Antidotes, supportive agents and other essentials in the management of acute toxic exposures and poisonings

A manual of specific and nonspecific poison antidotes*

Being as well prepared as possible for any poisoning will go a long way towards ensuring a favourable outcome.

Efficient management and treatment of episodes involving drug overdose, ingestion of or exposure to toxic substances and envenomation requires prospective preparation and planning. In many instances appropriate early therapeutic action is essential for a satisfactory outcome. Preparedness requires pre-arranged access to appropriate supportive care facilities, the means of effecting rapid, safe decontamination and the availability of supportive medicines and antidotes.

The general practitioner should have the necessary nonspecific antidotes or decontaminants to hand, and the facilities and accessories necessary to effect decontamination within the critical ½ - 1 hour after the event. Specific antidotes which need to be given early in the clinical course to be of benefit should also be available immediately. The spectrum of specific antidotes that should be stocked will depend upon the location and setting of the practice, the activities of local industries, the spectrum and prevalence of venomous creatures and the profile of the local population.

It is our experience that the practitioner close to a hospital relies heavily on hospital services and tends not to stock even basic decontaminants. Consequently, too often the opportunity for efficient and uncomplicated decontamination is lost because of inevitable delay and lack of practical preparedness.

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Hospitals should be prepared to deal with the widest possible spectrum of toxicity-related mishaps, with due regard to regional and environmental factors. From time to time, hospitals are called upon to deal with a number of casualties at one time and under these circumstances relatively large stocks of certain antidotes may be required to manage even the short emergency phase (e.g. atropine).

SUPPORTIVE AGENTS AND ANTIDOTES

Cumulative experience has led to the compilation of a spectrum of specific and nonspecific antidotes and supportive agents generally considered adequate to deal with most non-exotic poisoning-related emergencies. The basic list, together with dosage recommendations applicable to usual circumstances, is presented in Table I.

The doses and dosage regimens of scheduled agents listed in the table comply as far as possible with the guidelines contained in Medicines Control Council-approved manufacturers' package inserts (PIs) and these should be adhered to as far as possible. It makes good sense regularly to study the PIs of the antidotes and supportive agents in

*Keep this for reference.

stock in order to be prepared to deal efficiently with a poisoning-related casualty. Some emergencies, most notably cyanide poisoning, require an immediate and skilled response.

In the limited space available it is not possible to advise on appropriate medicines and dosage regimens for all possible eventualities, and appropriate texts should be consulted and specialist advice sought in difficult cases. Appropriate dosages for small children and frail adults present special difficulties and any medication which affects vital functions should be carefully and continuously monitored by a doctor. Imbalances in blood gases, pH and electrolytes increase the toxicity of both toxin and antidote and should be corrected as soon and as far as possible; adequate oxygenation should always enjoy top priority.

The earlier the antidote is administered, the greater will be the benefits in limiting morbidity.

ANTIDOTES AND SUPPORTIVE MEDICATIONS — GENERAL COMMENTS

- In all instances in which respiration is directly or indirectly compromised, adequate ventilation and oxygenation should precede antidote administration.
- The earlier the antidote is administered, the greater will be the benefits in limiting morbidity.
- Parenteral administration of antidote is preferable, if not attended by undue risk, since the desired effects are achieved rapidly and reliably.
- The half-life of an antidote may be much shorter than that of the agent against which it is directed and appropriate follow-up dosages may be necessary.
- Termination of antidote medication should be effected in carefully monitored stages in order to prevent serious rebound phenomena.
- An antidote may unmask physical dependence, underlying pathology or the effects of co-ingested toxin, e.g. naloxone may unmask life-threatening withdrawal symptoms in an opiate addict and flumazenil may precipitate seizures in a person taking a benzodiazepine regularly.
- A complex formed by a chelating agent and its toxic ligand, e.g. dimercaprol-lead complex, may itself reach toxic concentrations in renal tissues and its elimination should be appropriately aided by adequate hydration.

ACCESSORIES REQUIRED TO MANAGE THE EARLY PHASE OF POISONING

Accessories for management of the upper airways

Although it is self-evident that a laryngoscope and a suitable selection of blades and endotracheal tubes are essential for the management of the airways when poisoning-related complications arise, accessories necessary to treat small children should not be neglected.

Endotracheal intubation

The patient at risk of aspirating gastric contents should be intubated prior to gastric lavage. This is particularly true of three types of patient:

- the patient with a depressed level of consciousness and depressed vital functions
- the patient at risk of a seizure or who has ingested a seizure-inducing compound such as camphor, gamma-benzenehexachloride or isoniazid
- the patient who is to undergo gastric lavage because of ingestion of a potent toxin dissolved in a volatile hydrocarbon solvent.

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Sedation prior to endotracheal intubation

Patients in the second and third categories are particularly difficult to manage; the patient is often fully conscious and resists intubation if not adequately sedated. Adequate sedation in turn suppresses the gag reflex and makes the patient more vulnerable to aspiration. A parenteral benzodiazepine, diazepam or midazolam, should be used if sedation is indicated as the effects can be efficiently and rapidly reversed with flumazenil after gastric lavage has been completed, or at any other stage if necessary.

