INTRODUCTION
Acute poisoning is a common problem worldwide. In the United Kingdom (UK) it accounts for an estimated 10–20% of acute medical admissions and 5–10% of the workload of Accident and Emergency (A&E) departments.1–4 Episodes of self-poisoning in the UK continue to rise, with the rates being among the highest in Europe.5–7 The severity of poisoning has decreased over the past decade with the introduction of safer drugs, such as the selective serotonin reuptake inhibitors, but the total number of deaths from poisoning in the UK remains unchanged at more than 3,000 per year.2 This paper will address common pitfalls in the management of poisoned patients where clinical management could be improved and medicolegal problems avoided.

SUPPORTIVE CARE
Supportive care is the most important aspect of the management of poisoned patients.8 The majority of patients who present with self-poisoning develop minimal or no clinical effects, and therefore the aim is to identify as early as possible the 5% who will proceed to develop significant clinical features.9 As a general rule, complete elimination of a drug takes approximately the duration of five half-lives of the drug and so the patient needs to be supported during this phase with monitoring for and treatment of any secondary organ dysfunction or other features that develop.8

The management of the airway and breathing in all poisoned patients requires special attention. Failure to ventilate the patient sufficiently early may lead to general deterioration with complications such as pulmonary aspiration.

The mainstay of gut decontamination is the administration of activated charcoal within one hour of a significant ingestion of a toxin that binds to charcoal.10 Recent studies have shown that, in the UK, as few as 15% of patients are seen in hospital in the first hour after self-poisoning and further delays can occur during triage or while waiting in the A&E department.11, 12 It is important that those who have ingested a potentially serious overdose and have presented within one hour are rapidly identified and ‘fast tracked’ for administration of activated charcoal.

Multiple-dose activated charcoal (MDAC) increases the elimination of some drugs by interrupting their entero-enteric and entero-hepatic circulation.13 The dose given is 50 G (1 G/kg in children) of activated charcoal every four hours.13 Indications for MDAC are shown in Table 1.13 In addition to these indications, MDAC should be considered seriously in salicylate poisoning (to prevent delayed absorption) until the salicylate level peaks.8

| TABLE 1 |
| Indications for Multiple-Dose Activated Charcoal,13 |

To increase drug elimination in life-threatening overdose with:
- carbamazepine
- dapsone
- phenobarbitone
- quinine
- theophylline

To prevent delayed absorption in salicylate overdose

Gastric lavage is much less widely used now. Although there have been descriptive case reports of the removal of tablet debris during gastric lavage, no clinical studies have demonstrated that this has any impact on outcome.14 There is also the possibility that lavage may increase absorption by pushing tablets into the small intestine.15 It can also result in hypoxia and tachycardia.14 Gastric lavage should therefore only be considered if it can be carried out within one hour of a life-threatening ingestion and the patient should be monitored closely during the procedure.14

Whole bowel irrigation (WBI) with polyethylene glycol is a newer method of gut decontamination and although the current evidence for its use is based on volunteer studies and case reports, in our experience it is under-utilised in the management of poisoned patients. There are published reports describing the use of WBI in poisoning with a number of substances including iron, lithium, latex packets of cocaine in body-packers, lead and sustained-release preparations including verapamil.16 W hole bowel irrigation is generally well tolerated, and polyethylene glycol is not absorbed and does not result in significant changes in fluid or electrolyte balance.16 W hole bowel irrigation may be considered in potentially toxic ingestions of the substances listed in Table 2.16 The dosage of polyethylene glycol used for WBI is 1,500–2,000 mL/hr for adults, 1,000 mL/hr for children of six to twelve years and 500 mL/hr for children six months to six years of age; it should be continued until the rectal
effluent is clear. It can be given orally or via a nasogastric tube, although in practice, in view of the large volumes of polyethylene glycol that need to be administered, a nasogastric tube is almost always required.

A record of the exact weight of patients is important in clinical toxicology; the toxic dose of many compounds is dependent on the body weight, and the dose of some drugs used to treat poisoned patients is weight-dependent (e.g., N-acetylcysteine (NAC) for paracetamol poisoning). Many patients are not weighed, and weight is frequently estimated, often inaccurately. Weighing scales should be standard equipment in all clinical areas treating poisoned patients and all patients presenting after taking an overdose of any substance should have a formal body weight measurement as a standard part of their management.

The psychological aspect of the self-poisoned patient should not be forgotten. An assessment of mental state and the further risk of self-harm should be carried out in all patients who present with self-poisoning, ideally by a psychiatric nurse or psychiatrist. Care for these patients is a multidisciplinary responsibility, and nurses, physicians, psychiatrists and social workers all play key roles in the rehabilitation and future management of the patient.

