Poisoning

Lewis O Jones

Of 233,756 recorded hospital admissions for overdose between 1997 and 1999, 1149 (0.5%) resulted in death: equivalent to about 380 deaths per year. Equal numbers of males and females were involved and about 50% of the deaths involved opioids. 3.7% of all ICU admissions entered into the UK Intensive Care National Audit and Research Centre database had self or accidental poisoning as their primary reason for admission.

History

Information about the poisoning and the circumstances surrounding the presentation should be obtained from whatever sources are available. This may include the patient, accompanying friends or relatives, and paramedics attending the scene. The history should also include details of what drugs or substances have been taken, the estimated quantity, where and when it occurred, why (e.g. deliberate or accidental) and whether anyone else is involved.

The patient's medical history, including medications prescribed and self-administered (including ethanol), is relevant because this affects drug handling and may alter patient management.

The initial assessment of these patients should follow the ABC approach, with appropriate management being instituted when problems are encountered. Clues about the substance involved may be obtained at this time (Figure 1). During assessment of the conscious level pupil size and reaction should be noted (Figure 2).

If necessary, remove all the patient's clothes for further assessment, which will reduce the absorption of substances that may be on the clothes and which are readily absorbed through the skin (e.g. organophosphates). The patient's pockets should be searched for clues such as prescriptions, empty tablet packets or evidence of illegal drug use. The healthcare worker should ensure their personal protection against blood-borne viruses because there may be needles in the patient's pockets.

Hypothermia can mimic poisoning and occur as a result of environmental exposure due to a decreased level of consciousness and should be excluded at an early stage.

Investigations

The National Poisons Information Service (NPIS) recommends that all patients presenting with self-poisoning should have a blood sample taken at 4 hours to exclude significant paracetamol ingestion. It is not recommended that routine salicylate levels are taken in asymptomatic patients. Other investigations should be guided by the individual patient factors. Routine urine toxicology screening is seldom helpful in guiding acute management.

Initial assessment of the poisoned patient

Airway	Breathing	Circulation
Smell: ethanol	Respiratory rate: opioids and benzodiazepines both slow rate	Pulse rate: β-blockers (bradycardia)
Colour: blue – methaemoglobinaemia from amyl nitrate	Pattern: Kussmaul breathing may indicate salicylate ingestion	Blood pressure: hypotension (antihypertensives)
Burns: strong acid or alkali	Efficacy: organophosphates lead to muscle weakness	
Is there tablet residue that can be used in identification?	Secretions: increased (organophosphates); reduced (tricyclic antidepressants)	

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Management

Few drugs have specific antidotes, therefore for most patients the options available for treatment are:

- reduce absorption from the gastrointestinal tract
- increase elimination from the body
- treat the symptoms of end-organ failure.

Gastric lavage can be used for most poisons, but the recovery of tablet residue is variable and diminishes rapidly with time from ingestion. There is no published evidence for an improvement in clinical outcome in patients treated with lavage, but significant morbidity and mortality is associated with its use. It is recommended only within 60 minutes of ingestion of a potentially life-threatening overdose. Following the lavage, 50 g of activated charcoal should be instilled into the stomach to reduce further

Assessing pupil size

Small pupils	Large pupils
• Opioids	• Alcohol
• Organophosphates	• Anticholinergics
• Other cholinergics	• Amphetamines
	• β-blockers

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absorption of the drug. If the decision is made to lavage a patient with a decreased level of consciousness, an endotracheal tube should be inserted to prevent aspiration.

Single-dose oral activated charcoal: the efficacy of this drug is time dependent, with volunteer studies showing a mean reduction of absorption of 88.6% at 30 min, falling to 34.4% at 60 min after ingestion. A study comparing lavage and charcoal, nasogastric aspiration and charcoal or ipecachuana and charcoal showed a significant improvement in the nasogastric aspiration and charcoal group with respect to critical care admission.

It is currently recommended that most patients presenting within 1 hour of their poisoning are given a single dose of 50 g of activated charcoal. It is not recommended for use in patients who have ingested alcohols, boric acid, cyanide, iron, lithium, petroleum distillates or strong acids or alkalis.

