01-7 Poisoning

7 Poisoning

Poisoning SHL Thomas Comprehensive evaluation of the poisoned patient 132 General approach to the poisoned patient 134 Triage and resuscitation 134 Clinical assessment and investigations 134 Psychiatric assessment 135 General management 135 Poisoning by specific pharmaceutical agents 137 Analgesics 137 Antidepressants 138 Cardiovascular medications 140 Iron 140 Antipsychotic drugs 141 Antidiabetic agents 141 Pharmaceutical agents less commonly taken in poisoning 141 Drugs of misuse 141 Depressants 141 Stimulants and entactogens 143 Hallucinogens 143 Dissociative drugs 144 Volatile substances 144 Body packers and body stuffers 144 Chemicals and pesticides 144 Carbon monoxide 144 Organophosphorus insecticides and nerve agents 145 Carbamate insecticides 146 Paraquat 147 Methanol and ethylene glycol 147 Corrosive substances 147 Aluminium and zinc phosphide 148 Copper sulphate 148 Chemicals less commonly taken in poisoning 148 Chemical warfare agents 149 Environmental poisoning 149 Food-related poisoning 149 Plant poisoning 150

132 • POISONING Insets (Self-cutting) From Douglas G, Nicol F, Robertson C (eds). Macleod’s Clinical examination, 11th edn. Churchill Livingstone, Elsevier Ltd; 2005. (Chemical burn) www.firewiki.net. (Needle tracks) www.deep6inc.com. (Pinpoint pupil) http://drugrecognition.com/images. (Injected conjunctiva) http:// knol.google.com. Movement and muscles Tone, fasciculations, myoclonus, tremor, paralysis, ataxia Chest Evidence of aspiration, bronchoconstriction Reflexes Tendon reflexes, plantar responses, inducible clonus Eyes Miosis or mydriasis, diplopia or strabismus, lacrimation Skin Temperature, cyanosis, flushing, sweating, blisters, pressure areas, piloerection, evidence of self-harm Level of consciousness Presence of seizures, delirium, agitation or psychosis Psychiatric evaluation Features of psychiatric illness, mental capacity Mouth Dry mouth, excessive salivation Airway, breathing, circulation Respiration rate, oxygen saturation, pulse, BP, dysrhythmias Self-cutting Needle tracks Chemical burn Pinpoint pupil Injected conjunctiva

Abdomen Hepatic or epigastric tenderness, ileus, palpable bladder

Comprehensive evaluation of the poisoned patient Taking a history in poisoning • What toxin(s) have been taken and how much? • What time were they taken and by what route? • Has alcohol or any other substance (or substances, including drugs of misuse) been taken as well? • Obtain details from witnesses (e.g. family, friends, ambulance personnel) of the circumstances of the overdose • Assess immediate suicide risk in those with apparent self-harm (full psychiatric evaluation when patient has recovered physically) • Assess capacity to make decisions about accepting or refusing treatment • Establish past medical history, drug history and allergies, social

and family history • Record all information carefully

Comprehensive evaluation of the poisoned patient • 133

Clinical signs of poisoning by pharmaceutical agents and drugs of misuse. Cerebellar signs Some anticonvulsants, alcohol Phenothiazines, haloperidol, metoclopramide Extrapyramidal signs Any CNS depressant drug or agent (N.B. consider methaemoglobinaemia caused by dapsone, amyl nitrite etc.) Cyanosis Tachycardia or tachyarrhythmias: tricyclic antidepressants, theophylline, digoxin, antihistamines Bradycardia or bradyarrhythmias: digoxin, β-blockers, calcium channel blockers, opioids, organophosphates Heart rate Needle tracks Drugs of misuse: opioids etc. Hyperthermia and sweating: ecstasy, serotonin re-uptake inhibitors, salicylates Hypothermia: any CNS depressant drug, opioids, chlorpromazine Small: opioids, clonidine, organophosphorus compounds Large: tricyclic antidepressants, amphetamines, cocaine Reduced: opioids, benzodiazepines Increased: salicylates Paracetamol hepatotoxicity, renal toxicity Right upper quadrant /renal angle tenderness Epigastric tenderness NSAIDs, salicylates Rhabdomyolysis Amphetamines, caffeine Hypotension: tricyclic antidepressants, haloperidol Hypertension: cocaine, α-adrenoceptor agonists Respiratory rate Pupil size Body temperature Blood pressure Decontamination and enhanced elimination. One of the key aspects in the evaluation of a poisoned patient is deciding if decontamination and/or enhanced elimination is required. Blood Haemodialysis Haemoperfusion Kidneys Urinary alkalinisation Gastrointestinal tract Multiple-dose activated charcoal Enhancing elimination Direct eye contact Eye irrigation – remove contact lenses Wash eyes thoroughly for at least 15 mins with normal saline or water Remove particles from palpebral fissures If pain persists, insert fluorescein drops and perform slit-lamp examination for corneal damage Skin contact (hazardous chemicals/ pesticides) Remove clothing Wash with copious amounts of soap and water Gastrointestinal decontamination External decontamination Gastrointestinal tract Single-dose oral activated charcoal Gastric lavage

134 • POISONING General approach to the poisoned patient A general approach is shown on pages 132–133. In many countries, poisons centres are available to provide advice on management of suspected poisoning with specific substances. Information is also available online (p. 150). Triage and resuscitation Patients who are seriously poisoned must be identified early so that appropriate management is not delayed. Triage involves: • immediately assessing vital signs • identifying the poison(s) involved and obtaining adequate information about them • identifying patients at risk of further attempts at self-harm and removing any remaining hazards. Those with possible external contamination with chemical or environmental toxins should undergo appropriate decontamination (p. 133). Critically ill patients must be resuscitated (p. 174). The Glasgow Coma Scale (GCS) is commonly employed to assess conscious level, although not specifically validated in poisoning. The AVPU (alert/verbal/painful/unresponsive) scale is also a rapid and simple method. An electrocardiogram (ECG) should be performed and cardiac monitoring instituted in all patients with cardiovascular features or where exposure to potentially cardiotoxic substances is suspected. Patients who may need antidotes should be weighed if possible, so that appropriate weight-related doses can be prescribed. Substances unlikely to be toxic in humans should be identified so that inappropriate admission and intervention are avoided (Box 7.3). Clinical assessment and investigations History and examination are described on page 132. Occasionally, patients may be unaware of or confused about what they have taken, or may exaggerate (or, less commonly, underestimate) the size of the overdose, but rarely mislead medical staff deliberately. In regions of

the world where self-poisoning is illegal, patients may be reticent about giving a history. Toxic causes of abnormal physical signs are shown on page 133. The patient may have a cluster of clinical features (‘toxidrome’) suggestive of poisoning with a particular drug type, e.g. anticholinergic, serotoninergic (see Box 7.10), stimulant, sedative, opioid (see Box 7.12) or cholinergic (see Box 7.14) feature clusters. Poisoning is a common cause of coma, especially Acute poisoning is common, accounting for about 1% of hospital admissions in the UK. Common or otherwise important substances involved are shown in Box 7.1. In developed countries, the most frequent cause is intentional drug overdose in the context of self-harm, often involving prescribed or ‘over-the-counter’ medicines. Accidental poisoning is also common, especially in children and the elderly (Box 7.2). Toxicity also results from alcohol or recreational substance use, or following occupational or environmental exposure. Poisoning is a major cause of death in young adults, but most deaths occur before patients reach medical attention, and mortality is low (< 1%) in those admitted to hospital. In developing countries, the frequency of self-harm is more difficult to estimate. Because of their widespread availability and use, household and agricultural products, such as pesticides and herbicides, are common sources of poisoning and have a much higher case fatality. In China and South-east Asia, pesticides account for about 300 000 suicides each year. Snake bite and other forms of envenomation are also important causes of morbidity and mortality internationally and are discussed in Chapter 8. 7.3 Substances of very low toxicity • Writing/educational materials, e.g. pencil lead, crayons, chalk • Decorating products, e.g. emulsion paint, wallpaper paste • Cleaning/bathroom products (except dishwasher tablets and liquid laundry detergent capsules, which can be corrosive) • Pharmaceuticals: oral contraceptives, most antibiotics (but not tetracyclines or antituberculous drugs), vitamins B, C and E, prednisolone, emollients and other skin creams, baby lotion • Miscellaneous: plasticine, silica gel, most household plants, plant food, pet food, soil 7.2 Poisoning in old age • Aetiology: may result from accidental poisoning (e.g. due to delirium or dementia) or drug toxicity as a consequence of impaired renal or hepatic function or drug interaction. Toxic prescription medicines are more likely to be available. • Psychiatric illness: self-harm is less common than in younger adults but more frequently associated with depression and other psychiatric illness, as well as chronic illness and pain. There is a higher risk of subsequent suicide. • Severity of poisoning: increased morbidity and mortality result from reduced renal and hepatic function, lower functional reserve, increased sensitivity to sedative agents and frequent comorbidity. 7.1 Important substances involved in poisoning In the UK • Analgesics: paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) • Antidepressants: tricyclic antidepressants (TCAs), selective serotonin re-uptake inhibitors (SSRIs) and lithium • Cardiovascular agents: β-blockers, calcium channel blockers and cardiac glycosides • Drugs of misuse: depressants (e.g. opiates, benzodiazepines), stimulants and entactogens (e.g. amphetamines, MDMA, mephedrone, cocaine), hallucinogens (e.g. cannabis, synthetic cannabinoid receptor agonists, LSD) • Carbon monoxide • Alcohol In South and South-east Asia • Organophosphorus and carbamate insecticides • Aluminium and zinc phosphide • Oleander • Corrosives • Snake venoms (Ch. 8) (LSD = lysergic acid diethylamide; MDMA = 3,4-methylenedioxymethamphetamine, ecstasy)

health professional with appropriate training (p. 1187). This should occur after they have recovered from poisoning, unless there is an urgent issue, such as uncertainty about their capacity to decline medical treatment. General management Patients presenting with eye/skin contamination should

