

Antidotes and other substances used in poisonings

These notes are only guidelines and it is strongly recommended that poisons information centres be consulted in cases where there is doubt about the degree of risk or about appropriate management.

General care and non-specific treatment

All patients who show features of poisoning should generally be admitted to hospital. Patients who have taken poisons with delayed actions should also be admitted, even if they appear well; delayed-action poisons include acetylsalicylic acid, iron, lithium, paracetamol, paraquat, tricyclic antidepressants and warfarin. The effects of modified-release or prolonged-release preparations are also delayed. However, it is often impossible to establish with certainty the identity of the poison and the size of the dose but information on the type and timing of poisoning may be useful for symptomatic management. Few patients require active removal of the poison.

Most patients must be treated symptomatically and monitored. Particular care must be given to maintenance of respiration and blood pressure. Assisted ventilation may be required. Cardiac conduction defects and arrhythmias often respond to correction of underlying hypoxia, acidosis, or other biochemical abnormalities. Hypothermia which may develop in patients who have been unconscious for some hours is best treated by wrapping the patient in blankets to conserve body heat. Convulsions which are prolonged or recurrent may be controlled by intravenous diazepam. In some situations removal of the poison from the stomach by gastric lavage may be appropriate (see below). Activated charcoal can bind many poisons in the stomach and therefore prevent absorption. Active elimination techniques such as repeated administration of activated charcoal can enhance the elimination of some drugs after they have been absorbed (see below). Other techniques to enhance elimination of poisons after their absorption are only practical in hospital and are only suitable for a small number of patients and only to a limited number of poisons. Methods include haemodialysis and haemoperfusion. Alkalinization of urine can be used to increase the elimination of salicylates. Forced alkaline diuresis is no longer recommended.

Gastric lavage

The dangers of attempting to empty the stomach have to be balanced against the toxicity of the ingested poison, as assessed by the quantity ingested, the inherent toxicity of the poison, and the time since ingestion. Gastric emptying is clearly unnecessary if the risk of toxicity is small or if the patient presents too late. Emptying the stomach may be of value if undertaken within 1–2 hours after ingestion. The main risk is with inhalation of stomach contents and gastric lavage should **not** be undertaken in drowsy or comatose patients without assistance of an anaesthetist so that the airway can be protected by a cuffed endotracheal tube. Gastric lavage must **not** be attempted after corrosive poisoning or for hydrocarbon products which could be dangerous if aspirated.

Emesis

Induction of emesis for the treatment of poisoning is **not recommended**. There is no evidence that it prevents absorption of the poison and it may increase the likelihood of aspiration. Furthermore, the effects of the emetic substance may complicate diagnosis.

Prevention of absorption

Given by mouth **activated charcoal** can bind many poisons in the gastrointestinal system, thereby reducing their absorption. The sooner it is given, the more effective it is, but it may be effective for up to 1 hour after ingestion of the poison. It may be effective several hours after poisoning with modified-release preparations or drugs with anticholinergic (antimuscarinic) properties. It is relatively safe and particularly useful for prevention of absorption of poisons which are toxic in small amounts, for example, antidepressants. Furthermore, repeated doses of activated charcoal enhance the faecal elimination of some drugs (that undergo enterohepatic or enteroenteric recycling) several hours after ingestion and after they have been absorbed, for example phenobarbital, theophylline.

Activated charcoal

Powder (Powder for oral suspension), activated charcoal

Uses:

treatment of acute poisoning

Contraindications:

poisoning by hydrocarbons with high potential for harm if aspirated; poisoning by corrosive substances—may prevent visualization of lesions caused by poison

Precautions:

drowsy or unconscious patients—risk of aspiration (intubate before administration via nasogastric or gastric tube); not effective for poisoning with alcohols, clofenotane (dicophane, DDT), cyanides, malathion, and metal salts including iron and lithium

Dosage:

Poisoning (prevention of absorption), *by mouth* , **ADULT** 50–100 g as a single dose, as soon as possible after ingestion of poison; **INFANT** 1 g/kg as a single dose; **CHILD** 1–12 years, 25 g as a single dose (50 g in severe poisoning)

Poisoning (active elimination), *by mouth* , **ADULT** and **CHILD** over 1 year, 25–50 g initially, then 25–50 g every 4–6 hours; **INFANTS** 1 g/kg every 4–6 hours