Paracetamol remains the most common substance taken in overdose in the UK, accounting for 50% of all self-poisoning episodes and 100–200 deaths per year. The vast majority of cases of early, lone paracetamol poisoning are asymptomatic at presentation; therefore management is best guided by blood tests as discussed below. Because paracetamol overdose is the commonest form of self-poisoning in the UK, national guidelines have been produced and distributed as a poster in prose format to all A&E departments. In addition, we have recently reviewed this topic and produced an evidence-based flowchart to guide the management of patients presenting with paracetamol poisoning.

1. Risk factors for paracetamol poisoning
A number of factors may increase the risk of hepatotoxicity in patients with paracetamol poisoning and identify them as high risk; these are detailed in Table 3. Surprisingly, these are based on little evidence, and yet they have become established and, currently, we support their use. The standard treatment line on the Prescott nomogram is lowered by 50% and treatment line B is used for these ‘high risk’ patients (Figure 1). Prior to commencing treatment with NAC, a risk assessment should be made to determine whether the patient falls into a high- or low-risk treatment group for paracetamol toxicity; the appropriate treatment line on the nomogram should be followed.

![Image](https://via.placeholder.com/150)

**Table 2**

**Indications for Whole Bowel Irrigation (WBI).**

<table>
<thead>
<tr>
<th>Indications to WBI:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Large ingestions of agents not adsorbed to activated charcoal, e.g. lithium, iron</td>
</tr>
<tr>
<td>• Body packers, i.e. ingestion of drug-filled packets</td>
</tr>
<tr>
<td>• Large ingestions of sustained release or enteric-coated drugs, e.g. calcium channel blockers</td>
</tr>
</tbody>
</table>

**Contraindications to WBI: |

| Bowel obstruction or ileus |
| Significant gastrointestinal haemorrhage |
| Haemodynamic instability |

**Table 3**

**Risk factors in paracetamol overdose.**

| • Regular ethanol consumption in excess of currently recommended limits (21 units/week in males; 14 units/week in females) |
| • Regular use of enzyme-inducing drugs (e.g. phenytoin, carbamazepine, rifampicin, phenobarbitone) |
| • Conditions causing glutathione depletion (e.g. HIV, eating disorders, malnutrition, cystic fibrosis) |

2. Early paracetamol poisoning (less than 15 hours post-ingestion)
The decision to use NAC in patients with early paracetamol poisoning is based on the plasma paracetamol concentration plotted on the Prescott nomogram (Figure 1). Blood should be taken for a plasma paracetamol concentration on presentation (or four hours post-ingestion, whichever is later). N-acetylcysteine is an effective, safe antidote and if given within eight to ten hours of paracetamol ingestion provides almost 100% protection against the development of hepatic and renal toxicity. Therefore, in patients who present early, if the result of the plasma paracetamol concentration is available by eight hours post-ingestion, the decision to start NAC can be based directly on the plasma paracetamol concentration. However, in patients who present at more than eight hours after ingestion of a potentially hepatotoxic dose of paracetamol (>150 mg/kg or 75 mg/kg in high-risk patients), NAC should be started on presentation after blood is taken for a plasma paracetamol concentration; the NAC can be stopped if the plasma paracetamol concentration is found on analysis to be well below the relevant treatment line on the Prescott nomogram.
3. Late paracetamol poisoning (more than 15 hours post-ingestion)

This group is difficult to manage. In any patient presenting within eight to twenty-four hours of ingestion of a potentially hepatotoxic dose of paracetamol, NAC should be started immediately and blood taken for International Normalised Ratio (INR), liver function tests, serum creatinine and plasma (venous) bicarbonate.\(^{30, 32-7}\) The decision to continue the infusion will be determined by these blood results, the history and the clinical condition of the patient.\(^{21}\) While data strongly support the treatment line A (Figure 1) on the Prescott nomogram up to 15 hours,\(^{22}\) data beyond 15 hours are sparse and extrapolation of the line up to 24 hours amounts to guesswork, although this scheme is commonly used in practice. Furthermore, in late-presenting patients, the detection limit of the plasma paracetamol assay may not be sufficient to distinguish between toxic and non-toxic amounts.\(^{20, 38}\) Therefore, the plasma paracetamol concentration in late-presenting patients needs to be considered with caution and patients may need to be given NAC on the basis of ingestion of a potentially hepatotoxic dose of paracetamol (150 mg/kg or 75 mg/kg for ‘at risk’ groups).\(^{21}\) The maxim to be followed in practice is, ‘if in doubt, treat.’\(^{21}\)

The plasma paracetamol concentration cannot be used to assess patients presenting at more than 24 hours post-ingestion. In these patients, blood should be taken for INR, liver function tests, serum creatinine and plasma venous bicarbonate.\(^{30, 32-7}\) If the patient is asymptomatic and the blood results are normal he/she may be medically discharged;\(^{38, 39}\) if not, the National Poisons Information Service (NPIS) should be contacted for management advice.