undergo local decontamination measures. These are described on page 133. Gastrointestinal decontamination Patients who have ingested potentially life-threatening quantities of toxins may be considered for gastrointestinal decontamination if poisoning has been recent (p. 133). in younger people, but it is important to exclude other potential causes (p. 194). Urea, electrolytes and creatinine should be measured in all patients with suspected systemic poisoning. Arterial blood gases should be checked in those with significant respiratory or circulatory compromise, or after poisoning with substances likely to affect acid–base status (Box 7.4). Calculation of anion and osmolar gaps may help to inform diagnosis and management (Box 7.5). Potent oxidising agents may cause methaemoglobinaemia, with consequent blue discoloration of skin and blood, and reduced oxygen delivery to the tissues (Fig. 7.1). For some substances, management may be facilitated by measurement of the amount of toxin in the blood. Qualitative urine screens for potential toxins, including near-patient testing kits, have a limited clinical role. Psychiatric assessment Patients presenting with drug overdose in the context of self-harm should undergo psychiatric evaluation prior to discharge by a 7.5 Anion and osmolar gaps in poisoning Anion gap Osmolar gap Calculation [Na+ + K+] − [Cl− + HCO3 −] [Measured osmolality] − [(2 × Na) + Urea + Glucose]1 Reference range 12–16 mmol/L < 10 Common toxic causes of elevation2 Ethanol Ethylene glycol Methanol Salicylates Iron Cyanide Ethanol Ethylene glycol Methanol 1All units should be in mmol/L, except osmolality, which should be in mOsmol/kg. For non-SI units, the corresponding formula is [Measured osmolality (mOsmol/kg)] − [(2 × Na (mEq/L)) + Urea/2.8 (mg/dL) + Glucose/18 (mg/dL)]. 2Box 14.19 (p. 365) gives non-toxic causes. 7.4 Causes of acidosis in the poisoned patient Cause Normal lactate* High lactate Toxic Salicylates Methanol Ethylene glycol Paraldehyde Metformin Iron Cyanide Sodium valproate Carbon monoxide Other Renal failure Ketoacidosis Severe diarrhoea Shock *Unless circulatory shock is present, when it will be high in any case. Fig. 7.1 Methaemoglobinaemia. Causes Non-toxic • Congenital methaemoglobinaemias Toxic (Oxidising agents) • Organic nitrites • Nitrates • Benzocaine • Dapsone • Chloroquine • Aniline dyes • Chlorobenzene • Naphthalene • Copper sulphate Consequences • Haemoglobin–oxygen dissociation curve is shifted to the left (see Fig. 23.5) • Oxygen delivery to tissues is reduced • There is apparent 'cyanosis' • Breathlessness, fatigue, headache and chest pain occur • Delirium, impaired consciousness and seizures may occur in severe cases Treatment • Methylthioninium chloride ('methylene blue') 1–2 mg/kg (intravenous) is given • Reduces methaemoglobin (see below) • Used for symptomatic patients with severe methaemoglobinaemia (e.g. >30%) • Patients with anaemia or other comorbidities may need treatment at lower concentrations Cytochrome b5 reductase NADH NAD NADP* NADPH Methaemoglobin reductase Methylthioninium chloride (reduced) Methylthioninium chloride (oxidised) Methaemoglobin (Fe3+) Haemoglobin (Fe2+)

 for most substances and complications are common, especially pulmonary aspiration. It is contraindicated if strong acids, alkalis or petroleum distillates have been ingested. Use may be justified for life-threatening overdoses of those substances that are not absorbed by activated charcoal (see Box 7.6). Whole bowel irrigation This involves the administration of large quantities of osmotically balanced polyethylene glycol and electrolyte solution (1–2 L/ hr for an adult), usually by a nasogastric tube, until the rectal effluent is clear. It is occasionally indicated to enhance the elimination of ingested packets of illicit drugs or slow-release tablets such as iron and lithium that are not absorbed by activated charcoal. Contraindications include inadequate airway protection, haemodynamic instability, gastrointestinal haemorrhage, obstruction or ileus. Whole bowel irrigation may precipitate nausea and vomiting, abdominal pain and electrolyte disturbances. Urinary alkalinisation Urinary excretion of weak acids and bases is affected by

urinary pH, which changes the extent to which they are ionised. Highly ionised molecules pass poorly through lipid membranes and therefore little tubular reabsorption occurs and urinary excretion is increased. If the urine is alkalinised (pH > 7.5) by the administration of sodium bicarbonate (e.g. 1.5 L of 1.26% sodium bicarbonate over 2 hrs), weak acids (e.g. salicylates, methotrexate) are highly ionised, resulting in enhanced urinary excretion. Urinary alkalinisation is currently recommended for patients with clinically significant salicylate poisoning when the criteria for haemodialysis are not met (see below). It is also sometimes used for poisoning with methotrexate. Complications include alkalaemia, hypokalaemia and occasionally alkalotic tetany (p. 367). Hypocalcaemia may occur but is rare. Haemodialysis and haemoperfusion These techniques can enhance the elimination of poisons that have a small volume of distribution and a long half-life after overdose; use is appropriate when poisoning is sufficiently severe. The toxin must be small enough to cross the dialysis membrane (haemodialysis) or must bind to activated charcoal (haemoperfusion) (see Box 7.7). Haemodialysis can also correct acid–base and metabolic disturbances associated with poisoning (p. 135). Lipid emulsion therapy Lipid emulsion therapy is increasingly used for poisoning with lipid-soluble agents, such as local anaesthetics, tricyclic antidepressants, calcium channel blockers and lipid-soluble β-adrenoceptor antagonists (β-blockers) such as propranolol. It involves intravenous infusion of 20% lipid emulsion (e.g. Intralipid, suggested initial dose 1.5 mL/kg, followed by a continued infusion of 0.25 mL/kg/min until there is clinical improvement). It is thought that lipid-soluble toxins partition into the intravenous lipid, reducing target tissue concentrations. The elevated myocardial free fatty acid concentrations may also have beneficial effects on myocardial metabolism and performance by counteracting the inhibition of myocardial fatty acid oxidation produced by some cardiotoxins, enabling increased adenosine triphosphate (ATP) synthesis and energy production. Some animal studies have suggested efficacy and case reports of use in human poisoning have also been 7.7 Poisons effectively eliminated by multiple doses of activated charcoal, haemodialysis or haemoperfusion Multiple doses of activated charcoal • Carbamazepine • Dapsone • Phenobarbital • Quinine • Theophylline Haemodialysis • Ethylene glycol • Isopropanol • Methanol • Salicylates • Sodium valproate • Lithium Haemoperfusion • Theophylline • Phenytoin • Carbamazepine • Phenobarbital • Amobarbital 7.6 Substances poorly adsorbed by activated charcoal Medicines • Iron • Lithium Chemicals • Acids* • Alkalis* • Ethanol • Ethylene glycol • Mercury • Methanol • Petroleum distillates* *Gastric lavage contraindicated. Activated charcoal Given orally as a slurry, activated charcoal absorbs toxins in the bowel as a result of its large surface area. It can prevent absorption of an important proportion of the ingested dose of toxin, but efficacy decreases with time and current guidelines do not encourage use more than 1 hour after overdose, unless a sustained-release preparation has been taken or when gastric emptying may be delayed. Use is ineffective for some toxins that do not bind to activated charcoal (Box 7.6). In patients with impaired swallowing or a reduced level of consciousness, activated charcoal, even via a nasogastric tube, carries a risk of aspiration pneumonitis, which can be reduced (but not eliminated) by protecting the airway with a cuffed endotracheal tube. Multiple doses of oral activated charcoal (50 g 6 times daily in an adult) may enhance the elimination of some substances at any time after poisoning (Box 7.7). This interrupts enterohepatic circulation or reduces the concentration of free drug in the gut lumen, to the extent that drug diffuses from the blood back into the bowel to be absorbed on to the charcoal (‘gastrointestinal dialysis’). A laxative is generally given with the charcoal to reduce the risk of constipation or intestinal obstruction by charcoal ‘briquette’ formation in the gut lumen. Evidence suggests that single or multiple doses of activated charcoal do not improve clinical outcomes after poisoning with pesticides or oleander. Gastric aspiration and lavage Gastric

aspiration and/or lavage is very infrequently indicated in acute poisoning, as it is no more effective than activated charcoal

Poisoning by specific pharmaceutical agents • 137

7.8 Complications of poisoning and their management Complication Examples of causative agents Management Coma Sedative agents Appropriate airway protection and ventilatory support Oxygen saturation and blood gas monitoring Pressure area and bladder care Identification and treatment of aspiration pneumonia Seizures NSAIDs Anticonvulsants TCAs Theophylline Appropriate airway and ventilatory support IV benzodiazepine (e.g. diazepam 10–20 mg, lorazepam 2–4 mg) Correction of hypoxia, acid–base and metabolic abnormalities Acute dystonias Typical antipsychotics Metoclopramide Procyclidine, benzatropine or diazepam Hypotension Due to vasodilatation Vasodilator antihypertensives Anticholinergic agents TCAs IV fluids Vasopressors (rarely indicated; p. 206) Due to myocardial suppression β-blockers Calcium channel blockers TCAs Optimisation of volume status Inotropic agents (p. 206) Ventricular tachycardia Monomorphic, associated with QRS prolongation Sodium channel blockers Correction of electrolyte and acid–base abnormalities and hypoxia Sodium bicarbonate (e.g. 50 mL 8.4% solution, repeated if necessary) Torsades de pointes, associated with QTc prolongation Anti-arrhythmic drugs (quinidine, amiodarone, sotalol) Antimalarials Organophosphate insecticides Antipsychotic agents Antidepressants Antibiotics (erythromycin) Correction of electrolyte and acid–base abnormalities and hypoxia Magnesium sulphate, 2 g IV over 1–2 mins, repeated if necessary (NSAID = non-steroidal anti-inflammatory drug; TCA = tricyclic antidepressant) encouraging, with recovery of circulatory collapse reported in cases where other treatment modalities have been unsuccessful. No controlled trials of this technique have been performed, however, and efficacy remains uncertain. Supportive care For most poisons, antidotes and methods to accelerate elimination are inappropriate, unavailable or incompletely effective. Outcome is dependent on appropriate nursing and supportive care, and treatment of complications (Box 7.8). Antidotes Antidotes are available for some poisons and work by a variety of mechanisms (Box 7.9). The use of some of these in the management of specific poisons is described below. Poisoning by specific pharmaceutical agents Analgesics Paracetamol Paracetamol (acetaminophen) is the drug most commonly used in overdose in the UK. Toxicity is caused by an intermediate reactive metabolite that binds covalently to cellular proteins, 7.9 Specific antidotes used to treat poisoning Mechanism of action Examples of antidote Poisoning treated Glutathione repleters Acetylcysteine Methionine Paracetamol Receptor antagonists Naloxone Opioids Flumazenil Benzodiazepines Atropine Organophosphorus compounds Carbamates Alcohol dehydrogenase inhibitors Fomepizole Ethanol Ethylene glycol Methanol Chelating agents Desferrioxamine Iron Hydroxocobalamin Dicobalt edetate Cyanide DMSA Sodium calcium edetate Lead Reducing agents Methylthioninium chloride Organic nitrites Cholinesterase reactivators Pralidoxime Organophosphorus compounds Antibody fragments Digoxin Fab fragments Digoxin (DMSA = dimercaptosuccinic acid)