Adverse effects:

black stools; vomiting, constipation or diarrhoea; pneumonitis—due to aspiration

Specific antidotes

Paracetamol overdose

As little as 10–15 g or 150 mg/kg of paracetamol taken within 24 hours may cause severe hepatocellular necrosis and less frequently renal tubular necrosis. The only early features of poisoning, nausea and vomiting, usually settle within 24 hours. Persistence beyond this time, often with the onset of right subcostal pain and tenderness, usually indicates the development of liver damage which is maximal 3–4 days after ingestion. In spite of a lack of significant early symptoms, patients who have taken an overdose of paracetamol should be transferred to hospital urgently.

Administration of activated charcoal should be considered if paracetamol in excess of 150 mg/kg or 12 g, whichever is smaller, is thought to have been ingested within the previous hour.

Acetylcysteine or **methionine** protect the liver if given within 10–12 hours of ingesting paracetamol. Acetylcysteine, given intravenously is most effective within 8 hours of overdose, but is effective for up to and possibly beyond 24 hours. Alternatively, methionine may be given by mouth provided the overdose was ingested within 10–12 hours and the patient is not vomiting. However, acetylcysteine is the preferred treatment. Concurrent use of activated charcoal and specific oral antidotes should be avoided.

In remote areas methionine should be given, since administration of acetylcysteine outside hospital is not generally practicable. Once the patient is in hospital the need to continue antidote treatment can be assessed from plasma-paracetamol concentrations.

Acetylcysteine

Injection (Concentrate for dilution for infusion), acetylcysteine 200 mg/ml, 10-ml ampoule

Uses:

paracetamol overdose

Precautions:

asthma

Dosage:

Paracetamol overdose, *by intravenous infusion*, **ADULT** and **CHILD** initially, 150 mg/kg in 200 ml glucose 5% over 15 minutes, followed by 50 mg/kg in 500 ml glucose 5% over 4 hours, then 100 mg/kg in 1000 ml glucose 5% over 16 hours

Note. Children are given the same doses of acetylcysteine as adults, but the volume of infusion may need to be reduced to avoid fluid overload

Adverse effects:

hypersensitivity reactions including rashes, anaphylaxis

DL-Methionine

Tablets , DL-methionine 250 mg

Uses:

paracetamol overdosage

Precautions:

severe liver disease—may precipitate hepatic encephalopathy; avoid concurrent use with activated charcoal

Dosage:

Paracetamol overdosage, *by mouth* , **ADULT** and **child** over 6 years, 2.5 g initially, followed by 3 further doses of 2.5 g every 4 hours, **child** under 6 years 1 g initially, followed by 3 further doses of 1 g every 4 hours

Adverse effects:

nausea, vomiting, drowsiness, irritability

Opioid analgesic overdosage

Opioids cause varying degrees of coma, respiratory depression and pinpoint pupils. **Naloxone** is a specific antidote indicated if there is coma or bradypnoea. Naloxone has a shorter duration of action than many opioids so close monitoring and repeated injections are required depending on respiratory rate and depth of coma; naloxone may alternatively be given by intravenous infusion. The effects of some opioids such as buprenorphine are only partially reversed by naloxone.

Acute withdrawal syndromes may be precipitated by the use of naloxone in patients with a physical dependence on opioids or in overdosage with large doses; a withdrawal syndrome may occur in neonates of opioid-dependent mothers.

Naloxone hydrochloride

Injection (Solution for injection), naloxone hydrochloride 400 micrograms/ml, 1-ml ampoule

Uses:

opioid overdosage; postoperative respiratory depression (section 1.5)

Precautions:

physical dependence on opioids or other situations where acute withdrawal syndrome may be precipitated (see above); pregnancy (Appendix 2); breastfeeding (Appendix 3); cardiovascular disease

Dosage:

Overdosage of opioids, *by intravenous injection* , **ADULT** 0.8–2 mg repeated at intervals of 2–3 minutes to a maximum of 10 mg, if respiratory function does not improve, question diagnosis; **CHILD** 10 micrograms/kg; a subsequent dose of 100 micrograms/kg if no response