4. Management of established paracetamol-related hepatotoxicity

Meticulous supportive care is important in these patients\(^{30, 42}\) and we would advise that a poisons centre or a liver transplant unit should be contacted if there is evidence of hepatotoxicity at any stage or doubt about its management, particularly if markers of severe toxicity shown in Table 4 are present.\(^{42}\) This ensures that referral takes place before the criteria for liver transplantation are met and that appropriate intensive care support is provided.\(^{42, 43}\)

5. Staggered paracetamol poisoning

The plasma paracetamol concentration cannot be used to guide management in those patients who have taken a number of doses of paracetamol over a prolonged period of time. A baseline INR, liver function tests, serum creatinine and plasma venous bicarbonate should be taken, but the ingested dose is the most important factor and patients who have ingested more than 150 mg/kg over a 24-hour period (75 mg/kg for high-risk patients) should be treated with NAC.\(^{30, 44-7}\)
OPIOIDS

Naloxone has been used as a specific antidote for opioid poisoning since the 1960s. A frequent error in the management of opioid poisoned patients is to administer either excessive or insufficient doses of naloxone. The goal of naloxone treatment is reversal of respiratory depression to a minimum respiratory rate of ten (with adequate respiratory depth and oxygen saturation) and reversal of central nervous system (CNS) depression aiming for a Glasgow Coma Score of 13–14/15.

Naloxone can precipitate acute withdrawal syndrome (AWS) in chronic opioid users. The agitation, hypertension and tachycardia produced, although rarely life-threatening, may produce significant distress to both the patient and staff. The agitation that results from AWS makes it difficult to monitor the patient and patients in this state may opt to leave the A&E department against medical advice. In addition, vomiting commonly occurs in acute withdrawal and, in a patient who does not regain consciousness immediately after naloxone, this can result in aspiration.

The bolus dose required to reverse the depressant effects of an opioid depends on the quantity of the drug present at the receptor sites and the competitive relationship that exists between the opioid and the antagonist at the receptor site. This is generally between 0.4 mg and 2.0 mg IV, although this should not be given as a single large bolus. We would recommend that 2 mg of naloxone is made up in a 10 ml syringe with saline and given in 100–200 mcg boluses to a maximum of 10 mg, titrated according to the effect produced (see Figure 2).

The half-life of naloxone is between 30 and 100 minutes. Because the duration of action of most opioids exceeds that of naloxone, either repeated doses or an intravenous infusion of naloxone are often required. The protocol we recommend is that described by Goldfrank (Figure 2).

CARBON MONOXIDE POISONING

Carbon monoxide remains the commonest cause of death by poisoning in the UK. Two areas of particular concern are the clinical assessment of the patient and adequate oxygen therapy.

Patients should have a thorough neurological examination which should include heel-toe walking and other tests of cerebellar function. A carboxyhaemoglobin saturation level is of value in confirming the diagnosis but its level is not indicative of the severity of poisoning. An electrocardiogram (ECG) is essential in any patient with severe poisoning or in those with pre-existing heart disease because arrhythmias and myocardial ischaemia are a common cause of morbidity and mortality in severe carbon monoxide poisoning. Arterial blood gas analysis is also required in significant poisoning: oxygen saturation monitors are misleading as they measure both oxyhaemoglobin and carboxyhaemoglobin.

All patients should receive high flow oxygen through a tightly fitting facemask and this should be continued for at least 12 hours. The use of hyperbaric oxygen is controversial and six published randomised trials disagree on its efficacy. The trials each have limitations which include either too few patients, inclusion of patients who were exposed to other toxins in fires and different treatment protocols. Until further, well-controlled evidence is available we would recommend hyperbaric oxygen therapy in the groups of patients with carbon monoxide poisoning shown in Table 5.

CARDIOVASCULAR TOXICITY

Cardiovascular toxicity is a common cause of death in severely poisoned patients. The following three areas merit special attention.

1. Arrhythmias associated with poisoning
Arrhythmias associated with poisoning should not in general be treated with anti-arrhythmic agents as a first-line approach. Anti-arrhythmic agents have negative

### TABLE 4

Markers of severe paracetamol poisoning and indications for referral to a liver unit.

- Progressive coagulopathy, or INR >2 at 24 hours, INR >4 at 48 hours, INR >6 at 72 hours
- Renal impairment (creatinine >200 µmol/L)
- Hypoglycaemia
- Metabolic acidosis (pH <7.3, bicarbonate <18) despite adequate rehydration
- Hypotension despite fluid resuscitation
- Encephalopathy

### TABLE 5

Current recommendations for hyperbaric oxygen therapy.

- Any history of unconsciousness
- Carboxyhaemoglobin concentration of >40% at any time
- Presence of any neurological features (especially cerebellar signs)
- Pregnancy
- ECG changes
FIGURE 2
Flowchart for the management of opioid overdose.60
inotropic and chronotropic effects, and may lead to a deterioration in cardiovascular status, particularly in patients with arrhythmias due to a cardiotoxic agent. One should consider whether or not these drugs are really necessary; for example in poisoning with tricyclic antidepressants, administration of hypertonic sodium bicarbonate should be the first step in arrhythmia management. In other cases antidotes are indicated, e.g. Digibind® is preferable to pacing for bradyarrhythmias or anti-arrhythmic agents/DC cardioversion for tachy-arrhythmias in digoxin poisoning.

2. Cocaine-induced acute-coronary syndrome

The pathophysiology of cocaine-induced acute-coronary syndrome is different to that associated with atherosclerotic coronary artery disease; it is due primarily to coronary artery spasm rather than thrombosis and other pathological forms of occlusion. Management is therefore based on diazepam, aspirin, and buccal/intravenous nitrates as specific coronary artery vasodilators. Calcium channel antagonists such as verapamil may also be used. In patients with cocaine-induced myocardial infarction the use of thrombolytics is not usually necessary as the underlying aetiology is not thrombosis; the use of thrombolysis can further increase the risk of intracranial haemorrhage associated with cocaine use.

The initial drug of choice in treatment of cocaine-induced hypertension is diazepam, which reduces the central stimulation, tachycardia and hypertension associated with cocaine toxicity. A common error is to give beta-blockers, which may lead to worsening hypertension due to unopposed alpha-stimulation. Hypertension that does not settle with diazepam should be treated with intravenous nitrates.

3. Recovery from cardiac arrest

Some poisoned patients make a good recovery despite prolonged cardiac arrest and a common problem is that these patients are not resuscitated for long enough. A case has been reported of a successful outcome after 50 minutes of cardiopulmonary resuscitation (CPR) in a patient with a large imipramine overdose. This patient required 400 mmol of sodium bicarbonate in addition to standard adrenaline therapy. Poisoned patients who have developed a cardiac arrest are very different to other patients in the general population, or hospital in-patients who have a cardiac arrest, as they are more often fit young individuals with a better cardiorespiratory reserve.

ACIDOSIS

A metabolic acidosis is very common in poisoning although diabetic ketoacidosis is still missed; a bedside and laboratory assay of glucose should be carried out and urinalysis performed in all acidotic patients.

A patient with a high anion gap metabolic acidosis and high osmolal gap is very likely to be poisoned with ethylene glycol or methanol. The absence of a high anion gap metabolic acidosis does not, however, exclude methanol/ethylene glycol poisoning as the metabolic acidosis is due to the toxic metabolites, and metabolism of methanol/ethylene glycol can take between eight and thirty-six hours. Therefore, patients who present within the first eight to twenty-four hours of poisoning may have a normal blood gas and anion gap, and the diagnosis is usually made on the basis of a raised osmolal gap. The osmolal gap (normal value <10) is the difference between the measures serum osmolality (O₇) and the calculated osmolality (O₈) The formula for calculation of the calculated osmolality is: O₈ = 2(Na⁺ + K⁺) + urea + glucose. Common toxic causes of an elevated osmolal gap are methanol, ethanol, ethylene glycol and isopropanol. It is important to exclude ethanol as the cause of the elevated osmolal gap and so a serum ethanol concentration should also be measured; 3-7 mg/dL of ethanol approximates to 1 mOsm/L.

Management of methanol/ethylene glycol poisoning involves supportive care together with the use of competitive inhibitors of alcohol dehydrogenase (e.g. ethanol, 4-methylpyrazole) to reduce the formation of their toxic metabolites. In addition, aggressive bicarbonate therapy in patients with a metabolic acidosis decreases CNS transit of both ethylene glycol and methanol, and reduces optic nerve toxicity with methanol.

Ethanol remains the antidote of choice in most cases for ingestion of these substances. All patients who have ingested a significant amount of ethylene glycol or methanol should receive a loading dose of ethanol while awaiting confirmatory laboratory results. An infusion should then be commenced in patients with confirmed poisoning (usually on the basis of a history of methanol or ethylene glycol ingestion in association with a raised osmolal gap) aiming for a blood ethanol concentration of 100-150 mg/dL. Ethanol has unpredictable kinetics therefore patients who require an ethanol infusion should have hourly to two-hourly monitoring of blood ethanol concentrations until the serum ethanol concentration is 100-150 mg/dL, and then to four-hourly monitoring once this concentration is achieved. Patients with severe methanol/ethylene glycol poisoning (e.g. severe, resistant metabolic acidosis, acute renal failure, ocular toxicity with methanol poisoning) may require haemodialysis; the dose of ethanol should be increased in these patients, or ethanol put in the dialysate to maintain a serum ethanol concentration of 100–150 mg/dL.

Sodium bicarbonate is frequently used in the management of poisoned patients and the common indications are summarised in Table 6. Sodium bicarbonate is frequently used in the management of poisoned patients and the common indications are summarised in Table 6.
followed by further doses titrated to a pH of 7-45–7.5.\textsuperscript{102–4} It is important that drowsy patients are ventilated to prevent the potential carbon dioxide retention that can occur and result in a paradoxical intracellular acidosis in these patients treated with sodium bicarbonate.

**Rarer overdoses**

The most common area of mismanagement in the following, rarer overdoses is failure to recognise the potential severity of poisoning and instigate early appropriate treatment.

<table>
<thead>
<tr>
<th>TABLE 6</th>
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<tr>
<td><strong>Indications for use of sodium bicarbonate in poisoned patients.</strong>\textsuperscript{101}</td>
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</tbody>
</table>

- Severe metabolic acidosis associated with methanol, ethylene glycol, cyanide, salicylates
- Urinary alkalisation to enhance elimination of salicylate (and less commonly for phenobarbitone, chlorpropamide and some pesticides, e.g. 2,4D) or prevent renal deposition of myoglobin after severe rhabdomyolysis
- Cardiotoxicity caused by tricyclic antidepressants, dextropropoxyphene, flecanide, quinidine, procainamide, disopyramide, phenothiazines, chloroquine

**Chloroquine**

The mortality rate in published studies of chloroquine overdose is between 12–35%, among the highest in clinical toxicology.\textsuperscript{105,106} Ingestion of more than 5 g of chloroquine is probably the most accurate predictor of a fatal outcome; death is usually due to cardiotoxicity.\textsuperscript{107} The window of opportunity for treatment is short: the interval between ingestion and onset of symptoms is usually between one to three hours, with death within 12 hours.\textsuperscript{108} Studies have suggested that early management of severe chloroquine intoxication may have a cardioprotective effect and reduce the fatality rate.\textsuperscript{109,110} Chloroquine blood concentrations are not required for the institution of treatment. Clinical features, which primarily involve the cardiovascular and CNS, are more important. Activated charcoal should be given to patients presenting within one hour of ingestion of more than 15 mg/kg chloroquine.\textsuperscript{111} It is essential to intubate and ventilate early in the course of chloroquine poisoning if arrhythmias, hypotension, seizures or significant CNS depression are present. Anti-arrhythmic agents should be avoided if possible as they may precipitate further arrhythmias. Intravenous sodium bicarbonate is the treatment of choice for arrhythmias\textsuperscript{109,112} and should be used in patients with widened QRS and QTc intervals (1-2 ml/kg 8-4% sodium bicarbonate repeated as necessary aiming for a pH of 7-45–7.5). Oversedrive pacing is the treatment of choice for ventricular tachycardia or torsade de pointes.\textsuperscript{113} Inotropes may also be necessary for hypotension unresponsive to a fluid challenge.\textsuperscript{113,114} Plasma potassium should be monitored, although hypokalaemia may have a protective effect and should not be aggressively corrected in the early stages of poisoning as there is no total body deficit of potassium and attempted early correction can worsen cardiotoxicity.\textsuperscript{115} If hypokalaemia persists beyond eight hours, potassium should be replaced cautiously.\textsuperscript{115} High dose diazepam has been reported to have a specific cardioprotective action in severe chloroquine poisoning.\textsuperscript{111,116} It is recommended that after intubation 2 mg/kg of intravenous diazepam should be given over 30 minutes and then 1 to 2 mg/kg for two to four days.\textsuperscript{113,116} Continuous and aggressive cardiorespiratory support appears to be the most critical factor in survival.

**Salicylate**

Salicylate poisoning is much less common than ten years ago\textsuperscript{4} and for this reason doctors may fail to recognise its severity or treat such patients optimally. Delay in diagnosis was associated with a mortality of 15% compared to a much lower rate in those patients in whom early diagnosis and institution of therapy was made.\textsuperscript{118} We have recently reviewed the management of salicylate poisoning and proposed a management flowchart.\textsuperscript{119} The clinical effects of salicylate poisoning are shown in Table 7.\textsuperscript{120–5} Children and the elderly may suffer toxicity with lower ingested doses and at relatively lower plasma salicylate concentrations.

There is no antidote to salicylate poisoning, and management is directed towards preventing further absorption and enhancing elimination of the drug in patients with features of moderate or severe intoxication.\textsuperscript{119} The use of MDAC is controversial in salicylate overdose.\textsuperscript{126–9} We advocate its use, to prevent delayed absorption, until the salicylate level has peaked, which can be as late as 12–18 hours post-ingestion.\textsuperscript{8}

The plasma salicylate concentration should be determined on admission provided that the patient is more than four hours post-ingestion.\textsuperscript{119} As salicylates can delay gastric emptying and may form concretions in the stomach resulting in delayed absorption, the plasma salicylate concentration should be repeated every three to four hours to ensure the concentration does not continue to rise.\textsuperscript{119} The plasma salicylate concentration correlates very roughly with toxicity\textsuperscript{124,130} (see Table 7) although the presence of symptoms and signs and the degree of acidosis should be considered when interpreting the plasma salicylate concentration and deciding on further management.\textsuperscript{124,131} Metabolic acidosis is a particularly important negative predictor as it increases the CNS transit of salicylate and decreases salicylate renal elimination. After ingestion of enteric-coated preparations, plasma salicylate concentrations on admission are unreliable guides to the severity of
poisoning as levels may not peak until more than 12–18 hours after ingestion.\textsuperscript{132–4}

Patients with salicylate poisoning are often dehydrated because of vomiting, hyperventilation and sweating; rehydration is therefore an important aspect of management. Patients with severe salicylate poisoning are also at risk of pulmonary oedema, however, and it is important not to cause fluid overload; in the elderly or those with cardiac disease a central line may be necessary to guide rehydration.\textsuperscript{8}

Urinary alkalinisation is an effective method of increasing salicylate elimination and is indicated in patients with moderate salicylate poisoning (see Table 7).\textsuperscript{125} In adults this is achieved by administering 1L of 1·26% sodium bicarbonate over three to four hours and regularly checking the urinary pH with indicator paper aiming for a urinary pH 7·5–8·5; an increase in the infusion rate or bolus of 8·4% sodium bicarbonate may be required if an alkaline urine is not achieved as patients can have a significant base deficit.\textsuperscript{119} The plasma potassium should be monitored as the serum potassium can fall precipitously once adequate urinary alkalinisation is achieved and also it is very difficult to produce an alkaline urine if the patient is hypokalemic.\textsuperscript{119} We would therefore recommend adding 20–40 mmol potassium to each litre of intravenous fluid administered.

Haemodialysis reduces both the mortality and morbidity of poisoning, and, as well as being effective at increasing salicylate clearance it also corrects acid-base and fluid balance abnormalities.\textsuperscript{121} It should be considered if the patient has a metabolic acidosis resistant to correction with 8-4% sodium bicarbonate, especially if the pH is <7·2, the salicylate concentration is >800 mg/L in adults or 700 mg/L in children or elderly, or the patient has features of severe poisoning (see Table 7).\textsuperscript{120–5} It is important that alkalinisation is still achieved in those salicylate-poisoned patients undergoing haemodialysis in order to reduce plasma levels quickly, prevent acidemia and promote elimination of as much salicylate as possible via the kidneys.\textsuperscript{123}

Theophylline
Severe theophylline poisoning (ingestion of more than 3 g in adults or 40 mg/kg in children) is associated with a high mortality.\textsuperscript{8} Theophylline is most commonly used in sustained release formulations leading to delayed absorption in overdose and delayed onset of toxicity, as late as 12–24 hours post-ingestion.\textsuperscript{135}

A system has been proposed for grading the severity of theophylline intoxication and is shown in Table 8.\textsuperscript{136} Plasma theophylline concentrations can help confirm ingestion and may be of value in deciding upon elimination methods, but in the vast majority of poisoned patients they do not aid management.\textsuperscript{8} Management is most appropriately guided by the severity on the Sessler grading scheme (Table 8),\textsuperscript{136} bearing in mind that delayed effects occur in overdoses with sustained-release preparations.

All patients with theophylline poisoning should receive MDAC.\textsuperscript{13, 137, 138} Vomiting, which may be profuse, occurs in overdose in more than 70% of patients.\textsuperscript{139–41} It may respond to metoclopramide but is more likely to be controlled by a 5HT\textsubscript{3}-receptor antagonist such as ondansetron.\textsuperscript{142} All patients should have cardiac monitoring. Sinus or supraventricular arrhythmias not causing haemodynamic compromise are best left untreated.\textsuperscript{138} In non-asthmatic patients, symptomatic supraventricular tachycardia should be treated with propranolol (0·01–0·03 mg/kg IV) or esmolol (25–50 µg/kg), repeated according to response.\textsuperscript{143, 144} Asthmatic patients should be treated with verapamil or cautiously treated with esmolol (short half-life and relative beta 1 selectivity).\textsuperscript{145–7} Ventricular arrhythmias are treated with DC cardioversion or magnesium sulphate.\textsuperscript{8} Convulsions

