blood flow and release of norepinephrine from sympathetic nerve cells. (Martin VT, et al. Med Clin North Am 2001 Jul;85(4):911-41). Alternatively, a chocolate trigger may be explained by a premonitory food craving; and chocolate is consumed because of a response to a migraine attack and not a cause. Also, an urge to exercise may represent a premonitory symptom of migraine. The classic advice to avoid suspect triggers may be incorrect, and the migraineur should instead, be advised to become habituated to the provocative factor. (Martin PR. Managing headache triggers: think ‘coping’ not ‘avoidance.’ Cephalalgia 2010 May;30(5):634-7). Indeed, some adult patients advised to avoid chocolate and red wine would rather suffer an occasional migraine.

DEMYELINATING DISORDERS

LONG-TERM OUTCOME OF PEDIATRIC-ONSET MS

Researchers at University Hospital of Wales, Cardiff; and University of Bristol, UK studied the clinical features and disability in pediatric-onset multiple sclerosis (POMS) in a population-based cohort with long-term follow-up, and compared to a cohort of patients with adult-onset (AOMS) disease. Of 2068 patients identified with MS since 1985, 111 (5.4%) had POMS and in 110, disease onset was relapsing. Age of onset ranged from 4 to 17 years (mean, 15 years). Initial most frequent manifestations were motor in 52.8% and optic neuritis in 26.4%. No significant differences in sex ratio, familial recurrence, relapse rate, ethnicity or clinical symptoms at presentation were identified between POMS and AOMS. Compared to AOMS, POMS cases had a longer interval to second relapse (5 vs 2.6 years, p=0.04), less common primary progressive disease (0.9% vs 8.5%, p=0.003), longer time to develop secondary progressive disease (32 vs 18 years, p=0.0001), and longer to reach disability milestones (p<0.0001). Incomplete recovery from initial event was significantly associated with a shorter time to reach disability milestones (p=0.01). Patients with POMS become disabled at a younger age and have a poorer age-related prognosis than AOMS cases. (Harding KE, Liang K, Cossburn MD, et al. Long-term outcome of paediatric-onset multiple sclerosis: a population-based study. J Neurol Neurosurg Psychiatry 2013 Feb;84(2):141-7). (Respond: Professor Neil C Robertson, Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, University Hospital of Wales, Heath Park, Cardiff, CF14 4XN, UK. E-mail: robertsonnp@cardiff.ac.uk).

COMMENT. While prognosis of POMS appears more benign than that of AOMS in early disease, later stages of the disease are similar to AOMS and lead to an earlier disability.

FIBRONECTIN AGGREGATION AND REMYELINATION IN MS

Researchers at Universities of Groningen and Amsterdam, The Netherlands, and Universities of Cambridge and Edinburgh, UK examined the expression of the extracellular matrix molecule fibronectin on demyelinating injury and how this affects remyelination by oligodendrocytes progenitors. In lesions undergoing remyelination, fibronectin expression was transiently increased in demyelinated areas and declined as remyelination proceeded. In chronically demyelinated MS lesions, fibronectin expression
persisted as aggregates, resistant to degradation. Fibronectin aggregates within MS lesions contribute to failure of remyelination and are potential therapeutic targets for promoting remyelination. (Stoffels JMJ, de Jonge JC, Stancic M, et al. Fibronectin aggregation in multiple sclerosis lesions impairs remyelination. *Brain* 2013 Jan;136(Pt 1):116-31) (Response: Dr Wia Baron. E-mail: w.baron@umcg.nl).

**CHILDHOOD OBESITY AND RISK OF PEDIATRIC MS**

Researchers at Kaiser Permanente of Southern California studied a possible relation between childhood obesity and pediatric-onset multiple sclerosis (MS) or its potential precursor, clinically isolated syndrome (CIS), which encompasses optic neuritis (ON) and transverse myelitis (TM). Seventy-five newly diagnosed pediatric cases of MS or CIS were identified between 2004 and 2010; 41 (55%) were girls, and 54 (72%) were age 11-18. Onset of MS/CIS was uncommon at ages 2-11 years. Thirty-eight (50.7%) children or adolescents with MS/CIS were overweight or obese. Obesity was associated with a significantly increased risk of MS/CIS in girls but not in boys. Moderately and extremely obese patients were more likely to present with TM compared with normal/overweight children (p=0.003). (Langer-Gould A, Brara SM, Beaber BE, Loebnick C. Childhood obesity and risk of pediatric multiple sclerosis and clinically isolated syndrome. *Neurology* 2013 Feb 5;80(6):548-52). (Response: Dr Langer-Gould. E-mail: Annette.M.Langer-Gould@kp.org).

**COMMENT.** Childhood obesity is independently associated with an increased risk of pediatric-onset MS/CIS in girls but not in boys. The authors speculate that the rapid rise and high estrogenic exposure of obese, peripubescent girls coupled with inflammatory mediators released by adipose tissue accelerate MS/CIS onset in adolescence. Pregnancy in females and tobacco smoke among males (Palacios N, et al. *Ann Epidemiol* 2011 Jul;21(7):536-42), additional potential risk factors for MS, were not addressed in this study. The need to further address the progress of the childhood obesity epidemic is stressed, especially in girls.

**PERINATAL DISORDERS**

**MELATONIN AND EXPERIMENTAL PERINATAL ASPHYXIA**

Researchers from University College London, Hopital Robert Debre, and Universite Paris Diderot, Paris assessed the neuroprotective effects of melatonin combined with therapeutic hypothermia after transient hypoxia-ischemia in a piglet model of perinatal asphyxia. Melatonin administered intravenously 10 min after transient hypoxia-ischemia and repeated at 24 hr augments hypothermic neuroprotection based on improved cerebral energy metabolism, using magnetic resonance spectroscopy biomarkers and continuous EEG monitoring. The piglet model of H-I resembles the clinical setting in a neonatal intensive care unit. The observed benefits and safety profile of melatonin support consideration of phase I and II clinical studies of melatonin-augmented therapeutic hypothermia for neonatal encephalopathy. (Robertson NJ,