NOTE. Naloxone hydrochloride may be administered in the same doses by intramuscular or subcutaneous injection, but only if the intravenous route is not feasible (slower onset of action)

Overdosage of opioids, *by continuous intravenous infusion* using an infusion pump, **adult** 10 mg diluted in 50 ml glucose 5% intravenous infusion at a rate adjusted according to response

Adverse effects:

nausea, vomiting, sweating—may also be due to opioid withdrawal

Organophosphate and carbamate poisoning

Organophosphates are absorbed through the bronchi and intact skin as well as from the gastrointestinal tract. Initial treatment of organophosphate or carbamate poisoning includes prevention of further absorption by emptying the stomach by gastric lavage, moving patient to fresh air supply, removing contaminated clothing and washing contaminated skin. A clear airway must be maintained.

Organophosphates inhibit cholinesterases and thus prolong the effects of acetylcholine. Toxicity depends on the particular compound involved, and onset after skin exposure may be delayed. **Atropine** will reverse the muscarinic effects of acetylcholine and is used (in conjunction with oximes such as pralidoxime) with additional symptomatic treatment.

Additional treatment for carbamate poisoning is generally symptomatic and supportive. **Atropine** may be given but may not be required because of the rapidly reversible type of cholinesterase inhibition produced (oximes should not be given).

Atropine sulfate

Injection (Solution for injection), atropine sulfate 1 mg/ml, 1-ml ampoule

Uses:

organophosphate and carbamate poisoning; premedication (section 1.3); antispasmodic (section 17.5); mydriasis and cycloplegia (section 21.5)

Precautions:

children, elderly, Down syndrome; angle-closure glaucoma; myasthenia gravis; gastrointestinal disorders; prostatic enlargement; cardiac disorders; pyrexia; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions:** Appendix 1

Dosage:

Organophosphate poisoning, *by intramuscular or intravenous injection* (depending on severity of poisoning), **ADULT** 2 mg (**child** 20 micrograms/kg) every 5–10 minutes until the skin becomes flushed and dry and tachycardia develops

Iron poisoning and iron and aluminium overload

Mortality from iron poisoning is reduced by specific therapy with **deferoxamine** which chelates iron. Before administration of deferoxamine the stomach should be emptied by gastric lavage (with a wide-bore tube) within 1 hour of ingesting a significant quantity of iron or if radiography reveals tablets in the stomach. Deferoxamine is also used to diagnose and treat chronic iron overload. It is used in the diagnosis of aluminium overload and to treat aluminium overload in patients with end-stage renal failure undergoing maintenance haemodialysis.

Deferoxamine mesilate

Injection (Powder for solution for injection or infusion), deferoxamine mesilate 500-mg vial

Uses:

acute iron poisoning; chronic iron overload; aluminium overload

Precautions:

renal impairment (Appendix 4); eye and ear examinations before and at 3-month intervals during treatment; aluminium encephalopathy (may exacerbate neurological dysfunction); pregnancy (Appendix 2); breastfeeding (Appendix 3); children under 3 years (may retard growth)

Dosage:

Acute iron poisoning, *by slow intravenous infusion*, **ADULT** and **CHILD** initially 15 mg/kg/hour, reduced after 4–6 hours so that total dose does not exceed 80 mg/kg in 24 hours

Chronic iron overload, *by subcutaneous or intravenous infusion*, **ADULT** and **CHILD** lowest effective dose, usually within range of 20–60 mg/kg/day on 4–7 days a week

Aluminium overload in end-stage renal failure, *by intravenous infusion*, **ADULT** and **CHILD** 5 mg/kg, once a week during last hour of dialysis

Diagnosis of iron overload, *by intramuscular injection* , **ADULT** and **CHILD** 500 mg

Diagnosis of aluminium overload, *by intravenous infusion* , **ADULT** and **CHILD** 5 mg/kg during last hour of dialysis

RECONSTITUTION AND ADMINISTRATION. According to manufacturer's directions. For full details and warnings relating to administration for therapeutic or diagnostic purposes, see manufacturer's literature

