

GLOSSARY

CHRONIC DAILY HEADACHE (CDH) PATIENTS

Defined as daily headache sufferers who had been taking ≥ 1 analgesic/day for ≥ 1 year and who were classified as over-users

molecules), and determined which particles were the most active in relation to PrP content.

It was found that the most infectious units per mass of PrP were ~ 17 – 27 nm particles of ~ 300 – 600 kDa. Based on the assumption that the infectious particles were composed of PrP molecules of an average ~ 21.5 kDa each, this corresponded to oligomers comprising 14–28 PrP molecules.

Silveira *et al.* conclude that smaller subfibrillar particles have greater infectivity and converting activity than larger amyloid fibrils or plaques. This finding raises concerns that incomplete attempts to destabilize PrP^{Pres} aggregates for therapeutic reasons, or as a method of decontamination, could result in increased rather than reduced infectivity.

Christine Kyme

Original article Silveira JR *et al.* (2005) The most infectious prion protein particles. *Nature* 437: 257–261

Systematic review of trials for cholinesterase inhibitors

A systematic review of 22 clinical trials involving cholinesterase inhibitors for the treatment of Alzheimer's disease was recently conducted in Germany by Kaduszkiewicz and colleagues. Their findings indicate that current recommendations for the use of such drugs are not supported by the evidence.

The authors used MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews to identify randomized, double-blind, placebo-controlled trials that assessed the clinical efficacy of donepezil, rivastigmine or galantamine in terms of outcome in patients with Alzheimer's disease. Three researchers independently assessed each study for methodological quality using a pre-determined checklist of criteria, then discussed their findings to achieve joint assessments.

Although 19 of the 22 trials reported significant (though moderate) differences between the treatment groups and placebo, the authors found a number of methodological flaws in the trial designs. Trials commonly used several primary endpoints with no correction for multiple comparisons. Consequently, it was found that after correction for multiplicity, two of the five trials on rivastigmine did not show a significant benefit in terms of their primary endpoints. When trials used the last-observation-carried-forward

method for endpoint analyses, at least eight had included data from dropouts, which might have influenced the endpoint analysis.

The authors suggest that because of poor methodology and limited clinical benefits reported by trials, the scientific basis for the current recommendations on the use of cholinesterase inhibitors in Alzheimer's disease is open to question.

Christine Kyme

Original article Kaduszkiewicz H *et al.* (2005) Cholinesterase inhibitors for patients with Alzheimer's disease: systematic review of randomised clinical trials. *BMJ* 331: 321–327

Over-use of analgesics in chronic daily headache

A group of Italian researchers has reported that the dependence of patients with CHRONIC DAILY HEADACHE (CDH) PATIENTS on analgesics is similar to that of addicts on drugs of abuse. In the light of earlier evidence that over-use of analgesics can increase the frequency of headaches, this is a cause for concern.

During 2002 and 2003, Ferrari *et al.* recruited 122 consecutive CDH patients, 71 consecutive patients with episodic headache who occasionally took analgesics, and 115 consecutive substance-dependent drug addicts into their study. Evaluation using the Leeds Dependence Questionnaire (LDQ) showed CDH patients to be marginally more substance-dependent than drug addicts. They reported a greater need to take the drug each day and a reduced ability to cope without it, but scored much less than the addicts regarding compulsion to use the drug. The CDH and episodic groups both stated that the type of analgesic was less important than its effect, which strongly conflicted with the addicts' view of their drugs. Although the episodic group scored least for nearly all items, their total LDQ score was still greater than that reported elsewhere for non-substance-dependent subjects. Their response pattern was similar to the CDH group.

Despite this apparent dependency on analgesics, CDH patients differ from drug addicts in that their need is controlled by pain, not the drug. The authors have some concerns that the testing environment might have influenced results, but support the use of the LDQ in the clinical evaluation of headache patients,