A young woman who has taken an overdose of paracetamol (acetaminophen)

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Presenting problem

A 23-year-old lady, who is 34 weeks pregnant with her first child, is seen in the Accident and Emergency department after taking 28 paracetamol (500 mg) tablets 2 hours ago. She is 62 kg in weight. She did not co-ingest any other drug or alcohol. She complains of nausea and intermittent vomiting, but this has been consistent throughout her pregnancy.

What would your differential diagnosis include before examining the patient?

There is no real diagnostic difficulty in this case. The issue of greatest concern is that she has probably ingested 225 mg/kg of paracetamol, i.e. more than 150 mg paracetamol per kg of body weight. Hence she is at risk of developing hepatotoxicity and/or (more rarely) nephrotoxicity. The additional risk is that paracetamol can cross the placenta and this places the baby at risk. The onset of vomiting in this case is too early to be due to paracetamol-induced liver damage if, as she states, the timing of ingestion was only 2 hours ago. Paracetamol overdose per se, as well as pregnancy itself, can cause early-onset vomiting.

Examination

All her clinical observations (heart rate, blood pressure etc.) are within normal limits. She has no renal angle tenderness and no right upper quadrant tenderness. (Such signs might occur if she had taken the overdose at an earlier interval than stated, or in a staggered way, and was beginning to develop signs of renal or hepatic injury, respectively.) Her uterus is of a size that is in keeping with her stated gestation. She has a very low mood and odd affect.

Has examination narrowed down your differential diagnosis?

Examination of the patient reveals no evidence of current hepatotoxicity or nephrotoxicity, in keeping with the patient’s history of recent ingestion of paracetamol. However, if left untreated, she would be expected to develop liver damage from paracetamol within the next 24–36 hours. Her low mood indicates the need to apply the Beck’s depression scale (or to undertake some other form of immediate mood assessment), in order to determine her risk on the ward and the appropriate degree of nursing/psychiatric support. In view of the fact that she is pregnant, she may also have obstetric needs.
Initial investigations

Paracetamol levels are checked 4 hours after ingestion and the concentration plotted on a paracetamol treatment normogram (Fig. 11.1). Prothrombin ratio, liver function tests and venous bicarbonate concentrations are normal (Box 11.1).

Serum paracetamol concentrations should be measured in any patient who admits to taking excess paracetamol, anyone who has ingested white tablets and any patient with unexplained coma. Paracetamol concentrations within 4 hours of ingestion are not interpretable. Prothrombin ratio (PTR) is the most sensitive marker of ensuing liver dysfunction in paracetamol poisoning; it becomes elevated at 18–24 hours after significant ingestion, with ensuing hepatotoxicity. Prothrombin time is checked in this case, because of the need to be certain that ingestion has not taken place earlier than the patient states, i.e. to establish that there is no evidence of liver damage from paracetamol at presentation. Plasma venous bicarbonate is a useful early screening test for metabolic acidosis and can warn of impending liver damage from paracetamol.
How will you treat this patient?
This patient requires a full course (20½ hours) of the antidote for paracetamol poisoning, because her paracetamol level at 4 hours is above the normal treatment line (Fig. 11.1). She is not glutathione-deplete (e.g. due to alcoholism, anorexia or known human immunodeficiency (HIV) disease) or on enzyme-inducing agents (e.g. carbamazepine, phenobarbital, phenytoin or rifampicin) and so the lower, ‘high-risk’ treatment line is not used.

The antidote, intravenous N-acetylcysteine, will protect her liver and kidneys from paracetamol-induced hepatotoxicity. The dose is 150 mg/kg over 15 minutes, then 50 mg/kg over 4 hours and then 100 mg/kg over 16 hours. During infusion of the first two bags of N-acetylcysteine, up to 5% of patients develop an anaphylactoid reaction (flushing and wheezing). Watch out for this, and if it occurs, stop the infusion for at least 30 minutes and give an antihistamine drug. At the end of the infusion the patient needs to be clinically examined for upper quadrant tenderness or renal angle pain; if she is clinically well, however, she does not require further blood tests because N-acetylcysteine given within 10 hours of paracetamol ingestion offers virtually 100% protection from liver/renal injury.

There are, of course, two patients here: mother and fetus. Both paracetamol and N-acetylcysteine cross the placenta, and fortunately the fetus is fully protected by treating the mother with the antidote. Neither N-acetylcysteine nor paracetamol is known to be teratogenic (harmful) to the fetus. The mother will require a treatment for nausea that will not harm the baby — such as cyclizine. She also needs psychiatric evaluation to assess her ongoing suicidal risk. If you are in doubt about the care of a poisoned or potentially poisoned patient, doctors at a poisons information centre are there to help guide you on such issues. Keep a note of the poisons centre number with you.

Global issues
• Paracetamol poisoning is extremely common in the UK but also occurs in other parts of the world; paracetamol is called acetaminophen in the USA.
• Availability of the antidote N-acetylcysteine is not global. Up to 10 hours after an overdose, oral methionine (12 g orally 4-hourly, to a total of four doses) is a suitable alternative antidote for paracetamol poisoning if intravenous N-acetylcysteine is neither available nor affordable.
• The incidence of acute liver failure developing from paracetamol does not appear to be the same in every country. In Australia acute liver failure from paracetamol is rare but in the UK it is much more common; many factors dictate this risk.
• Do not forget the potential of drowsy patients having ingested a paracetamol/opioid combination. Check the paracetamol level in such patients!

<table>
<thead>
<tr>
<th>BOX 11.1</th>
<th>Initial investigations</th>
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</thead>
<tbody>
<tr>
<td>Paracetamol level at 4 hours after ingestion</td>
<td>350 mg/l</td>
</tr>
<tr>
<td>U&amp;Es</td>
<td>Normal</td>
</tr>
<tr>
<td>LFTs</td>
<td>Normal</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma venous bicarbonate</td>
<td>Normal</td>
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</tbody>
</table>

See Chapter 9 of *Davidson’s Principles and Practice of Medicine* (20th edn)