Poisons

Edited by Dr Nicholas Bateman MD FRCP FRCP(E)
Reader in Clinical Pharmacology, Scottish Poisons Information Bureau, Royal Infirmary, Edinburgh

Initial assessment and management

Sally M Bradberry BSc MB ChB MRCP, Assistant Director
J Allister Vale MD FRCP FRCPE FRCPG FFOM FAACT, Director
National Poisons Information Service (Birmingham Centre) and West Midlands Poisons Unit, City Hospital, Birmingham

Clin Med 2003;**3**:107–10

Initial assessment

Assessment of an acutely poisoned patient follows the established clinical method of:

- history
- examination, and
- investigation.

History

Acutely poisoned patients are frequently distressed, agitated, angry, inebriated, paranoid, potentially violent and/or liable to misinterpret verbal and/or visual cues. Such patients require sympathetic, careful and competent interview if vital information is not to be missed. It is preferable to take a history in the absence of attending family and friends, as many patients will conceal information in their presence. Similarly, if an interpreter is required, it is often inappropriate to invite a relative to act since domestic stress is frequently implicated in the poisoning episode.

If the patient is able to give an account of events, the identity and quantity of the substance(s) taken should be ascertained and the time and route of exposure confirmed. The information obtained may be unreliable because the patient either genuinely cannot remember what happened or wishes to conceal facts through embarrassment or fear. Further information about the quantity of tablets taken can normally be established by asking questions regarding the number of packets/strips involved and, if it is a prescription medication, observing the date of issue on the bottles/boxes etc. Useful information may be obtained from the ambulance attendance sheet. It is also usually possible to improve the accuracy of the timing of exposure by relating events to daily activities, television or radio programmes etc.

If pharmaceuticals have been taken, it should be established whether or not these were the patient's own, together with a list of any other prescribed or habitually taken preparations. Patients often do not use generic drug names, so it is important to clarify which product they mean (eg Anadin or Anadin Extra). All patients should be asked about their alcohol intake and other forms of substance abuse both habitually and at the time of poisoning. Other matters to determine are:

- precipitating events
- the patient's intent at the time of poisoning
- the degree of premeditation
- recent or previous episodes of self-harm
- the writing of a suicide note
- the patient's location at the time of poisoning
- whether others were present, and
- how the patient came to the attention of the medical services.

Important information may often be obtained from family and friends; for example, whether the patient is presently, or has previously been, under the care of the psychiatric services, if possible obtaining specific names and telephone contact numbers.

Medical and social history should be as comprehensive as circumstances allow and any previous case notes obtained at the earliest opportunity.

Examination

A thorough examination is imperative if vital diagnostic clues are not to be missed and alternative or coincidental diagnoses identified:

- Track marks may reveal an undisclosed illicit drug abuse problem.
- Atypical bruising may suggest domestic or other violence.
- Burns to oral mucous membranes may implicate ingestion of a corrosive substance.
- Solvents or alcohol may be smelled on the breath.

Although abnormal neurological signs are common in moderate to severe

Key Points

- **There should be a systematic approach to the poisoned patient**
- **Investigations depend on history and clinical features**
- **For most overdoses gut decontamination is not required**
- **Specific antidotes are indicated for relatively few poisons**

KEY WORDS: gut decontamination, management, overdose, poisoning

poisoning with many agents, with the exception of transient inequality of pupil size, lateralising neurological signs effectively exclude a diagnosis of acute poisoning unless they can be explained by pre-existing illness. There may be loss of oculocephalic and oculovestibular reflexes and/or the occurrence of transient pyramidal tract signs (hypertonia, hyperreflexia and extensor plantar responses) following poisoning with several drugs (eg carbamazepine, phenytoin, tricyclic antidepressants), from which patients can recover fully. Pupillary size, responses and movements may provide a clue to a diagnosis as part of typical 'clusters' of features (toxidromes) (see article on Self-poisoning in the UK: epidemiology and toxidromes below).

Table 1. Mechanisms of hypokalaemia in acute poisoning.

- Increased Na^+/K^+ ATPase activity
  - via cyclic AMP (eg β_2-agonists, theophylline)
  - via increased affinity for intracellular Na^+ (eg insulin)
- Competitive blockade of K^+ channels (eg barium, chloroquine)
- Gastrointestinal losses
- Alkalosis leading to a K^+ shift from ECF to ICF

AMP = adenosine monophosphate; ATP = adenosine triphosphate; ECF = extracellular fluid; ICF = intracellular fluid.

Table 2. Mechanisms of hyperkalaemia in acute poisoning.

- Inhibition of Na^+/K^+ ATPase activity (eg digoxin)
- Depletion of ATP (eg cyanide)
- Opening of K^+ channels (eg fluoride)
- Ingestion of a K^+ salt
- Acidosis leading to a K^+shift from ICF to ECF
- Rhabdomyolysis
- Acute renal failure

ATP = adenosine triphosphate; ECF = extracellular fluid; ICF = intracellular fluid.

Investigation

Haematological. Standard haematological investigations are rarely diagnostically helpful, although the prothrombin time may be prolonged following ingestion of anticoagulants or because of hepatic damage (eg in paracetamol poisoning).