138 • POISONING Salicylates (aspirin) Clinical features Salicylate overdose commonly causes nausea, vomiting, sweating, tinnitus and deafness. Direct stimulation of the respiratory centre produces hyperventilation and respiratory alkalosis. Peripheral vasodilatation with bounding pulses and profuse sweating occurs in moderately severe cases. Serious poisoning is associated with metabolic acidosis, hypoprothrombinaemia, hyperglycaemia, hyperpyrexia, renal failure, pulmonary oedema, shock and cerebral oedema. Agitation, delirium, coma and fits may occur,

especially in children. Toxicity is enhanced by acidosis, which increases salicylate transfer across the blood–brain barrier. Management Activated charcoal should be administered if the patient presents within 1 hour. Multiple doses may enhance salicylate elimination but are not routinely recommended. The plasma salicylate concentration should be measured at least 2 (symptomatic patients) or 4 hours (asymptomatic patients) after overdose and repeated in suspected serious poisoning, as concentrations may continue to rise for several hours. Clinical status, however, is more important than the salicylate concentration when assessing severity. Dehydration should be corrected carefully because of the risk of pulmonary oedema. Metabolic acidosis should be treated with intravenous sodium bicarbonate (8.4%), after plasma potassium has been corrected. Urinary alkalinisation is indicated for adults with salicylate concentrations above 500 mg/L. Haemodialysis is very effective for removing salicylate and correcting associated acid–base and fluid balance abnormalities. It should be considered when serum concentrations are above 700 mg/L in adults with severe toxic features, or in renal failure, pulmonary oedema, coma, convulsions or refractory acidosis. Non-steroidal anti-inflammatory drugs Clinical features Overdose of most non-steroidal anti-inflammatory drugs (NSAIDs) usually causes only minor abdominal discomfort, vomiting and/or diarrhoea, but convulsions can occur occasionally, especially with mefenamic acid. Coma, prolonged seizures, apnoea, liver dysfunction and renal failure may follow substantial overdose but are rare. Features of toxicity are unlikely to develop in patients who are asymptomatic more than 6 hours after overdose. Management Electrolytes, liver function tests and a full blood count should be checked in all but the most trivial cases. Activated charcoal may be given if the patient presents within 1 hour. Symptomatic treatment for nausea and gastrointestinal irritation may be needed. Antidepressants Tricyclic antidepressants Overdose with tricyclic antidepressants (TCAs) carries a high morbidity and mortality because of their sodium channel-blocking, anticholinergic and α-adrenoceptor-blocking effects. Clinical features Anticholinergic effects are common (Box 7.10). Severe complications include convulsions, coma and arrhythmias (ventricular causing cell death. This results in hepatic and occasionally renal failure. In therapeutic doses, the toxic metabolite is detoxified in reactions requiring glutathione, but in overdose, glutathione reserves become exhausted. Management Activated charcoal may be used in patients presenting within 1 hour. Antidotes for paracetamol act by replenishing hepatic glutathione and should be administered to all patients with acute poisoning and paracetamol concentrations above a ‘treatment line’ provided on paracetamol poisoning nomograms (Fig. 7.2). The threshold used for these nomograms varies between countries, however, and local guidance should be followed. Acetylcysteine given intravenously (or orally in some countries) is highly efficacious if administered within 8 hours of the overdose. However, efficacy declines thereafter, so administration should not be delayed in patients presenting after 8 hours to await a paracetamol blood concentration result. The antidote can be stopped if the paracetamol concentration is shown to be below the nomogram treatment line. Liver and renal function, International Normalised Ratio (INR) and a venous bicarbonate should also be measured. Arterial blood gases and lactate should be assessed in patients with reduced bicarbonate or severe liver function abnormalities; metabolic acidosis indicates severe poisoning. Anaphylactoid reactions are the most important adverse effects of acetylcysteine and are related to dose-related histamine release. Common features are itching and urticaria, and in severe cases, bronchospasm and hypotension. Most cases can be managed by temporary discontinuation of acetylcysteine and administration of an antihistamine. An alternative antidote is methionine 2.5 g orally (adult dose) every 4 hours to a total of four doses, but this may be less effective, especially after delayed presentation. Liver transplantation should be considered for paracetamol poisoning with life-threatening liver failure (p. 856). If multiple ingestions of paracetamol have taken place

over several hours (‘staggered overdose’) or days (e.g. chronic therapeutic excess), acetylcysteine may be indicated; specific treatment recommendations vary between countries. Fig. 7.2 Paracetamol treatment nomogram (UK). Above the treatment line, benefits of treatment outweigh risk. Below it, risks of treatment outweigh benefits. 0 0

10 12 Time since overdose (hr) Treatment line 14 16 18 20 22 24

Paracetamol concentration (mg/L) Too early to assess

solution) should be administered and repeated to correct pH. The correction of the acidosis and the sodium loading that results may bring about rapid improvement in ECG features and arrhythmias. Hypoxia and electrolyte abnormalities should also be corrected. Anti-arrhythmic drugs should only be given on specialist advice. Prolonged seizures should be treated initially with intravenous benzodiazepines (see Box 7.8). Selective serotonin and noradrenaline re-uptake inhibitors Selective serotonin re-uptake inhibitor (SSRI) antidepressants (e.g. fluoxetine, paroxetine, fluvoxamine, sertraline, citalopram, escitalopram) are increasingly used to treat depression and are less toxic in overdose than TCAs. The related serotonin– noradrenaline re-uptake inhibitors (SNRIs), such as venlafaxine and duloxetine, are also commonly used but are more toxic than SSRIs in overdose. Clinical features and management Overdose of SSRIs may produce nausea and vomiting, tremor, insomnia and sinus tachycardia. Agitation, drowsiness and convulsions occur infrequently and may be delayed for several hours. Serotonin syndrome may occur (see Box 7.10), especially if SSRIs are taken in combination or with other serotonergic agents. Cardiac arrhythmias occur infrequently and most patients require supportive care only. The toxic effects of SNRIs are similar but tachycardia, hypertension or hypotension and ECG changes (QRS and QT prolongation) may be more prominent and hypoglycaemia can also arise. Lithium Severe lithium toxicity is uncommon after intentional acute overdose but is more often encountered in patients taking therapeutic doses, frequently as a result of interactions with drugs such as diuretics or NSAIDs. Severe toxicity is more common after acute overdose in patients already taking chronic therapy (‘acute on chronic’ poisoning). Clinical features Nausea, diarrhoea, polyuria, dizziness and tremor may progress to muscular weakness, drowsiness, delirium, myoclonus, fasciculations, choreoathetosis and renal failure. Coma, seizures, ataxia, cardiac dysrhythmias such as heart block, blood pressure disturbances and renal failure may occur in severe poisoning. Management Activated charcoal is ineffective. Early gastric lavage is of theoretical benefit, but lithium tablets are likely to remain intact in the stomach and may be too large for aspiration via a lavage tube. Whole bowel irrigation is often used after substantial overdose but efficacy is unproven. Lithium concentrations should be measured immediately (symptomatic patients) or after at least 6 hours (asymptomatic patients) following acute overdose. The usual therapeutic range is 0.4–1.0 mmol/L. Adequate hydration should be maintained with intravenous fluids. Seizures should be treated as in Box 7.8. Haemodialysis should be considered for severe toxicity associated with high lithium concentrations (e.g. > 4.0 mmol/L after chronic or ‘acute on chronic’ poisoning, or > 7.5 mmol/L after acute poisoning). Lithium concentrations are reduced substantially during dialysis, but rebound increases occur after discontinuation and multiple sessions are usually required. tachycardia, ventricular fibrillation and, less commonly, heart block). Hypotension results from inappropriate vasodilatation or impaired myocardial contractility. Serious complications appear more common with dosulepin and amitriptyline.

Management Activated charcoal should be administered if the patient presents within 1 hour. A 12-lead ECG should be taken and continuous cardiac monitoring maintained for at least 6 hours. Prolongation of the QRS interval (especially if > 0.16 secs) indicates severe sodium channel blockade and a high risk of arrhythmia (Fig. 7.3). QT interval prolongation may also occur. Arterial blood gases should be measured in suspected severe poisoning. In patients with arrhythmias, significant QRS or QT prolongation or acidosis, intravenous sodium bicarbonate (50 mL of 8.4% Fig. 7.3 ECG in severe tricyclic antidepressant poisoning. This rhythm strip shows a broad QRS complex due to impaired conduction. II 7.10 Anticholinergic and serotonergic feature clusters Anticholinergic Serotonin syndrome Common causes Benzodiazepines Antipsychotics TCAs Antihistamines Scopolamine Benzatropine Belladonna Some plants and mushrooms (see Box 7.18) SSRIs MAOIs TCAs Amphetamines Tryptamines Buspirone Bupropion (especially in combination) Clinical features Cardiovascular Tachycardia, hypertension Tachycardia, hyper- or hypotension Central nervous system Delirium, hallucinations, sedation Delirium, hallucinations, sedation, coma Muscle Myoclonus Shivering, tremor, myoclonus, raised creatine kinase Temperature Fever Fever Eyes Diplopia, mydriasis Normal pupil size Abdomen Ileus, palpable bladder Diarrhoea, vomiting Mouth Dry Skin Flushing, hot, dry Flushing, sweating Complications Seizures Seizures Rhabdomyolysis Renal failure Metabolic acidosis Coagulopathies (MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin re-uptake inhibitor; TCA = tricyclic antidepressant)

