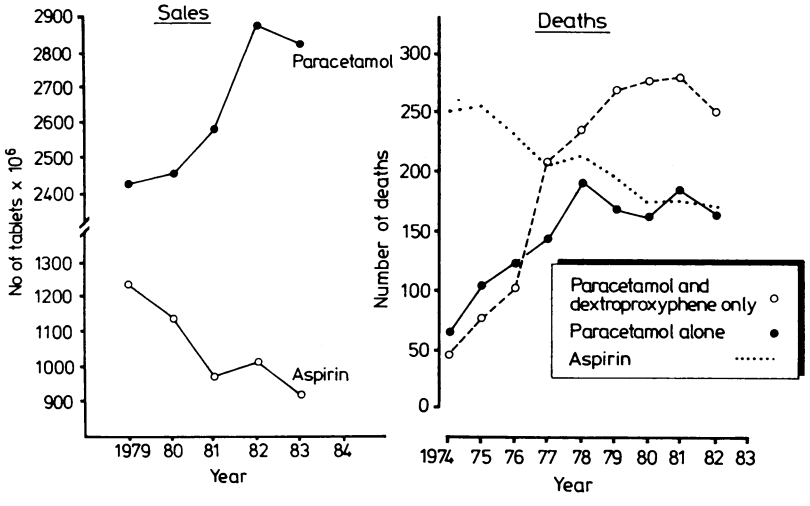
ABC of Poisoning

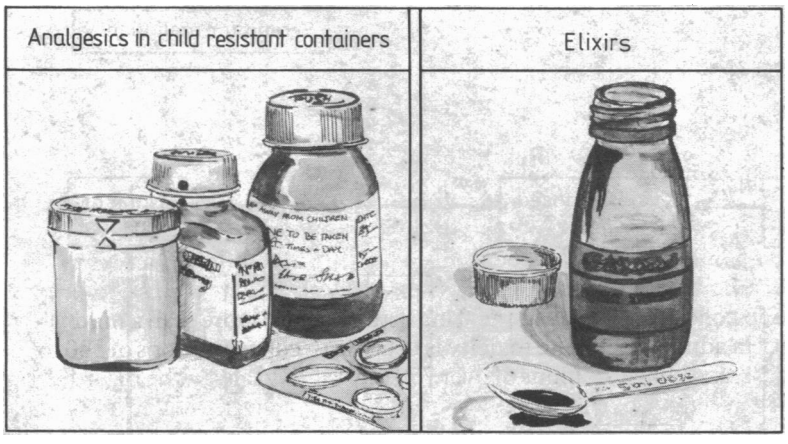
JOHN HENRY
GLYN VOLANS

ANALGESIC POISONING: I—SALICYLATES



Over the past 10-12 years there have been great changes in the epidemiology of analgesic poisoning. Hospital admissions for aspirin poisoning have fallen in line with reduced use, and there has been a similar, though smaller, decline in the number of deaths recorded. In contrast, the reported incidence of paracetamol poisoning originally did not parallel sales. There was a sharp increase in paracetamol related admissions and deaths in the mid-seventies, related probably to inappropriate publicity. More recently attention has turned to compound analgesics containing paracetamol and dextropropoxyphene (Distalgesic, Cosalgesic), which have been increasingly described as a cause of death. Effective treatments are available for poisoning from each of these three types of product. It is important, therefore, to consider carefully the presentation and management of cases of analgesic poisoning, and three articles in this series are directed to major analgesic problems.

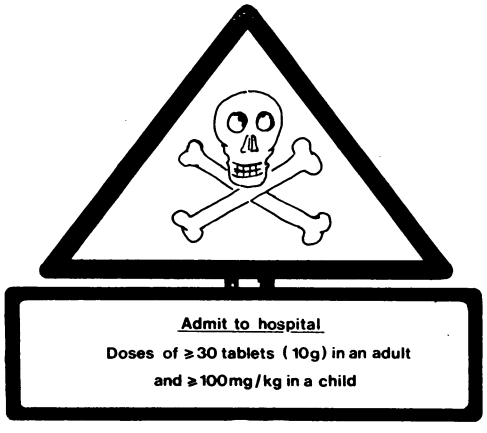
Accidental or deliberate?



Serious accidental analgesic poisoning in children is now uncommon. The use of child resistant closures for solid dose analgesics, smaller pack sizes, and the elimination of attractively coloured products have probably all helped to reduce this problem. Nevertheless, there is no room for complacency and so long as these drugs are widely available, doctors must continue to warn parents of the dangers, particularly when the analgesic is presented as a sweet tasting elixir.

Deliberate self poisoning is the motive behind most cases of adult analgesic poisonings, and the aspirin and paracetamol used are most often obtained without prescription.