Adverse effects:

anaphylaxis; flushing, urticaria, hypotension, shock (especially if given by too rapid intravenous infusion); gastrointestinal disturbances; fever, headache, arthralgia, myalgia; arrhythmias; renal impairment; blood disorders; neurological disturbances including neuropathy, paraesthesia, and dizziness; convulsions; Yersinia and mucormycosis infections; visual disturbances (including lens opacity and retinopathy) and hearing loss; rash; rarely, growth retardation (in young children); rarely, adult respiratory distress syndrome; pain on intramuscular or subcutaneous injection; local irritation on prolonged subcutaneous infusion; reddish-brown discoloration of urine

Heavy metal poisoning

Heavy metal poisoning may be treated with a range of antidotes including **dimercaprol** , **penicillamine** , **potassium ferric hexacyanoferrate** and **sodium calcium edetate** . Penicillamine is also used to promote excretion of copper in Wilson disease.

Dimercaprol

Oily injection (Solution for injection), dimercaprol 50 mg/ml in arachis (peanut) oil, 2-ml ampoule

Uses:

acute poisoning by antimony, arsenic, bismuth, gold, mercury, possibly thallium; adjunct (with sodium calcium edetate) in lead poisoning

Contraindications:

not indicated for iron, selenium or cadmium poisoning; severe hepatic impairment (unless due to arsenic poisoning)

Precautions:

hypertension; renal impairment (discontinue or use with extreme caution if renal failure occurs during treatment); any abnormal reaction such as hyperpyrexia should be assessed; elderly; pregnancy; breastfeeding

Dosage:

Poisoning by heavy metals, *by intramuscular injection* , **ADULT** 400–800 mg in divided doses on first day, then 200–400 mg daily in divided doses on the second and third days, then 100–200 mg daily in divided doses on subsequent days (single doses generally should not exceed 3 mg/kg, but in severe poisoning initial single doses up to 5 mg/kg may be required); **CHILD** calculate on basis of body-weight using same unit dose/kg as for adult in similar clinical circumstances

Adverse effects:

hypertension, tachycardia; malaise, nausea, vomiting, abdominal pain, salivation, lacrimation, sweating, burning sensation in the mouth, throat and eyes; feeling of constriction in throat and chest; headache, muscle spasms, tingling of the extremities; fever in children; local pain and abscess at injection site

Penicillamine

Capsules , penicillamine 125 mg [not included on WHO Model List], 250 mg

Tablets , penicillamine 125 mg [not included on WHO Model List], 250 mg

Uses:

poisoning by heavy metals, particularly lead and copper; Wilson disease; severe rheumatoid arthritis (section 2.4)

Contraindications:

hypersensitivity; lupus erythematosus

Precautions:

monitor throughout treatment including blood counts and urine tests; renal impairment (Appendix 4); pregnancy (Appendix 2); avoid concurrent gold, chloroquine or immunosuppressive treatment; avoid oral iron within 2 hours of a dose; **interactions:** Appendix 1

Blood counts. In Wilson disease, consider withdrawal if platelet count falls below 120 000/mm³ or white blood cells below 2500/mm³ or if 3 successive falls within reference range (can restart at reduced dose when counts return to reference range but permanent withdrawal necessary if neutropenia or thrombocytopenia recur)

Patient Advice. In Wilson disease warn patient to tell doctor immediately if sore throat, fever, infection, non-specific illness, unexplained bleeding and bruising, purpura, mouth ulcers or rash develop

Dosage:

Heavy metal poisoning, *by mouth*, **ADULT** 1–2 g daily in 4 divided doses before food (continue until urinary lead stabilised at less than 500 micrograms/day); **CHILD** 20–25 mg/kg daily in divided doses

Wilson disease, *by mouth* , **ADULT** 1.5–2 g daily in divided doses before food; maximum 2 g daily for 1 year then maintenance 0.75–1 g daily; **ELDERLY** 20 mg/kg daily in divided doses adjusted according to response; **CHILD** up to 20 mg/kg daily in divided doses; minimum 500 mg daily

Adverse effects:

initially nausea (less of a problem if taken with food and on retiring), anorexia, fever; taste loss (mineral supplements not recommended); blood disorders including thrombocytopenia, neutropenia, agranulocytosis and aplastic anaemia; proteinuria, rarely haematuria (withdraw immediately); haemolytic anaemia, nephrotic syndrome, lupus erythematosus-like syndrome, myasthenia gravis-like syndrome, polymyositis (rarely with cardiac involvement), dermatomyositis, mouth ulcers, stomatitis, alopecia, bronchiolitis and pneumonitis, pemphigus, Goodpasture syndrome and Stevens-Johnson syndrome also reported; male and female breast enlargement reported; rash early in treatment (usually allergic—may need temporary withdrawal), late rashes (reduce dose or withdraw treatment)