The orogastric tube for lavage

The bore of the orogastric tube for gastric lavage should be large enough to allow passage of particulate material: capsules, tablets or fragments thereof. Tubes need to be chosen with care: adults 36 - 42 French; children 24 - 32 French.

Endoscopy

Endoscopic removal of toxin is indicated when particulate toxic matter has formed radiologically

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Table I. **Antidotes and supportive agents for poisoning-related emergencies**

Agent	Indication	Mode of action	Dose
Acetylcysteine (see *N*-acetylcysteine)			
Activated charcoal (AC)	To enhance elimination of toxins which adsorb to AC and which reach the GIT via ingestion, hepatic elimination, hepatic secretion or by redistribution. Administer within 2 hours of ingestion.	Adsorbent	Adults: 50 - 100 g or 1 - 1.5 g/kg Children: < 1 yr 1 g/kg; 1 - 12 yrs 25 - 50 g Repeat or follow-up doses should be half the the initial dose. Administer as a watery suspension — 1 AC:8 diluent (v/v) — 240 ml of diluent per 30 g of AC. If possible administer sufficient AC to achieve a charcoal-to-toxin ratio of 10:1 or greater
Adrenaline	To counter the effects of acute anaphylaxis: bronchoconstriction, hypotension. Essential for cardiopulmonary resuscitation	Potent α- and β-receptor stimulation	Anaphylaxis: 0.3 - 0.5 ml of 1:1 000 adrenaline IM or SC, or 3 - 5 ml of 1: 10 000 IV (a standard ampoule contains 1 mg/ml or 1:1 000 adrenaline). Repeat until improvement occurs. For IV administration dilute tenfold — from 1 mg in 1 ml to 1 mg in 10 ml. A single dose is usually sufficient but 10% of patients will require a repeat dose or a part thereof. If venous access is difficult, endotracheal administration is an alternative route if endotracheal tube is *in situ*. Dose 2 mg by endotracheal route = 20 ml of a 1:10 000 solution.
Atropine	To counter the effects of: • cholinergic stimulation in poisoning by cholinesterase inhibitors, e.g. organophosphate and carbamate pesticides • for the treatment of bradycardia and severe bradydysrhythmias in a variety of poisonings • muscarinic receptor stimulation induced by certain mushroom toxins	Competitive antagonist of acetylcholine and other agonists on muscarinic cholinergic receptors	Adults: An initial trial dose of 1 - 2 mg IV should be given. If no adverse effects develop, further doses of 2 - 4 mg may be given at 10 - 15-min intervals Alternative dosage schedule: 0.05 mg/kg every 10 - 15 min IV until full atropinisation is achieved, followed by 0.05 mg/kg hourly in a continuous infusion. Patients with severe organophosphate poisoning may require unusually large doses of atropine. Children: an initial trial dose of 0.01 - 0.02 mg/kg followed by 0.05 mg/kg every 10 - 15 min thereafter Note: Over-treatment with atropine may induce atropine poisoning
Biperiden (Akineton; Knoll)	To counter extrapyramidal effects such as dystonia, pseudo-parkinsonism and akathisia induced by neuroleptic and other drugs which block dopamine receptors (e.g. metoclopramide)	Blocks centrally located muscarinic receptors and counters un-opposed cholinergic receptor-mediated effects	Slow IV injection: Adults: the usual dose is 2 - 5 mg Children: 0.04 mg/kg/dose The dose may be repeated every half hour if necessary, to a maximum of 4 doses per day
Calcium gluconate	To relieve muscle spasm and pain caused by *Latrodectus* spider bites and *Parabuthus* scorpion stings To precipitate fluoride and prevent formation of hydrofluoric acid in fluoride overdose	Inhibits the neuron-stimulatory effects of widow spider and scorpion neurotoxins. Prevents protonation of fluoride and forms an insoluble complex with fluoride	10 ml of a 10% solution, slowly IV over 10 - 20 min; may repeat every 3 - 4 hours (children: 50 mg/kg/dose IV, up to 500 mg/kg/24 h) Administer appropriate quantities of calcium gluconate (10 g) or magnesium sulphate (30 g) dissolved in 200 ml water, orally. Milk, calcium carbonate, or calcium lactate may also be given orally to bind the fluoride ions in the GI tract and prevent their systemic absorption. Alternatively, aluminum or magnesium based antacids may be used

