water diffusion that take place during the first week after brain injury at birth in 10 term infants. The sensitivity of diffusion MR imaging for detecting injury varied markedly with time after injury, being most sensitive between 2 and 4 days. During the first day after injury, diffusion MR imaging misses up to 30% of injuries in term infants. Thus, a "normal" diffusion MR scan obtained during the first day of life should be interpreted with caution.

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The accompanying editorial by Melhem notes the challenge that this study posed obtaining serial MRI studies in critically ill newborns—and considers the study's limitations. Whether diffusion MR will be able to demonstrate changes in a larger spectrum of neonatal disorders, such as those with hypoxia from respiratory compromise, or in premature infants, can only be determined with further studies.

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#### Arterial reocclusion after IV TPA

Alexandrov and Grotta used TCD to study patients with MCA occlusion treated with IV TPA. After initial partial or complete recanalization, reocclusion was observed in 34% of these patients. Reocclusion accounted for two-thirds of cases with neurologic deterioration following improvement and was associated with higher mortality.

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#### NSAIDs reduce AD incidence but . . .

Zandi et al. observed a reduced incidence of AD among users of NSAIDs in their 3-year follow-up assessment of the prospectively studied Cache County population. However, their data suggest a "lag" of several years between NSAID use and prevention of AD onset. This "lag" suggests that NSAIDs would not prevent progression from mild cognitive impairment in AD.

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#### Poverty and dementia: Cause or effect?

In a population-based study Anttila et al. show that dementia is associated with low-income level at old age and a decrease in income level from midlife. They note that the low old age income level is more likely to reflect the effects of the disease than the reverse.

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#### Migraine and impaired cognitive function

In a longitudinal birth cohort study done over a 23-year period Waldie et al. found that migraineurs have impaired verbal functioning and lessened academic success. However, the deficits are unrelated to duration of headache history, and are likely to be neurodevelopmental in origin rather than due to repeated vascular insults.

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## New pathomechanism of muscular dystrophy



A study of a patient with Ullrich congenital muscular dystrophy by Ishikawa et al. suggests that the loss of a link between interstitium and basal lamina may be a new molecular pathomechanism of muscular dystrophy.

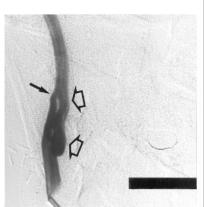
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### On-line video: Denny-Brown's treatment of Wilson's disease with BAL

In 1951, Denny-Brown and Porter reported that Wilson's disease could be treated effectively with BAL. This first demonstration that treatment of a biochemical disorder could alleviate dyskinesias, even in adults, is documented by Vilensky et al. in the films of Denny-Brown and the five initial patients—illustrating this historical landmark in neurology.

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## Carotid stenting for dissecting aneurysms



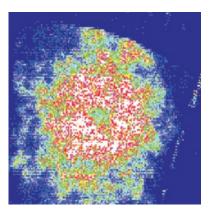


Binaghi et al. report stent angioplasty in two patients with spontaneous dissecting aneurysms of the cervical internal carotid artery. Repeat angiography at 1 year disclosed complete repair of the arteries.

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(Left) Initial. Arrow—true lumen; hollow arrow—false channel. (Right) One-year ICA.

## Neurogenic flare reaction in neuropathy



Bickel et al. analyzed the axon-reflex mediated flare reaction with laser Doppler scanning and found flare size but not intensity reduced in patients with suspected small fiber neuropathy.

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# **September 24 Highlights** *Neurology* 2002;59;795-797 DOI 10.1212/WNL.59.6.795

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