
At the end of Summer and into Autumn, we inevitably see an increase in cases of mushroom poisoning.



Enquiries to the Poisons Centre usually fall into three categories:

- (i) accidental mushroom ingestion by children
- (ii) accidental ingestion of toxic mushrooms
- (iii) deliberate ingestion of hallucinogenic mushrooms

Fortunately most cases of accidental ingestion involve relatively innocuous mushrooms and patients usually only develop mild GI symptoms such as nausea, vomiting, and diarrhoea. These symptoms occur soon after ingestion (<6 hrs) and in most cases treatment involves rehydration.

In rare cases, toxicity can be more severe. The most toxic native species in Ireland are *Cortinarius spp* (pictured) which can cause delayed renal dysfunction after a latent phase of a few days, and *Amanita phalloides* which can cause hepatic central lobular necrosis resulting in liver failure.

Correct identification of mushrooms can be difficult but we have a registry of mycologists who are willing to assist in mushroom poisoning cases. In severe cases, timely input from an expert mycologist can be useful in assisting clinical decisions. Ideally, any available mushroom fragments should be preserved and transported to the nearest mycologist but if this is not possible, digital photographs of the mushroom may be useful. Photographs should be close-up images showing the stalk, cap and underside of the mushroom.

Please discuss all cases of severe mushroom poisoning with the National Poisons Information Centre who can advise on storage and transport of mushroom samples if required.



The IMB recently highlighted recommendations from the European Agency Pharmacovigilance Risk Assessment Committee (PRAC) regarding the use of codeine in children. This follows a review of cases where serious adverse effects including respiratory depression and death were reported.

The PRAC now recommend that codeine should only be prescribed for acute short term use in children over 12 years of age, and not at all in children who undergo surgical removal of tonsils or adenoids for obstructive sleep apnoea. The review also concludes that children below 12 years of age may be at increased risk of morphine side effects including respiratory depression and there is no significant benefit from codeine compared to non-opioid painkillers.

The current guidelines on **TOXBASE®** recommend medical assessment for all children who have ingested any amount of codeine. Codeine linctus is currently licensed for use in children over 5 years but medical assessment is appropriate following therapeutic errors or ingestion of a codeine product by a child not on therapy. All patients should be observed until at least 4 hours post-ingestion. Respiratory rate, oxygen saturation, and GCS should be monitored closely. Naloxone may be required in severe cases.

Nail Polish Remover

Acetone: Poisoning with acetone nail polish removers is not uncommon but rarely results in severe toxicity. Over a 10 year period, we received almost one enquiry per week about ingestion of nail polish removers. The majority of cases involved accidental ingestion and 80% of patients remained asymptomatic. 14% experienced mild GI disturbances and 6 patients became drowsy.



Over a 10 year period, 6% of acetone cases reported to the poisons centre involved intentional ingestions of >150mls. When large amounts are taken there can be severe and prolonged CNS depression. Other symptoms can include hypotension, tachycardia, and metabolic acidosis.

A toxic dose of 2-3mls/kg of acetone has been suggested but most cases involve accidental ingestion by children and symptoms often do not correlate with the reported dose.

Observation for at least 4 hours is recommended in patients who may have taken > 1mL/kg of pure acetone. Complete recovery is expected with good supportive care.

Intentional Ingestion:

Severe CNS depression requiring intubation has been seen following repeated ingestions of large volumes of acetone containing nail polish remover:

| Episode | Volume | Features | