Diagnosis of acute poisoning

As all chemicals can act as poisons in the right quantity, effective lines of communication between the attending clinician or health worker, the laboratory and the toxicologist are essential.

Virtually all known chemicals can cause injury or death, depending on the dose of the substance. The lethal dose may vary widely. For example, 4 000 mg/kg of table salt will be lethal to 50% of a population of experimental animals (expressed as the LD_{50}), while the LD_{50} of arsenic trioxide is 1 - 2 mg/kg, and that of botulinum toxin 0.00001 mg/kg. A number of factors may contribute to toxicity: physico-chemical characteristics such as the pKa, lipid solubility, the route of entry (e.g. orally or percutaneously), the nature of the exposure (e.g. acute or chronic) and the susceptibility of the victim. This refers to factors such as the state of fetal development, childhood, advancing age and underlying pathology. In addition, the vehicle in which the agent is dissolved or suspended, and other formulation factors, may markedly influence toxicity. There is no entirely 'safe' chemical since all have the potential to cause death and injury under specific circumstances. It should also be emphasised that some adverse reactions to chemicals, such as allergic and idiosyncratic reactions, are not dose-related.[1,2]

In practice the critical factor is not whether or not a substance is poisonous, but whether someone is at risk from exposure to it. Risk is the probability that a substance will cause harm under specified conditions. This is reflected in a hazard rating on a scale of 1 - 3, where 3 indicates a high hazard rating (LD_{50} < 400 mg/kg), 2 is intermediate (LD_{50} of 400 - 4 000 mg/kg), and 1 is low (LD_{50} of 4 000 - 40 000 mg/kg). Safety, the opposite of risk, is the probability that harm will not occur under specified conditions.[2,3]

Virtually all known chemicals can cause injury or death, depending on the dose of the substance.

'Non-toxic ingestion' refers to the consumption of a non-edible agent or product usually not associated with harmful effects. The practical value of knowing that a product is 'usually non-toxic' prevents:

- an inappropriate response that causes panic
- over-treatment of the patient
- unnecessary visits to the doctor or hospital emergency facility.[4]

For an agent to be considered 'usually non-toxic', it should meet the following criteria:

- positive identification of the product, its ingredients, and its concentration
- positive assurance that it was the only product ingested.[1,4]

Because of unpleasant or disagreeable tastes, the quantity of 'non-edible' substances ingested accidentally is usually small. The average quantity of liquids swallowed accidentally by a child under the age of 5 years is 5 ml, and that by an adult 15 ml. In contrast, the quantity swallowed intentionally (by adults) is usually considerably larger, and should be taken into consideration when potential hazard or risk is assessed.

Table I lists the most frequently ingested household agents considered 'usually non-toxic'. This table is intended as a guide only, and should be used in conjunction with the information given above.[4,5]

For clinical purposes, poisons (including therapeutic drugs) may be divided into two broad categories:

- **Poisons (and their metabolites) which directly cause irreversible or slowly reversible structural or functional tissue damage in one or more organ systems.** These are also considered compounds with a high inherent toxicity (Table II). Arsenic and the organophosphates are good examples of poisons which may cause irreversible damage, long-lasting (slowly reversible) organ dysfunction, or lead to complications which may require extended periods of supportive therapy. Significant symptoms and signs of a substantial number of poisons in this group may appear late (1 - 3 days post

Table I. **Most frequently ingested household agents considered 'usually non-toxic'[4]**

Abrasives
Adhesives
Antacids
Antibiotics (most)

Baby products, cosmetics
Ballpoint pen inks
Bathtub floating toys
Bath oil (castor oil and perfume)
Bleach (< 3.5% hypochlorite)
Body conditioners
Bubble-bath soaps

Calamine lotion
Calcium sulphate (plaster of Paris)
Candles (beeswax or paraffin)
Caps (toy pistol, potassium chlorate)
Chalk (calcium carbonate)
Charcoal
Cigarettes or cigars (nicotine)
Clay (modelling)
Colognes
Contraceptives
Corticosteroids
Cosmetics
Crayons (marked 'non-toxic')

Dehumidifying packets (silica or charcoal)
Detergents (phosphate type, anionic)
Deodorants
Deodorisers (spray and refrigerator)

