REVIEW ARTICLE

THE MANAGEMENT OF ACUTE POISONING

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Self poisoning is among the most common causes of non-traumatic coma in patients younger than 35 yr, and accounts for approximately 10% of all acute medical admissions [8]. Anaesthetists may become involved in the care of these patients during emergency resuscitation or in the intensive care unit. In the U.S.A., acute self poisoning accounts for 5–30% of admissions to medical intensive care units [21, 23].

Classification

Self-poisoning accounts for 95% of all poison-related admissions. It is slightly commoner in females (female to male ratio approximately = 1.3:1) with a peak incidence in females younger than 25 yr, and between 20 and 35 yr for males [8]. About 50% of all overdoses involve a mixture of agents [8, 10, 21]. Self-poisoning is often an impulsive act with no clear intent to die and with a previous history of similar episodes [33].

Accidental poisoning occurs predominantly in children younger than 5 yr, and may be with medicines (usually those prescribed to a parent) or household products. Each year accidental poisoning in children accounts for about 24000 hospital admissions in England and Wales [5]. Only about 15% of the children presented to hospital with accidental poisoning develop symptoms from the agent ingested [23]. Fatal accidental poisoning is rare [35].

Non-accidental poisoning may occur as an extension of the syndrome of child abuse, usually in children younger than 30 months. This may be more common than is generally accepted [7], and has a fatal outcome more commonly than cases of accidental poisoning [23].

Homicidal poisoning is encountered rarely in clinical practice.

Diagnosis

Diagnosis is usually made from the history and circumstantial evidence. However, patients' statements about the nature and the quantity of the poison ingested are unreliable [39]. Witnesses, family, friends and ambulance personnel should be interviewed to establish details regarding the probable agents ingested and approximate time of ingestion. Alcohol is often taken in combination with one or more other agents.

Isolated signs and symptoms are of little diagnostic value in any poisoning incident, but identification of the agent can often be surmised from the history and examination. Various combinations of signs may be suggestive of specific commonly ingested poisons [11]; however, there is a poor correlation between drugs suspected on admission and those actually detected in the blood [21]. The agents used in deliberate self-poisoning undergo changing patterns, with various agents going in and out of vogue. Currently in the U.K., the agents encountered most commonly in deliberate self-poisoning are the benzodiazepines, paracetamol, aspirin and tricyclic anti-depressants [8]. Car exhaust poisoning is the method of suicide used most often by men aged 15–44 yr [29].

Toxicological screening should be considered in the urgent investigation of coma when the history, examination and biochemical analysis do not yield a diagnosis. About 50% of patients attending a casualty department with coma of unknown aetiology may be self-poisoning cases [10]. Appropriate samples should be collected early in the initial management of these patients so that they are available later if required for either diagnostic or medico-legal purposes. These samples should include:

- Gastric contents: 50 ml of vomit, aspirate or the first portion of a gastric lavage.
- Urine: 50 ml of the first sample voided after admission.
- Blood: 10 ml of lithium-heparinized blood, 10 ml of blood without anticoagulant, and 2 ml of fluoridized blood for ethanol assay. Care should be taken to avoid the use of swabs containing alcohol.

Ideally, all of these samples should be collected before administration of any medications which may confuse toxicological analysis.

Routine biochemical and haematological investigations may, rarely, suggest a diagnosis of acute poisoning. More often they provide a helpful baseline for later comparison. Many poisons cause fluid and electrolyte imbalance, renal or hepatic impairment, or acid-base imbalance.

The majority of patients admitted after acute
poisoning are conscious on arrival at the hospital; however, in unconscious patients organic brain damage should always be suspected if the history of poisoning is unsatisfactory and the depth of coma does not improve within 12 h.

MANAGEMENT

Before consideration of the active management of the poisoned patient, it should be emphasized that, for the majority of poisoned patients, only supportive care is needed. This led one reviewer to comment "It cannot be repeated too often that the primary object of the treatment of acute poisoning is not to collect as much 'poison' from the patient as possible, but to save life when this is threatened and to relieve pain and suffering... i.e. to save the patient, not to regain the poison" [22].

Immediate measures

Initial resuscitation in comatose patients should be conducted with the usual priorities: A-B-C-D-E:

Airway. Provide one if the patient's upper airway is obstructed. Protect the airway if the cough and gag reflexes are obliterated and secure the airway, when necessary, with tracheal intubation (this may include patients with marginally adequate protective reflexes who require gastric lavage).

Breathing. Assess the ventilatory efforts and assist where necessary. Assess gas exchange. Look for evidence of aspiration of gastric contents, toxic gases or foreign substances.

Circulation. Establish i.v. access early. Assess peripheral perfusion and begin resuscitation as required. Connect electrocardiographic monitoring and examine a rhythm strip.

Collect samples for future toxicological analysis if required.

Document the available history before ambulance personnel, relatives, etc. leave the hospital, and the level of coma.

Examine the patient thoroughly for associated injuries (e.g. pressure area necrosis), medical conditions which may have precipitated the overdose (e.g. toxic psychosis) or which may produce coma (e.g. hypoglycaemia).

Measures to limit absorption

The conventional belief that, after ingestion of poisons other than corrosives or petroleum distillates, the stomach should be routinely emptied by emesis or gastric lavage has been questioned by several authors [25, 27, 37].

Emesis should be induced only in fully conscious patients. It is less traumatic for the conscious patient than gastric lavage and is therefore the preferred technique of gastric emptying for children. However, the recovery of gastric contents by ipecacuanha-induced emesis is generally less than 50% [28, 37]. Syrup of ipecacuanha followed by an adequate volume of water induces vomiting in 90–95% of patients within 20–30 min, in both adults and children [13, 32]. Evidence that this emesis significantly reduces the absorption of commonly ingested poisons is less convincing. Therefore, although it only rarely causes serious sequelae, it is probably of little or no benefit to the majority of poisoned patients. The decision to empty the conscious patient's stomach by inducing emesis should be dependent upon the specific history of probable toxins, the estimated dose and the time since ingestion, rather than an automatic response to a history of acute poisoning.