Lethal doses

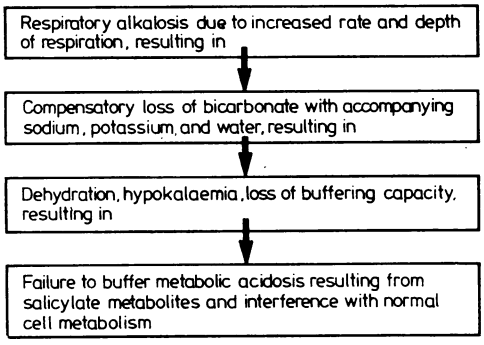


Our experience suggests that salicylate poisoning is often regarded complacently and that many deaths caused by salicylate poisoning could have been prevented.

The lethal acute dose in an adult is about 20-25 g, and 4 g is likely to be fatal as a single overdose in a small child, but considerably less than this can cause serious toxicity in infants. Unintentional therapeutic poisoning with aspirin is unfortunately a problem in children. Dosage regimens should be followed with care in children under 6 years. Parents should be made aware of the hazards of giving aspirin (even Junior Aspirin) to infants, since repeated doses can soon cause toxicity due to accumulation. Aspirin should not be given at all to children aged under 1 year. Oil of wintergreen and some teething gels also contain salicylates and occasionally cause accidental poisoning.

Aspirin (acetylsalicylic acid) is rapidly absorbed from the gut and quickly hydrolysed to salicylic acid. Its further metabolism is saturable, so that

Fluid and acid base balance in salicylate poisoning



(Children rarely develop respiratory alkalosis but progress more quickly to metabolic acidosis)

salicylic acid and its metabolites are eliminated slowly after overdosage. The effects from overdose are also influenced by continuing absorption since aspirin is poorly soluble in an acid solution and may dissolve poorly or precipitate out again in the gastric juice. The material thus produced coalesces to form a mass or a coating in the stomach, from which absorption may continue slowly over many hours.

The toxic effects of salicylates are complex and include acid-base disturbances, uncoupling of oxidative phosphorylation with inhibition of the production of high energy phosphates, and disordered glucose metabolism. Clinically, it is important to recognise the signs and symptoms of salicylate toxicity and to understand the factors influencing fluid and acid base balance.

Clinical features

- Nausea, vomiting, epigastric pain
- Excitability, tremor, tinnitus, and deafness
- Sweating (fever in children)
- Increased rate and depth of respiration, pulmonary oedema
- Dehydration, hypokalaemia, hyponatraemia, and hypernatraemia
- Respiratory alkalosis followed by metabolic acidosis
- Hyperglycaemia or hypoglycaemia
- Hypoprothrombinaemia
- Central nervous system depression occurs only in very severe cases, in late stages

The symptoms and signs of aspirin poisoning may not become apparent for many hours. There may be nausea and vomiting with abdominal pain and tinnitus progressing to deafness. The patient is hyperventilating, the skin is flushed, and sweating is usual. Disturbed consciousness and agitation are common. Coma in adults is rarely due to salicylates alone but is common in children. Less common complications include hyperpyrexia, hypoprothrombinaemia, hypoglycaemia, pulmonary oedema, and renal failure. Salicylates may also cause toxic liver damage in children.

The blood pH is usually normal or raised in the initial stages due to a respiratory alkalosis, but a metabolic acidosis may supervene if treatment is not started, and is the rule in children.

Management

Laboratory investigations in salicylate poisoning

- Haematology
  - Full blood count
  - Packed cell volume
  - Partial thromboplastin time
- Biochemistry
  - Urinary and blood electrolytes
  - Glucose
  - Liver function tests
  - Arterial blood gases
- Toxicology
  - Salicylate
  - Paracetamol
  - Save samples for other analyses
    - Blood
    - Gastric aspirate
    - Urine

Gastric aspiration or emesis should be carried out in all patients believed to have taken a toxic dose within the past 24 hours. Thereafter, decisions on treatment should be influenced by clinical and biochemical findings, including measurement of plasma salicylate values. During treatment with aspirin salicylate concentrations may sometimes reach as high as 300-380 mg/l and concentrations below 500 mg/l rarely cause more than a mild toxicity in adults. Moderate toxicity is usual with concentrations of 500 to 750 mg/l, and concentrations of over 750 mg/l should always be regarded as potentially fatal. Toxicity can occur in children at concentrations of 300 mg/l.

In suspected childhood poisoning it is important to obtain an initial salicylate concentration. The patient must not be discharged until a further sample has been measured four to six hours later. If the second level is higher, admission is necessary for further monitoring and management.

The need for symptomatic treatment with fluid and electrolyte replacement and glucose and vitamin K therapy where necessary is self evident and non-controversial. There is, however, continuing debate about the so called elimination techniques. Urinary salicylate excretion is increased if the urine pH is in excess of 7·5 and is optimal between pH 8·0 and 8·5. It has, therefore, been customary to recommend a fluid regimen sufficient to achieve this pH and to ensure a high urine output (forced alkaline diuresis). It has also been long apparent that the urine pH is a more important determinant of salicylate excretion than the urine flow and that inadequately monitored use of forced alkaline diuresis is both ineffective and dangerous because of the risks from hypokalaemia and fluid overload, especially pulmonary oedema. Recent reports have emphasised these observations and our recommended regimen for moderately severe

Treatment of salicylate poisoning

(1) Gastric aspiration, up to 24 hours after ingestion. Ipecacuanha syrup for children. Salicylate may remain undissolved in the stomach for many hours.

