1999;13:44, for previous comparison study of Ritalin and Adderal in ADHD).

## HEADACHE DISORDERS

### MIGRAINE PATHOPHYSIOLOGY AND TREATMENT

The proceedings of a symposium on "The scientific basis of migraine management" held Feb 1999 at Lake Louise, Alberta, Canada, are reported from the University of Calgary and other centers. (Becker WJ, et al. Can J Neurol Sci Nov 1999;26: Suppl 3).

**Pathophysiology.** Local vasodilatation of intracranial extracerebral blood vessels, and consequent stimulation of surrounding trigeminal sensory nervous pain pathways, causes release of vasoactive neuropeptides that sensitize neurons in the brain stem trigeminal nuclei and increase the pain response. The clinical effectiveness of 5-HT serotonergic agonists (triptan anti-migraine agents) is related to vasoconstriction, and inhibition of nociceptive transmission in peripheral nerve terminals in the meninges and in central terminals in brain stem sensory nuclei. (Hargreaves RJ, Shepheard SL. Pathophysiology of migraine - new insights. Can J Neurol Sci 1999;26:Suppl 3-S12-S19).

**Biology of Serotonin Receptors.** Serotonin receptors are highly heterogeneous (5-HT,1-7), and specific subtypes are associated with the pathogenesis or treatment of migraine headache. Availability of subtype selective 5-HT receptor agonists allow further proof of the neural/vascular hypothesis for migraine. (Hamel E. Can J Neurol Sci 1999;26:Suppl 3-S2-S6).

**Genetic basis of migraine.** Migraine etiology is multifactorial and genetically complex, with aggregation in families due to environmental and genetic tendencies. Familial hemiplegic migraine (FHM) is autosomal dominant, with 50% of families linked to chromosome 19p13 and mutations in a calcium channel alpha 1A subunit. FHM represents a CNS channelopathy. Migraine with or without aura may also be linked to chromosome 19p, or to Xq28 locus. (Gardner K. Can J Neurol Sci 1999;26:Suppl 3-S37-S43).

**Migraine prophylactic drug therapy.** The scientific evidence based on randomized double-blind, placebo controlled trials, rates migraine prophylactics in the following order of efficacy: metoprolol has an average score of 4.3 (maximum 5); divalproex 3.8; amitriptyline 2.3; atenolol 2.3; flunarazine 2.2; and propranolol 1.4. The placebo response varies from a 32% reduction in migraine frequency to a 7% increase in frequency in various trials. Migraine prophylaxis is largely disappointing, a minority having significant benefits that make the risk of adverse effects worthwhile. Other newer antimigraine agents include the antiepileptics, gabapentin and topiramate, and riboflavin. A combination of an antidepressant and a B-blocker may act synergistically, but monotherapy is often preferred. (Becker WJ. Evidence based migraine prophylactic drug therapy. Can J Neurol Sci 1999;26:Suppl 3-S27-S32).

COMMENT. This journal supplement provides an excellent review of the scientific advances in migraine mechanism and management. One paper also emphasizes the role of psychological treatments, especially relaxation training and biofeedback, in refractory migraine. The following report might also indicate the influence of psychological factors on the frequency of migraine attacks.

**Pulsing electromagnetic fields (PEMF) in treatment.** This novel therapy was studied by double-blind, placebo-controlled trial in 42 adults at the Orthopedic Surgery Service, Madigan Army Medical Center, Tacoma, WA (Sherman RA, et al. Headache Sept 1999;39:567-575). Exposure of the inner thighs to PEMFs for at least 3 weeks was considered an effective, short-term prophylactic treatment for migraine, but not in patients with tension headaches.

**Increased incidence of migraine headache** in female subjects of all ages is reported from the Mayo Clinic, following a study in Olmsted County, Rochester, MN, comparing the 1979-1981 period and 1989-1990. The peak incidence at age 20-29 years increased from 634 new cases per 100,000 person-years to 986 in a decade. (Rozen TD et al. Neurology Oct 1999;53:1468-1473).

**Increased brain serotonin synthesis in migraine** was demonstrated using PET in 11 women patients in comparison to 8 healthy controls. The results are consistent with reports of systemic alteration of serotonin metabolism in patients with migraine without aura. (Chugani DC et al. Neurology Oct 1999;53:1473-1479).

## SEIZURE DISORDERS

### VITAMIN B12 DEFICIENCY AND INFANTILE CONVULSIONS

The association of vitamin B12 deficiency and benign familial infantile convulsions (BFIC) is reported in one 4-month-old boy admitted to the University Hospital, Lund, Sweden, and in an additional 4 of 14 infants with BFIC who were found to have homocysteinuria or methylmalonic aciduria. The 4-mo-old presented with generalized tonic-clonic convulsions, partially responsive to vigabatrin. CT and initial EEGs were normal, and an ictal recording showed epileptiform activity over the left frontal region. Laboratory investigations were normal except for absent plasma cobalamin levels (<75 pmol/l), elevated plasma homocysteine (16.5 mcmol/l; N 5.3-11.0) and methylmalonic acid (0.88 mcmol/l; N<0.42), consistent with a diagnosis of vitamin B12 deficiency. The mother had anemia treated with intramuscular ferritin-sorbitol during the pregnancy. The infant received oral vitamin B12, 0.5 mg every 3 d, and seizures were controlled, except for a convulsion with fever. Treatment was discontinued at 7-12 months when laboratory tests were normal, and at 1.5 year follow-up, seizures had not recurred and development was normal. (Lundgren J, Blennow G. Vitamin B12 deficiency may cause benign familial infantile convulsions: a case report. Acta Paediatr Oct 1999;88:1158-1160). (Respond: Dr J Lundgren, Department of POediatrics, University Hospital, S-221 85 Lund, Sweden).

COMMENT. Infants of vegetarian mothers or those suffering from pernicious anemia may develop vitamin B12 deficiency in early infancy, leading to convulsions in susceptible infants. In the present case-report, the cause of the vitamin B12 deficiency is undetermined, but a genetic error in B12 metabolism cannot be excluded. The familial incidence of benign familial infantile convulsions (BFIC) indicates a genetic etiology, with linkage analysis mapped to chromosome 19. Environmental influences involving vitamin B12 metabolism in the mother and deficiency in the infant are also causative.

Infants with seizures in the first year of life should be examined for homocysteine and methylmalonic acid elevations in the plasma and a transient vitamin B12 deficiency, responsive to vitamin supplementation. Vitamin B12 is a