These data put into perspective the often quoted established 'safety' of the tricyclic antidepressants (TCAs), many of which were first available before or in the infancy of regulatory drug monitoring schemes or post-marketing surveillance studies. There are no similar bodies of safety data for most of the TCAs and older antidepressants; their 'established' safety results more from familiarity than hard data.

However, while PEM is an important addition to drug safety monitoring methodology, it cannot assess efficacy. General practitioners were asked to record on the follow-up form sent one year after the initial prescription, a simple question: was the drug effective? Apparently most GPs felt that fluvoxamine was not effective, yet only 38.4% of the sub-group analysed for the reason for stopping treatment recorded lack of efficacy as a factor. This is clearly a discrepant result. A number of reasons for this supposed low efficacy were discussed – all may be relevant, but the most significant is that PEM was not designed to study efficacy.

Efficacy is established in carefully designed and controlled double-blind studies using trained raters and specialised rating scales. Fluvoxamine has consistently been shown to be superior to placebo and to be as effective as other antidepressants (Wilde *et al*, 1993). Efficacy claims based on a PEM study would have been rightly criticised. Inferences regarding lack of efficacy are no more credible.

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Death during alcohol withdrawal

SIR: Circulatory collapse in delirium tremens or death during an alcohol withdrawal seizure are rare, but still occur. Much can be done to prevent this occurring by timely prescribing. Nurses giving sedation for alcohol withdrawal should be alert to the possibility that a dose may be vomited, in which case parenteral benzodiazepines or rectal diazepam may be indicated, particularly in a patient with a history of withdrawal seizures.

The typical ward regime of 6-hourly dosage may mean that a patient who had his last drink 12 hours before admission may go almost 18 hours before receiving his first dose of sedation. The nurse should be instructed to give the first dose at admission in most patients. An 'as required' dose enables the nurse to titrate dosage against symptoms.

Medication can be given while there is still some alcohol in the body, but not to a patient who is still intoxicated and unable to give true consent, and make a contract about the treatment plan. This applies if detoxification is to be carried out as an in-patient or as an out-patient. In out-patients, medication could be issued to the community nurse or relative, to commence when the patient is mentally clear enough to agree not to take alcohol.

There are serious risks in under-medicating individuals severely dependent on alcohol who precipitously cease alcohol intake for whatever reason.

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Glucocorticoids and the genesis of depressive illness

SIR: Dinan's integration of possible secondary neuroendocrine findings in depression supports the central role of glucocorticoids in its pathogenesis (*BJP*, March 1994, **164**, 365–371). The neuroendocrine changes quoted, and others not mentioned, specifically blunted hypoglycaemic response to the insulin stress test and subtle changes in the hypothalamo-pituitary-gonadal axis, are one of many areas of depressive phenomenology which may be secondary to hypercortisolaemia. High levels of exogenous steroids cause high intracellular sodium concentrations and eosinophilia, both of which have long been recognised in depression. Some evidence suggests that the characteristic sleep disturbances which are seen in both depression and Cushing's syndrome may be mediated by glucocorticoids (Shipley *et al*, 1992). A number of independent authors have documented that hypothalamo-pituitary adrenal (HPA) hyperactivity is associated with specific clinical features including psychomotor retardation, weight loss and cognitive decline (Miller & Nelson, 1987). High levels of cortisol have also been closely related to a variety of neuroanatomical changes including hippocampal atrophy which may be an important mechanism of steroid-related psychopathological change (Hauser, 1991).

While these associations only provide circumstantial support for the involvement of glucocorticoids in the pathogenesis of depressive disorders, recent research is more convincing. HPA axis status

tends to be state related in depression and when out of phase with the clinical picture strongly predicts prognosis. As noted by Dinan, cortisol hypersecretion often normalises before clinical recovery and this HPA alteration may be a newly recognised mechanism of action of antidepressant drugs. Correction of the glucocorticoid level may produce reversal of some neuroanatomical, cognitive and depressive features and as a result the role of steroid manipulation in the treatment of affective disorders is being explored.

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SHIPLEY, J. E., SCHTEINGART, D. E., TANDON, R., *et al* (1992) EEG sleep in Cushing's disease and Cushing's syndrome: comparison with patients with major depressive disorder. *Biological Psychiatry*, **32**, 146–155.

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SSRIs to treat sexual dysfunction

SIR: Power-Smith (*BJP*, February 1994, **164**, 249–250) recommended a beneficial role for fluoxetine in the treatment of erectile failure and sexual dysfunction. It was suggested that further investigation of the role of serotonin specific reuptake inhibitors (SSRIs) may usefully add to the understanding of sexual dysfunction as well as being for many a more acceptable form of treatment than existing options. In support, we report a case in which Paroxetine, another SSRI, was prescribed primarily to treat a patient with premature ejaculation with dramatic effect.

F, a 29-year-old married man, was referred with severe premature ejaculation dating from adolescence associated with erectile failure. Treatment from another sexual dysfunction clinic three years previously had been unsuccessful, the couple being unable to adhere to the Masters & Johnson approach prescribed at the time. Following his re-referral, the patient, as well as his wife, were negative about attempting the sensate focus programme in view of their previous failure. Considerable marital difficulties had intervened to compound the sexual dysfunction since the initial referral and the high level of frustration, anger and resentment was considered to be a serious obstacle to a behavioural approach. It was therefore decided to commence the patient on 20 mg paroxetine daily in view of its known effect in retarding ejaculation as well as its low frequency of other side-effects. At the follow-up appointment four weeks later, a dramatic improvement was noted in the patient's symptoms, with both partners expressing their delight at the result associated with a significant improvement in their relationship.

Power-Smith's report describes two elderly patients, both of whom had been initially commenced on fluoxetine for its antidepressant effect. The secondary benefit of retarded ejaculation for these patients was only appreciated following its discontinuation. In our experience, paroxetine maintains this benefit, despite a shorter half-life than fluoxetine, if prescribed on alternate days.

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