which has many similarities. It was hailed as a dramatic breakthrough in immunosuppression, is expensive, was greeted with scepticism, and has life-threatening side-effects (interstitial fibrosis) which require close supervision. Despite this it has gained universal acceptance and has made transplantation more widely available and has improved survival. No one begrudges its cost. Another possible useful comparison could be made with warfarin. This gained universal acceptance by virtue of the fact that it is obviously good. There is not a single clinical trial anywhere on warfarin in the literature. The point here is that Dr Healy chooses to ignore the very valuable anecdotal, but now extensive, clinical experience that clozapine is an improvement on previous treatments. Both academics (Cutting & Reveley, 1991) and clinicians (Launer, 1991) attest to the drug's superiority.

Turning to the Kane *et al* trial, (1988); Dr Healy's *post-hoc* criticism of this excellent piece of work is uncharitable. Firstly, it is not fair to say the patients had 1800 mg of chlorpromazine. This was a flexible-dose-ranging regime, 1800 mg/day being the most any one patient received. Furthermore, doses greater than 1000 mg were only allowable in the second half of the trial, to guard against possible over-treatment. Secondly, the patients were recruited from elsewhere having already fulfilled established criteria for resistance, and then underwent a further trial of resistance with haloperidol. It is not credible to suggest that the patients were systematically worsened by over-treatment at each and every stage of this filter. Thirdly, to pick over the details of whether Dr Kanes' patients were truly resistant or not misses the general point of the exercise. Clozapine is effective across the board in schizophrenia, and the point of its use is really whether there is a subset of particularly disabled patients, for whatever reason (treatment-refractory or neuroleptic-sensitive), in whom the drug may justify the risk of agranulocytosis (with monitoring, of course). The dismissive comparison with insulin-coma treatment is illogical. This is the 'It'll never fly' argument. To condemn something on the basis of past failure smacks of intellectual nihilism, implicitly suggesting all research endeavours are a waste of time.

In my opinion, Dr Healy is one of the UK's leading psychopharmacologists and he has valuably adopted a reasonable posture as a buffer to the evangelising about clozapine. My own stance would be that the early clinical-trial data is unequivocal, the Kane *et al* trial is indisputable, and the clinical impression of clozapine from its now numerous users are unambiguously impressive.

There have been a number of these exercises cautioning the use of clozapine (see also *Lancet* (1992)) and it invokes a hazy recollection of a Guinness commercial in the 1960s ... something about not liking it, but never having tried it!

CUTTING, J. & REVELEY, A. M. (1991) Expert opinion: clozapine. *Psychiatric Bulletin*, **15**, 617.

KANE, J., HONIGFELD, G., SINGER, J., *et al* (1988) Clozapine for the treatment resistant schizophrenic. *Archives of General Psychiatry*, **45**, 789–796.

LANCET (1992) Editorial. *Lancet*, **339**, 276–277.

LAUNER, M. (1991) Experience with clozapine. *Psychiatric Bulletin*, **15**, 223–224.

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Clozapine, cognition, and schizophrenia

SIR: Goldberg *et al* (*Journal*, January 1993, **162**, 43–48) argue that the cognitive deficits of schizophrenia are independent of the psychosis and as such do not respond to clozapine. They go on to postulate that the cognitions may actually deteriorate on clozapine and this may be due to the drug's anticholinergic properties. They subjected the patients to ten neuropsychological tests, some on two occasions, and used the Brief Psychiatric Rating Scale (BPRS) and the Clinical Global Impression scale (CGI) to rate their clinical change.

On the surface this seems totally exhaustive and an important development until we look at the 15 patients more closely. Six patients were on lithium before the clozapine phase and six were on lithium in the clozapine phase: four of these were the same patients continued on lithium so, in all, eight patients had received lithium either before or after clozapine. Of the seven patients who had never received lithium, one patient had received lorazepam and two had received anticonvulsants.

Lithium carbonate is described in the data sheet as being associated with memory impairment during long-term use and there is a theoretical risk of neuroleptic malignant syndrome possibly due to antidopamingeric actions when it is used with clozapine, and so the lack of change in the cognitions is not so simple to explain. In addition, many clinicians feel that benzodiazepines in long-term use may damage cognitive functions and the use of anticonvulsants, if given for epileptiform conditions (we are not told about this in the paper), may indicate long-standing brain damage.

