CARPHOLOGY by A Fo Ben

Pract Neurol 2010; 10: 124

Fatigue study out of control

You may have woken to the *Today Programme* on BBC Radio 4 reporting that another virus had been identified in a large proportion of patients with chronic fatigue syndrome—human gammaretrovirus, XMRV. But you were less likely to have looked at the paper, which compared affected patients with a control group. This study broke just about every rule in observational epidemiology; the control group was not described, the patients were highly selected, not all cases and controls were tested for the virus, the case or control status was known to the laboratory, possible confounding was neither discussed nor allowed for, and we don't know whether the laboratory studies were done in exactly the same way or at about the same time. A perfect example for an introductory course in epidemiology.

Science DOI: 10.1126/science.1179052

Combining treatment forces... for lymphoma

Primary CNS lymphoma has a notoriously poor prognosis. Most respond initially to radiotherapy but relapse is almost inevitable. High dose methotrexate followed by high dose radiotherapy has become the current standard, but with only 20–35% 5 year survival. The place of corticosteroids remains uncertain. A recent multicentre randomised controlled trial (79 patients) showed that high dose cytarabine combined with methotrexate gave complete remission in 46% (CI 31% to 61%) compared with 18% (6% to 30%) on methotrexate alone (p=0.006). Three year survival was 45% for the combination and 32% for methotrexate alone. CNS lymphoma remains enigmatic and challenging, and still with a grave prognosis, but these results give encouragement and a stimulus for further trials.

Lancet 2009;**374**:1512–20.

...and for pain

We urgently need improved treatments for chronic pain. A randomised double blind crossover study of 56 people with neuropathic pain (diabetic neuropathy and postherpetic neuralgia) found the combination of nortriptyline with gabapentin gave significantly more relief of pain intensity and pain related sleep disturbance than either used alone (mean pain score of combination compared with gabapentin −0.9 (95% CI −1.4 to −0.3, p=0.001), and to nortriptyline −0.6 (95% CI −1.1 to −0.1, p=0.02)). We might therefore recommend this combination to patients partially responsive to either drug, and who seek additional relief.

Lancet 2009;**374**:1252–61.

Migraine stroke

Clinical experience tells us that migraine increases stroke risk although the absolute risk remains low. A recent migraine meta-analysis (25 studies) found a significantly increased relative risk of ischaemic stroke but only in those with aura: 2.16 (95% CI 1.53 to 3.03) with aura compared with 1.73 (0.90 to 1.69) without aura. Women had almost double the risk of men; other factors were age <45 years, smoking and oral contraceptive use. Migraine did not influence the risks of myocardial infarction or cardiovascular death. The authors recommend that young women with migraine with aura, in particular, should be strongly advised to stop smoking, and to consider birth control methods other than oestrogen containing oral contraceptives. Migraine's trickiest question, should we identify and close a patent foramen ovale, remains unanswered.

BMJ 2009;**339**:b3914.

If we can't trust Big Pharma, who can we trust?

Changing a trial's primary outcome after getting the results is, at best, a shifting of the goalposts. However, sometimes study coordinators or sponsors cannot resist meddling with the protocol when intended results are not forthcoming. Of 20 off-licence trials for gabapentin, 12 were published: two-thirds had different primary outcomes in print than in the original protocol. Five of the eight studies showing statistically significant differences favouring gabapentin had had their primary outcomes changed. So, if that makes you question what you read, consider also what you cannot read: 6 of the 21 (29%) primary outcomes were not even reported.

N Engl J Med 2009;**361**:1963–71.

Cannibal polymorphs

Kuru is the prion spongiform encephalopathy endemic to Papua New Guinea and is spread primarily through cannibalisation. This cultural habit was localised to certain geographical highland regions, affecting predominantly women and children, but why did it spare some indigenous people? A study collected 3000 genetic samples, including 709 who had participated in tribal cannibalistic mortuary feasts; 152 later dying of kuru. A novel 127V prion protein gene polymorphism was absent from all who had succumbed to the disease but present exclusively in survivors from areas where kuru and cannibalism were endemic. This is some consolation to those of us fearing a Creutzfeldt–Jakob disease pandemic: in time the human race adapts and survives.

N Engl J Med 2009;**361**:2056–65.

A Fo Ben is always on the lookout for suitable carphology titbits, and comments on what has been included. Email the editor-in-chief if you come across one.