entitled "The safety and efficacy of clozapine in severe treatment–resistant schizophrenic patients in the UK"?

Firstly, their 54 "treatment-resistant" patients were not so treatment-resistant. They had had on average five past schizophrenic episodes, which means they had five times previously got better, to a greater or lesser extent, in response to treatment or without it. Furthermore, a number of unspecified patients were responding to pre-existing medication. Some were so "partially controlled" that it could only be gradually withdrawn and replaced by clozapine, and a few were "permitted" to stay on it and receive clozapine "in parallel" throughout the trial.

Then, the therapeutic results were, to say no more, unimpressive. Over half the cases (28) were outright failures and did not complete the six-month course: one because of suicide; 15 (28%) because they were "uncooperative" or "violated the protocol", which implied they remained too ill to accept clozapine, or retained enough sanity to refuse it; four because "the study drug was ineffective"; and seven (13%) because of adverse reactions.

In ordinary language, these *are* outright failures, even though the authors prefer to gloss over them as "early terminations". Of the remaining 26 cases, 19 were still, after six months, "moderately" or "markedly" or "severely" ill, and only 7 (12% of the whole series) had become "borderline or mildly ill". And of these 26, epileptic seizures developed in five.

Undaunted, the Study Group concludes that these results are "highly encouraging." They even contend, and this after only six months' observation, that their results "clearly show" that clozapine can have *long-term* benefits for these patients! Were that true, or even plausible, it would have made headlines long ago, since clozapine has been in use for 30 years (McKenna & Bailey, *BJP*, January 1993, **162,** 32–37).

They should re-examine the forgotten story of insulin coma therapy in schizophrenia (Bourne, 1953; Cramond, 1987). It too was a breakthrough, it too was dangerous as well as extremely costly and, in its heyday of universal use, it produced results far superior to these. And yet, in the end, it was an illusion.

BOURNE, H. (1953) The insulin myth. *Lancet*, **2**, 964.
CRAMOND, W. A. (1987) Lessons from the insulin story in psychiatry. *Australian and New Zealand Journal of Psychiatry*, **21**, 320.

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**Alzheimer's disease and Lewy body dementia**

SIR: In reference to our study (Förstl *et al*, *BJP*, March 1993, **162,** 385–392) Liberini *et al* (*BJP*, November 1993, **163,** 693–694) raise the possibility that responders to cholinesterase inhibitors, and in particular to tacrine, may turn out to show Lewy body pathology. They suggest that the solution to this might come from a post-mortem examination of responders.

As our own tacrine trial was the first to identify the presence of a subgroup of responders, constituting about one-third of those entering the study (Eagger *et al*, 1991), we have, where possible, attempted to carry out such a post-mortem follow-up. Since only a proportion of all patients maintained contact with our unit in order to obtain continued supplies of tacrine after the cessation of the trial, the sample under such study is liable to be biased. However, it is worth reporting that the first three brains studied, all from 'responders', did indeed show a considerable number of cortical Lewy bodies in addition to numerous plaques, tangles and β-amyloid deposits. Where it proved possible to obtain frozen tissue from the brains (in two out of the three cases) cholinacetyltransferase levels measured in Dr Elaine Perry's laboratory were found to be even lower than those in pure Alzheimer's disease.

Thus, although it is too early to reach a definite conclusion on the limited number of post-mortems carried out so far, preliminary results suggest that Liberini *et al*'s prediction may well turn out to be correct.

EAGGER, S., LEVY, R. & SAHAKIAN, B. (1991) Tacrine in Alzheimer's disease. *Lancet*, **337**, 989–992.

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**Anorexic siblings**

SIR: It is generally agreed that anorexia nervosa has a multi-determined aetiology (Garfinkel & Garner, 1982) and intrafamilial factors are rightly regarded as of particular importance (Hsu, 1990). Close attention is usually paid to the relationship between the sufferer and his/her parents (for example, see Bruch, 1988). I suspect, admittedly on anecdotal grounds, that the effects of siblings on each other may also be of importance, and recent considerable media publicity surrounding the 'diet twins' (for example, *Sunday Mirror*, 19 September 1993, p. 24: "Story all