Cholinesterase inhibitors are not beneficial in the treatment of mild cognitive impairment

Mild cognitive impairment (MCI) is a transitional condition between cognitive decline related to normal aging and dementia. Several clinical trials, some of which remain unpublished, have attempted to determine whether treatment with cholinesterase inhibitors (ChEIs) can slow or prevent the conversion of MCI to Alzheimer's disease (AD). To provide clinicians with a better risk–benefit profile for ChEIs in MCI treatment, Raschetti *et al.* have conducted a systematic review of published and unpublished randomized, controlled, trials of donepezil, galantamine, and rivastigmine, all of which are currently approved for the symptomatic treatment of mild to moderate AD.

A search of four electronic databases (MEDLINE, EMBASE, Cochrane, PsycINFO) and three registers (the Cochrane Collaboration Trial Register, Current Controlled Trials, and ClinicalTrials.gov) revealed three published and five unpublished trials that met the inclusion criteria. Although the study populations and trial durations were not homogenous, analysis showed that none of the ChEIs had any significant impact on the development of AD in patients with MCI.

Of concern to the authors was the high rate of adverse events reported in several trials, indicating that ChEIs not only confer little benefit but could actually be harmful to some patients with MCI. The authors conclude that the claims made by some of the trial investigators could not be justified by their data, and they question the scientific validity of the findings.

Original article Raschetti R *et al.* (2007) Cholinesterase inhibitors in mild cognitive impairment: a systematic review of randomised trials. *PLoS Med* **4:** e338

Ketogenic diet decreases pediatric seizure frequency within 2 months

The ketogenic diet (KD) is a high-fat, low-protein and low-carbohydrate diet that can be implemented as a treatment for children with intractable epilepsy. Currently, there is a lack of published data regarding both the length of time required to achieve seizure improvement in children who are on the KD and the time after which improvement is unlikely to occur.

To address these issues, Kossoff *et al.* performed a retrospective chart review of children with intractable epilepsy ($n = 118$, age range 0.3–15 years) who were started on the KD at two US hospitals between November 2003 and December 2006. In total, 99 (84%) children showed seizure improvement while on the KD. Of these, 75% responded within 14 days of diet initiation, 90% within 23 days, and all within 65 days. In this study, if seizure improvement did not occur by 65 days, it did not happen at all. Of the children who did show seizure improvement, 76% either maintained or continued to improve upon the initial level of seizure reduction over 6 months. Notably, in the subset of children who responded to the KD, initial improvement was much quicker in those who fasted for 1–2 days before initiation of the diet than in those who did not (median 5 versus 14 days), although fasting did not affect seizure reduction in the long term.

The authors conclude that the KD usually works very quickly, and even more rapidly if started after a fasting period. Conversely, if seizure frequency in children does not improve within 2 months of initiation of the KD diet, this therapy is unlikely to be effective and other treatments should be considered.

Original article Kossoff EH *et al.* (2007) When do seizures usually improve with the ketogenic diet? *Epilepsia* **49:** 329–333

Optical coherence tomography could quantify subclinical axonal loss in multiple sclerosis

Optical coherence tomography (OCT), a fast, noninvasive technique already used to measure retinal nerve fiber layer (RNFL) thickness and macular volume in glaucoma, is now being used to measure axonal damage and neuronal loss in patients with multiple sclerosis (MS). In a recently published paper, Pulicken *et al.* report that OCT can detect subclinical retinal changes, and they provide evidence for a relationship between RNFL thickness, macular volume and disease phenotype in MS.

Consistent with previous reports, the authors found that RNFL thickness was significantly decreased in patients with MS ($n = 326$) compared with healthy controls ($n = 94$; 92.7 μm