Eye make-up

Fabric softeners
Fertiliser (if no insecticides or herbicides added)
Fish bowl additives

Glues and pastes (for wood or paper)
Golf ball (core may cause mechanical injury)
Greases

Hair products (dyes, sprays, tonics)
Hand lotions and creams
Homeopathic medication (excl. herbal medicines)
Hydrogen peroxide (medicinal 3%)

Ice bricks (water and edible thickener)
Incense
Inedible markers
Ink (black and blue — non-permanent)
Iron filings (chemical sets)

Lanolin
Laxatives
Lipstick
Lozenges (without local anaesthetic)
Lubricant
Lubricating oils (lipid pneumonia when aspirated)

Magic markers
Make-up (eye, liquid, facial)
Matches
Mineral oil (unless aspirated)
Motor oil

Newspaper

Paint (indoor or latex)
Pencil (lead, graphite, colouring)
Perfumes
Peroxide 3%
Pet food
Petroleum jelly (Vaseline)
Phenolphthalein laxatives (Brooklax)
Plasticine
Play-Doh
Polaroid picture coating fluid
Porous-tip ink marking pens (koki)
Prussian blue (ferricyanide)
Putty (less than 60 g)

Rouge
Rubber cement
Shampoos (non-pediculicides)
Shoe polish (most do not contain aniline dyes)
Sesame oil
Silica
Silly putty (99% silicones)
Soap and soap products
Suntan preparations
Sweetening agents (saccharin, cyclamate)

Talc (not inhaled)
Teething rings (containing water, if sterile)
Thermometers (elemental mercury or alcohol)
Toilet water
Toothpaste (with or without fluoride)

Vaseline
Vitamins (without iron)

Water colours

Zinc oxide
Zirconium oxide

Adapted from Ellenhorn and Barceloux,[4] with permission

exposure). At this stage symptoms may not be expected, or the incident may have been partially forgotten. This can mean that the patient and/or doctor may not immediately (if at all) associate the cause of the symptoms with exposure, leading to delayed optimal therapeutic intervention. Examples include paracetamol and *Amanita phalloides* poisoning.

- **Poisons which do not cause tissue damage directly or which cause toxic effects which are rapidly and completely reversible**. Although many agents in this category have the potential to cause serious organ dysfunction or even death, appropriate supportive care during the acute phase will ensure complete recovery in most instances. Fortunately, most potential poisons dealt with in the clinical setting fall into this category. Consequently, most poisoned patients require treatment of symptoms and appropriate supportive care only. 'Supportive care' is the maintenance of normal respiratory, circulatory and renal function with monitoring of blood gases, acid/base balance, serum electrolyte and glucose levels, etc. Benzodiazepines and opiates taken in overdose, and even strychnine, are examples of poisons with a relatively low inherent toxicity.

When dealing with a suspected case of poisoning, one of the main priorities should be to attempt to identify poisons with a high inherent toxicity as soon as possible

Table II. **Examples of drugs and poisons with a high inherent toxicity***

Drug or poison	Specific treatment†	Reason for early antidotal/ active removal therapy
Carbon monoxide‡	Oxygen	Tissue damage (nervous system)
Cyanide‡, §	Oxygen. In serious poisoning: sodium nitrite/sodium thiosulphate or Kelocyanor (Restan)	Extremely toxic, often with a morbid course and death
Digoxin	Digoxin-specific antibodies	With massive overdose poisoned membranes can no longer maintain electrolyte gradients; this leads to extremely high potassium levels
Ethylene glycol‡, ¶	Ethanol, haemodialysis	Tissue damage (nervous system, kidney)
Isoniazid‡	Pyridoxine, haemodialysis	Tissue damage (nervous system)
Lithium carbonate**	Haemodialysis	Tissue damage (nervous system, kidney)
Metals and metalloids		
Arsenic**	Dimercaprol, penicillamine	Tissue damage (nervous system, liver, kidney) Tissue damage (gastrointestinal, liver, CVS)
Iron‡, **	Deferoxamine	Tissue damage (nervous system)
Lead**	Dimercaprol, calcium disodium edetate	Tissue damage (nervous system, kidney)
Mercury**	Dimercaprol, penicillamine	
Methanol‡, ¶	Ethanol, haemodialysis	Tissue damage (nervous system, blindness)
Methyl bromide	Dimercaprol, N-acetylcysteine	Tissue damage (nervous system, CVS, kidneys)
Mushrooms — cyclopeptides as in *Amanita phalloides***	Silibinin	Tissue damage (liver, kidney, heart, pancreas)
Organophosphates**	Obidoxime chloride, atropine	To prevent extended periods of intensive care
Paracetamol	N-acetylcysteine	Tissue damage (liver, kidney)
Paraquat (diquat)**, ††	Immediate, aggressive decontamination procedures plus activated charcoal or a watery slurry of clay	Multisystem failure (kidney, liver, nervous system, heart, lungs)
Salicylates‡	Haemodialysis	Tissue damage (nervous system)
Theophylline‡, **	Haemoperfusion	Tissue damage (nervous system)