Gastric aspiration and lavage is the only suitable way of emptying the stomach in the presence of obliterated laryngeal and pharyngeal reflexes. Airway protection is an essential part of the procedure. In the semi-conscious patient, airway protection may be achieved by placing the patient in the left-lateral, head-down position in the presence of an experienced anaesthetist with suction apparatus immediately to hand. In patients with more severely obtunded reflexes, it is safer to opt for elective tracheal intubation before gastric lavage.

Gastric aspiration and lavage via a wide-bore orogastric tube is indicated within 4 h of serious poisoning (i.e. the patient is comatose) with any of the commonly ingested poisons. The technique has been well described elsewhere [26]. Because the history is usually unreliable and gastric emptying is delayed by many poisons (notably aspirin and the tricyclic antidepressants), gastric lavage should be considered in any seriously poisoned patient up to 12 h after ingestion [12]. Conversely, with drugs which do not delay gastric emptying and which are absorbed rapidly from the gastrointestinal tract (e.g. paracetamol), gastric lavage may be ineffective as little as 2–4 h after ingestion.

Activated charcoal is a powerful, non-specific adsorbent which may be administered orally or via a gastric tube. Irreversibly binding the drugs within the bowel reduces blood concentration both by reducing drug absorption and by creating a negative diffusion gradient between the gut lumen and the blood, whereby drug diffuses from the circulation into the gut lumen—so called "gastrointestinal dialysis" [18]. It may be appropriate, therefore, to administer activated charcoal long after the original poisoning, and repeated administration is advocated as a safe, cheap and effective method of reducing drug concentrations in the blood. It is of demonstrable benefit after poisoning with several commonly ingested drugs, including aspirin [20] and paracetamol [19]. Anecdotal reports support the use of repeated administration of activated charcoal after a variety of other poisons. Enthusiasm for these relatively unproven uses, however, must be tempered by reports of serious consequences of pulmonary aspiration of activated charcoal [9, 24] and the minor risk of gastrointestinal obstruction after its use [36]. Furthermore, there are theoretical limitations. Drug elimination with activated charcoal is less effective in patients with severely impaired gastrointestinal motility—particularly relevant after poisoning with salicylates or with agents which have a significant anticholinergic action. Kirshenbaum and colleagues have questioned the clinical efficacy of multiple-dose
charcoal therapy after salicylate poisoning [16]. It is suggested also that clearance of parenterally administered medications used to treat intoxicated patients is increased by the charcoal, perhaps making treatment less effective.

Further pharmacokinetic data on the clearance of specific poisons are needed to determine the rational use of repeated charcoal regimens in a variety of clinical settings. Meanwhile, it provides a relatively safe technique of proven benefit in limiting drug absorption when given soon after ingestion of specific poisons. It is also probably of benefit in repeated doses in carefully selected clinical circumstances. Drugs which are well adsorbed to activated charcoal include benzodiazepines, antidepressants, anti-convulsants, barbiturates and theophylline. Salicylates and paracetamol are moderately well adsorbed.

Supportive care

All but a small minority of unconscious poisoned patients recover with supportive care alone. Conservative therapy is aimed at preventing complications such as hypoxaemia, aspiration, hypotension, acid-base and electrolyte imbalance, hypothermia, convulsions and the consequences of unconsciousness, whilst awaiting spontaneous elimination of the poison via the liver, kidneys, lungs and gut.

Respiratory complications are the commonest causes of death after acute poisoning, and immediate management must give priority to the airway, ventilation and prevention of aspiration. Having established an airway, it is important to assess the protective reflexes and consider the need for tracheal intubation. Whether or not gastric lavage is considered appropriate, a nasogastric tube should be inserted to prevent gastric dilatation. Hypoventilation is common after poisoning with sedatives, hypnotics, analgesics and many other drugs and chemicals. Hypoxia and hypercapnia may cause or exacerbate increased intracranial pressure, and should therefore be treated promptly. Specific antidotes may play a role in reducing the need for mechanical ventilation after poisoning with opioids or benzodiazepines (see Neurological complications).

Continued observation is essential in order to detect deterioration in the conscious level requiring a reappraisal of the need for airway protection or mechanical ventilation. Nurses should be given specific criteria by which to assess the need for referral to an anaesthetist. All patients requiring mechanical ventilation or tracheal intubation should be transferred to an intensive care unit for further monitoring.

Patients may present after long periods of respiratory depression, having already developed aspirational pneumonia or hypostatic pneumonia. The mainstay of treatment comprises endobronchial aspiration, physiotherapy and antibiotics.

Cardiovascular complications include hypotension, cardiac arrhythmias and cardiac arrest. A careful assessment of the patient's cardiovascular status should be made soon after presentation. The major factors contributing to hypotension in the presence of normal sinus rhythm are peripheral vasodilatation and myocardial depression, and the majority of patients respond to adequate intravascular volume repletion. In young, previously healthy patients, invasive monitoring is rarely required.

Arrhythmias may be caused by the toxin (e.g. poisoning with tricyclic antidepressants), hypoxia or hypercapnia, or may be secondary to the effects of the toxin on acid-base or electrolyte balance. A 12-lead ECG should be performed to provide a baseline and, in selected patients, continuous ECG monitoring is required. Patients suffering cardiac arrest as a direct result of a circulating toxin may be resistant to attempts to re-establish sinus rhythm. It is therefore worth persisting with external cardiac massage for longer than may otherwise be considered appropriate. Particular caution should be exercised in attributing any significance to the presence of fixed dilated pupils, which may reflect merely the actions of the toxin rather than any cerebral dysfunction.

