Antidepressant blood levels in acute overdose

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Summary
Plasma antidepressant levels and clinical condition were measured sequentially for at least 24 hr in eight patients who presented with acute antidepressant overdosage. There was no evidence to suggest that a knowledge of the drug plasma levels had anything to offer in the management of a patient whose overdose included a tricyclic antidepressant.

Introduction
Tricyclic antidepressants are widely prescribed drugs and feature prominently as agents used in self poisoning. A wide range of complications in overdose have been recognized: cardiac conduction disturbances and arrhythmias; respiratory depression; convulsions; hyperpyrexia and psychosis. Death can also occur (Sedal et al., 1972; Asberg et al., 1971). Interest has recently been aroused in the relationship between plasma levels of antidepressants and the various expressions of their effect. Considerable individual variation in plasma levels of drug have been demonstrated for a fixed oral dose, and plasma levels show a closer correlation with pharmacological action than does oral dose. Debate at present exists as to the precise significance of the plasma drug level related to the therapeutic response, but therapeutic levels of amitriptyline are rarely encountered above 200 ng/ml (Asberg et al., 1971; Braithwaite et al., 1972).

Any possible relationships between the plasma antidepressant levels and the physiological measures made on patients who presented with overdoses were investigated.

Method
Eight patients who had taken tricyclic antidepressant overdoses were studied. Blood was taken on admission and at approximately 6, 12 and 24 hr after. At the same time, a rating form was completed with special reference to severity of disturbances of consciousness. Temperature, pulse rate, ECG abnormalities and any other relevant findings were noted. The plasma was deep frozen and subsequently analysed by gas chromatography (Gifford, Turner and Pare, 1975).

Results
The condition of four patients was critical on general clinical grounds. They required supportive measures and were deeply unconscious for about 18 hr. In four of the eight patients the fall in plasma levels followed that of returning consciousness. In two patients the correlation was poor and in two the clinical condition deteriorated as the plasma drug level fell. There was no correlation between the plasma drug level and the clinical severity of the overdose, ECG changes, variations in temperature, pulse rate change, or anticholinergic side effects on return to consciousness. Ventricular ectopic beats occurred for the first time in a patient at a drug concentration of 320 ng/ml, the level having fallen from 510 ng/ml since admission.

All patients showed a reduction of plasma drug levels within 20 hr but gastric lavage even in the first 3 hr after drug ingestion did not prevent a further rise in plasma drug level. Plasma nortriptyline levels in no case rose above 50 ng/ml.

Conclusion
In half the patients the clinical condition improved as plasma drug level fell. Otherwise there was no correlation between plasma drug levels or their change with any of the parameters measured.

There was, therefore, no evidence to suggest that knowledge of plasma drug levels or sequential levels have anything to offer in the management of a patient whose overdose included a tricyclic antidepressant.

Acknowledgments
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### Table 1. Synopsis of significant findings

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Drugs taken</th>
<th>Gastric lavage</th>
<th>Drug serum level (ng/ml)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>Imipramine + Alcohol + Clordiazepoxide</td>
<td>No</td>
<td>On presentation 190, Maximum 220</td>
<td>Unconscious for 15 hr</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>Amitriptyline</td>
<td>Yes</td>
<td>288, Maximum 740</td>
<td>Clinically mild. Level rose as consciousness improved</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>Amitriptyline + Chlordiazepoxide</td>
<td>No</td>
<td>510, Maximum 510</td>
<td>Despite serum level falling required to be ventilated 20 hr after drug ingestion. Developed ventricular ectopic beats at a serum level of 320 ng/ml</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>Amitriptyline</td>
<td>Yes</td>
<td>300, Maximum 450</td>
<td>Clinically mild</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>Amitriptyline + Nitrazepam + Diazepam</td>
<td>Yes</td>
<td>620, Maximum 620</td>
<td>Clinically mild</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>Amitriptyline</td>
<td>Yes</td>
<td>300, Maximum 410</td>
<td>Clinically mild</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>Imipramine + Diazepam + Alcohol</td>
<td>Yes</td>
<td>580, Maximum 580</td>
<td>Unconscious for 36 hr. Hallucinated on recovery</td>
</tr>
<tr>
<td>8</td>
<td>43</td>
<td>Amitriptyline</td>
<td>Yes</td>
<td>110, Maximum 110</td>
<td>Time of overdose unknown. Clinically severe.</td>
</tr>
</tbody>
</table>

### References


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