140 • POISONING Digoxin and oleander Poisoning with digoxin is usually accidental, arising from prescription of an excessive dose, impairment of renal function or drug interactions. In South Asia, deliberate self-poisoning with yellow oleander (Thevetia peruviana), containing cardiac glycosides, is common. Clinical features Cardiac effects include tachyarrhythmias (either atrial or ventricular) and bradycardias, with or without atrioventricular block. Ventricular bigeminy is common and atrial tachycardia with evidence of atrioventricular block is highly suggestive of the diagnosis. Severe poisoning is often associated with hyperkalaemia. Non-cardiac features include delirium, headache, nausea, vomiting, diarrhoea and (rarely) altered colour vision. Digoxin poisoning can be confirmed by elevated plasma concentration (usual therapeutic range 1.3–2.5 mmol/L). After chronic exposure, concentrations

> 5 mmol/L suggest serious poisoning. Management Activated charcoal is commonly administered to patients presenting soon after acute ingestion, although evidence of benefit is lacking. Urea, electrolytes and creatinine should be measured, a 12-lead ECG performed and cardiac monitoring instituted. Hypoxia, hypokalaemia (sometimes caused by concurrent diuretic use), hypomagnesaemia and acidosis increase the risk of arrhythmias and should be corrected. Significant bradycardias may respond to atropine, although temporary pacing is sometimes needed. Ventricular arrhythmias may respond to intravenous magnesium (see Box 7.8). If available, digoxin-specific antibody fragments should be administered when there are severe refractory ventricular arrhythmias or bradycardias. These are effective for both digoxin and yellow oleander poisoning. Iron Overdose with iron can cause severe and sometimes fatal poisoning, with toxicity of individual iron preparations related to their elemental iron content. Clinical features Early features include gastrointestinal

disturbance with the passage of grey or black stools, progressing to hyperglycaemia, leucocytosis, haematemesis, rectal bleeding, drowsiness, convulsions, coma, metabolic acidosis and cardiovascular collapse in severe cases. Early symptoms may improve or resolve within 6–12 hours, but hepatocellular necrosis can develop 12–24 hours after overdose and occasionally progresses to hepatic failure. Gastrointestinal strictures are late complications. Management Activated charcoal is ineffective but gastric lavage may be considered in patients presenting soon after substantial overdose, although efficacy is unknown. Serum iron concentration should be measured at least 4 hours after overdose or earlier if there are features of toxicity. Desferrioxamine chelates iron and should be administered immediately in patients with severe features, without waiting for serum iron concentrations, as well as symptomatic patients with high serum iron concentrations (e.g. > 5 mg/L). Desferrioxamine may cause hypotension, allergic reactions and occasionally pulmonary oedema. Otherwise, treatment is supportive and directed at complications. Cardiovascular medications Although not common, cardiovascular drug overdose is important because features of toxicity are often severe. Beta-blockers Major features of toxicity are bradycardia and hypotension; heart block, pulmonary oedema and cardiogenic shock occur in severe poisoning. Those with additional sodium channel-blocking effects (e.g. propranolol, acebutolol, carvedilol) may cause seizures, delirium and coma, while sotalol, which also blocks potassium channels, may cause QTc prolongation and torsades de pointes (Box 7.8 and p. 476). Management Intravenous fluids may reverse hypotension but care is required to avoid pulmonary oedema. Bradycardia and hypotension may respond to high doses of atropine (up to 3 mg in an adult) or an infusion of isoproterenol. Glucagon (5–10 mg over 10 mins, then 1–5 mg/hr by infusion) counteracts β-blockade by stimulating intracellular cyclic adenosine monophosphate (cAMP) production and is now more commonly used. In severe cases, ‘hyperinsulinaemia euglycaemic therapy’ has been used, as described under calcium channel blockers below. The efficacy of lipid emulsion therapy in severe poisoning with lipid-soluble β-blockers, such as propranolol, carvedilol and oxprenolol, is uncertain. Calcium channel blockers L-type calcium channel blockers are highly toxic in overdose. Dihydropyridines (e.g. nifedipine, amlodipine) cause vasodilatation, whereas diltiazem and verapamil have predominantly cardiac effects, including bradycardia and reduced myocardial contractility. Clinical features Hypotension due to vasodilatation or myocardial depression is common and bradycardias and heart block may also occur, especially with verapamil and diltiazem. Gastrointestinal disturbances, delirium, metabolic acidosis, hyperglycaemia and hyperkalaemia may also be present. Management Hypotension should be corrected with intravenous fluids, taking care to avoid pulmonary oedema. Persistent hypotension may respond to intravenous calcium gluconate (10 mg IV over 5 mins, repeated as required). Isoproterenol and glucagon may also be useful. Successful use of intravenous insulin with glucose (10–20% dextrose with

> insulin initially at 0.5–2.0 U/kg/ hr, increasing to 5–10 U/kg/hr according to clinical response), so-called ‘hyperinsulinaemia euglycaemic therapy’, has been reported in patients unresponsive to other strategies. The mechanism of action remains to be fully elucidated, but in states of shock myocardial metabolism switches from use of free fatty acids to glucose. Calcium channel blocker poisoning is also associated with hypoinsulinaemia and insulin resistance, impeding glucose uptake by myocytes. High doses of insulin inhibit lipolysis and increase glucose uptake and the efficiency of glucose utilisation. Cardiac pacing may be needed for severe unresponsive bradycardias or heart block. Lipid emulsion therapy has also been used in severe poisoning with apparent benefit, although evidence is largely anecdotal.

Arterial blood gases and plasma lactate should be taken after metformin overdose; acidosis should be corrected with intravenous sodium bicarbonate (250 mL 1.26% solution or 50 mL 8.4% solution, repeated as necessary). In severe cases, haemodialysis or haemodiafiltration is used. Pharmaceutical agents less commonly taken in poisoning An overview of the clinical features and management for drugs less commonly involved in poisoning is provided in Box 7.11. Drugs of misuse Drugs of misuse are common causes of toxicity requiring hospital admission. Management has recently become more complex because of the emergence of ‘novel psychoactive substances’ (NPS). These are often chemically related to traditional drugs of misuse, but with structural modifications made to evade legal control. The constituents of branded NPS products are often unknown and knowledge about the clinical features and management of NPS toxicity is limited. Depressants These produce CNS depression, including drowsiness, ataxia, delirium and coma, sometimes with respiratory depression, airway compromise, aspiration pneumonia and respiratory arrest Antipsychotic drugs Antipsychotic drugs (p. 1198) are often prescribed for patients at high risk of self-harm or suicide and are often taken in overdose. Clinical features Anticholinergic features (see Box 7.10) including drowsiness, tachycardia and hypotension, are common and convulsions may occur. Acute dystonias, including oculogyric crisis, torticollis and trismus, may occur after overdose with typical antipsychotics like haloperidol or chlorpromazine. QT interval prolongation and torsades de pointes can occur with some typical (e.g. haloperidol) and atypical (e.g. quetiapine, amisulpride, ziprasidone) agents. Management Activated charcoal may be of benefit if given early. Cardiac monitoring should be undertaken for at least 6 hours. Management is largely supportive, with treatment directed at complications (see Box 7.8). Antidiabetic agents Overdose is uncommon but toxic effects can be severe. Clinical features Sulphonylureas, meglitinides (e.g. nateglinide, repaglinide) and parenteral insulin cause hypoglycaemia when taken in overdose, although insulin is non-toxic if ingested by mouth. The duration of hypoglycaemia depends on the half-life or release characteristics of the preparation and may be prolonged over several days with long-acting agents such as glibenclamide, insulin zinc suspension or insulin glargine. Features of hypoglycaemia include nausea, agitation, sweating, aggression, delirium, tachycardia, hypothermia, drowsiness, convulsions and coma (p. 738). Permanent neurological damage can occur if hypoglycaemia is prolonged. Hypoglycaemia can be diagnosed using bedside glucose strips but venous blood should also be sent for laboratory confirmation. Metformin is

uncommonly associated with hypoglycaemia. Its major toxic effect is lactic acidosis, which can have a high mortality, and is particularly common in older patients and those with renal or hepatic impairment, or when ethanol has been co-ingested. Other features of metformin overdose are nausea, vomiting, diarrhoea, abdominal pain, drowsiness, coma, hypotension and cardiovascular collapse. There is limited experience of overdose involving thiazolidinediones (e.g. pioglitazone) and dipeptidyl peptidase 4 (DPP-4) inhibitors (e.g. sitagliptin) but significant hypoglycaemia is unlikely. Management Activated charcoal should be considered for recent substantial overdose. Venous blood glucose and urea and electrolytes should be measured and measurement repeated regularly. Hypoglycaemia should be corrected using oral or intravenous glucose (50 mL of 50% dextrose); an infusion of 10–20% dextrose may be required to prevent recurrence. Intramuscular glucagon can be used as an alternative, especially if intravenous access is unavailable. Failure to regain consciousness within a few minutes of normalisation of the blood glucose can indicate that a central nervous system (CNS) depressant has also been ingested, the hypoglycaemia has been prolonged, or there is another cause of coma (e.g. cerebral haemorrhage or oedema). 7.11 Clinical features and specific management of drugs less commonly involved in poisoning Substance Clinical features Management Anticonvulsants Carbamazepine, phenytoin Cerebellar signs Convulsions Cardiac arrhythmias Coma Multiple-dose activated charcoal (carbamazepine) Sodium valproate Coma Metabolic acidosis Haemodialysis for severe poisoning Isoniazid Peripheral neuropathy Convulsions Activated charcoal IV pyridoxine Theophylline Cardiac arrhythmias Convulsions Coma Multiple-dose activated charcoal Antimalarial drugs Chloroquine Acidosis and hypokalaemia Visual loss Convulsions, coma ECG changes and arrhythmias Correction of pH (but not potassium) Monitoring and treatment of cardiac rhythm High-dose diazepam with mechanical ventilation Quinine Tremor, tinnitus, deafness, ataxia, convulsions, coma Haemolysis ECG changes and arrhythmias Retinal toxicity Correction of pH (but not potassium) Monitoring and treatment of cardiac rhythm Multiple-dose activated charcoal No effective treatment for visual loss

