Oral poisoning: an update

Catherine Ward MBBS BSc Hons FRCA
Mark Sair PhD MRCP FRCA

Key points
The mainstay treatment of poisoning is resuscitation and supportive care.
Poisoning should be considered in any patient exhibiting bizarre behaviour, a reduced conscious level, or unexplained physiological instability.
Ipecac is no longer recommended in the treatment of acute poisoning.
Activated charcoal should be given within 60 min of ingestion of poison but may have an effect for up to 2 h or longer post-ingestion.
Acetaminophen levels are mandatory in all cases of adult overdose.

Oral poisoning: an update
Acute poisoning accounts for >100,000 hospital admissions per year in the UK with in excess of 4000 deaths reported in England and Wales per annum. Although the majority of poison-related deaths occur in the community, reduction of in-hospital morbidity and mortality remains an important challenge. The largest proportion of enquiries to the National Poisons Information Service (NPIS) and Guy’s and St Thomas’ Poisons Unit (GTPU) are concerning pre-school children. A recent report indicated that 85% of poisonings occur in the home. Drugs accounted for the majority, but industrial chemicals and household products were involved in a significant number. Only one-third of cases were deliberate. The medications most commonly taken were acetaminophen, non-steroidal analgesics, and antidepressants.

The NPIS was commissioned by the Health Protection Agency and consists of five regional centres that operate a 24 h information service to health-care staff on the diagnosis, treatment, and management of poisoning. GTPU ceased to be a provider to NPIS in November 2005 and operates independently with support from Guy’s and St Thomas’ Foundation Trust. Toxbase, the UK online toxicology database, was established in 1998 and NPIS recommends it as the first point of contact for registered health-care professionals. The website provides easily accessible information on acute poisoning and its management.

Initial approach to the poisoned patient
Poisoning should be considered in any patient exhibiting bizarre behaviour, a reduced conscious level, or unexplained metabolic, cardiovascular, or respiratory instability. All cases are managed as acute medical emergencies using an ABC approach regardless of the agent used. Rare exceptions include patients poisoned with organophosphates, where health-care workers first need to protect themselves from the agent, and cyanide poisoning, where the antidote for cyanide is immediately required. All cases require:
- resuscitation;
- risk assessment;
- substance identification;
- specific treatment (if available);
- a period of observation.

A focused and detailed poisoning history and examination are required to identify specific physical signs of poisoning followed by the selective use of antidotes and laboratory tests (Table 1). Most poisoned patients require supportive treatment only.

A risk assessment should be performed by obtaining specific information from ambulance personnel or witnesses regarding the nature, timing, and amount of drug or poison. One-third of cases involve more than one toxin and alcohol is a common contributing factor. The patient’s clothing should be checked for notes or blister packets, which may give a clue to quantity and type of drug ingested. In cases of deliberate self-harm, there may be previous hospital admissions to aid diagnosis. The patient’s general practitioner should be contacted for previous history as family or witness sources are often unreliable.

Supportive care and monitoring
Patients suspected of being exposed to a poison or drug should be monitored in an appropriate clinical environment. Where coma is inevitable, patients should be intubated pre-emptively or at the first sign of deterioration in level of consciousness. Tracheal intubation will protect the airway and allow early administration of activated charcoal (AC) via a nasogastric tube if required. Patients who are at risk of cardiac instability and acidosis should have continuous ECG and invasive arterial pressure monitoring with regular blood gas analysis. Body temperature and serum glucose should be checked and i.v. dextrose administered if required.
whether given alone or combined with AC. 

Induced emesis

Ipecac induces vomiting by both direct gastrointestinal effects and central nervous system actions. It is administered at a dose of 30 ml in adults followed by water 240 ml. Emesis typically occurs within 20 min and persists for 30–120 min. Several studies have compared ipecac with single-dose AC. Ipecac conveys no benefit, whether given alone or combined with AC. 

Gastric decontamination

There is much debate regarding the use of the so-called ‘decontamination triangle’ of forced emesis, gastric lavage, and single-dose AC. Decontamination strategies are not without side-effects and the risk/benefit ratio should be considered before administration. The American Academy of Clinical Toxicology and European Association of Poisons Centres state that gastrointestinal decontamination should not be administered routinely.

Investigations

Acetaminophen levels are considered mandatory in all cases of adult overdose and should be taken 4 h post-exposure. Salicylate levels are not recommended in the asymptomatic patient. Screening for substances of abuse can be achieved quickly with readily available commercial urine kits. Other laboratory tests include full blood count, urea and electrolytes, lactate, liver function tests, and coagulation studies. Where poisoning is caused by specific agents, for example, methanol or carbamazepine plasma levels are taken 4 hourly to allow refinement of risk assessment and to gauge the response to enhanced elimination techniques. A chest radiograph may indicate pulmonary oedema, which is suggestive of poisoning with narcotics or salicylates. Abdominal radiographs can identify packets of drugs smuggled in ‘body packers’. Radiological investigations are otherwise rarely required in the setting of acute poisoning.

