should be used only to assure patient compliance or to confirm toxicity due to overdose or adverse interaction". The following case is paradigmatic of the reasons why I find the previous statement too restrictive.

Case report. A 51-year-old Caucasian man, suffering from a moderate depressive illness, was referred to the psychiatric day hospital. On admission he had already been on clomipramine orally 150 mg daily for eight weeks with no clinical response, but at the same time no troublesome side-effects. He was otherwise healthy, with no concurrent medical problems and on no other medications.

It was agreed to increase gradually the dose of the antidepressant and after four weeks on clomipramine 250 mg daily, which is the *British National Formulary*'s (*BNF*) higher limit, the mental state was still unchanged and the only side-effect, easily tolerated, was dry mouth.

It was decided to measure the antidepressant plasma level and the result was that the combined plasma levels of clomipramine and its metabolites had reached dangerous toxic levels, 980 ng/ml, against a higher recommended level of 450 ng/ml. As a consequence the medication was discontinued; on examination there were no signs of toxicity and the electrocardiogram (ECG) resulted within normal limits.

In the review by Preskorn *et al* (1989) it is shown how the central nervous system (CNS) and cardiotoxicity are related to plasma levels. On the other hand the plasma levels reached on a certain dose in an individual are completely unpredictable: the rate at which the drug is metabolised varies greatly from person to person, with a single dose giving rise to a greater than tenfold range of plasma levels (Asberg, 1976). In the case just presented a daily dose within *BNF* limits resulted in plasma levels that in the review of Preskorn are considered of major cardiotoxic risk, this without any warning side-effects. If the authors' recommendations had been followed, the plasma level would not have been sought, this with potential serious consequences. For these reasons it is my opinion that the choice to request antidepressant plasma levels should be considered by the clinician any time *BNF* limits are approached and in every case with individual or epidemiological risk factors for cardiovascular system (CVS) or CNS toxicity.

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Sir: In our article we stated that "some adverse effects (e.g. CNS and CVS toxicity) do seem... to be related to plasma levels". While this is true in general, it is also true that individuals differ greatly in their tolerance to the adverse effects of tricyclic and related antidepressants. The case described here, we feel, illustrates this point.

The patient cited was taking a high dose of clomipramine which afforded a high plasma level of clomipramine and its metabolite. The drug was stopped despite there being no signs of toxicity or ECG changes. We feel a more rational approach in patients on high dose tricyclics is simply to perform an ECG (and monitor carefully for other adverse effects). If the ECG is found to be normal then the drug may be continued.

The two approaches described here would have led to two different methods of treatment: discontinuation or continuation of clomipramine. We feel this case illustrates how plasma levels of tricyclics can be misused, provoking clinicians to assume toxicity where there is none. Our experience is that plasma levels much higher than those quoted here are often used safely and therapeutically. We have observed that high plasma levels are not always associated with CNS or CVS toxicity, making plasma level monitoring of limited value.

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Sir: Taylor and Duncan (*Psychiatric Bulletin*, September 1995, **19**, 548–550) are correct in stating that well defined therapeutic levels have only been accepted for a few tricyclics. We feel that their conclusion, that therapeutic drug monitoring is only useful for assessing compliance or confirming toxicity, neglects another major advantage: detection of asymptomatic toxicity.

While tricyclics have many side-effects, some of which can be serious and life-threatening, toxicity may also be present in the absence of clinical symptoms (Preskorn, 1993). There is a marked increase in central nervous system toxicity when levels exceed 300 μg/l (Preskorn & Jerkovich,