

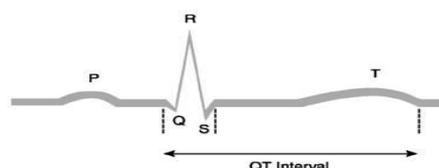
We are currently in the process of updating and revising our website [www.poisons.ie](http://www.poisons.ie) where you will find general background information and contact details for the Poisons Centre.

Please note that our website does not include toxicity information or advice for treating patients and you should continue to use [www.toxbase.org](http://www.toxbase.org) for this purpose.

You will also notice that the homepage highlights an alternative phone-number for members of the public; this number is not a 24 hour service and does not automatically reroute to the Poisons Information Service in the UK after 10pm. Please continue to use the phone-number specifically for healthcare professionals: **01-809 2566**.

## Venlafaxine

Our enquiries about venlafaxine have steadily increased over the last few years and it is now one of the top 20 agents involved in poisoning. Venlafaxine non-selectively inhibits reuptake of serotonin, noradrenaline, and dopamine. Toxicity is usually associated with doses of >7mg/kg. Drowsiness is common following overdose, and in severe cases there may be coma and seizures. Wide QRS and prolonged QT interval have been reported and appear to be dose related (Howell 2007, Batista 2013). Despite this, significant ventricular arrhythmias are not commonly reported (Isbister 2009). Prolonged QT interval may increase the risk for torsade de pointes; correct acidosis, hypoxia, hypokalaemia,



hypocalcaemia and hypomagnesaemia. Treat torsade de pointes with magnesium sulphate (2 grams in adults and 25-50 mg/kg in children intravenously over 30-120 seconds, repeated twice at intervals of 5-15 minutes if necessary).

In rare cases of overdose serotonin syndrome may occur. Monitor U&Es and creatinine concentration. Hyperpyrexia should be treated with conventional cooling methods and benzodiazepines. Cyproheptadine and chlorpromazine may be useful in severe cases; discuss with the Poisons Information Centre.

**Further Reading:** Howell C, Wilson AD, Waring WS. Cardiovascular toxicity due to venlafaxine poisoning in adults: a review of 235 consecutive cases. *Br J Clin Pharmacol.* 2007; 64: 192-197.

Isbister G. Electrocardiogram changes and arrhythmias in venlafaxine overdose. *Br J Clin Pharmacol.* 2009 May; 67(5):572-6

Batista M, Dugernier T, Simon M *et al.* The spectrum of acute heart failure after venlafaxine overdose. *Clin Toxicol (Phila).* 2013 Feb;51(2):92-5

## Spring Cleaning Hazards!

**DRAIN CLEANERS:** These products usually contain caustic agents like sodium hydroxide, potassium hydroxide or sulphuric acid. They can cause severe damage to the gastrointestinal tract particularly if the pH is  $>12$  or  $<2$ . When drain cleaners are ingested there is usually an immediate burning sensation around the lips, in the mouth, and the back of the throat. In some cases there can be oedema and airway obstruction. Metabolic disturbances may occur as a direct effect of a strong acid or as a result of corrosive tissue injury. Surgical referral is indicated in patients who develop significant oesophageal or abdominal pain, metabolic acidosis, or circulatory collapse. Patients with evidence of oropharyngeal burns, drooling, vomiting, pain or dysphagia should have an early endoscopy to grade local injury. The value of corticosteroids is controversial and should be discussed with senior colleagues.

Contini S, Scarpignato C. **Caustic injury of the upper gastrointestinal tract: a comprehensive review.** World J Gastroenterol. 2013 Jul 7; 19(25):3918-30.

**WHITE SPIRIT:** This petroleum distillate is commonly found in household products such as paint remover, furniture polish and window cleaners. It is poorly absorbed from the gastrointestinal tract and accidental ingestion of small amounts rarely causes systemic toxicity. The main complication following ingestion is chemical pneumonitis as a result of pulmonary aspiration. Features may progress over 36 hours and can include wheeze, breathlessness, hyperventilation, dyspnoea, tachypnoea, bronchospasm, hypoxia, cyanosis, fever and leucocytosis. Large deliberate ingestions may cause CNS depression, coma, respiratory collapse, seizures, and cardiac arrhythmias. Severe repeated diarrhoea can occur and has been associated with perianal injury including rash, blistering, excoriation and burns. Analgesia and prophylactic antibiotics may be useful.

Cassidy N, Duggan E, McDonnell CO *et al.* **Peri-anal injury following ingestion of White Spirit.** Clin Toxicol (Phila). 2014 Mar; 52(3): 236.

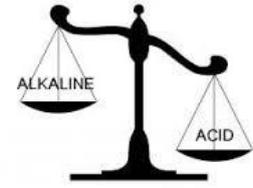


**BLEACH:** Most domestic bleaches contain a low concentration of sodium hypochlorite and they are classed as irritants rather than caustics. Large volumes may cause corrosive injury to the GI tract but small accidental ingestions rarely cause more than local irritation in the mouth and mild gastrointestinal features. A small glass of milk or water is often sufficient in these cases.