Activated charcoal

Most drugs and chemicals are absorbed by AC. It creates weak van der Waals forces that bind with the substance in the gastrointestinal tract. The numerous charcoal particles provide a large enough surface area to prevent further absorption. AC should be administered orally or nasogastrically via a 16 F tube in the intubated patient. The charcoal to toxin ratio is 10:1. It has been shown to reduce acetaminophen absorption up to 2 h after ingestion. AC is unpalatable and can cause vomiting, thus in children it can be mixed with ice cream. Patients should also be warned that it will make their stools black. It is not recommended in poisoning with lithium, iron, alcohol, methanol, ethylene glycol, petroleum distillates,
corrosives, acids, or alkalis. Repeated doses of 25 g per 4–6 hourly can be of benefit for poisoning with slow release formulations, for example, salicylate, barbiturates, theophylline, quinine, digoxin, carbamazepine, phenytoin, and dapsone. Multiple doses interrupt the enterohepatic circulation of the drug, reducing the plasma levels, and there are data that this reduces the duration of toxicity. A major but rare adverse effect from repeat doses is acute bowel obstruction from charcoal concretions, which is particularly likely in the presence of an anticholinergic ileus.

### Whole bowel irrigation

Whole bowel irrigation (WBI) aims to reduce the time for ingested substances to be absorbed. It requires the administration of polyethylene glycol (PEG) 1.5–2 litres solution per hour and is best administered through a 12 F feeding tube. The head of the bed should be elevated to 45º to prevent aspiration. If emesis occurs, then the infusion should be discontinued for 30 min and restarted at half the normal rate. Metoclopramide can be helpful as an antiemetic due to its prokinetic effects. Current recommendations are that the PEG is administered until the effluent is clear. The technique is not used routinely but may be considered where poisoning includes sustained release or enteric coated tablets. It may also be used for drugs for which charcoal is known to be ineffective, for example, alcohols, boric acid, cyanide, iron, lithium, hydrocarbons, acids, and alkalis. It has been used with some success in the treatment of body packers, heavy metal, and battery ingestion. WBI is contraindicated in patients with an unprotected airway, haemodynamic instability, bowel obstruction, bowel perforation, or an ileus.

### Increased elimination

Alkaline diuresis enhances the elimination of weak acids such as salicylates and some herbicides. Sodium bicarbonate is administered and the pH of the urine measured to keep the urinary pH 7.5–8.5. Weak acids become charged in alkaline urine resulting in a concentration gradient drawing more toxin into the renal tubular system. Hypokalaemia can result from this technique and should be corrected aggressively. Alkaline diuresis should be used with caution in patients with renal impairment or cardiac disease.

### Haemodialysis

Haemodialysis is helpful in ethylene glycol, methanol, lithium, theophylline, and salicylate poisoning. The usefulness of this technique depends on the pharmacological properties of the ingested drug. The drug or poison should have a low volume of distribution (<1 litre kg⁻¹), a low molecular weight (<500 Da), low protein binding, and low water solubility.

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**Fig 1** Acetaminophen metabolism.
Salicylates

Patients with salicylate poisoning may present with tinnitus, deafness, hyperventilation, epigastric pain, vomiting, hyperthermia, sweating, dehydration, respiratory alkalosis, metabolic acidosis, and electrolyte disturbances. Agitation and confusion may indicate the development of cerebral oedema which can be fatal. Treatment includes rehydration, treatment of acid–base disturbance, and close monitoring of plasma levels. AC should be administered as soon as possible even in delayed presentations. The use of multidose AC is debatable, but should be considered if the plasma salicylate level continues to increase or if a slow release preparation has been taken. Alkalinization of the urine may increase the elimination of salicylate and should be considered in patients with signs of toxicity or in patients with plasma levels more than 300 mg litre\(^{-1}\). In patients with levels more than 700 mg litre\(^{-1}\), haemodialysis should be considered.

Benzodiazepines

Deaths associated with benzodiazepine overdose are due to mixed overdoses, especially alcohol and other drugs. Clinical manifestations are associated with drowsiness, respiratory depression, dysarthria, and ataxia. Coma is not common but is most often seen in the elderly or patients who have ingested alcohol or other drugs. Treatment is supportive. The use of flumazenil is controversial as it has many side-effects and is rarely indicated. Adverse effects include ventricular tachycardia, raising intracranial pressure, withdrawal in chronic abusers, and seizures if used in the presence of tricyclic antidepressants. It can be used to reverse benzodiazepine coma so as to avoid intubation, but this should be limited to situations of benzodiazepine overdose where no other drugs have been taken (Table 2).