Renal complications may result from the direct effects of the toxin (e.g. in aspirin, paracetamol or heavy metal poisoning), from a period of hypotension, from rhabdomyolysis with myoglobinuria, or from sepsis related to aspiration pneumonia. For further information beyond the scope of this article, the reader is referred to an extensive review of nephrotoxins by Abuelo [1].

Myoglobinuria should be suspected in any patient with evidence of a prolonged period of coma before admission (i.e. pressure area discoloration with poor capillary refill), with a history of prolonged seizures or with tissue hypoxia (e.g. from carbon monoxide poisoning).

Any comatose or hypotensive patient, or any patient with a history of poisoning with a known nephrotoxin, should be catherized, and the urine output maintained at least at 0.5 ml kg\(^{-1}\) h\(^{-1}\). This is achieved with volume resuscitation in the first instance followed, if necessary, by an infusion of dopamine in a small dose (2–4 \(\mu g\) kg\(^{-1}\) min\(^{-1}\)) and the judicious use of diuretics. Urinalysis before intervention may aid diagnosis by pointing to a renal or pre-renal cause, and occasionally by displaying the granular casts of acute tubular necrosis or the eosinophils of an acute interstitial nephritis.

When rhabdomyolysis is suspected, urinalysis of myoglobin should be performed, but treatment should be started promptly without awaiting the results of urinalysis. Urine output should be maintained at least at 1.5–2 ml kg\(^{-1}\) h\(^{-1}\) with aggressive volume loading and mannitol, and the urinary pH should be kept greater than 6.5 in order to prevent myoglobin from precipitating in the renal tubules.

Loop diuretics have the theoretical disadvantage of acidifying the urine, therefore mannitol is preferred for maintaining the diuresis. Blood samples should be taken for measurement of the urea, creatinine, potassium, calcium and creatine phosphokinas concentrations. In severe cases, hypocalcaemia may result from a shift of extracellular calcium into injured muscle. Serum potassium concentrations may increase rapidly because of muscle breakdown,
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necessitating early intervention with calcium, glucose and insulin infusion, or dialysis.

Hepatic and gastrointestinal complications. Gastric stasis may occur in any comatose patient, or in response to anticholinergic or opioid effects. Early decompression with a nasogastric tube should be performed to reduce the risk of regurgitation and aspiration. Stress ulcer prophylaxis may also be appropriate in selected patients.

Fulminant hepatic failure is a well recognized complication of serious poisoning with paracetamol, carbon tetrachloride or Amanita phalloides. These patients require early referral to a specialist liver unit.

Neurological complications include depression of conscious level, seizures, cerebral oedema and peripheral nerve injuries as a result of prolonged pressure. It is important to exclude metabolic or traumatic causes, and any patient whose level of consciousness appears inappropriately depressed for the history of poisoning should be suspected of having an intracranial haemorrhage. Lateralizing signs are rarely attributable directly to the toxin.

Correct nursing care is essential to protect the patient from the complications of prolonged coma. The presence of pressure area necrosis, neuropraxias, corneal abrasions and other sequelae of coma must be documented on admission to the unit, both to alert the nurses to areas requiring special attention, and to provide medico-legal protection.

The role of specific antagonists such as naloxone and flumazenil to antagonize central nervous system depression is controversial [2]. Reversal of coma can undoubtedly make management of the patient easier; however, acute antagonism of opioids with naloxone, or of benzodiazepines with flumazenil, may provoke severe withdrawal reactions. Antagonism of benzodiazepines with the specific antagonist, flumazenil, may be counterproductive in patients who have taken a mixture of drugs. For example, in the commonly encountered poisoning with both tricyclic antidepressants and benzodiazepines, acute antagonism of the benzodiazepines may induce seizures which had previously been suppressed. Moreover, for both antagonists the action of the antagonism is short-lived, therefore the patient may become comatose unexpectedly as the antagonist wears off.

Seizures may result from metabolic disturbance, cerebral hypoxia, or as a direct toxic effect (e.g. after poisoning with tricyclic antidepressants or theophylline). Urgent control is essential and is usually achieved initially with i.v. diazepam. Thereafter, consideration must be given to further anticonvulsant therapy (e.g. with phenytoin, phenobarbitone or clonazepam). Resistant subjects may require an infusion of thiopentone. Some of these agents cause further respiratory depression and elective tracheal intubation and artificial ventilation may be necessary. Detection of further seizures may be difficult in the patient undergoing ventilation, and monitoring should include continuous recording with a cerebral function monitor if neuromuscular blockers are used.

Cerebral oedema should be anticipated in any patient who has suffered a hypoxic cardiac arrest, a period of profound hypotension or severe carbon monoxide poisoning. Treatment to prevent secondary brain injury should include elective intubation and mechanical ventilation to moderate hypocapnia, with careful control of cerebral perfusion pressure by maintaining the mean arterial pressure within the normal range for that patient, and by avoiding fluid overload. Mannitol and loop diuretics may have a role after specialist consultation, and in severe cases intracranial pressure monitoring may be appropriate to direct therapy.

Metabolic complications may take almost any form in acute poisoning. The concentrations of urea, electrolytes and blood glucose should be checked routinely. In some patients, blood-gas analysis is also required.

Hypothermia is a common complication of prolonged coma outside hospital, and may be exacerbated by drugs which prevent the usual responses of vasoconstriction and shivering. Passive rewarming should be achieved with warm blankets. Active external rewarming is discouraged, as it may produce peripheral vasodilatation when cardiac function is still depressed by a reduced core temperature. I.v. fluids should be warmed and, during artificial ventilation, warm water bath humidifiers should be added to the breathing system. In extreme cases (< 32 °C) resistant to these techniques, it may be necessary to rewarm actively with warm water gastric or bladder instillation or by peritoneal lavage. Temperature should be monitored centrally (oesophageal or nasopharyngeal) and the ECG should be monitored for arrhythmias.