(2) Fluid and electrolyte replacement: treat according to biochemical results, especially for hypokalaemia and hypoglycaemia

(3) Correct metabolic acidosis with bicarbonate

(4) Vitamin K for hypoprothrombinaemia

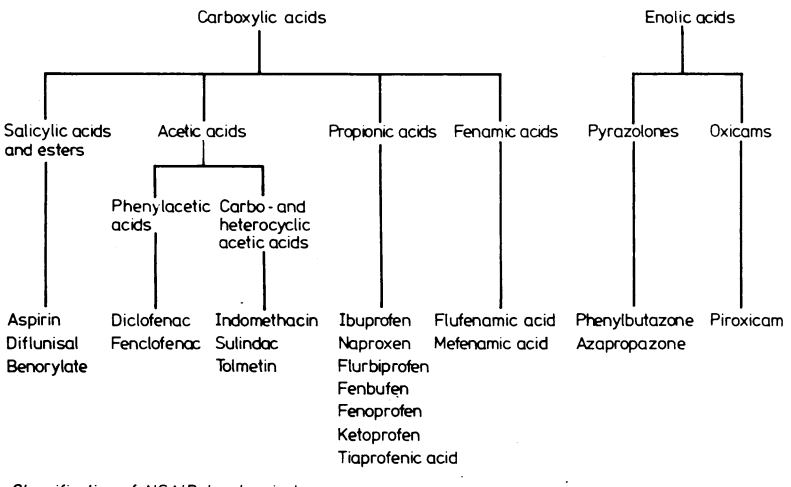
(5) Arrange haemodialysis – or alternatives in severe cases – see text

poisoning is designed to ensure an alkaline diuresis without producing an excessive urine flow.

On the other hand, because of vomiting, hyperventilation, and sweating, the patient is usually quite dehydrated, and fluid replacement is essential; the central venous pressure should be monitored in severe cases. Once adequate rehydration has been achieved, the plasma salicylate concentrations may fall considerably and will then provide a more realistic indication of severity and the need for further treatment.

In serious poisoning (plasma salicylate levels over 800 mg/l after rehydration or 1000 mg/l before rehydration) or when renal failure or pulmonary oedema complicate the picture haemodialysis is preferable since it can be used to correct fluid and electrolyte imbalance at the same time as effectively removing salicylate. Peritoneal dialysis and haemoperfusion are alternative but less efficient treatments for salicylate poisoning.

Overdose with non-steroidal anti-inflammatory agents



Classification of NSAIDs by chemical groups

In spite of their widespread usage the non-steroidal anti-inflammatory drugs are infrequently taken in overdose. Most of these compounds appear to be less toxic than aspirin and seldom cause more than mild drowsiness and gastrointestinal symptoms. Notable exceptions are: *benorylate*, an ester of aspirin and paracetamol, which causes primarily the effects of paracetamol; *mefenamic acid*, which causes a high incidence of convulsions but which is readily treated with diazepam and has not caused any deaths; *phenylbutazone* and *oxyphenbutazone*, which in acute overdose cause more severe gastrointestinal disturbances, including haematemesis together with coma, convulsions, and renal and hepatic failure. Aplastic anaemia has also been reported as a late effect. The withdrawal of oxyphenbutazone and the restricted use of phenylbutazone should ensure that few if any further cases will occur.

Ibuprofen preparations

Brand	Tablet/capsule sizes (mg)	Manufacturer
	Prescription only	
Apsifen	200, 400	APS
Brufen	200, 400, 600	Boots
Ebufac	400	DDSA
Fenbid	300 sustained release	SK and F
	Non-prescription	
Ibuprofen	200	Evans
Maxagesic	200	Wigglesworth
Nurofen	200	Boots
Proflex	200	International Laboratories

In contrast to these drugs, there is evidence that the derivatives of propionic acid are of low toxicity even after large overdoses. This is particularly well documented for ibuprofen. From August 1983 ibuprofen has been available without prescription from chemists (though not from other outlets). The National Poisons Information Service is monitoring all cases of overdose with this drug and when possible is correlating clinical reports with plasma concentrations of ibuprofen. We encourage reporting of all such cases to us since it is important to prove in practice that the recent change in the availability of non-prescription analgesics does indeed represent a move towards greater safety.

Court H, Volans GN. Poisoning after overdose with non-steroidal anti-inflammatory drugs. *Adverse Drug Reactions Bulletin* 1984;3:1-21.

Dr John Henry, MRCP, is consultant physician and Dr Glyn Volans, MD, FRCP, is director, National Poisons Information Service, Guy's Poisons Unit, New Cross Hospital, London SE14 5ER. The data for the first illustration are taken, by permission, from Meredith TJ, Vale JA. Epidemiology of analgesic overdose in England and Wales. *Human Toxicology* 1984;3(suppl):615.