Repeated-dose activated charcoal: the use of multiple-dose activated charcoal attempts to interrupt the enterohepatic and entero-enteric circulation of the drug, reducing the plasma levels with a 'gut dialysis'. It should be considered only if a patient has taken a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine or theophylline**.** For these drugs there are data to confirm enhanced elimination, though no studies have demonstrated clinical benefits. The current recommended regimen for repeated-dose activated charcoal is 50 g, immediately followed by doses of 25–50 g at 4-hour intervals.

Induced emesis with syrup of ipecachuana is not recommended for use in acute ingestion because it does not increase elimination of the drug.

Whole-bowel irrigation is an option for potentially toxic ingestions of sustained-release or enteric-coated drugs. It also has theoretical value for patients who have ingested substantial amounts of iron (due to the high morbidity and the lack of other options for gastrointestinal decontamination) or packets of illicit drugs, and in those who have ingested substantial amounts of poisons not adsorbed to activated charcoal.

Increased elimination: a number of methods may be used to increase elimination; they include alkaline diuresis, haemodialysis, peritoneal dialysis, exchange transfusion and charcoal haemoperfusion.

Alkaline diuresis – renal elimination of weak acids such as salicylates and some herbicides can be increased by the intravenous administration of sodium bicarbonate. Alkalinization alone is as effective as traditional forced alkaline diuresis, and reduces the risk of complications resulting from fluid overload, cerebral or pulmonary oedema and electrolyte disturbance. The urine pH should be monitored closely to ensure that the desired change has been achieved (aiming for a urinary pH of 7.5–8.5).

Haemodialysis and peritoneal dialysis – the characteristics that predict the successful removal of a toxin by dialysis include low volume of distribution (< 1 litre/kg), the presence of the toxin in the central compartment, low endogenous clearance, a low molecular weight (< 500 Da), low protein binding and high water solubility. To be clinically effective, dialysis should improve the removal of a toxin by at least 30% compared with total body clearance. It is currently recommended for use in poisoning from methanol, ethylene glycol, isopropanol, lithium and salicylates.

Charcoal haemoperfusion and exchange transfusion have been attempted, but have no specific indications.

Specific poisons and their treatment

Opioids

The clinical features of opioid intoxication include:

- impaired conscious level
- respiratory depression
- pupillary constriction
- nausea and vomiting
- histamine release
- reduced gastrointestinal motility
- urinary retention.

Naloxone antagonizes the effect of the opioids at the mu and kappa receptors. It has a mean half-life of 64 min compared with morphine which has a half-life of 90–120 min in normal adults. Rapid reversal of the symptoms occurs following intravenous administration of naloxone, 400–800 µg, but it may induce withdrawal symptoms in those who are opioid dependent. Caution has to be taken in those who have been poisoned with long-acting opioids (e.g. methadone) and a prolonged period of observation is recommended in these cases. If a response is seen to the naloxone, but the respiratory depression then recurs, a naloxone infusion can be considered.

Benzodiazepines

Benzodiazepines commonly cause drowsiness, ataxia, dysarthria and nystagmus. Coma, hypotension and respiratory depression may occur but usually only if other CNS depressants, including alcohol, are involved. Coma usually lasts only a few hours in the young but in elderly people it may be more prolonged and relapsing. The respiratory depressant effects of benzodiazepines are more serious in patients with underlying lung disease.

Flumazenil (*Anexate*) is a benzodiazepine antagonist and like naloxone it has a shorter half-life than the drugs it antagonizes. It is not licensed or recommended for use as a diagnostic test, especially in mixed overdoses, where the benzodiazepine may be neuro- or cardioprotective against tricyclic antidepressants. In these circumstances, reversing the effect of the benzodiazepine could precipitate seizures or cardiac dysrhythmias.

Tricyclic antidepressants

Tricyclic antidepressants are highly toxic to the CNS and the cardiovascular system. Their main mode of toxicity is via their anticholinergic effects. The symptoms and signs seen in significant poisoning are given in Figure 3.