Hyperthermia may occur in acute intoxication with, for example, tricyclic antidepressants, cocaine or amphetamines, or as part of the syndrome of neuroleptic malignant syndrome after phenothiazine overdosage. In severe cases, active cooling with sedation, paralysis and ventilation with unheated gases may be required to control core temperature.

Measures to enhance elimination of the poison

Fewer than 5% of cases of acute poisoning merit treatment with specific techniques to increase drug elimination [34], “Gastrointestinal dialysis” with activated charcoal has already been discussed, and for those drugs which are readily adsorbed to activated charcoal it provides the safest mechanism of enhancing drug clearance. More invasive techniques are rarely justified. In cases of serious poisoning, specialist advice should be sought from the regional poisons centre.

Forced diuresis should be considered only for those patients in whom toxicological analysis has demonstrated the presence in the blood of a toxic agent in sufficient amount to cause severe poisoning. Brisk diuresis maintains a small concentration gradient between the renal tubular fluid and the renal capillary bed, thereby minimizing tubular reabsorption of toxins. Manipulation of the urinary pH may further decrease tubular reabsorption of the targeted drug by ensuring that it remains mostly in the ionized form. Therefore, for weak acids (such as salicylates or barbiturates), forced alkaline diuresis is most effective, whilst for weak bases (such as
phencyclidine) forced acid diuresis is more appropriate. The technique is ineffective for drugs which are strongly protein-bound (e.g. tricyclic antidepressants, carbamazepine, phenytoin) or which have a large apparent volume of distribution (e.g. paracetamol, lithium, tricyclic antidepressants). Regimens to establish a forced alkaline or forced acid diuresis have been described well elsewhere [34]. The technique, however, carries significant risk of causing fluid overload with pulmonary oedema or cerebral oedema, or of causing severe disturbance of electrolyte and acid–base balance. This risk is accentuated in the elderly, or those with cardiac or renal impairment, and should be balanced against the likelihood of significantly altering the patient's clinical outcome.

Extracorporeal elimination techniques—haemodialysis and haemoperfusion—have not yet been assessed adequately clinically in acute poisoning, and there remain many difficulties in assessing the efficacy of these invasive techniques [4, 38]. Their use should currently be limited to a carefully selected group of patients, and specialist help should always be sought. For extracorporeal elimination techniques to be helpful the following criteria are suggested [4]:

1. The drug or toxin should either diffuse readily through the dialysis membrane or be readily taken up by an absorbent. Protein-bound drugs and large molecules are removed inefficiently by dialysis, and can be removed more effectively by haemoperfusion (in which the blood is directly over sorbent particles to which toxins or drugs are adsorbed by surface forces). However, although salicylates are protein-bound, the plasma binding sites are saturated quickly even at normal therapeutic plasma concentrations, therefore a large proportion of the drug exists in the unbound form.

2. A significant proportion of the poison should be present in the plasma water, or be capable of rapid equilibration with it. Drugs with a large volume of distribution and high lipid solubility are therefore difficult to eliminate. If movement of the drug from the extravascular compartment back into the intravascular compartment is slower than the plasma clearance achieved, a rebound of the plasma concentration occurs on stopping dialysis/haemoperfusion.

3. The pharmacological effect of the toxin should be directly related to its concentration in the blood.

4. Dialysis or haemoperfusion should add significantly to other body mechanisms of elimination.

Peritoneal dialysis achieves considerably less clearance of plasma than can be achieved with haemodialysis, and has no established role in the management of acute poisoning.

Haemodialysis or haemoperfusion has a clearly established role in the treatment of severe salicylate overdose or poisoning with death cap mushrooms (Amanita phalloides) [4]. Clearance of alcohol, ethanol, barbiturates, anticonvulsants, benzodiazepines, lithium, cardiac glycosides and many other less commonly encountered poisons can certainly be enhanced with extracorporeal techniques; however, it remains unclear if this influences clinical outcome favourably. Clearance of paracetamol and the tricyclic antidepressants is not enhanced by haemodialysis or haemoperfusion, and extracorporeal elimination techniques have no role in the management of patients after poisoning with these agents.

Use of specific antidotes

The toxic effects after poisoning with specific agents may be decreased or prevented by administration of their specific antidotes. Such antidotes may directly influence the metabolism of the poison, preventing or reducing the formation of harmful metabolites (e.g. acetylcysteine in paracetamol poisoning), may compete for drug receptor sites (e.g. flumazenil in benzodiazepine overdose; naloxone in opioid overdose) or may bind with the poison to form less toxic chelates which are more easily excreted (e.g. Fab fragments in severe cardiac glycoside overdose). A broader definition of an antidote includes any substance which can favourably influence the onset, severity or duration of the toxic effects of a poison. The currently available antidote therapies and their clinical use has recently been reviewed comprehensively by Lheureux, Even-Aadin and Askenasi [17] and emergency departments should keep a reference list of antidotes and their mode of administration for quick reference.

FEATURES AND TREATMENT OF SPECIFIC POISONS

It is proposed not to give here detailed aspects of management, but to provide a ready, practical referral list, and to point out aspects of care peculiar to specific intoxicants.

Analgesics

Salicylate intoxication

A large number of salicylate preparations are available to the community, many of which do not mention the name "aspirin". Oil of wintergreen is methyl salicylate and is highly toxic.

Pharmacology. In normal therapeutic doses, acetyl salicylic acid is de-acetylated by plasma esterases and eliminated by conjugation. The volume of distribution is normally low but, when metabolic acidosis develops, tissue penetration increases.