 experience, often accompanied by heightened sexual arousal. Physical dependence occurs within a few weeks of regular high-dose use. Withdrawal can start within 12 hours, causing intense craving, rhinorrhoea, lacrimation, yawning, perspiration, shivering, piloerection, vomiting, diarrhoea and abdominal cramps. Examination reveals tachycardia, hypertension, mydriasis and facial flushing. Commonly encountered opioids and clinical features of poisoning are shown in Box 7.12. Needle tracks may be visible in intravenous users and there may be drug-related paraphernalia. Methadone may also cause QTc prolongation and torsades de pointes. Features of opioid poisoning can be prolonged for up to 48 hours after use of long-acting agents such as methadone or oxycodone. Use of the specific opioid antagonist naloxone (0.4–2 mg IV in an adult, repeated if necessary) may obviate the need for intubation, although excessive doses may precipitate acute withdrawal in chronic opiate users and breakthrough pain in those receiving opioids for pain management. Repeated doses or an infusion are often required because the half-life of the antidote is short compared to that of most opiates, especially those with prolonged elimination. Patients should be monitored for at least 6 hours after the last naloxone dose. Rare complications of naloxone therapy include fits, ventricular arrhythmias and pulmonary oedema. (Box 7.12). Other complications of coma include pressure blisters or sores and rhabdomyolysis. Effects are potentiated by other CNS depressants, including alcohol. Essential supportive care is detailed in Box 7.8. Antidotes are available for some depressants. Benzodiazepines Benzodiazepines (e.g. diazepam) and related substances (e.g. zopiclone) are of low toxicity when taken alone in overdose but can enhance CNS and respiratory depression when

taken with other sedative agents, including alcohol. They are more hazardous in the elderly and those with chronic lung or neuromuscular disease (see Box 7.12). The specific benzodiazepine antagonist flumazenil (0.5 mg IV, repeated if needed) increases conscious level in patients with benzodiazepine overdose, but carries a risk of seizures and is contraindicated in patients co-ingesting pro-convulsants (e.g. TCAs) and those with a history of epilepsy. Opioids Toxicity may result from misuse of illicit drugs such as heroin or from intentional or accidental overdose of medicinal opiates. Intravenous or smoked heroin gives a rapid, intensely pleasurable 7.12 Stimulant, sedative and opioid feature clusters Stimulant Sedative hypnotic Opioid Common causes Amphetamines MDMA (‘ecstasy’) Ephedrine Pseudoephedrine Cocaine Cannabis Phencyclidine Cathinones (e.g. mephedrone) Benzylpiperazine Benzodiazepines Barbiturates Ethanol GHB Heroin Morphine Methadone Fentanyl and derivatives Oxycodone Dihydrocodeine Codeine Pethidine Buprenorphine Dextropropoxyphene Tramadol Clinical features Respiratory Tachypnoea Reduced respiratory rate and ventilation1 Reduced respiratory rate and ventilation Cardiovascular Tachycardia, hypertension Hypotension1 Hypotension, relative bradycardia Central nervous system Restlessness, anxiety, anorexia, insomnia Delirium, hallucinations, slurred speech Delirium, hallucinations, slurred speech Hallucinations Sedation, coma1 Sedation, coma2 Muscle Tremor Ataxia, reduced muscle tone Ataxia, reduced muscle tone Temperature Fever Hypothermia Hypothermia Eyes Mydriasis Diplopia, strabismus, nystagmus Normal pupil size Miosis Abdomen Abdominal pain, diarrhoea – Ileus Mouth Dry – – Skin Piloerection Blisters, pressure sores Needle tracks2 Complications Seizures Myocardial infarction Dysrhythmias Rhabdomyolysis Renal failure Intracerebral haemorrhage or infarction Respiratory failure1 Aspiration Respiratory failure2 Non-cardiogenic pulmonary oedema Aspiration 1Especially barbiturates. 2IV use. (GHB = gamma hydroxybutyrate; MDMA = 3,4-methylene-dioxymethamphetamine)

include mephedrone and methylenedioxypyrovalerone. Tolerance is common, leading regular users to seek ever higher doses. Toxic features usually appear within a few minutes of use and last 4–6 hours, or substantially longer after a large overdose. Sympathomimetic stimulant and serotonergic effects are common (see Boxes 7.10 and 7.12). Some users develop hyponatraemia as a result of excessive water-drinking or inappropriate vasopressin (antidiuretic hormone, ADH) secretion. Muscle rigidity, pain and bruxism (clenching of the jaw), hyperpyrexia, rhabdomyolysis, metabolic acidosis, acute renal failure, disseminated intravascular coagulation, hepatocellular necrosis, acute respiratory distress syndrome (ARDS) and cardiovascular collapse have all been described following MDMA use. Cerebral infarction and haemorrhage have been reported, especially after intravenous amphetamine use. Management is supportive and directed at complications (see Box 7.8). Hallucinogens Cannabis Derived from the dried leaves and flowers of Cannabis sativa, cannabis produces euphoria, perceptual alterations and conjunctival injection, followed by enhanced appetite, relaxation and occasionally hypertension, tachycardia, slurred speech and ataxia. Effects occur 10–30 minutes after smoking or 1–3 hours after ingestion, and last 4–8 hours. High doses may produce anxiety, delirium, hallucinations and psychosis. Psychological dependence is common, but tolerance and withdrawal symptoms are unusual. Long-term use is thought to increase the lifetime risk of psychosis. Serious acute toxicity is uncommon and supportive treatment is all that is required. Synthetic cannabinoid receptor agonists Large numbers of synthetic cannabinoid receptor agonists (SCRAs), synthetic compounds sometimes referred to collectively as ‘spice’, are now used as legal alternatives to cannabis; examples include PB-22, 5F-

PB-22, 5F-AKB-48, STS-135, SF-ADB and MDMB-CHMICA. They are usually sprayed on to a herbal smoking mix and packaged as smoking products with appealing brand names. These may contain more than one SCRA and content may change with time. The toxic effects of SCRAs differ from those of cannabis, being generally more marked and including agitation, panic, delirium, hallucinations, tachycardia, ECG changes, hypertonia, dyspnoea and vomiting. Coma, respiratory acidosis, seizures, hypokalaemia and renal dysfunction are also reported. Treatment of intoxication is supportive. Tryptamines These are predominantly 5-hydroxytryptamine (5-HT, serotonin; especially 5-HT2a) agonists with associated stimulant effects. Typical clinical features include hallucinations, agitation, delirium, hypertension, tachycardia, sweating, anxiety and headache. Serotonin syndrome may occur (see Box 7.10), especially if tryptamines are used in combination with other serotonergic agents. Naturally occurring examples are psilocin and psilocybin, found in ‘magic mushrooms’, and dimethyltryptamine (DMT) in traditional ayahuasca brews. Synthetic tryptamines, such as alpha-methyltryptamine (AMT), have been encountered recently. Gamma hydroxybutyrate Gamma hydroxybutyrate (GHB), and the related compounds gamma butyrolactone (GBL) and 1,4 butanediol are sedative liquids with psychedelic and body-building effects. As well as sedative hypnotic features (see Box 7.12), toxicity may cause nausea, diarrhoea, vertigo, tremor, myoclonus, extrapyramidal signs, euphoria, bradycardia, convulsions, metabolic acidosis, hypokalaemia and hyperglycaemia. Coma usually resolves abruptly within a few hours but occasionally persists for several days. Dependence may develop in regular users, who experience severe, prolonged withdrawal effects if use is discontinued suddenly. Management is largely supportive. All patients should be observed for a minimum of 2 hours and until symptoms resolve, with monitoring of blood pressure, heart rate, respiratory rate and oxygenation. Withdrawal symptoms may require treatment with very high doses of benzodiazepine. Stimulants and entactogens These are sympathomimetic and serotonergic amines that have overlapping clinical features, depending on the balance of their stimulant (see Box 7.12) and serotonergic (see Box 7.10) effects. As well as traditional drugs such as cocaine, amphetamines and ecstasy, the group includes many more recently emerging novel psychoactive substances, including cathinones (e.g. mephedrone), piperazines (e.g. benzylpiperazine), piperadines (e.g. ethylphenidate), benzofurans (e.g. 5-aminopropylbenzofuran) and NBOMe compounds (e.g. 25I-NBOMe). Cocaine Cocaine is available as a water-soluble hydrochloride salt powder suitable for nasal inhalation (‘snorting’), or as insoluble free-base (‘crack’ cocaine) ‘rocks’ that, unlike the hydrochloride salt, vaporise at high temperature and can be smoked, giving a more rapid and intense effect. Effects appear rapidly after inhalation and especially after smoking. Sympathomimetic stimulant effects predominate (see Box 7.12). Serious complications usually occur within 3 hours of use and include coronary artery spasm, leading to myocardial ischaemia or infarction, hypotension and ventricular arrhythmias. Cocaine toxicity should be considered in younger adults presenting with ischaemic chest pain. Hyperpyrexia, rhabdomyolysis, acute renal failure and disseminated intravascular coagulation may occur. A 12-lead ECG and ECG monitoring should be undertaken. ST segment elevation may occur in the absence of myocardial infarction and troponin T estimations are the most sensitive and specific markers of myocardial damage. Benzodiazepines and intravenous nitrates are useful for managing patients with chest pain or hypertension. Acidosis should be corrected and physical cooling measures used for hyperthermia. Beta-blockers may be contraindicated because of the risk of unopposed α-adrenoceptor stimulation, but this is debated. Coronary angiography should be considered in patients with myocardial infarction or acute coronary syndromes. Amphetamines and cathinones Amphetamine-related compounds include amphetamine sulphate (‘speed’), methylamphetamine (‘crystal meth’) and 3,4-methylenedioxymethamphetamine (MDMA,