*Examples are those in which antidotes or special toxin removal procedures may prevent permanent tissue damage or serious complications (paraquat and carbon monoxide excluded).
†The degree of poisoning, together with drug or poison levels, usually determines the specific treatment regimen.
‡Causes marked metabolic acidosis.
§Included because of its potential to cause death within minutes. Most patients who recover have no permanent sequelae.
¶Causes alterations in the osmolar gap.
**Gastrointestinal disturbances prominent.
††Survival only possible if oral activated charcoal or a watery slurry of clay combined with a cathartic (preferably magnesium sulphate or sorbitol), is given as soon as possible to prevent absorption. Once absorbed it is doubtful whether an antidote or special toxin removal procedure will prevent tissue damage.

(Table II). This allows timely antidotal or special decontamination procedures so that severe tissue damage and complications can be avoided. Agents with a low inherent toxicity need to be identified early where the use of a specific antidote may avoid relatively risky treatment regimens. An example is the treatment of an opiate overdose with naloxone, rather than with mechanical ventilation, which may predispose to respiratory infection and other complications.[5,6]

GUIDELINES FOR EARLY IDENTIFICATION OF A POISON

History

While vital functions are being assessed/stabilised, a proper history should be obtained. Important information includes the nature of the poison, degree of exposure and time since exposure. Since it is often difficult to obtain a reliable history from the poisoned patient (up to 50% of histories are incorrect as to the substance, quantity or even actual exposure), the clinician must rely on a high index of suspicion and be aware of the toxins that possess a high inherent toxicity (Table II). Communication with family, friends, traditional healers, general practitioners and local pharmacists may provide useful information. Relatives or friends should be asked not to leave the premises until the clinician has had the opportunity to question them. A special effort should be made to obtain specimens and containers involved.

Clinical evaluation/physical examination

Symptoms and signs provide valuable clues to the causative toxic agent. Although manifestations of acute poisoning may be wide and varied, patients who have ingested poisons with high inherent tissue-damaging potential often present with severe and persistent gastrointestinal symptoms and signs (Table II). Hypotension, cardiac dysrhythmias, seizures, acid-base and electrolyte disturbances (acidosis and hyperkalaemia), and signs of liver and renal impairment usually also indicate serious poisoning.

Patients who have ingested poisons with high inherent tissue-damaging potential often present with severe and persistent gastrointestinal symptoms and signs.

Although the diagnosis of acute poisoning can seldom be made on the basis of a single symptom or sign, specific poisonings are associated with clusters of clinical features which may be of diagnostic value. In the context of a condition caused by a poisonous substance, a set of associated symptoms and signs is referred to as a toxidrome. Toxidromes may be useful when attempting to identify the cause of a poison-induced symptom/sign complex. An example in point is the association of a garlicky smell on the breath with vomiting, profuse bloody diarrhoea, delayed hair loss and distinctive lines in nails, which is pathognomic of arsenic poisoning. Toxidromes and their causes are listed in the introductory chapters of most standard toxicology textbooks. A given toxidrome, however, must be interpreted with caution since it may not be specific, and hence pathognomonic, but may apply to more than one poisonous agent and may even be mimicked by a disease state unrelated to poisoning. Although toxidromes are useful when dealing with an unidentified toxic agent, they may be misleading and their use fraught with pitfalls for the unwary and inexperienced.