In salicylate intoxication, prolongation of elimination occurs, the conjugation pathway rapidly becomes saturated and elimination is by the clearance of free salicylate via the kidneys. Salicylate clearance is pH-dependent, increasing 10-fold from a serum pH of 6 to that of 7.5.

Salicylates have a contradictory effect on acid–base balance. CNS stimulation of the respiratory centre may lead to respiratory alkalosis, whereas salicylate itself results in the accumulation of organic acid metabolites. The interaction between these two elements is variable and can be assessed only by frequent measurement of blood-gas tensions and acid–base state. Other important metabolic effects are hypo- or hyperglycaemia, and hypokalaemia from compensatory renal excretion.

There is increased risk of permeability-related oedema, although left ventricular failure may also occur secondary to cardiac arrhythmias, hypokalaemia or fluid overload. Clotting defects may...
Mild intoxication
Observe fluid balance.
Forced diuresis with large fluid turnover (4 litre/24 h).
Repeat salicylate concentration measurement 2 h later to check that concentration is decreasing.

Moderate–severe intoxication
Admit to ITU regardless of the level of consciousness.
Administer activated charcoal orally or via a nasogastric tube: 5 g 4-hourly for six doses.
Observe airway, ventilatory frequency, mental state and core temperature.
Measure acid–base balance 2-hourly.
Forced alkaline diuresis.
Maintain careful fluid balance charts and observe for fluid overload, pulmonary oedema and pulmonary aspiration.
Haemodialyse if:
1. "Severe" concentration does not decrease after 2 h of therapy.
2. "Moderate" concentration increases to the "severe" range after 2 h of therapy.
3. Onset of acute renal failure or pulmonary oedema secondary to fluid overload, unresponsive to diuretic therapy.

Table I. Summary of management of salicylate poisoning

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Management</th>
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<tbody>
<tr>
<td>Asymptomatic</td>
<td>Monitor urinary pH. If &lt; 7.2, give 1 litre of saline 0.3 mol litre⁻¹ with sodium bicarbonate 100 mmol i.v. over the subsequent 2 h, and review urinary pH. Do not give more than 300 mmol of sodium per 24 h. Repeat measurement of the blood salicylate concentration after 2 h. If a &quot;moderate&quot; concentration has increased to the &quot;severe&quot; range, or there has been no decrease from the severe range, commence renal dialysis, or refer for renal dialysis. If there has been a decrease in the salicylate concentration, try to maintain the urinary pH &gt; 7.2 with the use of sodium bicarbonate 50–100 mmol added to 1 litre of saline 0.3 mol litre⁻¹. Potassium chloride 60–120 mmol should be added to each 1 litre of i.v. solution. Observe serum sodium, potassium and bicarbonate concentrations and pH. Avoid fluid overload, metabolic alkalosis, hypernatraemia and hypokalaemia. Should there be doubt about the fluid balance or the patient develops pulmonary oedema, pulmonary artery occlusion pressure monitoring is essential. A small pulmonary artery occlusion pressure should be aimed for.</td>
</tr>
<tr>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
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<tr>
<td>Severe</td>
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</table>

Occur because of inhibition of Factor VII production by salicylate.

Presentation. Restlessness, irritability and hallucinations; tinnitus; tachycardia; hyperventilation; pyrexia, sweating; occasionally, pulmonary oedema.

General management (table 1). Gastric lavage if ingestion < 24 h. Activated charcoal in repeated doses via a nasogastric tube. Check salicylate concentration, blood-gas tensions, and concentrations of electrolytes, clotting factors and blood glucose.

In severe intoxication (fig. 1), check also serum concentrations of proteins and calcium, and liver function tests. Hyperpyrexia is rare, but may require treatment.

Fluids and electrolytes. Ensure intravascular volume repletion with colloid, then give 1 litre of saline 1 mol litre⁻¹ or 0.3 mol litre⁻¹ every 4–6 h. Monitor urinary pH. If < 7.2, give 1 litre of saline 0.3 mol litre⁻¹ with sodium bicarbonate 100 mmol i.v. over the subsequent 2 h, and review urinary pH. Do not give more than 300 mmol of sodium per 24 h. Repeat measurement of the blood salicylate concentration after 2 h. If a "moderate" concentration has increased to the "severe" range, or there has been no decrease from the severe range, commence renal dialysis, or refer for renal dialysis. If there has been a decrease in the salicylate concentration, try to maintain the urinary pH > 7.2 with the use of sodium bicarbonate 50–100 mmol added to 1 litre of saline 0.3 mol litre⁻¹. Potassium chloride 60–120 mmol should be added to each 1 litre of i.v. solution. Observe serum sodium, potassium and bicarbonate concentrations and pH. Avoid fluid overload, metabolic alkalosis, hypernatraemia and hypokalaemia. Should there be doubt about the fluid balance or the patient develops pulmonary oedema, pulmonary artery occlusion pressure monitoring is essential. A small pulmonary artery occlusion pressure should be aimed for.

Paracetamol intoxication

Pharmacology. Paracetamol is converted initially in hepatocytes to the potentially toxic metabolite n-acetyl-p-benzoquinoneimine (NABQI), which is conjugated rapidly to glutathione within the cell. In paracetamol overdose, glutathione stores are overwhelmed and unconjugated NABQI binds to proteins within the cell, producing necrosis. Increased concentration of intracellular calcium appears to play a fundamental role in the induction of cellular injury.

Paracetamol-induced liver damage is likely to be worse in patients taking hepatic enzyme-inducing agents, such as barbiturates or alcohol.

Paracetamol intoxication may also be complicated by renal failure and myocardial necrosis.

