

severity of poisoning is less below a plasma-salicylate concentration of 500 mg/litre (3.6 mmol/litre), unless there is evidence of metabolic acidosis. Activated charcoal can be given within 1 hour of ingesting more than 125 mg/kg of aspirin. Fluid losses should be replaced and intravenous sodium bicarbonate may be given (ensuring plasma-potassium concentration is within the reference range) to enhance urinary salicylate excretion (optimum urinary pH 7.5–8.5).

Plasma-potassium concentration should be corrected before giving sodium bicarbonate as hypokalaemia may complicate alkalisation of the urine.

Haemodialysis is the treatment of choice for severe salicylate poisoning and should be considered when the plasma-salicylate concentration exceeds 700 mg/litre (5.1 mmol/litre) or in the presence of severe metabolic acidosis, convulsions, respiratory failure, pulmonary oedema or persistently high plasma-salicylate concentrations unresponsive to urinary alkalisation.

Opioid poisoning

Opioids (narcotic analgesics) cause varying degrees of coma, respiratory depression, and pinpoint pupils. The specific antidote naloxone hydrochloride p. 869 is indicated if there is coma or bradypnoea. Since naloxone has a shorter duration of action than many opioids, close monitoring and repeated injections are necessary according to the respiratory rate and depth of coma. When repeated administration of naloxone is required, it can be given by continuous intravenous infusion instead and the rate of infusion adjusted according to vital signs. All children should be observed for at least 6 hours after the last dose of naloxone. The effects of some opioids, such as buprenorphine, are only partially reversed by naloxone. Dextropropoxyphene and methadone have very long durations of action; patients may need to be monitored for long periods following large overdoses.

Naloxone reverses the opioid effects of dextropropoxyphene. The long duration of action of dextropropoxyphene calls for prolonged monitoring and further doses of naloxone may be required. Norpropoxyphene, a metabolite of dextropropoxyphene, also has cardiotoxic effects which may require treatment with sodium bicarbonate p. 607 or magnesium sulfate p. 618, or both. Arrhythmias may occur for up to 12 hours.

Paracetamol poisoning

In cases of **intravenous** paracetamol poisoning contact the National Poisons Information Service for advice on risk assessment and management.

Toxic doses of paracetamol may cause severe hepatocellular necrosis and, much less frequently, renal tubular necrosis. Nausea and vomiting, the only early features of poisoning, usually settle within 24 hours. Persistence beyond this time, often associated with the onset of right subcostal pain and tenderness, usually indicates development of hepatic necrosis. Liver damage is maximal 3–4 days after paracetamol overdose and may lead to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Therefore, despite a lack of significant early symptoms, children who have taken an overdose of paracetamol should be transferred to hospital urgently.

To avoid underestimating the potentially toxic paracetamol dose ingested by obese children who weigh more than 110 kg, use a body-weight of 110 kg (rather than their actual body-weight) when calculating the total dose of paracetamol ingested (in mg/kg).

Acetylcysteine p. 870 protects the liver if infused up to, and possibly beyond, 24 hours of ingesting paracetamol. It is most effective if given within 8 hours of ingestion, after which effectiveness declines. Very rarely, giving acetylcysteine by mouth [unlicensed route] is an alternative

if intravenous access is not possible—contact the National Poisons Information Service for advice.

Neonates less than 45 weeks corrected gestational age may be more susceptible to paracetamol-induced liver toxicity, therefore, treatment with acetylcysteine should be considered in all paracetamol overdoses, and advice should be sought from the National Poisons Information Service.

Acute overdose

Hepatotoxicity may occur after a single ingestion of more than 150 mg/kg paracetamol taken in less than 1 hour. Rarely, hepatotoxicity may develop with single ingestions as low as 75 mg/kg of paracetamol taken in less than 1 hour.

Children who have ingested 75 mg/kg or more of paracetamol in less than 1 hour should be referred to hospital. Administration of charcoal, activated p. 866 should be considered if paracetamol in excess of 150 mg/kg is thought to have been ingested within the previous hour.

Children at risk of liver damage and, therefore, requiring acetylcysteine, can be identified from a single measurement of the plasma-paracetamol concentration, related to the time from ingestion, provided this time interval is not less than 4 hours; earlier samples may be misleading. The concentration is plotted on a paracetamol treatment graph, with a reference line ('treatment line') joining plots of 100 mg/litre (0.66 mmol/litre) at 4 hours and 3.13 mg/litre (0.02 mmol/litre) at 24 hours. Acetylcysteine treatment should commence immediately in children:

- whose plasma-paracetamol concentration falls on or above the *treatment line* on the paracetamol treatment graph;
- who present 8–24 hours after taking an acute overdose of more than 150 mg/kg of paracetamol, even if the plasma-paracetamol concentration is not yet available; acetylcysteine can be discontinued if the plasma-paracetamol concentration is later reported to be below the *treatment line* on the paracetamol treatment graph, provided that the child is asymptomatic and liver function tests, serum creatinine and INR are normal.

The prognostic accuracy of a plasma-paracetamol concentration taken after 15 hours is uncertain, but a concentration on or above the *treatment line* on the paracetamol treatment graph should be regarded as carrying a serious risk of liver damage. If more than 15 hours have elapsed since ingestion, or there is doubt about appropriate management, advice should be sought from the National Poisons Information Service.

'Staggered' overdose, uncertain time of overdose, or therapeutic excess

A 'staggered' overdose involves ingestion of a potentially toxic dose of paracetamol over more than one hour, with the possible intention of causing self-harm. Therapeutic excess is the inadvertent ingestion of a potentially toxic dose of paracetamol during its clinical use. The paracetamol treatment graph is unreliable if a 'staggered' overdose is taken, if there is uncertainty about the time of the overdose, or if there is therapeutic excess. In these cases, children who have taken more than 150 mg/kg of paracetamol in any 24-hour period are at risk of toxicity and should be commenced on acetylcysteine immediately, unless it is more than 24 hours since the last ingestion, the patient is asymptomatic, the plasma-paracetamol concentration is undetectable, and liver function tests, serum creatinine and INR are normal.

Rarely, toxicity can occur with paracetamol doses between 75–150 mg/kg in any 24-hour period; for some children this may be within the licensed dose, but ingestion of a licensed dose of paracetamol is not considered an overdose. Clinical judgement of the individual case is necessary to determine whether to treat those who have ingested this amount of paracetamol.

Although there is some evidence suggesting that factors such as the use of liver enzyme-inducing drugs (e.g.