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Carbocysteine (Mucosirop; Fisons)	Treatment of paracetamol overdose, and only where *N*-acetylcysteine is not immediately available	Theoretically restores depleted glutathione stores. (Animal studies, however, indicate that it does not offer adequate protection against liver damage.)	150 mg/kg (3 ml/kg of a 250 mg/5 ml solution or 1 ml/kg of a 750 mg/5 ml solution) orally, every 4 hours for 24 hours. The safety of late or prolonged administration (> 24 hours) has not been established
Chlorpheniramine (Chlor-Trimeton; Scherag)	Acute drug-induced hypersensitivity reactions, especially skin manifestations	H_1-receptor antagonist	Adults: parenteral: the usual IM, IV (over 1 minute), or subcutaneous dosage range is 5 - 20 mg as a single dose. Doses up to 40 mg/d may be administered parenterally. Oral dose (maximum 24 mg/d: 4 mg 3 - 4 times daily or 8 - 12 mg, 2 - 3 times a day Children: orally or IM, 0.35 mg/kg/day in 4 divided doses, or 2 mg (break the 4 mg tablet in half) every 94 - 6 hours up to 12 mg in 24 hours. The 8-hour and 12-hour allergy tablets are not recommended
Cholestyramine	Digoxin poisoning	Reduces serum digoxin levels	4 - 8 g orally 3 - 4 times a day for 1 - 6 days
Dantrolene	Malignant hyperthermia	Inhibits Ca^{++} release from the sarcoplasmic reticulum, re-establishes the myoplasmic calcium equilibrium and increases the percentage of bound calcium. Changes associated with malignant hyperthermia may thus be reversed or attenuated	1 mg/kg by rapid IV injection. The dose may be repeated, to a cumulative dose of 10 mg/kg. Reversal is usually achieved with a cumulative dose of 2.5 mg/kg. Oral doses of 1 - 2 mg/kg 4 times daily for 1 - 3 days may be necessary to prevent recurrence of malignant hyperthermia symptoms
Desferrioxamine (Desferal; Ciba-Geigy)	Iron poisoning. Spontaneous vomiting, diarrhoea, leucocytosis and hyperglycaemia, within 6 hours of overdose, usually indicates blood levels of > 54 µmol/l (300 µg/l), which requires chelation therapy. Iron levels of: 54 - 90 µmol/l (300 - 500 µg/l) — brief chelation 90 - 180 µmol/l (500 - 1 000 µg/l) — chelation and supportive treatment > 180 µmol/l — prolonged chelation and vigorous supportive treatment	Chelation of ferrous iron	In acute iron poisoning: Adults: continuous IV administration is the preferred route (see package insert of Desferal). The recommended initial rate for infusion is 15 mg/kg/h and should be reduced after 4 - 6 hours, so that the total dose does not exceed a recommended 80 mg/kg over a 24-hour period. The usual initial dose is 1 g at a rate of 50 mg/kg/h, followed by 500 mg 4 hourly at a rate of 125 mg/h. Doses of 15 mg/kg/h for 24 - 48 hours have been used in severe cases. Some experts recommend the IM route for mild cases and the IV route for severe poisonings. The usual IM dose in adults is 1 g initially, followed by 500 mg every 4 - 12 hours, depending on severity and response to therapy (maximum 6 g in 24 hours) Children: the IV dose per kg is the same in children as in adults. The recommended IM paediatric dose is 50 mg/kg per dose every 6 hours for 12 - 24 hours, depending on the severity and response to therapy

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Dextrose (50% solution)	To counter hypoglycaemia induced by hypoglycaemic agents and various toxins, e.g. ethanol intoxication	Increases blood glucose concentrations	50 ml by slow IV injection; may be repeated if necessary. Caution: 50% dextrose may be harmful in a patient with acute cerebrovascular pathology and it is therefore prudent to measure the blood sugar with a reagent strip prior to giving dextrose if this can be done without undue delay
Diazepam	Seizures	Anticonvulsant. Benzodiazepines exert their pharmacological effect at the site of the GABA synapse, increasing the affinity of the receptor for GABA	Adults: 5 - 10 mg slowly IV (max. rate 5 mg/min). Paediatric: 0.2 - 0.5 mg/kg, repeated every 5 min as needed. Caution: IV benzodiazepines may cause or exacerbate respiratory depression and hypotension. Diazepam may take a while to reach its peak effect (15 min) in certain patients
Dicobalt edetate (Kelocyanor; Restan)	Known cyanide poisoning	Chelates cyanide to form a non-toxic complex (which also reduces the potential toxicity from cobalt itself)	Adult dose: 300 mg IV over 1 min, followed immediately by 50 ml 50% dextrose using the same needle. If there is no immediate response, a second dose of 300 mg, followed by dextrose, may be given. If there is no response to the second dose after 5 min, a third dose followed by dextrose should be given. It is recommended that the IV injection be given steadily over 1 min Caution: Cobalt-containing compounds are potentially toxic and should be used only in patients with known severe cyanide poisoning. This product should not be used as a precautionary measure
Digoxin immune fab	Severe digoxin poisoning associated with hyperkalaemia, life-threatening cardiac dysrhythmias or digoxin levels ≥ 6 - 10 ng/ml	Forms a complex with digoxin, which is excreted by the kidney	Ten vials constitute the average dose, although significantly lower doses have often given satisfactory results. The package insert should be consulted for details. Side-effects include hypersensitivity reactions and hypokalaemia. Serum potassium levels should be monitored and potassium given when indicated
Dimercaprol (British Anti-Lewisite, BAL)	Acute mercury, arsenic and gold poisoning. Also useful as an adjunct to disodium edetate in the treatment of lead, copper, thallium, bismuth and antimony poisoning	Chelating agent	Adults: 200 - 400 mg twice daily by deep IM injection on the first day; 100 - 200 mg twice daily on the second and third days; 50 - 100 mg twice daily on subsequent days. As a general guideline single doses should not exceed 3 mg/kg; however, in severe acute poisoning, single doses of 5 mg/kg may be required initially. Therapy should continue for 7 - 10 days Children: 2.5 - 4 mg/kg in accordance with the foregoing Note: The abovementioned regimen represents an average dosage schedule and should be modified if necessary, depending on the metal involved. If side-effects of BAL treatment become unacceptable after 12 - 48 hours, penicillamine may be used as a substitute
Dobutamine	Inotropic agent	Selective β_1-receptor stimulant	2 - 40 µg/kg/min as required by IV infusion

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Dopamine	Inotropic and vasoactive agent used to treat severe hypotension refractory to plasma expanders and to increase renal blood flow and glomerular filtration rate	Dose-dependent, direct and indirect stimulation of dopaminergic receptors, as well as α_1-, β_1- and β_2-adrenergic receptors	IV infusion: 2.5 µg/kg/min to improve renal perfusion, 5 - 20 µg/kg/min to improve cardiac contractility and/or elevate the blood pressure
Edetate calcium disodium (calcium disodium versenate)	Chelating agent of choice for the treatment of acute or chronic lead poisoning	Chelating agent	The usual adult dose is 1 g twice daily IV or IM or 50 - 75 mg/kg/day for 5 days, followed by a 2-day interruption if a repeated dose is considered. The usual paediatric dose is 1 000 - 1 500 mg/m²/day IV (given over a period of 8 - 12 hours) or IM for 3 - 5 days, followed by a 2-day interruption if a repeated course of therapy is necessary. For intravenous use, $CaNa_2EDTA$ is diluted in either 5% dextrose or 0.9% saline and is administered slowly (1 g/250 - 500 ml fluid). Intramuscular administration results in good absorption, but pain occurs at the injection site. The primary adverse reaction of $CaNa_2EDTA$ is nephrotoxicity. To minimise nephrotoxicity, adequate urine production should be ensured prior to and during treatment. Warning related to IV administration: the IM route is preferred in patients with lead encephalopathy and cerebral oedema, since these patients may experience a lethal increase in intracranial pressure following IV infusion
Ethanol (see also fomepizole)	To prevent toxic sequelae of methanol and ethylene glycol ingestion	Ethanol is a preferential substrate for the enzyme hepatic alcohol dehydrogenase, the enzyme responsible for the breakdown of methanol and ethylene glycol to toxic metabolites. It therefore retards conversion of parent compound to toxic metabolites: methanol to formaldehyde and formic acid; ethylene glycol to glyco-aldehyde and glycolate	Oral regimen Loading dose: 0.8 - 1 ml/kg of a ≥ 95% ethanol solution OR 1.5 - 2 ml/kg of a 40% ethanol solution (as in brandy, gin, cane spirits, etc.) in 180 ml (6 oz) of orange juice over 30 min Maintenance dose for average drinker: 0.15 ml/kg/h of a ≥ 95% ethanol OR 0.3 ml/kg/h of a 40% ethanol solution. The aim is to maintain plasma ethanol concentrations in the region of 1 - 1.3 g/l IV regimen: prepare a 10% ethanol solution in 5% dextrose solution: remove 100 ml from 1 litre 5% dextrose and replace with 100 ml absolute alcohol (99.5% ethanol) or 105 ml of 95% ethanol Loading dose of a 10% ethanol solution: 8 - 10 ml/kg over 30 min to achieve blood alcohol concentration of 1 - 1.3 g/l Maintenance dose for average drinker using 10% ethanol solution: 1.3 ml/kg/h to achieve a target blood alcohol concentration of 1 - 1.3 g/l Note: Based on pharmacokinetic theory, ethanol therapy should be continued for 5 days Caution: The use of ethanol in children has not been satisfactorily researched

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Flumazenil (Anexate; Roche)	To reverse the effects of benzodiazepines	Competes with benzodiazepines for receptor sites in the CNS	An initial trial dose of not more than 0.2 mg should be administered IV over 1 min. If the response to the trial dose is satisfactory, 0.2 - 0.5 mg may be administered over 30 seconds at 1-min intervals until CNS depression is reversed, up to a maximum cumulative dose of 3 mg. Appropriate supplementary doses at 30 - 60-min intervals may be necessary to counter recurring sedation Caution: A series of small doses should be administered at appropriate intervals and not a single large bolus dose. Flumazenil should not be routinely administered to patients in a coma of unknown aetiology or in suspected mixed drug overdose; it should not be given to patients with hypoxaemia, airway obstruction, severe hypotension, cardiac arrhythmias, seizures or a history of seizure disorders, or signs or symptoms of tricyclic antidepressant overdose. It is intended as an adjunct to, but not a substitute for, proper maintenance of airways, circulatory access and support, GI decontamination, and clinical evaluation
Fomepizole	Methanol and ethylene glycol poisoning	Fomepizole is a competitive alcohol dehydrogenase inhibitor, with an 8 000 times greater affinity for alcohol dehydrogenase than ethanol. It prevents the metabolism of ethylene glycol and methanol to toxic metabolites, e.g. glycolic acid and formic acid respectively	IV loading dose: 15 mg/kg followed by 10 mg/kg every 12 hours for 4 doses, and then 15 mg/kg every 12 hours. Therapy should be continued until ethylene glycol or methanol levels are less than 20 mg/dl and the patient is asymptomatic, with a normal pH. All doses must be administered as a slow IV infusion over 30 min. If haemodialysis is employed, the frequency of dosing should be increased to every 4 hours
Furosemide	Induction of diuresis	Loop diuretic	20 mg IV per bolus injection as required to initiate and maintain adequate urinary flow
Glucagon	Severe β-adrenergic blocker and calcium channel blocker overdose	Positive inotropic and chronotropic effects are believed to be due to increased cyclic-AMP formation and increased intracellular levels of calcium – effects are independent of β_1- and β_2-receptors	50 - 150 µg/kg (3 - 10 mg) IV over 1 min followed by infusion of 1 - 5 mg/h Note: Glucagon should not be administered at concentrations greater than 1 mg/ml
Ipecacuanha (see syrup of ipecacuanha)			

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Isoprenaline	Inotropic agent of choice when bradycardia is prominent, e.g. after poisoning by β-adrenoceptor-blocking drugs	Competitively antagonises the effect of β-blockers by stimulation of β_1- and β_2-receptors	0.02 - 1 µg/kg/min infused by a constant infusion pump. The infusion rate should be adjusted to clinical response. The dilution can vary, but generally 1 mg is diluted in 100 ml of fluid
Labetalol	Used in cocaine, amphetamine and amphetamine-like substances induced cardiotoxicity, tachycardia and artrial hypertonia	Has both α- and β-blocking properties, may be preferable to propranolol for cardiotoxicity secondary to these agents. Membrane-stabilising properties	IV: initial dose of 20 mg by slow injection over 2 min. Repeat with 40 - 80 mg every 10 - 15 min. Alternatively, 1 - 2 mg/kg given as a bolus followed by an infusion of 0.5 - 4 mg/min, until desired blood pressure is reached. Maximum total dose 300 mg
Lignocaine	Anti-arrhythmic agent used to treat ventricular tachyarrhythmias	Class IB antiarrythmic agent. Acts by depressing diastolic depolarisation and automaticity in the ventricles. It has little effect on atrial tissue and does not signifi-depress myocardial contractility or AV conduction, in therapeutic doses	100 mg (1 - 1.5 mg/kg) by bolus injection IV over 1 min. Additional boluses of 0.5 - 0.75 mg/kg (25 - 50 mg) can be given every 5 - 10 min if needed up to a maximum of 3 mg/kg, followed by 2 - 4 mg/min by IV infusion; gradually reduce the rate to 1 - 2 mg/min; continue as needed, as guided by blood levels (ideally). Monitor clinically for toxicity. Infusion should be maintained for only 6 - 24 hours and then discontinued so that the patient's need for antiarrhythmic therapy can be reassessed
Magnesium citrate	To increase GIT transit time and produce bowel evacuation. The use of cathartics (e.g. saline cathartics or sorbitol), with or without activated charcoal, has recently been challenged and they are not routinely recommended for GIT decontamination. Cathartics can induce fluid and electrolyte disturbances, particularly in children	Osmotic cathartic	Magnesium citrate 6% solution: adults 150 - 300 ml; children 6 - 12 years 0.5 ml/kg, to a maximum of 200 ml, may be administered every 4 - 6 hours until stools are clear. Cathartics should not be administered to children under the age of 6 years
Magnesium sulphate	To increase GIT transit time and produce bowel evacuation. The use of cathartics (e.g. saline cathartics or sorbitol), with or without activated charcoal, has recently been challenged and they are not routinely recommended for GIT decontamination. Cathartics can induce fluid and electrolyte disturbances, particularly in children	Osmotic cathartic	Adults: orally 10 - 15 g in a glass of cold water. Children: 0.25 g/kg (approximately 5 - 10 grams) every 4 - 6 hours diluted in a glass of cold water. Cathartics should not be administered to children under 6 years old
	In large fluoride ingestions, to precipitate fluoride and prevent formation of hydrofluoric acid	Prevents protonation of fluoride	Administer an appropriate volume of a mixture of calcium gluconate (10 g) and magnesium sulphate (30 g) dissolved in 200 ml water