**Table 2 Common antidotes**

<table>
<thead>
<tr>
<th>Indicated in poisoning with</th>
<th>Antidote</th>
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</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>Flumazenil</td>
</tr>
<tr>
<td>Ethylene glycol, methanol</td>
<td>Fomepizole and ethanol (10% for i.v. use)</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Atropine</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Factor II, VII, IX, X concentrate</td>
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<tr>
<td>Cyanide</td>
<td>Dicobalt edetate, hydroxycobalamin</td>
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<tr>
<td>Digoxin</td>
<td>Digibind</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>Glucagon</td>
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<tr>
<td>Methaemoglobinemia</td>
<td>Methylen blue</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>N-acetylcysteine</td>
</tr>
<tr>
<td>Opiate</td>
<td>Naloxone</td>
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**Fig 2** Acetaminophen nomogram (permission from Prof. PA. Routledge, Therapeutics and Toxicology Centre, Cardiff University).
Opiates
Increasing doses of opioids progressively produce euphoria, pinpoint pupils, sedation, respiratory depression, and apnoea. Complications include hypotension, convulsions, non-cardiogenic pulmonary oedema, and compartment syndrome from prolonged immobility. Where this is suspected, serum CK and urinary myoglobin should be measured to look for evidence of rhabdomyolysis. Naloxone should be given in 100 μg boluses i.v. to a maximum of 2 mg with the aim of reversing the opiate effect and reversing respiratory depression. This antidote can precipitate an acute agitated withdrawal state and when giving it staff should be mindful of their own safety. Naloxone can be administered i.v., i.m., s.c., or via the tracheal route. It has a short half-life (20 min if given i.v.) and therefore may be needed as an infusion since respiratory depression may reoccur. It can rarely cause ventricular dysrhythmias and hypertension and drowsiness at very high doses.

Tricyclic antidepressants
Tricyclic antidepressants cause 250 fatalities each year in the UK. The predominant cause of death is cardiac depression by sodium channel blockade with resultant decrease in cardiac output. Overdose presents with a sinus tachycardia, mydriasis, coma, hyporeflexia, convulsions, ECG changes, and hypotension. A QRS interval of >120 ms indicates cardiac toxicity and is predictive of ventricular arrhythmias and seizures. Treatment includes prevention of absorption using AC. Sodium bicarbonate is given as a loading dose (8.4% 1–2 ml kg$^{-1}$) followed by an infusion or intermittent bolus. Sodium bicarbonate should be administered even in the absence of a significant metabolic acidosis as it helps to stabilize the Na channels in the myocardium and prevent cardio-toxicity. Convolusions can be treated with benzodiazepines initially, but anaesthesia with propofol may be required. Phenytoin is the anti-arrhythmic of choice and glucagon can be helpful if there is evidence of myocardial depression.

Selective serotonin reuptake inhibitors
These drugs include citalopram, fluoxetine, flovoxamine, paroxetine, and sertraline. Nausea, vomiting, agitation, tremor, nystagmus, drowsiness, dysrhythmias, and mild hypertension are the most common features of overdose. Convulsions have been reported up to 10 h post-ingestion. If administered with other drugs like cocaine, tricyclics MAOIs, or MDMA which release serotonin or affect its reuptake, this may result in serotonin syndrome. Serotonin syndrome consists of a triad of altered mental status, neuromuscular hyperactivity, and autonomic instability, similar in presentation to neuroleptic malignant syndrome—hyperpyrexia, acidosis, arrhythmias, and rhabdomyolysis are seen. Treatment is supportive but should include AC up to 1 h post-ingestion. Convulsions should be treated with benzodiazepines and phentoin. Cryoheptadine and chlorpromazine are 5HT-2A antagonists and have successfully been used to treat serotonin syndrome, but there are no controlled trials to support the use of either agent. If rhabdomyolysis is suspected, urinary alkalization and volume replacement may be helpful to reduce renal failure. Fluid resuscitation including 225 mmol of 8.4% sodium bicarbonate over 2 h is administered to increase urine pH to >7. If renal failure occurs, haemodialysis or haemofiltration is required.

Methanol and ethylene glycol
Methanol and ethylene glycol poisoning results in a severe high anion gap metabolic acidosis. Both are metabolized via the enzyme alcohol dehydrogenase resulting in formation of acids (formic, glycolic, and oxalic, respectively) which accumulate in the body and are responsible for neurological damage and death. Overdose with these agents can be treated with oral or nasogastric ethanol because of its greater affinity for alcohol dehydrogenase. However, maintaining plasma alcohol levels in the correct range is difficult and time-consuming, particularly if the patient is undergoing dialysis. Fomepizole blocks the metabolism of methanol and ethanol and can be injected 12 hourly. It is expensive and not widely available. Folate deficiency in primates is predictive of poor outcome in methanol toxicity and it is suggested that folate be given in a dose of 1 mg kg$^{-1}$ day$^{-1}$ for 48 h. Summary
Acute poisoning is relatively common and is the cause of significant morbidity and mortality. NPIS and Toxbase provide a 24 h information service for all aspects of poisoning. Treatment of poisoning remains largely supportive. Few drugs have antidotes and therefore treatment is aimed at reducing further absorption of the drug, increasing its elimination, and treating the side-effects. Gastric decontamination with AC is time-dependent, but can significantly reduce drug absorption. Forced emesis and gastric lavage are no longer recommended.

References

Please see multiple choice questions 5–7