‘ecstasy’). Synthetic cathinones

144 • POISONING ingested. Cocaine, for example, presents a much higher risk than heroin because of its high toxicity and lack of a specific antidote. Patients suspected of body packing or stuffing should be admitted for observation. A careful history taken in private is important, but for obvious reasons patients may withhold details of the drugs involved. The mouth, rectum and vagina should be examined as possible sites for concealed drugs. A urine toxicology screen performed at intervals may provide evidence of leakage, although positive results may reflect earlier drug use. Packages may be visible on plain abdominal films (Fig. 7.4) but ultrasound and computed tomography (CT) are more sensitive. One of these (preferably CT) should be performed in all suspected body packers. Antimotility agents are often used by body packers to prevent premature passage of packages; it can take several days for packages to pass spontaneously, during which the carrier is at risk from package rupture. Whole bowel irrigation is commonly used to accelerate passage and is continued until all packages have passed. Surgery may be required when there is mechanical bowel obstruction or when evolving clinical features suggest package rupture, especially with cocaine. Chemicals and pesticides Carbon monoxide Carbon monoxide (CO) is a colourless, odourless gas produced by faulty appliances burning organic fuels. It is also present in vehicle exhaust fumes and sometimes in smoke from house fires. It binds with haemoglobin and cytochrome oxidase, reducing tissue oxygen delivery and inhibiting cellular respiration. CO is a common cause of death by poisoning and most patients die before reaching hospital. Clinical features Early features include headache, nausea, irritability, weakness and tachypnoea. The cause of these non-specific features may not be obvious if the exposure is occult, such as from a d-Lysergic acid diethylamide d-Lysergic acid diethylamide (LSD) is a synthetic ergoline usually ingested as small squares of impregnated absorbent paper (often printed with a distinctive design) or as ‘microdots’. The drug causes perceptual effects, such as heightened visual awareness of colours or distortion of images. Hallucinations may be pleasurable or terrifying (‘bad trip’). Other features are delirium, agitation, aggression, dilated pupils, hypertension, pyrexia and metabolic acidosis. Psychosis may sometimes last several days. Patients with psychotic reactions or CNS depression should be observed in hospital, preferably in a quiet, dimly lit room to minimise external stimulation. A benzodiazepine that can be used for sedation is required, avoiding antipsychotics if possible, as they may precipitate cardiovascular collapse or convulsions. Dissociative drugs Ketamine, its N-ethyl derivative methoxetamine and phencyclidine (now rarely encountered) produce a sense of dissociation from reality, often associated with visual and auditory distortions. Memory loss, impaired consciousness, agitation, hallucinations, tremors and numbness may also occur. Long-term ketamine (and probably methoxetamine) use can cause severe chronic cystitis with dysuria, frequency, urgency, haematuria and incontinence. Treatment of intoxication is supportive. Volatile substances Inhalation of volatile nitrites (e.g. amyl nitrite, isobutyl nitrite), often sold in bottles or vials as ‘poppers’, is reported to produce a feeling of pleasure and warmth, relax the anal sphincter and prolong orgasm. These potent vasodilators commonly provoke headache, dizziness, hypotension and tachycardia. They also oxidise haemoglobin to produce methaemoglobinaemia, with resulting breathlessness and delirium. Severe cases are treated with methylthioninium chloride (‘methylene blue’, see Fig 7.1). Several volatile solvents found in household products, such as propane, butane, toluene and trichloroethylene, have a mild euphoriant effect if inhaled. Serious toxic effects can occur, including reduced level of consciousness, seizures and cardiac arrhythmias; there is also a risk of asphyxia from some methods of inhalation. Nitrous oxide is an anaesthetic gas, but small canisters of it are sold for the

domestic production of whipped cream and the contents of these can be transferred to balloons for inhalation. The gas has euphoriant effects (‘laughing gas’), but hazards include asphyxia from inhalation without oxygen, or vitamin B12 inactivation from chronic use leading to megaloblastic anaemia, psychosis and other neurological sequelae. Body packers and body stuffers Body packers (‘mules’) attempt to smuggle illicit drugs (usually cocaine, heroin or amphetamines) by ingesting multiple small packages wrapped in several layers of clingfilm or in condoms. Body stuffers are those who have ingested unpackaged or poorly wrapped substances, often to avoid arrest. Both groups are at risk of severe toxicity if the packages rupture. This is more likely for body stuffers, who may develop symptoms of poisoning within 8 hours of ingestion. The risk of poisoning depends on the quality of the wrapping, and the amount and type of drug Fig. 7.4 Abdominal X-ray of a body packer showing multiple drug-filled condoms.

complex allows reactivation of the enzyme but, subsequently, loss of a chemical group from the OP–enzyme complex prevents further enzyme reactivation. After this process (termed ‘ageing’) has taken place, new enzyme needs to be synthesised before function can be restored. The rate of ‘ageing’ is an important determinant of toxicity and is more rapid with dimethyl (3.7 hrs) than diethyl (31 hrs) compounds (Box 7.13) and especially rapid after exposure to nerve agents (soman in particular), which cause ‘ageing’ within minutes. Clinical features and management OP poisoning causes an acute cholinergic phase, which may occasionally be followed by the intermediate syndrome or organophosphate-induced delayed polyneuropathy (OPIDN). The onset, severity and duration of poisoning depend on the route of exposure and agent involved. faulty domestic appliance. Subsequently, ataxia, nystagmus, drowsiness and hyper-reflexia may develop, progressing to coma, convulsions, hypotension, respiratory depression, cardiovascular collapse and death. Myocardial ischaemia may result in arrhythmias or myocardial infarction. Cerebral oedema is common and rhabdomyolysis may cause myoglobinuria and renal failure. In those who recover from acute toxicity, longer-term neuropsychiatric effects are common, such as personality change, memory loss and concentration impairment. Extrapyramidal effects, urinary or faecal incontinence, and gait disturbance may also occur. Poisoning during pregnancy may cause fetal hypoxia and intrauterine death. Management Patients should be removed from exposure as soon as possible and resuscitated as necessary. A high concentration of oxygen should be administered via a tightly fitting facemask; this reduces the half-life of carboxyhaemoglobin from 4–6 hours to about 40 minutes. Measurement of carboxyhaemoglobin is useful for confirming exposure; levels > 20% suggest significant exposure but do not correlate well with the severity of poisoning, partly because concentrations fall rapidly after removal of the patient from exposure, especially if supplemental oxygen has been given. An ECG should be performed in all patients with acute CO poisoning, especially those with pre-existing heart disease. Arterial blood gas analysis should be checked in those with serious poisoning. Pulse oximetry may provide misleading oxygen saturations because carboxyhaemoglobin and oxyhaemoglobin are both measured. Excessive intravenous fluid administration should be avoided, particularly in the elderly, because of the risk of pulmonary and cerebral oedema. Convulsions should be controlled with diazepam. Hyperbaric oxygen therapy is controversial. At 2.5 atmospheres, this reduces the half-life of carboxyhaemoglobin to about 20 minutes and increases the amount of oxygen dissolved in plasma 10-fold, but systematic reviews have not consistently shown improved clinical outcomes. The logistical difficulties of transporting sick patients to hyperbaric chambers and managing them

therein are substantial. Organophosphorus insecticides and nerve agents Organophosphorus (OP) compounds (Box 7.13) are widely used as pesticides, especially in developing countries. Case fatality following deliberate ingestion is high (5–20%). Nerve agents, developed for chemical warfare, are derived from OP insecticides and are much more toxic. They are commonly classified as G (originally synthesised in Germany) or V ('venomous') agents. The 'G' agents, such as tabun, sarin and soman, are volatile, absorbed by inhalation or via the skin, and dissipate rapidly after use. 'V' agents, such as VX, are contact poisons unless aerosolised, and contaminate ground for weeks or months. The toxicology and management of nerve agent and pesticide poisoning are similar. Mechanism of toxicity OP compounds inactivate acetylcholinesterase (AChE), resulting in the accumulation of acetylcholine (ACh) in cholinergic synapses (Fig. 7.5). Initially, spontaneous hydrolysis of the OP–enzyme 7.13 Organophosphorus compounds Nerve agents • G agents: sarin, tabun, soman • V agents: VX,VE Insecticides Dimethyl compounds Diethyl compounds • Dichlorvos • Fenthion • Malathion • Methamidophos • Chlorpyrifos • Diazinon • Parathion-ethyl • Quinalphos Fig. 7.5 Mechanism of toxicity of organophosphorus compounds and treatment with oxime. Acetylcholinesterase enzyme 'Ageing': reactivation not possible Organophosphate Enzyme–substrate complex Elimination of 'leaving group' Reactivation with oxime Spontaneous reactivation AChE–OH + X–P–OR1 O OR2 AChE–O–X–P–OR1 O OR2 AChE–O–P–OR1 + AChE–O–P–OR O OR2 OXIME N–OH O O• AChE–OH + HO–P–OR1 O OR2 AChE–OH + OXIME O OR2 N–P–OR1 XH

 given rapidly after exposure. Oximes reactivate AChE that has not undergone 'ageing' and are therefore less effective with dimethyl compounds and nerve agents, especially soman. Oximes may provoke hypotension, especially if administered rapidly. Intravenous magnesium sulphate has been reported to increase survival in animals and in small human studies of OP poisoning; however, further clinical trial evidence is needed before this can be recommended routinely. Ventilatory support should be instituted before the patient develops respiratory failure. Benzodiazepines may be used to treat agitation, fasciculations and seizures and for sedation during mechanical ventilation. Exposure is confirmed by measurement of plasma or red blood cell cholinesterase activity but antidote use should not be delayed pending results. Plasma cholinesterase is reduced more rapidly but is less specific than red cell cholinesterase. Values correlate poorly with the severity of clinical features but are usually < 10% in severe poisoning, 20–50% in moderate poisoning and > 50% in subclinical poisoning. The acute cholinergic phase usually lasts 48–72 hours, with most patients requiring intensive cardiorespiratory support and monitoring. Cholinergic features may be prolonged over several weeks with some lipid-soluble agents. Intermediate syndrome About 20% of patients with OP poisoning develop weakness that spreads rapidly from the ocular muscles to those of the head and neck, proximal limbs and the muscles of respiration, resulting in ventilatory failure. This 'intermediate syndrome' generally develops 1–4 days after exposure, often after resolution of the acute cholinergic syndrome, and may last 2–3 weeks. There is no specific treatment and supportive care is needed, including maintenance of airway and ventilation. Organophosphate-induced delayed polyneuropathy Organophosphate-induced delayed polyneuropathy (OPIDN) is a rare complication that usually occurs 2–3 weeks after acute exposure. It is a mixed sensory/motor polyneuropathy, affecting long myelinated neurons especially, and appears to result from inhibition of enzymes other than AChE. It is a feature of poisoning with some OPs such as triorthocresyl phosphate but is less common with nerve agents. Early clinical features are muscle cramps followed by numbness and paraesthesiae, proceeding to flaccid paralysis of the lower and subsequently the upper limbs, with foot and wrist drop and a high-stepping gait, progressing to paraplegia. Sensory loss may also be present but is