Metabolic. Hypokalaemia (Table 1) is a common complication of acute poisoning, while hyperkalaemia (Table 2) is less frequent. Hypoglycaemia is typically caused by an overdose with insulin or oral hypoglycaemic agents; it complicates ethanol intoxication, particularly in children, and is a well-documented feature of severe paracetamol-induced liver damage. Hyperglycaemia can occur in intoxication with sympathomimetic drugs (eg theophylline). Hypocalcaemia is a feature of poisoning with ethylene glycol and fluoride salts, and complicates hydrofluoric acid burns. Undisclosed paracetamol overdose is a strong diagnostic possibility in any patient who presents with plasma aminotransferase activity of more than 5,000 iu/l.

Arterial blood gas analysis. Arterial blood gas analysis should be undertaken in any patient with respiratory insufficiency, hyperventilation or when metabolic acid-base disturbance is suspected. The cause of a metabolic acidosis should be promptly clarified. The anion and osmolal gaps provide useful information in this regard, particularly if there is a potential history of methanol or ethylene glycol ingestion. Poisons that cause a high anion gap metabolic acidosis are listed in Table 3.

Concentration of ingested poison. Emergency measurement of the concentration of ingested poison is indicated only when the result will influence management. Such agents are listed in Table 4. Plasma paracetamol concentrations should be measured in all unconscious poisoned patients since it is important to diagnose an overdose at a stage when administration of N-acetylcysteine might prevent liver damage and death.

Table 3. Poisons causing a high anion gap metabolic acidosis.

- Poisons causing a lactic acidosis
  - Type A (hypoxic)
    - any toxin causing cardiorespiratory depression
    - any toxin causing convulsions
    - carbon monoxide
    - methaemoglobin-forming agents
  - Type B (non-hypoxic)
    - cyanide
    - hydrogen sulphide
- Salicylate
- Ethylene glycol
- Methanol
- Ethanol
- Poisons causing uraemia

Table 4. Agents for which assays should be available on a 24-hour basis.*

- Acetylcholinesterase
- Carbamazepine
- Carboxyhaemoglobin
- Digoxin
- Ethanol
  (monitoring of treatment in ethylene glycol and methanol poisoning)
- Ethylene glycol
- Iron
- Lithium
- Methaemoglobin
- Methanol
- Paracetamol
- Paraquat (qualitative urine test)
- Phenobarbital
- Phenytoin
- Salicylate
- Theophylline

* *Note*: some assays will be available only from a specialised toxicology laboratory.

In contrast, routine requests for a salicylate concentration cannot be justified, as it is unlikely that a clinically significant concentration will be present in a patient without the typical signs of salicylism. Emergency toxicological screening in an unconscious patient is appropriate only when the result of the screen will alter management.

Radiology. Radiology can be used to confirm ingestion of metallic objects (eg coins, button batteries) or injection of elemental mercury or iron salts. Hydrocarbon solvents may be seen as a slightly opaque layer floating on the top of the gastric contents with the patient upright, or outlining the small bowel.

ECG. An ECG is of limited diagnostic value, although tachycardia with prolongation of the PR and/or QRS intervals in an unconscious patient should prompt consideration of tricyclic antidepressant overdose. With increasing cardiotoxicity, it may be impossible to detect P waves and the pattern then resembles ventricular tachycardia. Overdose with cardiac glycosides or potassium salts also induces characteristic ECG changes.

Initial management

Symptomatic and supportive care

Intoxicated patients often present a clinical, ethical and legal dilemma. If it is considered that the patient is competent to refuse or accept medical advice and treatment, the patient's wishes should be respected. However, if the patient's capacity to consent is diminished, treatment should be instituted as necessary. Calm reassurance and an attempt to address the patient's immediate needs can often diffuse a volatile situation. Restraint is rarely required and, if it is necessary, patient and staff safety is paramount. When sedation is indicated, a benzodiazepine is preferred; alternatively, haloperidol may be used.

Most acutely poisoned patients require only symptomatic and supportive care to ensure an uncomplicated recovery, though some will benefit from the use of a specific antidote (Table 5). If the clinical presentation suggests inadequate ventilation caused by an opiate and/or a benzodiazepine, it is reasonable to give a resuscitative dose of intravenous naloxone (≥1.2 mg) and/or flumazenil (≥500 μg).

Gut decontamination: position statements

In a series of joint position statements,[1–6] the American Academy of Clinical Toxicology and the European Association of Poison Centres and Clinical Toxicologists have addressed the roles of gastric lavage, ipecac syrup, single- and multidose activated charcoal, whole bowel ingestion and cathartics.

Gastric lavage. The position statement on gastric lavage[1] concluded that lavage should not be *considered* unless a patient had ingested a potentially life-threatening amount of a poison and the procedure could be undertaken within one hour of ingestion.

Syrup of ipecacuanha . The position statement on syrup of ipecacuanha[2] concluded that there is no evidence from clinical studies that ipecac improves the outcome of poisoned patients. It was recommended that routine administration of ipecac syrup should be abandoned.