Presentation. Early (< 24 h): nausea and vomiting; confusion (occasionally); signs may be masked by additional drug ingestion. Late (> 24 h): severe vomiting; jaundice; evidence of acute hepatic failure, including encephalopathy, bruising and hypoglycaemia.
weight in 5% glucose 500 ml over 4 h, followed by 200 ml over 15 min, followed by 50 mg/kg body weight in 5% glucose 1000 ml over 16 h.

Occasionally, a histamine-mediated reaction develops in response to acetylcysteine.

Other aspects of management. Check clotting factors, electrolyte concentrations and liver function tests. Monitor capillary blood glucose concentration hourly. Monitor the patient's level of consciousness. Give glucose by i.v. infusion, to a total of 300 g daily. Observe for onset of renal failure. Renal dialysis may be necessary.

If ingestion was more than 24 h before presentation, and intoxication is assumed to be moderate to severe, observe for evidence of hepatocellular failure (deteriorating level of consciousness; increasing prothrombin time; pH less than 7.3) and introduce routine therapy for liver failure (these patients should be treated in an intensive therapy unit).

Referral to a centre particularly interested in the management of patients with paracetamol intoxication should be considered under the following circumstances [15]:
- pH < 7.3 more than 24 h after ingestion
- Prothrombin time > 45 s at 48 h
- Prothrombin time > 50 s at 72 h
- Increasing serum creatinine concentration
- Rapid development of grade 2 encephalopathy
- Liver transplantation may be considered under the following circumstances [15]:
  - pH < 7.3
  - Prothrombin time > 100 s
  - Serum creatinine concentration > 300 μmol litre⁻¹
  - Coma grade 3 or 4
  - Increasing prothrombin time from day 3 to day 4 after overdose.

Cocaine intoxication

Pharmacology. Cocaine (benzoylmethylecgonine) is absorbed from all mucosal surfaces and is most commonly taken i.v., by insufflation (intranasal) and by smoking (pulmonary). When it is insufflated, the peak action occurs at 30 min and lasts 60 min. The pharmacokinetic properties of i.v. cocaine are similar to those of smoked or inhaled cocaine.

"Crack" is the poorly water-soluble alkaloid form of cocaine, and is smoked. The onset of action is within minutes, and is dissipated within 20 min.

If ingested with alcohol, cocaine may be metabolized in the liver to a longer lasting more lethal metabolite [31].

Presentation. Clinical effects are the result of both peripheral and central nervous system stimulation. CNS stimulation: Euphoria, agitation, confusion; seizures; hyperthermia. Peripheral vasomotor stimulation by noradrenaline results in tachycardia and hypertension.

Complications. Transient ischaemic attacks; cerebral haemorrhage; cardiac arrhythmias; hyperthermia leading to disseminated intravascular coagulation, cerebral oedema and rhabdomyolysis with acute renal failure; acute psychosis—paranoia, hallucinations and aggressive behaviour.

Differential diagnosis is from other conditions causing hypoxia, seizures, or both. The clinical picture may mimic neuroleptic malignant syndrome or acute withdrawal from sedative or hypnotic drugs.
TABLE II. Summary of pharmacology of antidepressant drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
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<tbody>
<tr>
<td><strong>Tricyclic</strong></td>
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<tr>
<td>Amitriptyline</td>
<td>Anticholinergic</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Alpha-adrenergic agonist</td>
</tr>
<tr>
<td>Lofeperidine</td>
<td>Life-threatening cardiotoxicity</td>
</tr>
<tr>
<td><strong>Tetracyclic</strong></td>
<td></td>
</tr>
<tr>
<td>Manaserine</td>
<td>Cardiotoxic in mild overdose</td>
</tr>
<tr>
<td><strong>Triazolopyridine derivative</strong></td>
<td></td>
</tr>
<tr>
<td>Trazadone</td>
<td>Unrelated to tricycles</td>
</tr>
<tr>
<td>Aralkylketone</td>
<td>Toxicity is mild—drowsiness, dizziness, occasionally coma</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Serotonin uptake inhibitor</td>
</tr>
<tr>
<td><strong>Trifluoro-oxypropylamine derivative</strong></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Plasma half-life 2–3 days</td>
</tr>
<tr>
<td><strong>Dibenzoxapines</strong></td>
<td></td>
</tr>
<tr>
<td>Amoxapine, loxapine</td>
<td>Block dopamine receptors</td>
</tr>
<tr>
<td></td>
<td>Mild cardiotoxicity</td>
</tr>
<tr>
<td></td>
<td>High incidence of convulsions</td>
</tr>
<tr>
<td></td>
<td>Rhabdomyolysis and acute renal failure may occur</td>
</tr>
<tr>
<td></td>
<td>Management: Aggressive anticonvulsant therapy, early intubation. Diazepam ineffective in controlling seizures</td>
</tr>
</tbody>
</table>

or ethanol. Other drugs which may result in a similar presentation include the hallucinogens and anticholinergics.

**General management.** It is essential to exclude medical causes for agitation—for example hypoxia from pneumonia, meningitis or sepsicaemia.

The most important aspect of care is to control the psychomotor agitation and hence to prevent complications. Place in a single room where close monitoring is possible, but where intrusion is minimal.

Check oxygen saturation, ECG, core temperature and capillary blood glucose. Commence i.v. fluids and ensure intravascular volume repletion. Give Parentrovite ampoules 1 and 2 i.v. Cool by surface cooling if core temperature > 40°C.

**Indications for tracheal intubation and artificial ventilation:** uncontrollable hyperthermia; extreme agitation with danger of aspiration; uncontrollable convulsions; deep coma with danger of aspiration.

**Sedation.** Sedate with diazepam i.v. until agitation and seizures stop. If the required dose causes respiratory depression, tracheal intubation and artificial ventilation may be necessary. Continue regular doses of diazepam—for example 10 mg 4–6 hourly.

