Two prospective measures, the staff rating of appropriateness of admission and Rajotte score, emerged as reliable predictors of violent incidents. What information were the staff using to make their ratings? Admission SCL-90 scores did not in themselves predict aggression but might they be related to the staffs' judgements? Using multiple regression to predict the Rajotte score from specific SCL-90 scales there was a significant effect (0.04). High scores on the Rajotte scale were predicted by low depression scores and by a borderline effect of high hostility scores.

From these results, self-injury would be predicted at admission by low admission Rajotte scores (<28), high SCL-90 depression self-rating and low SCL-90 hostility scores. The likelihood of external assault would be greater in cases where there was a high admission Rajotte score (>46), low SCL-90 depression rating, and high hostility self rating.

In addition, the low v. high 'appropriateness of admission' groups were compared on the general and specific scales of the admission SCL-90. The high appropriateness group had significantly greater scores at admission on the Global Symptom Index, and on the sub-scales for obsessive-compulsive, depression, anxiety, paranoid ideation and psychoticism on admission.

Comment

The subjective approach to psychopathology worked surprisingly well in this disturbed group of patients (80% SCL-90s completed on admission). Along with the non-medical staffs' 'appropriateness of admission' rating and Rajotte scale, these measures could be used to predict subsequent assaults, self-injury and total violent incidents. Future research could concentrate on the apparently primitive subjective mood dimension of hostility/depression, and on the potential value of the perceptions and views of the non-medical members of the multidisciplinary team in psychiatric intensive care.

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A full list of references and statistical data are available on request to Dr Hyde.

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Expert opinion

Antidepressants and murder*

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A 44-year-old man was treated with amitriptyline by his general practitioner for 'mild depression'. Shortly after starting treatment he was said to have become 'beserk'; he hit his wife and a family friend with an iron bar and attempted to sever their heads with a kitchen knife. He was found guilty of manslaughter on the grounds of substantially diminished responsibility and sentenced to life imprisonment.

Following the homicidal behaviour 16 amitriptyline tablets were found to be missing and the assailant's blood concentration of the drug was 'higher than expected' (presumably higher than that expected if he had taken only therapeutic doses). The man appealed against his sentence and an expert medical witness expressed the opinion to the Court of Appeal that the appellant (who had no previous convictions) had experienced a rare side effect of an overdose of amitriptyline and was in a manic state when he carried out the murderous act. His counsel argued that he was no longer a danger to society and should be given his freedom (Dyer, 1991).

As the case is currently *sub judice* further details are not in the public domain and available for comment. It is therefore not possible to offer an opinion on the particular case, but the important theoretical and practical medico-legal aspects that it raises will be discussed.

*Invited opinion on DYER, C. (1991) Murder on antidepressants. *British Medical Journal*, **303**, 331–332.

The most important of these is the possible causal connection between amitriptyline and homicide. To establish such a relationship between a drug and an adverse reaction (i) the reaction should be an authoritatively documented unwanted effect of the drug; (ii) the reaction should not be a manifestation of the illness being treated or of a concurrent disorder; (iii) no other substance that could have caused the reaction should have been taken at the time of the reaction; (iv) there should be a close temporal relationship between the reaction and the administration of the drug, backed up if possible by the demonstration of the parent compound and/or its metabolites in body fluids; (v) the reaction should disappear on discontinuing treatment; and (vi) reappear with a rechallenge test (Edwards, 1981).

In the case under consideration the published information did not indicate that any other substance (including alcohol) that could have caused the homicide was being taken at the time of the offence. Nor was there any mention as to how many days after starting treatment with amitriptyline the homicide occurred, the plasma amitriptyline concentration or the timing of the sample in relation to the act. Violent behaviour did not continue for long following the incident as the assailant was said to have returned to his normal state within days. A rechallenge test was either not considered, not carried out (possibly for ethical reasons) or not reported.

From the information available it is also impossible to say if homicide was a manifestation of the disorder that was treated with amitriptyline or of a concomitant illness. All of the possible causes of homicide, including manic-depressive illness, schizophrenia, an organic psychosis and a personality disorder, would have to be considered. If no alternative explanation for the homicide can be offered the focus of further discussion should be on the possible role of amitriptyline.