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Clinical features} & \textbf{Dose ingested} & \textbf{Salicylate concentration} & \textbf{Dose ingested} \\
\hline
\textbf{Adults} & \textbf{Children/Elderly} & \textbf{Clinical features} & \textbf{Adults} & \textbf{Children/Elderly} \\
\hline
\textbf{Mild} & \textbf{>150 mg/kg} & \textbf{300–600 mg/L} & \textbf{250–450 mg/L} & \textbf{Lethargy, nausea, vomiting, tinnitus, dizziness} \\
\hline
\textbf{Moderate} & \textbf{>250 mg/kg} & \textbf{600–800 mg/L} & \textbf{450–700 mg/L} & \textbf{Mild features and tachypnoea, sweating, hyperpyrexia, dehydration, restlessness} \\
\hline
\textbf{Severe} & \textbf{>500 mg/kg} & \textbf{>800 mg/L} & \textbf{>700 mg/L} & \textbf{Moderate features and metabolic acidosis, hypotension, CNS features (e.g. coma, seizures), renal failure} \\
\hline
\end{tabular}
\caption{Clinical features of salicylate poisoning.}
\end{table}
should be treated with intravenous diazepam; if these are resistant to treatment, the patient should be intubated and ventilated. Plasma potassium concentration should be monitored frequently (every one to two hours in severely poisoned patients) as hypokalaemia is a potentially life-threatening consequence of theophylline poisoning. The blood glucose should be checked, as hyperglycaemia is also common.

It is likely that MDAC is almost as effective as charcoal haemoperfusion in the management of severe theophylline poisoning. If MDAC is not possible, however, e.g. paralytic ileus, charcoal haemoperfusion should be considered in patients with severe (grade 3 and 4) poisoning.

**Iron**

The clinical course of iron poisoning may be divided into four stages. During the initial 30 minutes to several hours after ingestion, the corrosive effects of iron result in gastrointestinal upset leading to nausea and vomiting, abdominal pain and diarrhoea. In severe cases gastrointestinal haemorrhage and shock can occur. The second phase, during which the clinical effects usually abate, lasts from six to twenty-four hours after ingestion. This phase can be deceptively reassuring as the asymptomatic patient during this phase can still go on to develop severe toxicity. Phase three occurs from 12–48 hours after ingestion and may include severe lethargy, coma, convulsions, gastrointestinal haemorrhage, shock, metabolic acidosis, hepatic failure with hypoglycaemia, coagulopathy, pulmonary oedema and renal failure. Phase four occurs between two and five weeks if the patient survives. Scarring from the initial corrosive damage can result in small bowel strictures and pyloric stenosis.

It is important when assessing the ingested dose of iron that the elemental content of different iron preparations is considered (see Table 9). Undissolved iron tablets are radiopaque, and an abdominal X-ray (AXR) should be taken in all patients to determine the need for gut decontamination. However the absence of radiopaque material on AXR does not exclude iron ingestion. If any tablets are visible on the AXR, whole bowel irrigation should be undertaken.

### TABLE 8

**Grading scheme for patients with theophylline intoxication.**

<table>
<thead>
<tr>
<th>Severity grade</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vomiting, abdominal pain, diarrhoea, anxiety, tremor, sinus tachycardia &gt;120 bpm, plasma potassium 2.5–3.5 mmol/L</td>
</tr>
<tr>
<td>2</td>
<td>Haematemesis, disorientation, supraventricular tachycardia, frequent ectopics, mean arterial blood pressure at least 60 mmHg but unresponsive to standard therapy, plasma potassium &lt;2.5 mmol/L, arterial pH &lt;7.2 or &gt;7.6, rhabdomyolysis</td>
</tr>
<tr>
<td>3</td>
<td>Non-repetitive seizure, sustained ventricular tachycardia, mean arterial blood pressure &lt;60 mmHg and unresponsive to standard therapy</td>
</tr>
<tr>
<td>4</td>
<td>Recurrent seizures, ventricular fibrillation, cardiac arrest</td>
</tr>
</tbody>
</table>

**TABLE 9**

**Elemental iron content of iron preparations in the UK.**

<table>
<thead>
<tr>
<th>Iron preparation</th>
<th>Usual dosage</th>
<th>Amount of elemental iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous fumarate</td>
<td>200 mg</td>
<td>65 mg</td>
</tr>
<tr>
<td>Ferrous gluconate</td>
<td>300 mg</td>
<td>35 mg</td>
</tr>
<tr>
<td>Ferrous succinate</td>
<td>100 mg</td>
<td>35 mg</td>
</tr>
<tr>
<td>Ferrous sulphate (dried)</td>
<td>200 mg</td>
<td>60 mg</td>
</tr>
<tr>
<td>Ferrous sulphate (dried)</td>
<td>300 mg</td>
<td>60–5 mg</td>
</tr>
</tbody>
</table>

