mately 50 for dothiepin and amitriptyline, to less than five for mianserin, and virtually nil for the selective serotonin reuptake inhibitors (SSRIs) and modified tricyclic antidepressants like lofepramine.[7] These figures relate to deaths by suicide and do not account for increased accidents due to cognitive impairment and sedation caused by the tricyclic antidepressants or to the effects of such drugs on cardiac function, which may occur after therapeutic doses.[8] Surely with the widespread use of the tricyclic antidepressants by both general practitioners and psychiatrists there should be more concern regarding the use of such drugs particularly now that equally effective and much safer second generation antidepressants such as the SSRIs are widely available. Does this mean that the medical profession only reacts to the threat of litigation in changing its prescribing habits rather than acting proactively to ensure that the efficacy of antidepressant treatment is combined with a better quality of life for the patient due to improved compliance and reduced drug side effects?

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COMMENTARY

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Litigation and the toxicity of psychotropic drugs

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What is striking about Leonard's[6] clarion call to the litigants and the legal profession is that he made similar calls over the last number of years,[4,5] issuing dire predictions of the poor defence a hapless psychiatrist would have in the wake of a completed suicide as a result of an antidepressant overdose, when safer drugs were available. Such a spate of litigation has not followed nor, have the regulatory authorities expressed an interest in the matter. This is simply because a case against a doctor is unlikely to be successful when he or she is acting in accordance with a recognised body of practice within that profession, even though others hold the opposite view, provided of course there is no evidence of overt negligence such as failing to assess current suicidal ideation. Indeed in circumstances where active suicide ideation is present, to only prescribe an antidepressant, even if it were an SSRI, could be deemed negligent if suicide follows since such a patient should be hospitalised.

The comparison between the potential for litigation with fatal overdose of tricyclic antidepressants and benzodiazepines dependence is flawed since the source of the problems with benzodiazepines was their potential to cause dependence even with therapeutic doses. By contrast the problem with tricyclic antidepressants arises when they are taken in excess of the therapeutic dose. Notwithstanding the recognised and much publicised risks with benzodiazepines, the civil suits brought against the manufacturers have, to date, been unsuccessful. Moreover benzodiazepines can themselves be fatal in overdose but litigation for this has never arisen. If, as is claimed, older antidepressants are so dangerous and so toxic, is it not surprising that their prescription has not plummeted in a similar manner to that observed with benzodiazepines?

Whilst Leonard correctly states that the suicide rate among males in the 25-34 year old age group is increasing, it is inaccurate to attribute this increase to antidepressant overdose. For example, in 1992, of the 657 male suicides among the 25-34 age group, 22 (3.3%) died by antidepressant overdose alone.[7] A further inaccuracy is found in his claim that physical methods of suicide are being replaced by the use of poisons. In England and Wales poisoning accounted for 33% of suicides whilst this fell to 22% between 1990 and 1993. Moreover his perspective on the role of antidepressants in suicide is distorted since antidepressant overdose alone accounted for 18% of suicides by poisoning but for only 4% of suicides by any method.[8]

The fatal toxicity index of antidepressants is much cited as evidence for the danger of at least some of the older antidepressants. However, Leonard has failed to point out that a recent study by Jick *et al*[3] has demonstrated that the relative risk of suicide (suicide index) by any method is greater for at least one SSRI than for the tricyclic antidepressants. As this information is in the public domain, is a doctor who prescribed an SSRI for a patient who then dies by, say, hanging, potentially open to litigation also? It is likely that overdose toxicity is not the only link between antidepressants and suicide and undue focus on the overdose potential may detract from full and thorough assessment of suicide risk, irrespective of method.

The cognitive effects of psychotropic drugs and their potential to cause road traffic accidents is recognised. However, the direction of causality has never been established since patients with depressive illness are cognitively

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impaired anyway – only studies of the cognitive effects of antidepressants on already depressed patients would clarify this. Indeed the population attributable risk associated with cognitive impairment is unknown.

The tricyclic antidepressants do indeed have a well known list of side effects at therapeutic doses although some of these can be beneficial, at least in the initial stages of treatment. In particular, the sedative side effects obviate the need for anxiolytics or hypnotics. However, the SSRIs also have side effects and limitations although these are different from the tricyclics and include sexual dysfunction, their preclusion from use in the lactating woman and the serotonin syndrome. Leonard hails the side-effects profile of the SSRIs as an advantage over the older antidepressants leading also to improved compliance in a clinical setting. Indeed studies of drop-out rates from randomised controlled trials confirm that drop-outs due to side effects are higher among the tricyclic than among the SSRI groups.[1] However, when the drop-out rates for specific antidepressants is compared against SSRIs the situation is reversed in favour of the tricyclic.[2] Moreover, there is no evidence that the drop-out rate from a drug trial is a suitable proxy for assuming compliance in a clinical setting.

Modern psychiatrists are fortunate in having access to a variety of antidepressants of which the SSRIs, among others, represent a major development. Given the established benefits derived by the majority of patients from both the TCAs and the SSRIs, and the current state of knowledge, opinion and rhetoric about the relative effects of both classes of drugs on the suicide rate, doctors would be ill-advised to respond to the threat of litigation. Defensive medicine and knee-jerk practice is no substitute for sound clinical judgement.

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The *Uniform requirements for manuscripts submitted to biomedical journals*[1] has two paragraphs on statistical guidelines. These have been explained and elaborated by Bailar and Mosteller.[3]

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