Homicide is not an established unwanted effect of this drug, but there have been previous publications suggesting that tricyclic antidepressants induce aggression (Waring, 1977; Rampling, 1978) and, following the appearance of Dyer's report, Sugarman & Hughes (1991) reported a 46-year-old patient with no past history of violent behaviour who assaulted his wife and daughter the day after taking amitriptyline. Each spring the patient (and his mother) had bouts of irritability, overactivity, severe sleep disturbance and 'related symptoms', while at the age of 21 he had an episode consistent with a diagnosis of mild mania. In his most recent bout of psychiatric disorder he developed delusions of infidelity and the belief that his daughter was illegitimate. After taking 75 mg of amitriptyline at night he woke at 4 a.m. with his thoughts racing and he stabbed his daughter with a pair of scissors. He had the urge to gouge his wife's eyes out and he attempted to strangle her. Subsequently he thought that he had killed his family and in hospital he had to be restrained from attacking the nursing staff. The patient was treated with small doses of chlorpromazine and 'settled' in four days.

There are a number of mechanisms by which antidepressants could possibly cause or contribute to hostile and homicidal behaviour. It is thought that they can cause a manic swing or a toxic psychotic reaction; it is also theoretically possible that their anxiolytic-sedative properties can lead to a paradoxical disinhibition as is said to occur during treatment with benzodiazepines.

Tricyclic antidepressants have long been thought to cause a switch from depression to mania, so much so that this is standard teaching and warnings of the possibility are included in drug data sheets. Such swings have been reported with most, if not all, antidepressants but there remains a question mark over the relationship between drug and manic switch. Most studies have been uncontrolled and the criteria for diagnosing a manic reaction were not accurately described in the publications. In a study that was controlled it was found that the rate of induction of mania by tricyclics was not greater than that expected from the natural history of bipolar affective disorder (Lewis & Winokur, 1982). Furthermore, it was shown in a study of patients treated between 1920 and 1981 that the proportion who swung from depression to mania (and vice versa) did not significantly increase after the introduction of antidepressants into clinical practice in the 1950s (Angst, 1987). More recently a comparison of the drug treatment that patients with manic-depressive illness were receiving at the time of switching from depression to mania with the treatment they were having when there was no switch showed that switches occurred regardless of the treatment status (Solomon *et al*, 1990). These studies suggest that mania is more likely to be a spontaneous swing than to be drug-induced.

Manic attacks were reported as lasting varying periods ranging from four to 13 months prior to the introduction of modern treatments and a mean of just over seven and a half weeks since (Coryell & Winokur, 1982). The cases reported by Dyer (1991) and Sugarman & Hughes (1991) remitted within days, suggesting that their abnormal behaviour was not typical of mania. Furthermore mania, although associated with hostility in some patients, very rarely leads to homicidal behaviour.

The second possibility that we have to consider is a drug-induced psychotic reaction. Such reactions were reported within a few years of the introduction of antidepressants into clinical practice (Shader & Dimascio, 1977), but only rarely are they associated with hostile behaviour.

The third mechanism by which hostility could possibly have been mediated is through amitriptyline's anxiolytic-sedative effects. This drug, like other antidepressants, has antianxiety as well as antidepressant properties. Depression and anxiety go hand in hand and it is possible that any anxiolytic effect results from the treatment of associated depression. Alternatively, the antidepressant could have a specific pharmacological effect on anxiety (just as some other psychotropic drugs have been shown to be less specific in their actions than originally assumed). If this is the case amitriptyline could have released hostility by disinhibition as has been alleged during treatment with benzodiazepines. Against this view, however, is a critical review that led to the conclusions that there was little convincing evidence that benzodiazepines caused aggression and that, on the contrary, they assuaged feelings of hostility in most patients (Bond & Lader, 1979). A similar argument can therefore be offered against the suggestion that amitriptyline provokes aggression through its anxiolytic-sedative effect. Any hostility that occurs as part and parcel of a depressive disorder is likely to be ameliorated, rather than exacerbated, by its antidepressant action.

Finally, although we cannot extrapolate from animal experiments because of species differences, there is a considerable body of pharmacological evidence that suggests antidepressants have anti-aggressive effects rather than provoke aggression (Delini-Stula & Vassort, 1979).

The balance of probabilities, as assessed from everyday clinical experience and the studies referred to, suggests that murder does not occur as an adverse reaction to tricyclic antidepressants. There are, however, suggestions in the literature that these drugs may induce aggression on rare occasions, although the mechanism by which this comes about is unclear. In the case under discussion it is impossible to comment further without knowing all the legal and medical facts. It is a matter of public record that at his trial the accused was judged to have had an abnormality of mind such that his responsibility was substantially diminished; whether or not he was unresponsible for his behaviour and thus should be given his liberty are matters that only the Court of Appeal can decide.

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