Thus there were only four patients who had not received lithium, lorazepam or anticonvulsants and even they were tested over a range of 3–24 months after starting clozapine. It is acknowledged that 60% of patients take a year to respond to clozapine (Meltzer *et al*, 1989) and it is therefore possible that even these four patients had not had a long enough trial of the drug.

My own experience of lithium and clozapine was one patient who, after the lithium was stopped, went on to pass school examinations and recommence driving. He remains well on clozapine monotherapy after nearly three years.

I would suggest that there is no conclusion to be drawn from this paper, except that it is impossible to 'dissect' the causes of cognitive deficits in polypharmacy patients (taking preparations such as lithium) who may also have brain damage. Clozapine not only improves the psychiatric symptoms but also it has been demonstrated over long-term use (13 years) that 39% of treatment-resistant schizophrenic patients found employment, compared with 3% before the clozapine was started (Lindstrom, 1989).

MELTZER, H. Y., BASTANI, B., KWON, K. Y., *et al* (1989) A prospective study of clozapine in treatment-resistant schizophrenic patients. *Psychopharmacology*, **99**, S68–72.

LINDSTROM, L. H. (1989) A retrospective study on the long-term effect of clozapine in 96 schizophrenic and schizo-affective patients during a 13-year-period. *Psychopharmacology*, **99**, 84–86.

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Mentally ill sex offenders

SIR: We read with interest Craissati & Hodes' article on mentally ill sex offenders (*Journal*, December 1992, **161**, 848–849). We have published a paper concerning a series of patients with schizophrenia who had sexually assaulted young women in direct response to command hallucinations (Jones *et al*, 1992). We would like to stress the importance of careful examination of the mental states of schizophrenic patients who are charged with such offences, and that this needs to be done as soon as possible after the offence. Craissati & Hodes suggest that within their group of patients, the majority having schizophrenia, the offences were primarily driven by feelings of sexual disinhibition; recent work from Canada might suggest an alternative hypothesis.

Rogers *et al* (1990) studied a forensic population which included a group of patients who were found by the research team to exhibit command hallucinations. In 50% of cases the patients had not reported these symptoms, or denied having them, to the original assessment team. Many patients (44%) reported that they frequently responded to hallucinatory commands with unquestioning obedience. We would agree that patients with schizophrenia might commit offences driven indirectly by their psychosis via disinhibition. It is also important to exclude direct effects of their psychosis on offending behaviour via delusions and hallucinations.

It may appear that a patient with schizophrenia has committed a sex offence due to sexual disinhibition. An alternative hypothesis might be that they had command hallucinations at the material time of the offence and this has been missed, or the patients had actively tried to hide these symptoms from the assessment team.

JONES, G. H., HUCKLE, P. L. & TANAGHOW, A. (1992) Command hallucinations, schizophrenia and sexual assaults. *Irish Journal of Psychological Medicine*, **9**, 47–49.

ROGERS, R., GILLIS, J. R., TURNER, R. E., *et al* (1990) The clinical presentation of command hallucinations in a forensic population. *American Journal of Psychiatry*, **147**, 1304–1307.

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Mabi bark tea

SIR: I wish to comment on Drs Hassiotis & Taylor's paper (*Journal*, September 1992, **161**, 404–407). We have published results of our phytochemical studies of mabi bark tea (Seaforth & Mohammed, 1988; Seaforth *et al*, 1992). We have not yet found any "quinoline alkaloids" in mabi bark tea.

Drs Hassiotis & Taylor stated that the subject "C had boiled it (mabi bark) in water along with sugar and nutmeg", and that she was consuming about two-thirds of a pint of the drink daily during the week before admission. Perhaps the nutmeg could have been responsible for the ill-effects of this particular drink.

The literature describes nutmeg/mace (*Myristica fragrans*) as the source of hallucinogenic agents! (see Schultes & Hofmann, 1980; Der Marderosian &