**Other medications.** Do not use neuroleptic agents. Beta-adrenergic antagonists should be avoided unless the patient is heavily sedated, because this may lead to increased alpha-adrenergic activity and increasing hypertension.

**Management of cardiac arrhythmias and hypertension.** Supraventricular tachycardias are common and are often caused by hyperthermia and agitation, requiring no specific antiarrhythmic therapy.

Ventricular tachycardias should be treated appropriately, the patient sedated and the lungs ventilated artificially. Lignocaine may be considered as a temporary measure, and alpha–beta-block (labetalol) or beta-block (atenolol or propranolol) may be used when the patient is undergoing artificial ventilation.

Severe hypertension which has failed to respond to sedation and artificial ventilation should be treated with vasodilators such as labetalol, or sodium nitroprusside by i.v. infusion.

**Treatment of rhabdomyolysis.** Rhabdomyolysis is generally associated with severe muscle pain and contractures, and is frequently complicated by acute renal failure (ARF) which may require dialysis. The management of acute rhabdomyolysis has been discussed earlier in this review.

**Additional investigations.** Check concentrations of serum creatine phosphokinase and urine myoglobin; perform blood and urine drug screen (including alcohol); a computed tomography scan is advisable in order to exclude complicating intercerebral pathology; blood and urine cultures.

**Amphetamines and MDMA (Ecstasy)**

Amphetamines may be injected, inhaled or taken orally.

**Pharmacology:** Methyl amphetamine (ice) is available as crystals and is smoked. It is 20 times as potent as amphetamine sulphate, with effects which are similar. 3,4-Methylene dioxyamphetamine (MDMA) has fewer side effects in the usual dose of 200 mg taken orally, but sudden death from ventricular fibrillation has been reported.

**Presentation** is similar to that following intoxication with cocaine.

**Management.** Similar to management of cocaine intoxication. Clearance of amphetamine is increased by urinary acidification, but this should be avoided in the presence of rhabdomyolysis.
Heroin (diamorphine)

Heroin deaths are caused generally by respiratory depression with or without pulmonary aspiration. This may occur with first use, change in drug access (variability in purity) or loss of tolerance after a period of abstinence.

Presentation: coma, with slow ventilatory frequency (terminating in apnoea); pinpoint pupils (not present in pethidine intoxication).

Diagnosis. Classically, a temporary reversal of coma and respiratory depression is achieved with naloxone 0.8–2 mg i.v. Antagonism may require larger doses of naloxone if the intoxication is caused by pethidine, buprenorphine, or dextropropoxyphene, and may be suppressed by the presence of other drugs.

Treatment. Some authors suggest the use of i.v. naloxone to maintain antagonism. In our opinion, this requires very careful titration, and we consider it safer to intubate the trachea and ventilate the lungs until the intoxicant effect has worn off spontaneously.

Complications include pulmonary aspiration, non-cardiogenic pulmonary oedema, rhabdomyolysis and infective complications in i.v. drug abusers.

Drug couriers. "Body packers" as they are termed, smuggle drugs by concealment in and around the body. Should the drug be swallowed in a container (e.g. condom, plastic bag or vial), leakage may lead to severe toxicity. A recent plane journey may be an indication for an abdominal x-ray. Surgical removal from the bowel may be indicated.

Psychoactive Drugs

Pharmacology. The antidepressant agents have differing activities, summarized in table II.

Tricyclic intoxication

Presentation. Cardiovascular and neurological features dominate the clinical picture.

Cardiac: hypotension; cardiac arrhythmias (ventricular and atrial); ECG abnormalities (PR, QRS and QTc prolongation). A right bundle branch block pattern is characteristic [3]. With QRS > 0.1 s, convulsions are likely; QRS > 0.16 s, ventricular arrhythmias are likely. Terminally, refractory hypotension may occur, leading to electromechanical dissociation (EMD).

CNS: convulsions; agitation; hallucinations; coma and respiratory depression.

General management. In any patient with evidence of a cardiac arrhythmia, twitching or respiratory depression, the trachea should be intubated and the lungs ventilated. Therefore, in the majority of severe intoxications, even if the patient is still conscious, he/she should undergo elective ventilation.

This management is recommended because respiratory depression, hypercapnia and hypoxia often precipitate cardiac arrhythmias; acidosis, whether respiratory or metabolic, enhances cardiotoxicity; and intubation of the trachea and ventilation of the lungs ensure preservation of the airway and safe use of anticonvulsants (e.g. benzodiazepines) which are less negatively inotropic than phenytoin.
(generally relieved by procyclidine 5-10 mg i.v.); coma and convulsions; hypothermia; neuroleptic malignant syndrome (confusion, muscle pain and rigidity, rhabdomyolysis, fever).

**General management**: supportive care; maintain pH > 7.4; ensure a normal serum potassium concentration.

**Management of tordes de pointes**: d.c. shock and cardiac pacing 20 beat min⁻¹ greater than the patient’s sinus rhythm; infusion of isoprenaline 2-6 µg min⁻¹ may be tried whilst pacing is established.

**Sedative and Hypnotic Agents**

**Benzodiazepine overdose**

Death is caused by respiratory depression and aspiration of vomitus, but note that these drugs are often taken in combination with other drugs, resulting in a confusing clinical picture.

In our opinion, flumazenil should not be used for treatment because it may precipitate convulsions or acute withdrawal syndromes, and it has a short half-life (1-2 h), making repetitive doses and continued monitoring necessary.

**Management**: supportive care with intubation and ventilation if required.

**Carbon monoxide poisoning**

In England and Wales, approximately 1000 people die every year from carbon monoxide poisoning. Most of these patients do not reach hospital. Common sources of carbon monoxide are car exhaust fumes, improperly maintained and ventilated heating systems, smoke from fires, and household gas.