Activated charcoal. Although activated charcoal is widely used in an attempt to reduce poison absorption, the position statement recommended that single-dose activated charcoal should not be administered routinely in the management of poisoned patients.[3] Activated charcoal may be *considered* if a patient had ingested up to one hour previously a potentially toxic amount of a poison known to be adsorbed by charcoal. (Toxins not well adsorbed by charcoal are listed in Table 6.) There are insufficient data to support or exclude its use after one hour[3] and no evidence that

Table 6. Poisons poorly adsorbed by activated charcoal.

- Acids and alkalis
- Ethanol
- Ethylene glycol
- Iron
- Lithium
- Methanol

Table 5. Antidotes of value in acute oisoning.

Poison	Antidote
• Anticoagulants (oral)	Vitamin K
• Benzodiazepines	Flumazenil
• β-adrenoceptor blockers	Atropine Glucagon
• Carbon monoxide	Oxygen
• Cyanide	Oxygen Dicobalt edetate Hydroxocobalamin Sodium thiosulphate Sodium nitrite
• Digoxin	Digoxin–specific antibody fragments
• Ethylene glycol	Ethanol Fomepizole
• Iron salts	Desferrioxamine
• Methaemoglobinaemia	Methylthioninium chloride (methylene blue)
• Methanol	Ethanol Fomepizole
• Opioids	Naloxone
• Organophosphorus insecticides	Atropine Pralidoxime
• Paracetamol	N-acetylcysteine

administration of activated charcoal improves clinical outcome.

Whole bowel irrigation. Theoretically, the more quickly a poison passes through the gut, the less it is absorbed. Whole bowel irrigation (WBI) using polyethylene glycol electrolyte solutions does not result in absorption of fluid and electrolytes, even though large volumes (1,500–2,000 ml/hr) are administered rapidly via a nasogastric tube. Some volunteer studies have shown substantial decreases in the bioavailability of ingested drugs, but there is no conclusive evidence that WBI improves the outcome of the poisoned patient.[4] Based on volunteer studies, WBI may be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs.

Cathartics. Osmotic and saline cathartics have no role in the management of the poisoned patients.[5]

Enhancing poison elimination

Urine alkalinisation

The principle behind urine alkalinisation is that weakly acidic poisons can be 'trapped' in the urine by increasing their ionisation, thereby enhancing their elimination. Urine alkalinisation increases the elimination of salicylate, phenobarbital, chlorpropamide, 2,4-dichlorophenoxyacetic acid and mecoprop. However, with the exception of salicylate poisoning, urine alkalinisation cannot be recommended as sole therapy in cases of poisoning due to these agents. Multiple dose activated charcoal is superior in the case of phenobarbital, while supportive care is invariably adequate in the case of chlorpropamide. A substantial diuresis is required in addition to urine alkalinisation to achieve clinically important chlorophenoxy herbicide (2,4-D and mecoprop) elimination.

Multiple dose activated charcoal

Multiple dose activated charcoal therapy involves the repeated administration of oral activated charcoal to enhance the elimination of drug already absorbed into the body. It is thought to increase poison elimination by interrupting the enteroenteric and, in some cases, the enterohepatic circulation of drugs. In addition, any unabsorbed drug still present in the gut will be adsorbed to activated charcoal, thereby reducing drug absorption. Elimination of drugs with a prolonged elimination half-life following overdose and small volume of distribution (<1 l/kg body weight) is particularly likely to be clinically significantly enhanced by this treatment.

Although many studies in animals and volunteers have demonstrated that multiple dose activated charcoal significantly increases drug elimination, this therapy has not yet been shown in a controlled study in poisoned patients to reduce morbidity and mortality. Further studies are required to establish its role and the optimal dosage regimen of charcoal. Based on experimental and clinical studies, multiple dose activated charcoal should be considered only if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine or theophylline.[6]

Clinical experience in adults suggests that charcoal should be administered in an initial dose of 50–100 g and then at a rate of not less than 12.5 g/hr, preferably via a nasogastric tube. A total of 200 g is usually suficient to load the small bowel of an adult.

Haemodialysis

Dialysis is of little value for poisons with a large volume of distribution (eg tricyclic antidepressants) because the plasma contains only a small proportion of the total amount of drug in the body. Haemodialysis significantly enhances the elimination of salicylate, lithium, methanol, isopropanol, ethylene glycol and ethanol, and is the treatment of choice for all cases of severe poisoning with these agents. Haemofiltration and peritoneal dialysis are more widely available than haemodialysis, but they are much less efficient in increasing poison elimination.

References

1 Vale JA. Position statement: gastric lavage. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:711–9.

2 Krenzelok EP, McGuigan M, Lheureux P. Position statement: ipecac syrup. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:699–709.

3 Chyka PA, Seger D. Position statement: single-dose activated charcoal. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:721–41.

4 Tenenbein M. Position statement: whole bowel irrigation. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:753–62.

5 Barceloux D, McGuigan M, Hartigan-Go K. Position statement: cathartics. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:743–52.

6 Vale JA, Krenzelok EP, Barceloux GD. Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1999;**37**:731–51.