Central nervous system (CNS)[7]

CNS depression is one of the most common manifestations of acute poisoning. Substances usually implicated include alcohol, anticonvulsants, benzodiazepines, tricyclic antidepressants, organophosphates, carbamates and salicylates. A combination of alcohol with other CNS depressants is particularly hazardous.

- **Lateralising neurological signs**. With the exception of transient inequality of pupil size, lateralising neurological signs effectively exclude a diagnosis of acute poisoning unless the signs are due to a pre-existing condition.
- **Pyramidal tract signs**. An overdose of tricyclic antidepressant agents, and the earlier generations of antihistamines with prominent anticholinergic prop-

erties, often induces hypertonia, hyperreflexia and extensor plantar responses.

- **Extrapyramidal signs**. An overdose of metoclopramide, a phenothiazine or a butyrophenone antipsychotic agent, may induce an acute dystonic reaction. Dystonia also often occurs in association with carbon monoxide poisoning.
- **Seizures.** Compounds usually implicated include camphorated oil, chlorinated hydrocarbons (e.g. gamma benzene hexachloride), organophosphates and the carbamates. Medicinal agents include carbamazepine, the salicylates (aspirin and mefenamic acid), the tricyclic antidepressants, theophylline, carbon monoxide, caffeine and the sympathomimetic appetite suppressants.
- **Agitation/restlessness.** Overdose with agents such as ethanol, tricyclic antidepressants, theophylline and carbamazepine is known to cause agitation. Other causes, such as hypoxia, should always first be excluded.
- **Pupils.** The opioids, cholinesterase inhibitors, barbiturates, chloral hydrate, pilocarpine and the phenothiazines often induce miosis. In contrast, the antimuscarinic and sympathomimetic agents, the tricyclic antidepressants, carbamazepine and diphenhydramine, among others, often cause mydriasis. Non-medicinal chemicals that may induce dilated pupils include ethanol, methanol, LSD, cocaine, cyanide and certain neurotoxic snake venoms.
- **Anosmia.** Loss of the sense of smell is diagnostic of berg adder bite.

Cardiovascular system

- **Tachycardia.** Antimuscarinic drugs, sympathomimetic drugs, theophylline and cholinesterase inhibitors (nicotinic effect) all cause tachycardia.
- **Bradycardia**. Cholinesterase inhibitors (via muscarinic effects), digitalis, η-blocking agents, central-acting sympatholytic antihypertensive drugs and opioids may all cause bradycardia.
- **Hypertension**. Antimuscarinic and sympathomimetic agents and, frequently, tricyclic antidepressants (sympathomimetic and antimuscarinic effects) may be implicated.

A dry, hot, flushed skin is typical of atropine poisoning.

- **Hypotension**. Tricyclic antidepressants (ζ-blocking effects), antipsychotic drugs, η-blocking agents, barbiturates, and central-acting antihypertensive drugs may be implicated.
- **ECG**. See under 'Special investigations'.

Respiratory system

- **Hyperventilation**. Salicylate, theophylline and sympathomimetic drugs are often implicated.
- **Hypoventilation**. Opioids, sedative-hypnotics, cholinesterase inhibitors, central-acting sympatholytic drugs and cyanide cause hypoventilation.

Skin

Blisters on the skin are occasionally found in poisoned patients and are associated with a wide variety of drug overdoses, but especially with phenobarbitone overdose. A dry, hot, flushed skin is typical of atropine poisoning. Heavy perspiration is common in organophosphate poisoning and in latrodectism.

Absence of clinical signs of toxicity

In poisoning with certain substances, the onset of toxic manifestations may be delayed. During this latent period clinical evaluation will reveal no clear abnormal findings. Symptoms and signs of poisoning with *Amanita phalloides* mushrooms, methyl bromide, organophosphates, paracetamol, and the superwarfarin rodenticides, may not immediately be evident and may be delayed for varying periods of time — for hours (organophosphates) or days (*Amanita phalloides* mushrooms).