**Pharmacology.** Carbon monoxide has an affinity for haemoglobin which is 200-250 times that of oxygen. Carbon monoxide combines with haemoglobin to form carboxyhaemoglobin, and the affinity for oxygen of the remaining haem is increased. Carbon monoxide toxicity is caused by cellular anoxia, and possibly also inhibition of cellular respiration as a result of binding to other haem proteins. The elimination half-life of carbon monoxide is reduced from 250 min when the subject is breathing air, to 59 min breathing 100% oxygen, and is reduced further to 22 min when 100% oxygen is breathed at 2.2 atm.

The severity of poisoning depends on the concentration of carbon monoxide in the air, the duration of exposure and the person’s general health.

**Presentation.** Repeated exposure: headache; fatigue; poor memory and concentration; dizziness and paraesthesia; visual disturbances; chest pain; diarrhoea and abdominal pain.

Acute exposure: carboxyhaemoglobin < 10%—generally no symptoms; carboxyhaemoglobin > 60%—coma, leading to cardiorespiratory arrest.

Late sequelae may include neuropsychiatric sequelae which may develop weeks after exposure (memory loss, impaired intellect, signs of cerebellar and mid-brain damage).

Signs of poisoning include: cherry red skin, coma, hyper-reflexia, convulsions and cardiac arrhythmias.

**General management.** Remove from site; administer 100% oxygen via tight fitting face mask (where there is respiratory depression or difficulty with airway control, intubate the trachea and ventilate the lungs with 100% oxygen); in cases of severe poisoning, assume cerebral oedema and treat accordingly.

Indications for hyperbaric oxygen therapy include: a conscious patient with a carboxyhaemoglobin > 20%; depressed level of consciousness, but able to maintain airway; recovery of consciousness after an initial carboxyhaemoglobin > 40%.

Contraindications to hyperbaric oxygen therapy via a single person chamber include: artificial ventilation; inability to maintain an airway; hypovolaemia or dependence on cardiac inotropes; cardiac arrhythmias potentially requiring urgent intervention; asthma.

These contraindications arise because of the practical difficulties of managing such patients in single person hyperbaric oxygen chambers, and the limited availability of compressed air chambers in which medical attendants can also be pressurized. All patients fulfilling the indications for hyperbaric oxygen therapy should be discussed with the regional hyperbaric oxygen facility. (The availability of hyperbaric oxygen facilities may be ascertained by contacting the Diving Diseases Research Centre, who provide a 24-h service. Tel.: 0752-261-910.)

**Lithium intoxication**

**Pharmacology.** This metal is eliminated by the kidney, therefore renal failure may lead to accumulation. Other circumstances which may lead to toxicity when lithium is being used for treatment include dehydration and concomitant administration of non-steroidal anti-inflammatory agents or diuretics.

**Presentation.** Neurological: confusion, agitation; hyper-reflexia, hypertension, tremor; ataxia; convulsions. Gastrointestinal: vomiting. Metabolic: hyponatraemia; diabetes insipidus; renal failure.

The therapeutic range in blood is lithium 1.0-1.4 mmol litre⁻¹. In acute poisoning the lithium concentration is generally > 5.0 mmol litre⁻¹.

**General management**: gastric lavage up to 4 h after ingestion; forced diuresis. In the presence of neurological symptoms, renal failure, or both, haemodialysis should be performed.

**APPENDIX**

**OTHER POISONINGS**

Space does not allow for details about other poisons. Readers are referred to the following texts for further information on the management of specific poisons:

**Alcohols and ethylene glycol**


Anticonvulsants
Dupuis RE, Lichtman SN, Pollack GM. Acute valproic acid
overdose—clinical course and pharmacokinetic disruption of


Mauro LS, Mauro VF, Brown DL, Somani P. Enhancement of
phenytoin elimination by multiple dose activated charcoal. Annals of

Beta-2 agonists and theophylline poisoning
Vale JA. Poisoning with respiratory drugs. Prescribers' Journal

Cardiac drugs
Martin SS, Phelps SJ, Maney KL. Treatment of severe digitalis
intoxication with digoxin-specific antibody fragments: a clinical

Chloroquine poisoning
Riou B, Barriot P, Rimailho A, Baud FJ. Treatment of severe
318: 1-6. Consensus Committee, Société de Réanimation de Langue
Française. Treatment of Acute Chloroquine Poisoning. Intensive and
Critical Care Digest 1992; 11: 5.

Inhalation agents as poisons
Blain PG. Sulphur mustard and nerve agents, organophosphorus
poisonings—chemical warfare agents. Care of the Critically Ill

Mushroom poisoning

Langer M, Verconci S, Constantino D. In: Vincent JL, ed. Update in
Intensive Care and Emergency Medicine. Berlin: Springer-
Verlag, 1990; 482-493.

Paraquat poisoning
Volans GN, Byatt GM. Poisoning from domestic products.

Quinine intoxication

Sedatives
Flanagan RJ, Ruprah M, Meredith TJ, Ramsay JD. An
introduction to the clinical toxicology of volatile substances. Drug

Henry JA. Volatile substance abuse. Care of the Critically Ill

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arrhythmias after an acute overdose of trimylic anti-
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Value of emergency toxicological investigations in differential
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Alcohander GJM, Williams R. Intravenous aacetylcysteine in
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Does multiple-dose charcoal therapy enhance salicylate
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18. Levy G. Gastrointestinal clearance of drugs with activated
charcoal. New England Journal of Medicine 1982; 307:
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absorption in man. Part 1. Clinical Pharmacology and
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Geller E. Acute poisoning treated in the intensive care unit:
A case series. Israel Journal of Medical Sciences 1989; 25:
98-102.
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aspiration of oral activated charcoal. British Medical Journal
R, Rashkin MC. Prospective evaluation of gastric emptying
in the self poisoned patient. American Journal of
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