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Methionine	Antidote for paracetamol overdose or poisoning	Enhances the synthesis of glutathione. Used as an alternative to *N*-acetylcysteine for paracetamol poisoning, to prevent hepatic damage. Use only if *N*-acetylcysteine is not available	2.5 g orally 4-hourly for 4 doses (10 g over 12 hours) Most effective if treatment is initiated within 12 hours of the overdose Caution: If there are signs of liver damage before initiation of treatment, or during the course thereof, parenteral *N*-acetylcysteine should be used instead of oral methionine
Methylene blue	Treatment of drug- or toxin-induced methaemoglobinaemia. Causative agents include nitrates and nitrites; cresol, phenol; cetrimide, dapsone and primaquine	Methylene blue acts as an electron carrier for the hexose monophosphate pathway, which reduces methaemoglobin to haemoglobin	Initial dose adult/child: 1 - 2 mg/kg/dose (0.1 - 0.2 ml/kg/dose) IV over 5 min as needed every 4 hours. Improvement is noted shortly after administration if diagnosis is correct Repeat doses: Additional doses may be required, especially for substances with prolonged absorption, slow elimination, or those that form metabolites that produce methaemoglobin. Doses of greater than 15 mg/kg may cause haemolysis
Methylprednisolone	Prevention of oesophageal stricuture formation (efficacy controversial) due to ingestion of corrosives. Consider administration in third-degree, deep or circumferential burns, no more than 48 hours post ingestion, in patients without active upper GIT bleeding or at risk of perforation	Anti-inflammatory agent	40 mg (20 mg for children < 2 years) 8 hourly IV; as soon as feeds are tolerated administer 2 mg/kg/day orally for 3 weeks before tapering the dose
N-acetylcysteine (Parvolex; Glaxo)	Antidote for paracetamol overdose or poisoning	A derivative of the naturally occurring amino acid-L-cysteine, indicated for paracetamol overdose. It is converted to cysteine *in vivo* and acts by stimulating hepatic glutathione synthesis	Adult dose: IV infusion, initially 150 mg/kg in 200 ml 5% dextrose over 60 minutes; then 50 mg/kg in 500 ml 5% dextrose over the next 4 hours by continuous infusion; followed by 100 mg/kg in 1 litre 5% dextrose over 16 hours * Although there are no clear guidelines with regard to the duration of IV acetylcysteine therapy, there are strong indications that a 48-hour regimen is superior to the 24-hour regimen, especially in seriously poisoned patients and in cases where therapy is started late. The manufacturer's dosage regimen covers only the first 20 - 24 hours. The recommended dose for the second 24 hours is 150 mg/kg in 1 litre 5% dextrose water over 24 hours. The above represents a minimum dosage requirement. A third day of therapy could be considered in serious cases Paediatric dose: As for adult dose Oral regimen: Oral acetylcysteine is effective in the treatment of paracetamol overdose Dose: Oral, loading dose of 140 mg/kg followed by 70 mg/kg 4-hourly for 17 doses (over a period of 72 hours)

Table I. **Continued**

Agent	Indication	Mode of action	Dose
			* Solutions should be diluted to 5% in water or fruit juice/soft drink. Capsules or powder should be taken with adequate amounts of fluid (250 ml) Note: Although most effective when given early, within 8 - 12 hours of overdose, it is never too late to give *N*-acetylcysteine IV. It is of substantial benefit and it can be life-saving if initiated late, up to 96 hours or longer after overdose, even in patients with advanced hepatoxicity. *N*-acetylcysteine has been shown not to contribute to hepatic injury already present
Naloxone (Narcan; Boots)	To reverse the effects of opiates and opioids on the CNS	Naloxone is a competitive opioid antagonist almost completely devoid of agonistic effects	IV (preferable) or IM. The initial adult dose is 0.4 - 2 mg. If improvement does not occur immediately with IV administration, it may be repeated at 2 - 3 min intervals, to a maximum of 10 mg. (The diagnosis should be reconsidered if 2 - 3 doses fail to produce a response.) In children, the initial dose is 0.01 mg/kg, followed by 0.1 mg/kg if necessary Caution: If addiction is suspected or evident the lowest appropriate dose should be used in order to prevent violent withdrawal symptoms
Neostigmine	An alternative to physostigmine in severe and life-threatening anticholinergic (atropine-like) poisoning	Rapidly reversible cholinesterase inhibitor	0.25 mg slowly IV, 3 - 6 hourly as required. Max. per 24h: 3 mg IV Note: Administer under ECG control. Keep atropine available as antidote. Neostigmine does not readily cross the blood-brain barrier
Nitrite/sodium thiosulphate regimen (Tripac-Cyano; Covan)	Cyanide poisoning	The nitrites oxidise haemoglobin to methaemoglobin, which has a much higher affinity for cyanide. Thiosulphate mediates the conversion of free cyanide to less toxic thioxyanate	Adults: The patient should immediately be made to inhale 0.3 ml amyl nitrite, emptied onto a gauze swab, after which 10 ml of sodium nitrite is administered IV over 3 min; this should be followed 5 minutes later by 50 ml of 50% sodium thiosulphate solution IV over 10 min. A repeat dose of both sodium nitrite and thiosulphate may be given after 2 hours if necessary
Noradrenaline	Used in the treatment of severe hypotension resistant to plasma expanders and dopamine	Chiefly α_1-receptor stimulant with some β_1- and β_2-activity	2.5 - 10 µg/min by IV infusion. Adjust rate to maintain a low normal BP (80 - 100 mmHg systolic). Normal maintenance dosage range 2 - 4 µg/min
Obidoxime (Toxogonin; Merck)	Obidoxime is a cholinesterase reactivator used in the treatment of organophosphate poisoning. To be administered only in atropinised patients	It restores cholinesterase activity by reversal of phosphorylation of the enzyme. Cholinesterase reactivators should only be used in conjunction with atropine and other	Adults: An initial dose of 1 ampoule toxogonin 250 mg/ml IV (3 - 5 mg/kg). If a satisfactory response is obtained after the first dose, 1 or 2 further ampoules should be given at 2-hourly intervals, up to a total dose of 750 mg/day. May also be given IM Children: A single dose of 4 - 8 mg/kg is recommended. May be diluted in NS solution Caution: Only of value if administered within 24 hours of