Special investigations

A sample of the suspected toxic substance or the material ingested is crucial for rapid and positive identification of a poison. Identification can often be achieved by simple inspection. Health care providers should be encouraged to collect, inspect and send the suspected toxic material to the laboratory as soon as possible. If the suspected toxic substance is not initially brought in with the patient, a special effort should be made to send family or friends, or even the police, to collect specimens and containers. Obtaining the original toxic substance or container is more valuable and reliable for rapid and positive identification of a poison than depending on laboratory analysis of blood, urine or other body fluids.[5]

The toxicology laboratory

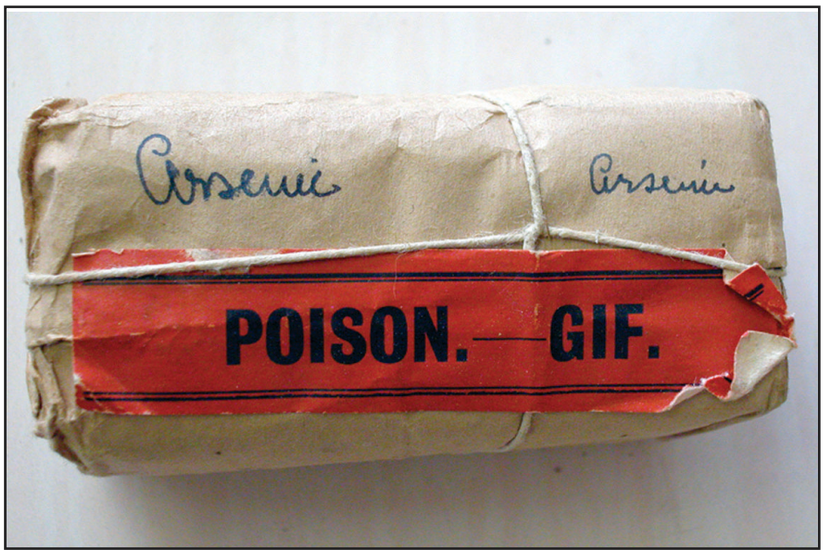
Laboratory analyses play an important role in the identification or exclusion of poisons. In addition, the laboratory may be able to assist in quantifying the severity of exposure. Because of time limitations, expense, and the large number (thousands) of potentially toxic substances commonly encountered, standard toxicology screening procedures cannot cover all the possibilities. Contrary to the per-

ceptions of most clinicians, routine toxicology screening tests are primarily designed to identify, or eliminate, a limited number of drugs and non-drug chemicals which are commonly involved in poisoning. If none of the compounds for which the tests were designed are identified, the test is reported as being negative. Consequently, a negative screening test does not imply that poisoning has not occurred but only that the compounds tested for are not the culprits. In the normal course of events fewer than 50 compounds are routinely screened for. Therefore, the use of a toxicology screen without an understanding of its possibilities and limitations may be misleading or even hazardous. If the screen is negative, but a diagnosis of poisoning cannot be excluded clinically, the toxicologist should be consulted for an opinion on appropriate additional special investigations and/or an appropriate course of action. It needs to be stressed that when a medical emergency is thought to be the result of an unidentified poison, efforts should be directed at identification or elimination of those agents with high inherent toxicity.[5]

In most cases of poisoning, standard special investigations are often more rewarding for diagnostic purposes than a toxicology screen.

Effective lines of communication between the attending clinician or health worker, the laboratory and the toxicologist are essential.

Quantitative determination of toxins is needed for relatively few substances, e.g. paracetamol, salicylates, theophylline, lithium, digoxin and metals. For some of these, depending on the elimination rate of the substance, two plasma levels some hours apart may be needed to determine whether concentrations are rising or falling, before deciding if a specific therapy is needed or can be discontinued.



Non-toxicological investigations

In most cases of poisoning, standard special investigations, such as serum electrolyte, glucose, arterial blood gases, blood urea nitrogen, the ion and osmolal gap measurements, as well as liver and kidney function tests, full blood count, clotting profile (prothrombin time and INR), urinalysis and ECG, are often more rewarding for diagnostic purposes than a toxicology screen.