Arrhythmias are best treated by correcting any hypoxia or acidosis. Even in the absence of a metabolic acidosis sodium bicarbonate, 50 mmol (50 ml of 8.4%), should be given intravenously to an adult with arrhythmias or significant ECG abnormalities. It is thought the bicarbonate alters the binding of tricyclic antidepressants to the myocardium and there is some evidence that the sodium load stabilizes the fast sodium channels of the myocardium as well. Further doses of bicarbonate may be required depending on clinical response. Anti-arrhythmic drugs should be avoided.

Seizures should be treated with intravenous benzodiazepines.

Symptoms and signs of tricyclic antidepressant poisoning

Peripheral effects

- Sinus tachycardia and other cardiac arrhythmias
- Hot dry skin
- Dry mouth
- Dilated pupils
- Urinary retention
- Skin blisters

Central effects

- Ataxia
- Nystagmus
- Drowsiness
- Increased tone and hyperreflexia
- Extensor plantar reflexes
- Divergent squint
- Hypotension and hypothermia
- Fits
- During recovery confusion, agitation and visual hallucinations

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Phenytoin is contraindicated because it increases the risk of cardiac arrhythmias. Glucagon, 1 mg i.v. every 3 min, has been used to correct myocardial depression and hypotension. Glucagon increases intracellular cGMP production by direct stimulation of adenyl cyclase, leading to improved cardiac myocyte contractility. If a response is seen, a glucagon infusion should be started, and if severe hypotension persists despite the above measures the use of inotropes, vasopressors or even an intra-aortic balloon pump should be considered.

Carbon monoxide

Carbon monoxide binds to haemoglobin much more avidly than oxygen, leading to a marked impairment of peripheral oxygen delivery, resulting in coma, cerebral oedema and metabolic acidosis. Carbon monoxide is a product of incomplete combustion and poisoning typically arises either acutely during exposure to smoke in a confined space (e.g. in a house fire) or chronically from exposure to faulty heating equipment. The indicators of severe poisoning include:

- any new objective acute neurological signs (e.g. increased tone, upgoing plantars)
- coma
- need for ventilation
- ECG evidence of infarction or ischaemia
- clinically significant acidosis
- initial carboxyhaemoglobin more than 30%.

The half-life of carboxyhaemoglobin is reduced from 240 min to about 40 min when a patient breathes 100% oxygen. All patients with suspected carbon monoxide poisoning should be treated with inspired oxygen as close to 100% as possible. Those with a decreased level of consciousness, metabolic acidosis or cardiac ischaemia at presentation are at risk of long-term neurological sequelae which may be reduced with early hyperbaric oxygen therapy (three treatments in the first 24 hours).

Paracetamol

Paracetamol ingestion alone is seldom a cause for admission to critical care, but paracetamol is the most commonly taken drug in mixed overdose and for this reason knowledge of its management is important. Timely treatment of this poisoning avoids all the life-threatening complications.

Patients who have ingested a large amount of paracetamol are usually asymptomatic until end-organ damage occurs 48 hours or more from ingestion. The toxicity is due to an active metabolite, N-acetyl-p-benzoquinone imine (NAPQI), which under normal conditions binds to glutathione, rendering it inactive and allowing renal excretion. In overdose this pathway can be overwhelmed, leading to systemic release of NAPQI, which is toxic to the liver and kidneys. Patients with induced cytochrome P450 systems from chronic alcohol excess or regular medications (including the anti-epileptics) are at higher risk because they produce more NAPQI. Those who are glutathione depleted (anorexics, the malnourished or those with terminal malignancy) are also at high risk because they will be unable to bind the excess toxins.

A serum paracetamol level should be taken 4 hours after the ingestion and compared with the appropriate line on the Prescott nomogram to ascertain if treatment is required. If the level is deemed treatable, the glutathione donor N-acetylcysteine should be commenced. Regular checks of the liver function tests and INR allow any hepatotoxicity to be followed. As well as the manifestations of fulminant hepatic failure, paracetamol poisoning can cause acute renal failure requiring renal replacement therapy. ◆

FURTHER READING

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Kerr G W, McGuffie A C, Wilkie S. Tricyclic antidepressant overdose: a review. *Emerg Med J* 2001; **18:** 236–41.

Toxbase. www.spib.axl.co.uk The National Poisons Information Service website which contains comprehensive information on all aspects of poisons and poisoning.

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