Table I. **Continued**

Agent	Indication	Mode of action	Dose
		supportive measures in moderate to severe organophosphate poisoning	exposure; administer only after atropinisation is achieved and in conjunction with atropine. Toxogonin administration should begin about 5 minutes after initiation of atropine therapy. Contraindicated in carbamate poisoning
Penicilliamine (Penicillamine; Eli Lily Metalcaptase; Knoll)	Arsenic, copper, gold, lead, mercury and zinc poisoning	Chelating agent	For chelation therapy: Adult dose: Oral usually 0.5 - 1.5 g daily in 4 divided doses Paediatric dose: Oral 20 - 40 mg/kg daily in 4 divided doses
Phentolamine	Severe hypertension due to α_1-receptor agonists, e.g. clonidine, methylphenidate and phenylephrine; methysergide and monoamine oxidase inhibitors	Short acting α-receptor antagonist. Causes peripheral vasodilation	Adults: For short-term control of severe hypertension the usual adult dose is 5 mg given slowly at a rate not exceeding 0.2 - 2 mg/min Children: 0.1 mg/kg
Phenylephrine	To elevate blood pressure in patients with severe acute hypotension and low peripheral resistance where positioning and plasma expanders have failed	α_1-receptor stimulant	One ampoule contains 10 mg in 1 ml (1% solution). The usual adult SC or IM dose is 2 - 5 mg (range: 1 - 10 mg). The initial dose should not exceed 5 mg. The maximum dose is 10 mg. Do not repeat doses more often than every 10 - 15 min. For direct IV administration the dose is 0.2 mg (range 0.1 - 0.5 mg). For direct IV administration a 0.1% solution should be prepared (add 1 ampoule to 9 ml sterile water). Infusion solutions are prepared by adding 1 ampoule to 500 ml 5% dextrose. Initial dose; 100 - 180 µg/min. Maintenance dose: 40 - 60 µg/min
Physostigmine (Antilirium; not readily available)	Severe and life-threatening anticholinergic (atropine-like) poisoning, unresponsive to standard therapy	Rapidly reversible inhibition of centrally and peripherally located cholinesterase enzymes	1 - 3 mg IV slowly over 2 - 5 min, under ECG control; a second dose may be given after 10 min if necessary Caution: Not recommended in tricyclic antidepressant overdose as it has been associated with seizures and fatal dysrhythmias
Polystyrene sulphonate Na (Kexelate Al Pharm	Lithium overdose or poisoning	Inhibits the absorption of lithium	30 g orally or rectally every 6 hours
Pyridoxine	To counter the seizure-inducing effects of isoniazid overdose	Probably counteracts effects of isoniazid-induced decrease of GABA	5 g IV over 30 - 60 min to control seizures; repeat doses should be given until seizures are controlled. If dose of isoniazid ingested is known, 1 g of IV pyridoxine should be administered for each 1 g of isoniazid ingested
Salbutamol (Ventolin; Allen & Hanburys)	To counter the effects of agents causing bronchospasm: β-adrenoceptor blocking agents and irritant fumes and gases	Selective β_2-receptor stimulant	Per nebuliser 1 - 2 ml of nebuliser solution diluted to a total volume of 4 ml with normal saline. Slowly IV: 4 µg/kg, repeat as necessary
Silibinin (Legalon; Madaus — not readily available)	Poisoning by *Amanita phalloides* and other mushrooms containing cyclopeptide toxins	Prevents the uptake of toxins by hepatocytes	Dose: 20 - 50 mg/kg/day IV, continued for 48 - 96 hours. Optimally, should be given within the first 48 hours of mushroom ingestion. Silibinin is not available as a licensed drug in SA In addition, administer 0.25 - 0.5 million units of penicillin G IV, twice daily