variable. Initially, tendon reflexes are reduced or lost but mild spasticity may develop later. There is no specific therapy for OPIDN. Regular physiotherapy may limit deformity caused by muscle-wasting. Recovery is often incomplete and may be limited to the hands and feet, although substantial functional recovery after 1–2 years may occur, especially in younger patients. Carbamate insecticides Carbamate insecticides such as bendiocarb, carbofuran, carbaryl and methomyl inhibit a number of tissue esterases, including AChE. The mechanism, clinical features and management of toxicity are similar to those of OP compounds. However, clinical features are usually less severe and of shorter duration, because the carbamate–AChE complex dissociates quickly, with a half-life of 30–40 minutes, and does not undergo ageing. Also, carbamates penetrate the CNS poorly. Intermediate syndrome Acute cholinergic syndrome This usually starts within a few minutes of exposure and nicotinic or muscarinic features may be present (Box 7.14). Vomiting and profuse diarrhoea are typical following ingestion. Bronchoconstriction, bronchorrhoea and salivation may cause severe respiratory compromise. Excess sweating and miosis are characteristic and the presence of muscular fasciculations strongly suggests the diagnosis, although this feature is often absent, even in serious poisoning. Subsequently, generalised flaccid paralysis may develop and affect respiratory and ocular muscles, resulting in respiratory failure. Ataxia, coma, convulsions, cardiac repolarisation abnormalities and torsades de pointes may occur. Management The airway should be cleared of excessive secretions, breathing and circulation assessed, high-flow oxygen administered and intravenous access obtained. Appropriate external decontamination is needed (p. 133). Gastric lavage or activated charcoal may be considered if the patient presents sufficiently early. Seizures should be treated as described in Box 7.8. The ECG, oxygen saturation, blood gases, temperature, urea and electrolytes, amylase and glucose should be monitored closely. Early use of sufficient doses of atropine is potentially life-saving in patients with severe toxicity. Atropine reverses ACh-induced bronchospasm, bronchorrhoea, bradycardia and hypotension. When the diagnosis is uncertain, a marked increase in heart rate associated with skin flushing after a 1 mg intravenous dose makes OP poisoning unlikely. In OP poisoning, atropine (2 mg IV) should be administered and this dose should be doubled every 5–10 minutes until clinical improvement occurs. Further bolus doses should be given until secretions are controlled, the skin is dry, blood pressure is adequate and heart rate is > 80 bpm. Large doses may be needed, but excessive doses may cause anticholinergic effects (see Box 7.10). In severe poisoning requiring atropine, an oxime such as pralidoxime chloride or obidoxime is generally recommended, if available, although efficacy is debated. This may reverse or prevent muscle weakness, convulsions or coma, especially if 7.14 Cholinergic features in poisoning* Muscarinic Nicotinic Respiratory Bronchorrhoea, bronchoconstriction Reduced ventilation Circulation Bradycardia, hypotension Tachycardia, hypertension Higher mental function Anxiety, delirium, psychosis Muscle – Fasciculation, paralysis Temperature Fever – Eyes Diplopia, miosis, lacrimation Mydriasis Abdomen Vomiting, profuse diarrhoea – Mouth Salivation – Skin Sweating – Complications Coma, seizures, respiratory depression *Both muscarinic and nicotinic features occur in OP poisoning. Nicotinic features occur in nicotine poisoning and black widow spider bites. Cholinergic features are sometimes seen with some mushrooms.

and acute tubular necrosis occur because of renal calcium oxalate precipitation. Hypocalcaemia, hypomagnesaemia and hyperkalaemia are common. Methanol poisoning causes headache, delirium and vertigo. Visual impairment and photophobia develop, associated with optic disc and

retinal oedema and impaired pupil reflexes. Blindness may be permanent, although some recovery may occur over several months. Pancreatitis and abnormal liver function have also been reported. Management Urea and electrolytes, chloride, bicarbonate, glucose, calcium, magnesium, albumin, plasma osmolarity and arterial blood gases should be measured in all patients with suspected methanol or ethylene glycol toxicity. The osmolar and anion gaps should be calculated (see Box 7.5). Initially, poisoning is associated with an increased osmolar gap, but as toxic metabolites are produced, an increased anion gap develops, associated with metabolic acidosis. The diagnosis can be confirmed by measurement of ethylene glycol or methanol concentrations but assays are not widely available. An antidote, ideally fomepizole but otherwise ethanol, should be administered to all patients with suspected significant exposure while awaiting the results of laboratory investigations. These block alcohol dehydrogenase and delay the formation of toxic metabolites until the parent drug is eliminated in the urine or by dialysis. The antidote should be continued until ethylene glycol or methanol concentrations are undetectable. Metabolic acidosis should be corrected with sodium bicarbonate (e.g. 250 mL of 1.26% solution, repeated as necessary). Convulsions should be treated with an intravenous benzodiazepine. In ethylene glycol poisoning, hypocalcaemia should be corrected only if there are severe ECG features or if seizures occur, as this may increase calcium oxalate crystal formation. In methanol poisoning, folinic acid should be administered to enhance the metabolism of the toxic metabolite, formic acid. Haemodialysis or haemodiafiltration should be used in severe poisoning, especially if renal failure is present or there is visual loss in the context of methanol poisoning. It should be continued until acute toxic features are no longer present and ethylene glycol/methanol concentrations are undetectable. Corrosive substances Products containing strong acids (e.g. hydrochloric or sulphuric acid) or alkalis (e.g. sodium hydroxide, calcium carbonate) may be ingested, accidentally or intentionally, causing gastrointestinal pain, ulceration and necrosis, with risk of perforation. External decontamination (p. 133), if needed, should be performed after initial resuscitation. Gastric lavage should not be attempted and neutralising chemicals should not be administered after large ingestions because of the risk of tissue damage from heat release. Cardiorespiratory monitoring is necessary and full blood count, renal function, coagulation and acid–base status should be assessed. An erect chest X-ray should be performed if perforation is suspected and may show features of mediastinitis or gas under the diaphragm. Strong analgesics should be administered for pain. Severe abdominal or chest pain, abdominal distension, shock or acidosis may indicate perforation and should prompt an urgent CT scan of chest and abdomen and surgical review. In the absence of perforation, drooling, dysphagia, stridor or oropharyngeal burns suggest possible severe oesophageal and OPIDN are not common features of carbamate poisoning. In spite of this, case fatality can be high for some carbamates, depending on their formulation. Atropine may be given intravenously as for OP poisoning (p. 146). Diazepam may be used to relieve anxiety. The use of oximes is unnecessary. Paraquat Paraquat is a herbicide that is widely used across the world, although it has been banned in the European Union and some other countries for several years. It is highly toxic if ingested, with clinical features including oral burns, vomiting and diarrhoea, progressing to pneumonitis, pulmonary fibrosis and multi-organ failure. Exposure can be confirmed by a urinary dithionite test, while the plasma paraquat concentration indicates prognosis. There is no specific antidote but activated charcoal is commonly administered. Immunosuppression with glucocorticoids and cyclophosphamide is sometimes used but evidence for benefit is weak. Irrespective of treatment, death is common and may occur within 24 hours with substantial poisoning or after 1–2 weeks with lower doses. Methanol and ethylene glycol Ethylene glycol (1,2-ethanediol) is found in antifreeze, brake fluids and, in lower concentrations, windscreen washes. Methanol is present in some

antifreeze products and commercially available industrial solvents, and in low concentrations in some screen washes and methylated spirits. It may also be an adulterant of illicitly produced alcohol. Both are rapidly absorbed after ingestion. Methanol and ethylene glycol are not of high intrinsic toxicity but are converted via alcohol dehydrogenase to toxic metabolites that are largely responsible for their clinical effects (Fig. 7.6). Clinical features Early features of poisoning with either methanol or ethylene glycol include vomiting, ataxia, drowsiness, dysarthria and nystagmus. As toxic metabolites are formed, metabolic acidosis, tachypnoea, coma and seizures may develop. Toxic effects of ethylene glycol include ophthalmoplegia, cranial nerve palsies, hyporeflexia and myoclonus. Renal pain Fig. 7.6 Metabolism of methanol and ethylene glycol. Ethanol or fomepizole Inhibits Alcohol dehydrogenase Ethylene glycol Glycoaldehyde Glycolic acid Formaldehyde Formic acid TOXIC METABOLITES Glyoxylic acid Oxalic acid Methanol

 vegetable oil to reduce the release of toxic phosphine, but the benefit is uncertain. Copper sulphate This is used as a fungicide. If it is ingested, clinical features of toxicity include nausea, vomiting, abdominal pain, diarrhoea, discoloured (blue/green) secretions, corrosive effects on the gastrointestinal tract, renal or liver failure, methaemoglobinaemia, haemolysis, rhabdomyolysis, convulsions and coma. Treatment is as for other corrosive substances (see above) and should address complications, including use of methylthioninium chloride for methaemoglobinaemia (see Fig. 7.1). Chelation therapy is unlikely to be beneficial after acute exposure. Chemicals less commonly taken in poisoning An overview of the clinical features and management for chemicals less commonly involved in poisoning is provided in Box 7.15. damage and early endoscopy by an experienced operator should be considered. Delayed endoscopy (e.g. after several days) may carry a higher risk of perforation. Aluminium and zinc phosphide These rodenticides and fumigants are a common means of self-poisoning in northern India. The mortality rate for aluminium phosphide ingestion has been estimated at 60%; zinc phosphide ingestion appears less toxic, at about 2%. When ingested, both compounds react with gastric acid to form phosphine, a potent pulmonary and gastrointestinal toxicant. Clinical features include severe gastrointestinal disturbances, chest tightness, cough and breathlessness progressing to ARDS and respiratory failure, tremor, paraesthesiae, convulsions, coma, tachycardia, metabolic acidosis, electrolyte disturbances, hypoglycaemia, myocarditis, liver and renal failure, and leucopenia. Ingestion of a few tablets can be fatal. Treatment is supportive and directed at correcting electrolyte abnormalities and treating complications; there is no specific antidote. Early gastric lavage is sometimes used, often with 7.15 Clinical features and specific management of chemicals less commonly involved in poisoning Substance Clinical features Management Lead e.g. Chronic occupational exposure, leaded paint, water contaminated by lead pipes, use of kohl cosmetics Abdominal pain Microcytic anaemia with basophilic stippling Headache and encephalopathy Motor neuropathy Nephrotoxicity Hypertension Hypocalcaemia Prevention of further exposure Measurement of blood lead concentration, full blood count and blood film, urea and electrolytes, liver function tests and calcium Abdominal X-ray in children to detect pica Bone X-ray for ‘lead lines’ Chelation therapy with DMSA or sodium calcium edetate Petroleum distillates e.g. White spirit, kerosene Vomiting Aspiration pneumonitis Gastric lavage contraindicated Activated charcoal ineffective Oxygen and nebulised bronchodilators Chest X-ray to assess pulmonary effects Organochlorines e.g. DDT, lindane, dieldrin, endosulfan Nausea, vomiting Agitation Fasciculation Paraesthesiae (face, extremities) Convulsions Coma Respiratory depression Cardiac arrhythmias Hyperthermia Rhabdomyolysis Pulmonary oedema Disseminated intravascular coagulation Activated charcoal (with nasogastric aspiration for liquid preparations) within 1 hr of ingestion