Potassium ferric hexacyanoferrate

Prussian Blue

Powder for oral solution , potassium ferric hexacyanoferrate

Uses:

thallium poisoning

Contraindications:

constipation; paralytic ileus

Dosage:

Treatment of thallium poisoning, *by duodenal tube* , **ADULT** 125 mg/kg in 100 ml of mannitol 15% twice daily (until urinary thallium stabilized at 500 micrograms or less/day)

Adverse effects:

constipation, dark stools

Sodium calcium edetate

Infusion (Concentrate for solution for infusion), sodium calcium edetate 200 mg/ml, 5-ml ampoule

Uses:

lead poisoning

Precautions:

renal impairment

Dosage:

Treatment of lead poisoning, *by intravenous infusion* , **ADULT** and **CHILD** up to 40 mg/kg twice daily for up to 5 days; repeated if necessary after interval of 48 hours

DILUTION AND ADMINISTRATION. According to manufacturer's directions

Adverse effects:

renal tubular necrosis; nausea, diarrhoea, abdominal cramps; thrombophlebitis (if given too rapidly or as too concentrated a solution), fever, malaise, headache, myalgia, thirst, chills, histamine-like responses (sneezing, nasal congestion, lacrimation) and transient hypotension

Methaemoglobinaemia

Methylthioninium chloride can lower the levels of methaemoglobin in red blood cells and is used in the treatment of methaemoglobinaemia. In large doses, it may cause methaemoglobinaemia and therefore methaemoglobin levels should be monitored during treatment.

Methylthioninium chloride

Methylene Blue

Injection (Solution for injection), methylthioninium chloride 10 mg/ml, 10-ml ampoule

Uses:

acute methaemoglobinaemia

Contraindications:

severe renal impairment; methaemoglobinaemia due to chlorate or induced by sodium nitrite in treatment of cyanide poisoning

Precautions:

G6PD deficiency—may cause haemolytic anaemia; monitor blood methaemoglobin throughout treatment; pregnancy; breastfeeding

Dosage:

Acute methaemoglobinaemia, *by slow intravenous injection* over several minutes **ADULT** and **CHILD** 1–2 mg/kg as a single dose; may be repeated after 1 hour if required

ADMINISTRATION. According to manufacturer's directions

Adverse effects:

nausea, vomiting, abdominal pain, chest pain, headache, dizziness, confusion, profuse sweating; hypertension or hypotension reported; haemolytic anaemia—in G6PD deficiency; methaemoglobinaemia—with high dosage; bluish skin discoloration; blue saliva, urine and faeces

Cyanide poisoning

Cyanide poisoning may be treated with **sodium nitrite** followed by **sodium thiosulfate** .

Sodium nitrite

Injection (Solution for injection), sodium nitrite 30 mg/ml, 10-ml ampoule

Uses:

cyanide poisoning (together with sodium thiosulfate)

Precautions:

monitor plasma methaemoglobin levels; severe cardiovascular or cerebrovascular disease

Dosage:

Cyanide poisoning, *by intravenous injection* over 5–20 minutes, **ADULT** 300 mg (followed by sodium thiosulfate); further dose of 150 mg after 30 minutes if symptoms recur; **child** 4–10 mg/kg (initially lower dose)

Adverse effects:

vasodilatation resulting in syncope, hypotension, tachycardia, flushing, headache; methaemoglobinaemia; cyanosis, dyspnoea, tachypnoea, nausea, vomiting and abdominal pain

Sodium thiosulfate

Injection (Solution for injection), sodium thiosulfate 250 mg/ml, 50-ml ampoule

Uses:

cyanide poisoning (together with sodium nitrite); pityriasis versicolor (section 13.1)

Dosage:

Cyanide poisoning, after sodium nitrite, *by slow intravenous injection* over about 10 minutes, **ADULT** 12.5 g; further dose of 6.25 g after 30 minutes if symptoms recur; **child** 400 mg/kg