Table I. **Continued**

Agent	Indication	Mode of action	Dose
Sodium bicarbonate 4.2% IV solution	For the management of metabolic acidosis. To enhance renal elimination of acidic compounds, e.g. salicylate, barbitone, phenobarbitone and lithium	Alkalinisation of renal filtrate promoting ion-trapping of acidic compounds	1 - 2 mEq/kg over 3 - 4 hours in a solution constituted of 2 mEq bicarbonate per 15 ml of 5% dextrose in 0.45% saline; repeat if necessary to obtain a target urinary pH 7.5 - 8 Note: 8.4% and 4.2% $NaHCO_3$ solutions contain 1 mEq/ml and 0.5 mEq/ml of $NaHCO_3$, respectively Caution: Monitor pH and electrolytes and supplement potassium appropriately, particularly in children; a high urinary output should be maintained
Sorbitol	To shorten GIT transit time and to counter constipation. The use of cathartics (e.g. saline cathartics or sorbitol), with or without activated charcoal, has recently been challenged and they are not routinely recommended for GIT decontamination. Cathartics can induce fluid and electrolyte disturbances, particularly in children	Osmotic cathartic	Sorbitol (70% solution) — adults: 50 - 150 ml; children: 2 ml/kg
Succimer	Orally active chelating agent for the treatment of lead poisoning	Chelating agent. After absorbtion, succimer is biotransformed to a mixed disulfide with cysteine. It produces a lead diuresis with subsequent lowering of blood levels	In adults the optimal dose appears to be 30 mg/kg/d for 5 days. The usual oral dose of succimer for the treatment of lead poisoning in children, with blood levels above 45 mg/dl, is 10 mg/kg every 8 hours for 5 days, followed by 10 mg/kg every 12 hours for an additional 14 days. Transient elevations in serum transaminase have been observed and patients with a history of hepatic disease should, therefore, be observed closely
Syrup of ipecacuanha (Ipecac)	To induce emesis, if not contraindicated, to clear the stomach of ingested toxins. The use of ipecac has recently been discouraged, because there does not appear to be any supportive risk-benefit literature to justify its use	Ipecac acts locally by irritating the gastric mucosa and centrally by stimulating the chemoreceptor trigger zone	Adults: 15 - 30 ml. Repeat after 20 - 30 min if necessary Children: < 6 months — not recommended; 6 - 8 months 5 ml; 8 - 12 months 10 ml; 1 - 3 years 15 ml; > 3 years 15 - 30 ml Note: Use ipecac syrup (USP), or equivalent formulation in which the total ether-extractable alkaloids do not exceed 8 mg/5 ml. In all instances ipecac should be followed by a drink of water — a full glass in the case of adults
Vitamin C	To reduce methaemoglobin formed by oxidising agents.	Reduction of methaemaglobin to haemoglobin.	1 g slowly IV followed by 200 mg orally 3 times daily. Note: Suitable for use in patients with glucose 6 phosphate dehydrogenase deficiency
Vitamin K_1 (phytomenadione: Kanakion; Roche)	Vitamin K_1 (phytonadione, phytomenadione: Konakion) is a specific antidote to counter the effects of warfarin and long-acting anticoagulant rodenticide poisoning, and should be administered to	Bypasses inhibition of vitamin K_1-epoxide reductase enzyme	IV vitamin K_1 is preferable in severe cases where rapid correction is required Adults: Initially, 2.5 - 10 mg up to 25 mg may be administered IV, diluted in N/saline or 5% dextrose, at a rate not exceeding 5% of the total dose per minute. In

Table I. **Continued**

Agent	Indication	Mode of action	Dose
	any patient with a prolonged PT or INR. Menadione (vitamin K_3, Synkayvite) should not be used		maximally anticoagulated individuals, repeat doses at 6 - 8-hour intervals may be required if response is not adequate. (Initial IV doses of 25 - 400 mg have been required in actively haemorrhaging patients.) Adult oral dose: Absorption is inconsistent: large daily maintenance doses (100 - 125 mg/day) may be required for prolonged periods (1.5 - 8 months) in severe overdose, whereas 20 - 100 mg/day may be adequate in less severe poisoning Children IV: 1 - 5 mg. Repeat in 6 - 8 hours, if necessary Children orally: 2.5 - 10 mg Caution: IV administration is associated with a small risk of anaphylaxis

visible concretions or masses in the stomach, e.g. iron-containing tablets and slow-release formulations in general. Disc batteries can also be removed in this way.

Temperature measurement

Anticholinergic and antihistamine toxins may decrease the patient's ability to perspire to the extent that the temperature rises to life-threatening levels; toxins may also directly or indirectly cause hypothermia which, in turn, may cause or precipitate cardiac dysrhythmias. It is imperative that the temperature be carefully and regularly monitored in the acute situation; a special suitably calibrated instrument is required to measure low body temperatures.

Measurement of the respiratory minute volume

Slow irregular respiratory efforts with long apnoeic periods are almost invariably indicative of respiratory depression. However, ventilation may be inadequate in the patient with a normal or increased respiratory rate. Consequently, the respiratory minute volume should be measured with a Wright's or other respirometer in all instances in which ventilatory depression is suspected. Flow rates of less than 4 l/min are indicative of respiratory depression and appropriate ventilatory support should receive immediate attention.

FURTHER READING

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Although it is not possible to be fully prepared for all poisoning-related eventualities, it is possible to take proactive steps to deal with the commonly encountered poisonings and overdoses responsible for more than 90% of incidents.

In addition to the medicines, equipment and accessories necessary to support vital functions, arrangements should be made to have readily available specific antidotes and agents required to counter the effects and to prevent systemic absorption of toxins.