Cardiac monitoring Pyrethroid insecticides e.g. Cypermethrin, permethrin, imiprothrin Skin contact: dermatitis, skin paraesthesiae Eye contact: lacrimation, photophobia and oedema of the eyelids Inhalation: dyspnoea, nausea, headaches Ingestion: epigastric pain, nausea, vomiting, headache, coma, convulsions, pulmonary oedema Symptomatic and supportive care Washing contaminated skin makes irritation worse Anticoagulant rodenticides e.g. Brodifacoum, bromadialone and warfarin Abnormal bleeding (prolonged) Monitor INR/prothrombin time Vitamin K1 by slow IV injection if there is coagulopathy Fresh frozen plasma or specific clotting factors for bleeding (DMSA = dimercaptosuccinic acid)

7.16 Chemical warfare agents Examples Clinical effects Antidotes* Nerve agents Tabun Sarin Soman VX See page 145 and Box 7.13 Atropine Oximes (p. 145) Blistering agents Nitrogen/sulphur Mustard Lewisite Eyes: watering, blepharospasm, corneal ulceration Skin: erythema, blistering Respiratory: cough, hoarseness, dyspnoea, pneumonitis None Choking agents Chlorine Phosgene Eyes: watering, blepharospasm, corneal ulceration Respiratory: cough, hoarseness, dyspnoea, pneumonitis None Blood agents Cyanide Cardiovascular: dizziness, shock Respiratory: dyspnoea, cyanosis CNS: anxiety, headache, delirium, convulsions, coma, fixed dilated pupils Other: vomiting, lactic acidosis Dicobalt edetate Hydroxocobalamin *Appropriate resuscitation, decontamination and supportive care are essential after exposure to all chemical warfare agents. Use appropriate personal protective equipment. 7.17 Clinical features of chronic arsenic poisoning Gastrointestinal tract • Anorexia, vomiting, weight loss, diarrhoea, increased salivation, metallic taste Neurological • Peripheral neuropathy (sensory and motor) with muscle wasting and fasciculation, ataxia Skin • Hyperpigmentation, palmar and plantar keratosis, alopecia, multiple epitheliomas, Mee’s lines (transverse white lines on fingernails) Eyes • Conjunctivitis, corneal necrosis and ulceration Bone marrow • Aplastic anaemia Other • Low-grade fever, vasospasm and gangrene, jaundice, hepatomegaly, splenomegaly Increased risk of malignancy • Lung, liver, bladder, kidney, larynx and lymphoid system Chemical warfare agents Some toxins have been developed for use as chemical warfare agents. These are summarised in Box 7.16. Environmental poisoning Arsenism Chronic arsenic exposure from drinking water has been reported in many countries, especially India, Bangladesh, Nepal, Thailand, Taiwan, China, Mexico and South America, where a large proportion of the drinking water (ground water) has a high arsenic content, placing large populations at risk. The World Health Organisation (WHO) guideline value for arsenic content in tube well water is 10 µg/L. Health effects associated with chronic exposure to arsenic in drinking water are shown in Box 7.17. In exposed individuals, high concentrations of arsenic are present in bone, hair and nails. Specific treatments are of no benefit in chronic arsenic toxicity and recovery from the peripheral neuropathy may never be complete, so the emphasis should be on prevention. Fluorosis Fluoride poisoning can result from exposure to excessive quantities of fluoride (> 10 ppm) in drinking water, industrial exposure to fluoride dust or consumption of brick teas. Clinical features include yellow staining and pitting of permanent teeth, osteosclerosis, soft tissue calcification, deformities (e.g. kyphosis) and joint ankylosis. Changes in the bones of the thoracic cage may lead to rigidity that causes dyspnoea on exertion. Very high doses of fluoride may cause abdominal pain, nausea, vomiting, seizures and muscle spasm. In calcium-deficient children, the toxic effects of fluoride manifest even at marginally high exposures to fluoride. In endemic areas, such as Jordan, Turkey, Chile, India, Bangladesh, China and Tibet, fluorosis is a major public health problem, especially in communities engaged in physically strenuous agricultural or industrial

activities. Dental fluorosis is endemic in East Africa and some West African countries. Food-related poisoning Paralytic shellfish poisoning Paralytic shellfish poisoning is caused by consumption of bivalve molluscs (e.g. mussels, clams, oysters, cockles and scallops) contaminated with saxitoxins, which are concentrated in the shellfish as a result of constant filtration of toxic algae during algal blooms (e.g. ‘red tide’). Symptoms develop within 10–120 minutes of eating the contaminated shellfish and include gastrointestinal disturbances, paraesthesia around the mouth or in the extremities, ataxia, mental state changes and dysphagia. In severe cases, paralysis and respiratory failure can develop. There is no specific antidote and treatment is supportive. Most cases resolve over a few days. Ciguatera poisoning Ciguatera toxin and related toxins are produced by dinoflagellate plankton that adhere to algae and seaweed. These accumulate in the tropical herbivorous fish that feed on these and in their larger predators (e.g. snapper, barracuda), especially in the

 Further information Books and journal articles Bateman DN, Jefferson R, Thomas SHL, et al. (eds). Oxford desk reference: toxicology. Oxford: Oxford University Press; 2014. Benson BE, Hoppu K, Troutman WG, et al. Position paper update: gastric lavage for gastrointestinal decontamination. Clin Toxicol 2013; 51:140–146. Chyka PA, Seger D, Krenzelok EP, et al. Position paper: single-dose activated charcoal. Clin Toxicol 2005; 43:61–87. Thompson JP, Watson ID, Thanacoody HK, et al. Guidelines for laboratory analyses for poisoned patients in the United Kingdom. Ann Clin Biochem 2014; 51:312–325. Websites curriculum.toxicology.wikispaces.net/ Free access to educational material related to poisoning. toxbase.org Toxbase, the clinical toxicology database of the UK National Poisons Information Service. Free for UK health professionals but registration is required. Access for overseas users by special arrangement. Low-cost smartphone app available. toxnet.nlm.nih.gov US National Library of Medicine’s Toxnet: a hazardous substances databank, including Toxline for references to literature on drugs and other chemicals. who.int/gho/phe/chemical_safety/poisons_centres/en/ World directory of poisons centres held by the WHO, including interactive map and contact details. Pacific and Caribbean. Human exposure occurs through eating contaminated fish, even if well cooked. Nausea, vomiting, diarrhoea and abdominal pain develop within a few hours, followed by paraesthesia, ataxia, blurred vision, ataxia and tremor. Convulsions and coma can occur, although death is uncommon. Fatigue and peripheral neuropathy can be long-term effects. There is no specific treatment. In the South Pacific and Caribbean, there are approximately 50 000 cases per year, with a case fatality of 0.1%. Scombrotoxic fish poisoning Under poor storage conditions, histidine in scombroid fish (e.g. tuna, mackerel, bonito, skipjack and the canned dark meat of sardines) may be converted by bacteria to histamine and other chemicals. Within minutes of consumption, flushing, burning, sweating, urticaria, pruritus, headache, colic, nausea and vomiting, diarrhoea, bronchospasm and hypotension may occur. Management is with nebulised salbutamol, intravenous antihistamines and, occasionally, intravenous fluid replacement. Plant poisoning A substantial number of plants and fungi are potentially toxic if consumed, with patterns of poisoning depending on their geographical distribution. Some toxic examples and the clinical features of toxicity are shown in Box 7.18. 7.18 Some poisonous plants and fungi, with their clinical effects Species (common name) Toxins Important features of toxicity Plants Abrus precatorius (jequirity bean) Abrin Gastrointestinal effects, drowsiness, delirium, convulsions, multi-organ failure Ricinus communis (castor oil plant) Ricin Aconitum napellus (aconite, wolf’s bane, monkshood) Aconitum ferox (Indian aconite, bikh) Aconite Gastrointestinal effects, paraesthesiae, convulsions, ventricular tachycardia Atropa belladonna (deadly nightshade) Datura stramonium (Jimson weed, thorn apple) Brugmansia spp. (angel’s trumpet) Atropine, scopolamine, hyocyamine Anticholinergic toxidrome (see Box 7.10)

Colchicum autumnale (autumn crocus) Colchicine Gastrointestinal effects, hypotension, cardiogenic shock Conium maculatum (hemlock) Toxic nicotinic alkaloids Hypersalivation, gastrointestinal effects, followed by muscular paralysis Digitalis purpurea (foxglove) Nerium oleander (pink oleander) Thevetia peruviana (yellow oleander) Cardiac glycosides Cardiac glycoside toxicity (p. 140) Laburnum anagyroides (laburnum) Cytosine Gastrointestinal effects; convulsions in severe cases Taxus baccata (yew) Taxane alkaloids Hypotension, bradycardia, respiratory depression, convulsions, coma, arrhythmias Fungi Amanita phalloides (death cap mushroom) Amatoxins Gastrointestinal effects, progressing to liver failure Cortinarius spp. Orellanine Gastrointestinal effects, fever, progressing to renal failure Psilocybe semilanceata (‘magic mushrooms’) Psilocybin, psilocin Hallucinations

---

Revision #1
Created 2026-01-08 16:24:31 UTC by Omar Ayman
Updated 2026-01-08 16:24:31 UTC by Omar Ayman