- **Urine.** Brown discolouration of urine may be due to the presence of haemoglobin (due to intravascular haemolysis), myoglobin secondary to rhabdomyolysis (see later) or metabolites of paracetamol. Urinary oxalate crystals are a common, but not invariable, feature of ethylene glycol intoxication.
- **Clotting profile**. Prolongation of the prothrombin time or the INR may be caused either by ingestion of vitamin K antagonists (e.g. super warfarin rat poisons), or by liver necrosis secondary to paracetamol or hepatotoxic mushroom poisoning, among others. A prolonged clotting time may be indicative of boomslang bite.
- **Hypoglycaemia**. Low glucose concentrations may be due to an overdose of oral antidiabetic agents (e.g. sulphonylureas) or insulin. It may also be a complication of severe paracetamol or *Amanita phalloides* (hepatotoxic mushroom) poisoning.
- **Hyperglycaemia** is often associated with an overdose of sympathomimetic agents or theophylline.
- **Liver function abnormalities**. Abnormalities, with or without jaundice, are common with advanced paracetamol, arsenic or hepatotoxic mushroom (e.g. *Amanita phalloides*) poisoning.
- **Nephrotoxicity**. Acute renal failure may occur in aminoglycoside, heavy metal, arsenic and ethylene glycol poisoning. Poisons that cause rhabdomyolysis with myoglobinuria (many poisons) may indirectly cause renal failure.
- **Hypocalcaemia**. Low calcium

levels are a complication of fluoride and ethylene glycol poisoning.

- **ECG abnormalities**. A number of toxins induce well-recognised ECG changes that are, to a greater or lesser extent, specific and may confirm, or cast doubt on, the compound or substance thought to be involved. These changes include a prolonged QT interval (e.g. phenothiazines), a widened QRS interval (e.g. tricyclic antidepressants and quinidine), atrioventricular conduction block (e.g. digoxin, tricyclic antidepressants and phenytoin) and ventricular arrhythmias (e.g. tricyclic antidepressants, digoxin and theophylline).[7]
- **Water, electrolyte and acid-base disturbances** are common complications of acute poisoning and this topic is discussed in the article on p. 466.

IMPORTANT CLINICAL ENTITIES WHICH MAY BE ASSOCIATED WITH ACUTE POISONING

Serotonin syndrome

This syndrome may be caused by drugs, or combinations of drugs, which increase serotonin activity in the brain. It usually occurs when two or more drugs, which increase serotonin availability by different mechanisms, are used simultaneously. It is a syndrome that presents with at least 3 of the following features: altered mental status (confusion, hypomania), agitation, myoclonus, hyperreflexia, sweating, shivering, tremor, diarrhoea, incoordination, and fever. The syndrome may be difficult to distinguish from the neuroleptic malignant syndrome. Hyperthermia is a characteristic finding. Tachycardia, hypertension and tachypnoea are common. Hypotension and respiratory failure, and even a DIC, may develop in severe cases. The creatine kinase (CK) levels are usually elevated. Patients being treated with antidepressant agents who take drugs of abuse, such as the amphetamines and cocaine, are particularly vulnerable. This syndrome is often a complication of drug abuse in the 'rave' party setting.[8]

Rhabdomyolysis

This is a syndrome resulting from skeletal muscle damage, with release of muscle cell contents into the plasma (myoglobinaemia), manifesting as myoglobinuria. Renal failure can occur secondary to rhabdomyolysis. Common causes of rhabdomyolysis include drug abuse/overdose and alcohol abuse, or following trauma, seizures, and infections. Although alcohol and drug abuse/overdose are implicated in many cases, the actual rhabdomyolysis may be due to secondary causes, such as seizures, trauma, metabolic acidosis, hypoxia, coma, immobilisation, muscle compression, or occlusion of the regional blood supply. Beta-receptor stimulation and hyperdynamic states, such as malignant hyperthermia, neuroleptic malignant syndrome, and hypokalaemia have been documented to cause rhabdomyolysis, as well as prolonged physical activity, agitation, and compartment syndrome.

References available on request.

IN A NUTSHELL

When dealing with a suspected toxic exposure or poisoning, one of the major priorities should be to attempt to identify agents with a high inherent toxicity as soon as possible.

Early identification will allow timeous antidotal or special decontamination procedures so that severe tissue damage or complications can be avoided.

Patients who have ingested poisons with a high inherent tissue-damaging potential often present with severe and persistent gastrointestinal symptoms and signs.

The suspected toxic substance or the material ingested is crucial for rapid and positive identification of a poison.