

Estrogen and migraine attacks

The study by E. Anne MacGregor and Allan Hackshaw presents evidence for an association between estrogen withdrawal and attacks of migraine without aura, as well as evidence for an association between high estrogen states and attacks of migraine with aura.

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Triptan treatment of menstrual migraine

Silberstein et al. studied frovatriptan in a three-way crossover trial in menstrually associated migraine (MAM) comparing placebo vs frovatriptan 2.5 mg QD vs frovatriptan 2.5 mg BID. Six days of treatment were started 2 days before anticipated MAM. The incidence of MAM headache in the 6-day perimenstrual periods was 67% for placebo, 52% for frovatriptan 2.5 mg QD, and 41% for frovatriptan 2.5 mg BID.

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The editorial accompanying these two articles by Elizabeth Loder notes that the MacGregor and Hackshaw article provides evidence that there is a subset of women with migraine for whom the hormonal changes associated with menstruation are a principal, sometimes sole, headache trigger, and in whom attack symptoms are intensified. The Silberstein et al. trial demonstrates a dose-response curve and establishes treatment efficacy over a broad range of endpoints, including headache duration, associated symptoms, and use of rescue medication. The use of a loading dose contributed to the more impressive results of this study vs other placebo-controlled trials of triptan prophylaxis for menstrual migraine, which all assessed the use of naratriptan. However, Loder points out that timing is critical in short-term prevention regimens for menstrual migraine, with success requiring treatment initially prior to headache onset. In the Silberstein et al. study regular menstrual periods were a requirement for entry, yet almost one third of subjects in each treatment period inaccurately assessed the date on which they should begin medication. Treatment effects are modest, and comparative trials are now necessary to establish the place of this regimen in the context of treatment alternatives.

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Radiosurgery for cerebral AVMs in hereditary hemorrhagic telangiectasia

Cerebral HHT AVMs are usually small (<2 cm) and multiple, and can cause severe intracerebral hemorrhage. Maarouf et al. reported two patients with seven cerebral HHT AVMs that were treated using LINAC radiosurgery yielding complete occlusion of the seven AVMs without side effects.

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Donepezil and neuropsychiatric symptoms

In a placebo-controlled study Holmes et al. showed that donepezil was effective in the treatment of neuropsychiatric symptoms and in reducing caregiver distress in patients with mild to moderate Alzheimer disease. Randomized withdrawal of donepezil was associated with cognitive decline, a re-emergence of neuropsychiatric symptoms, and greater caregiver distress.

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“Despite [some] limitations...the study provides the best evidence to date that donepezil has beneficial effects in . . .mild to moderate AD with neurobehavioral symptoms.”

The accompanying editorial by Nathan Herrmann and David Knopman notes that behavioral and psychological symptoms of dementia are common, serious problems that affect patient and caregiver quality of life. The benefit seen in the Holmes et al. study must be considered in the context of the strengths and limitations of its methodology: a withdrawal design in which all patients were treated with open label donepezil for 12 weeks after which

they were randomized to ongoing treatment with donepezil or placebo. A limitation of this design was the high dropout rate of placebo-treated patients as well as a concern that sudden withdrawal of donepezil may have a specific drug withdrawal syndrome. The authors conclude that the study clearly demonstrates that once therapy with ChEIs is initiated and benefit on cognition and behavior is evident, discontinuing therapy, at least within the first 3 to 6 months, will likely result in significant behavioral worsening and cognitive decline, and should be avoided.

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Parkinson disease, psychosis, and mood disorders

Marsh et al. report that patients with PD with psychosis have high rates of comorbid nonpsychotic psychiatric disturbances, especially affective disorders. These additional disturbances were associated with greater morbidity and caregiver distress. Psychosis was a primary predictor of caregiver burden whereas depressive symptoms were associated with enhanced motoric disability.

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Initial chemotherapy in gliomatosis cerebri

Initial chemotherapy with either procarbazine-CCNU-vincristine (PCV) regimen or temozolomide was investigated by Sanson et al. in 63 patients with diffuse gliomatosis cerebri. They found a 33% clinical response and 26% radiologic response, with lower toxicity and comparable efficacy for temozolomide regimen.

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Temozolomide as initial treatment in gliomatosis cerebri

Levin et al. studied 11 radiotherapy-naïve patients with gliomatosis cerebri who received temozolomide. Objective response was documented in 45% with progression free survival of 55% at 12 months. Thus, radiotherapy to extensive brain regions can be deferred until disease progresses.

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The accompanying editorial by Marc C. Chamberlain reviews the clinical features of gliomatosis cerebri (GC). MRI has changed the conceptualization of GC. CT imaging visualizes GC poorly due to the subtle widespread infiltration of white matter and lack of focal tumor mass and contrast enhancement. MR sequences utilizing FLAIR (or T2-weighted images) have better tumor visualization assisting both in diagnosis and treatment. Oligodendroglial tumors, the common tumor accounting for GC in both reports, are often treatment sensitive. These studies provide data to help in design of a randomized clinical trial for the treatment of GC.

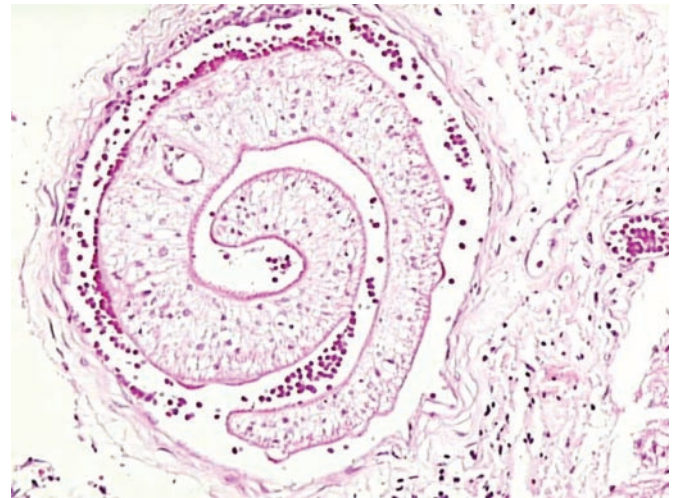
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Genotype distributions published in *Neurology*

Kocsis et al. review the reasons why testing of Hardy-Weinberg equilibrium is essential in population genetic studies. Was this test adequately used for articles in *Neurology*? The authors tested 123 genotypes described in 54 articles published between 1999 and 2002. Unreported deviations from equilibrium were found in 19 genotype distributions in 11 articles. Additional information could have been obtained from these articles by recalculating the Hardy-Weinberg equilibrium. [*Neurology's* "Information for Authors" is being modified to reflect the need for such testing in genetic studies.]

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Schistosoma mansoni myelopathy



Adult *S. mansoni* worm in spinal subarachnoid vein.

Carod Artal et al. report 13 patients with *Schistosoma mansoni* myelopathy. Three different syndromes were seen: an acute flaccid paraplegia, a mid-thoracic myelopathy with spastic paraparesis, and a cauda equine syndrome.

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