*Oxygen-based bleaches* however contain hydrogen peroxide and even small amounts can liberate oxygen gas causing possible venous or arterial gas embolism. All patients require observation for at least 4 hours following ingestion of any amount of hydrogen peroxide. Chest and abdominal X-rays should be obtained to detect perforation or gas embolism if the patient is symptomatic.

## METFORMIN *and lactic acidosis:*



Metformin is a biguanide agent used as first line therapy in the treatment of non-insulin dependent diabetes. The exact mechanism of action of metformin has been difficult to elucidate but recent work by Madiraju *et al* provides compelling evidence that it decreases hepatic gluconeogenesis by inhibiting the mitochondrial enzyme glycerophosphate dehydrogenase. This causes a shift in the ratio of NADH/NAD and the resultant rise in NADH impairs formation of glucose from lactate. Lactate levels then rise.

Despite widespread use of metformin, there remains uncertainty about the risk of lactic acidosis in therapeutic use and in overdose. A comprehensive Cochrane Review (Salpeter 2010) showed no evidence of an increased risk of lactic acidosis with therapeutic use of metformin. However this review excluded cases of acute overdose. Both hyperlactadaemia (lactate >2mmol/L) and acidosis (pH <7.35) are well described in metformin overdose (Vecchio 2014). Lactic acidosis, as defined by pH <7.35 with a lactate of >5mmol/L, is less common but has been observed in larger overdoses (McNamara 2015). A recent review of intentional overdoses concluded that deaths were associated with a serum pH nadir of less than 6.9, a lactate concentration of greater than 25 mmol/L and a metformin concentration greater than 50 micrograms/mL (Dell'Aglio 2009).

Minor features of toxicity can include GI upset, sweating, headache and generalised weakness. More severe features may include lactic acidosis, confusion, CNS depression, hypothermia, hypotension, and renal failure. Rarely, ventricular dysrhythmias, and respiratory insufficiency can occur.

Patients should be observed for at least 6 hours with monitoring of blood glucose, U&Es, creatinine, LFTs, and blood gases including lactate. Treatment is supportive. Metformin has a large volume of distribution so dialysis does not enhance clearance in patients with normal renal function.

### Further Reading:

- Dell'Aglio DM, Perino LJ, Kazzi Z, *et al*. Acute metformin overdose: examining serum pH, lactate level, and metformin concentrations in survivors versus nonsurvivors: a systematic review of the literature. *Ann Emerg Med* 2009; 54: 818-823.
- Madiraju AK, Erion DM, Rahimi Y *et al*. Metformin suppresses gluconeogenesis by inhibiting mitochondrial glycerophosphate dehydrogenase. *Nature* 2014; 510:542-6
- McNamara K, Isbister G. Hyperlactataemia and clinical severity of acute metformin overdoses. *Intern Med J*. 2015 Feb 9 [Epub ahead of print]
- Vecchio S, Giampreti A, Petrolini VM, *et al* *Clin Toxicol (Phila)*. 2014 Feb; 52(2):129-35. 2013 Nov 28. Metformin accumulation: lactic acidosis and high plasmatic metformin levels in a retrospective case series of 66 patients on chronic therapy.

## AISE “Accidentology project”



Laundry detergent capsules contain concentrated detergents that can potentially cause harm to children if swallowed or splashed onto skin or eyes. The NPIC is currently taking part in a preliminary 6 month study with other European poisons information centres to determine the circumstances and outcomes of accidental paediatric exposures to all liquid detergent capsules. The study involves carrying a short survey with parents/carers in the days following a poisoning incident with these detergent capsules. This research has been commissioned by A.I.S.E. (International Association for Soaps, Detergents and Maintenance Products), the official representative body of this industry in Europe, and has been approved by the Beaumont Hospital Ethics Committee.

It is envisaged that the NPIC will also participate in a larger European wide study looking at the circumstances of paediatric exposures to household products including liquid detergent capsules, laundry and dishwashing products. This project is expected commence in the coming months and will run for a number of years. We anticipate that the results will be used to inform future safety measures that may be indicated for packaging, storage and handling of these products.

## DAFFODIL BULBS

Daffodil bulbs continue to cause inadvertent poisoning due to mistaken identity when people use them instead of onions. All parts of the daffodil plant contain toxic compounds (Lycorine and calcium oxalate) and ingestion can cause rapid onset of gastrointestinal features. Severe vomiting, diarrhoea, and abdominal pain can persist for 3-4 hours. Some patients may also develop hypotension, convulsions, and CNS depression. In most cases, symptoms will resolve within 12 hours. Treatment is supportive with fluid replacement and anti-emetics as required.



Handling the bulbs can cause skin rash due to the presence of calcium oxalate crystals.

**Further Reading:** Matulkova P, Gobin M, Evans M, *et al.* Gastro-intestinal poisoning due to consumption of daffodils mistaken for vegetables at commercial markets, Bristol, United Kingdom. *Clin Toxicol (Phila)* 2012 Sep; 50(8):788-90

### Contributors:

Elaine Donohoe (Specialist in Poisons Information), Dr Edel Duggan (Medical Director) National Poisons Information Centre, Beaumont Hospital, Dublin 9, Tel: (01) 837 9964 / 809 2566. Fax: (01) 836 8476.



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