Blood should be taken four hours after ingestion for determination of the serum iron concentration. If desferrioxamine is to be given before four hours for severe poisoning, blood should be taken for determination of the serum iron level just prior to its administration as once desferrioxamine has been given colorimetric assay methods may underestimate the amount of free serum iron. A blood level taken more than six to eight hours after ingestion may underestimate the amount of free iron because of distribution into the tissues. For sustained-release preparations an initial serum concentration should be checked at four hours and again two to four hours later. The serum iron concentration should not be interpreted in isolation but in the context of the patients clinical condition and an accurate history of the ingested dose. Measurement of the total iron binding capacity is of no value in the management of these patients.

There have been no controlled studies looking at the use of desferrioxamine in iron poisoning; we would, however, recommend its use in patients with hypotension, shock, severe lethargy, coma or convulsions or a serum iron level >90 mmol/L. Patients with a serum iron concentration of 55–90 mmol/L should be observed for 24–48 hours post-ingestion. They do not require chelation therapy unless they develop symptoms, or have haematemesis or melaena. The recommended initial dose of desferrioxamine is 15 mg/kg/hour, reduced after two to four hours up to a maximum of 80 mg/kg in 24
hours. More rapid infusion rates can cause hypotension, and there is a risk of pulmonary complications such as ARDS with doses of more than 80 mg/kg/24 hrs. Chelation with desferrioxamine should be continued until the urine has returned to a normal colour, symptoms have abated and all radioactivities have disappeared. Haemodialysis or haemofiltration may be required to remove the iron-desferrioxamine complex in patients with renal failure.

**CYANIDE**

Although rare, acute cyanide poisoning requires immediate action as it produces its effects, which include metabolic acidosis and CNS, cardiac and respiratory depression, rapidly. The immediate diagnosis of cyanide poisoning is difficult despite improvements in blood cyanide detection methods. This poses a therapeutic dilemma for the clinician who must rapidly decide whether to administer specific antidotes, some of which are themselves toxic. The blood cyanide concentration is considered the gold standard in confirmation of acute cyanide poisoning; they are, however, rarely of use in emergency management because they cannot be carried out rapidly enough to guide treatment. A sample should be taken before antidote administration for cyanide quantification at a later stage.

Many patients suffering from smoke inhalation or burns may also have cyanide toxicity and may present with a lactic acidosis not responding to oxygen administration. A recent study has shown that immediate and serial measurements of plasma lactate concentrations are useful in assessing the severity of cyanide poisoning in patients in whom the diagnosis is strongly suspected on a clinical basis. In burn victims without severe burns, a plasma lactate concentration of >90 mg/dL (10 mmol/L) is a sensitive and specific indicator of cyanide intoxication. Decontamination is an important aspect of management; it is vital that medical staff treating the patient do not become poisoned. If hydrogen cyanide gas or liquid cyanide is involved, protective clothing and breathing apparatus is necessary and if the patient is intubated a closed circuit should be used. In cyanide salt exposure, contaminated clothing should be removed and placed in sealed bags, and the skin washed with soapy water.

Meticulous supportive care is important in the management of cyanide poisoning. All patients should receive high-flow oxygen and comatose patients will require intubation. Patients who present with an established metabolic acidosis should be treated with 1–2 ml of 8.4% sodium bicarbonate to correct the acidosis.

The other aspect of the management of cyanide poisoning is the use of antidotes. Dicobalt edetate can be associated with severe adverse effects including cardiotoxicity, facial and laryngeal oedema, bronchospasm and rashes. These effects are more likely to occur if it is administered in the absence of cyanide ions or if the drug is injected too rapidly. If it should therefore be used only if the diagnosis of cyanide poisoning is certain and the patient has severe clinical features; adrenaline and facilities for intubation should be available. If the diagnosis is uncertain or dicobalt edetate is unavailable, the patient should be treated with a combination of intravenous sodium thiosulphate and sodium nitrite. Hydroxocobalamin (at a dose of 5 g for an adult) is a newer cyanide antidote and is both effective and well tolerated. Currently the concentrated form of hydroxocobalamin is not widely available in the UK.

**DECLARATION OF INTERESTS**

AL Jones is a scientific advisor for GlaxoSmithKline on analgesics; PI Dargan has acted as a scientific advisor to GlaxoSmithKline and received funding to attend scientific meetings. The Medical Toxicology Unit at the National Poisons Information Service is supported by AstraZeneca-Novartis, Boots Healthcare and Bass Breweries.

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