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Toxicity of antidepressants

SIR: Beaumont (*Journal*, April 1989, **154**, 454–458) has contributed in an imaginative way to the debate concerning the prescription of antidepressant medication. The principal issue reviewed in his article is that of toxicity in overdose.

A number of authors have addressed the issue of calculating the relative risk of fatal poisoning associated with antidepressants, notably Leonard (1986) and Cassidy & Henry (1987). While there is no definitive way of arriving at a calculation which will precisely predict the pattern of fatalities following overdosage with antidepressant agents (since the necessary data is unavailable), these authors provide a 'fatal toxicity index' which attempts to predict the number of deaths per million prescriptions of each drug.

The results are striking, and perhaps can be illustrated even more clearly by the extrapolations below. The total number of prescriptions for antidepressant medications in 1987, in the UK, was around 7 009 000 (Pers. Comm., ICI Pharmaceuticals). We can therefore use Cassidy & Henry's formula to predict that if only a single antidepressant agent were to be administered throughout the UK, we could expect the following consequences: exclusive use of dothiepin would result in 350 deaths per annum; amitriptyline, 326; and doxepin, 219. In contrast, use of the 'newer' antidepressants would compare as follows: trazodone, 95 deaths per annum; and lofepramine, 0. Since the body of evidence available would suggest little difference in efficacy between the spectrum of antidepressant agents, the justification for using the older, more toxic antidepressants seems tenuous. Additionally, the newer compounds have superior adverse effect profiles.

In the light of current political developments, we are likely to be subjected to progressively greater pressure to 'rationalise' our prescribing habits. Our fear is that this will involve the production of Regional Health Board and hospital formularies which will attempt to restrict our antidepressant prescribing to that of the cheapest products available. Already, in the Grampian area, we are being urged to use amitriptyline, imipramine, and doxepin.

We agree that there seems little need to use other than a small fraction of the antidepressant medications available to us. However, we suggest that restricting our clinical freedom to the use of lofepramine, trazodone, one of the serotonin re-uptake blockers, and a single MAOI (for example phenelzine) might substantially reduce the 'human cost' of our prescribing.

We are faced with balancing financial considerations against those of fatality in overdose. Since doctors are generally poor at predicting suicide attempts (Barraclough *et al*, 1974), it is currently inevitable that our patients will continue to kill themselves with the tools which we supply. Which is the greater cost?

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Toxicity of hospital water?

SIR: We have recently reported (King & Birch, 1989) that toxic concentrations of heavy metals in drinking water may occur at Victorian mental hospitals with independent water supplies. The problem is compounded by compulsive water drinking among chronically psychotic patients, which is often difficult to detect and is probably under-diagnosed (Noonan & Ananth, 1977; Lee *et al*, 1989). Heavy metal neurotoxicity masquerading as psychiatric illness seems a real possibility in some of our institutions, especially where maintenance has been neglected.

We are unsure how widespread such hazards are in practice, and should be interested in hearing from anyone working in older hospitals where discoloured water may indicate corroded pipework.

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Phobia and childhood parental loss

SIR: The recent report by Tweed *et al* (*Journal*, June 1989, **154**, 823–828) that agoraphobia with panic attacks and, to a lesser extent, simple phobia in an adult community sample are associated with parental loss or separation in childhood is an important contribution to our understanding of the aetiology of phobic disorders. However, certain limitations imposed by their method, particularly as they affect the interpretation of the negative results, should be noted.

Any interview procedure that screens for categorical cases will inevitably misclassify a proportion of borderline subjects. So long as there is no consistent bias in favour of over or under-diagnosis, this misclassification will not affect the estimation of prevalence rates for a disorder. However, the presence of false positives in the case group will confound the search for factors associated with the disorder in question, and studies of correlates based on unmodified survey data are likely to underestimate the significance of any associations. This problem can be overcome in two ways, either by excluding borderline subjects from studies of correlates (Robins, 1985), or else by verifying the subjects' case/non-case status according to particular rules in a follow-up case-control study. The advantage of the latter strategy is that it allows a more sensitive estimation of the significance of associations, particularly if there is pairwise matching of cases and controls.

The findings of Dr Tweed *et al* have been derived from a simple comparison of screen-positive and screen-negative survey subjects. This probably does not detract from the significance of the association reported between phobic disorders and childhood parental loss; indeed, a more rigorous approach might have demonstrated a stronger link. Where this study may have failed to do justice to the data is with regard to possible associations between childhood parental loss and other disorders such as social phobia and generalised anxiety disorder, and between anxiety disorders and specific maternal or paternal loss.

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Flaubert's complaint

SIR: I was interested to read in a recently published biography of Gustave Flaubert (Lottman, 1989) that he suffered from epilepsy, probably of temporal lobe origin (Gastaut & Gastaut, 1982). The biography also contains ample evidence of Flaubert's compulsive promiscuity and passion for writing, which be described as his "idée fixe". In a letter to one of his many female lovers he remarks, "I write a love letter to write, and not because I love". His great interest in religious matters is well known to any reader of his works, which include *Herodias, La Tentation de Saint Antoine*, and *Legend de Saint Julian Hospitalor*. Of himself he once said, "One must live as a bourgeois and think as a demi-god".

Several authors, including Trimble (1986), have drawn attention to a specific interictal syndrome associated with temporal lobe epilepsy and consisting of disorders of sexual function, hypergraphia, and hyperreligiosity. It seems probable that Flaubert suffered from this syndrome, but unlike many other fellow-sufferers, he was a genius able to turn his own pathology into art.

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The damnation of benzodiazepines

SIR: The paper by Kraupl Taylor (*Journal*, May 1989, **154**, 697–704) is timely. His use of the term 'anxiety illness' applies to most of the multitude suffering from various forms of disabling and often chronic anxiety. A look back to the condition of such patients before benzodiazepines became available about 30 years ago reminds us of the very unsatisfactory medication (e.g. barbiturates and amphetamines) commonly prescribed, not to mention the physical treatments and even psychosurgery resorted to in desperation by those seeking relief from intolerable anxiety. With the benzodiazepines, the improvement for many by way of the relief of symptoms was impressive. They were able to live "tolerable and reasonably normal lives, taking fairly full advantage of their abilities". Many were able to go out alone,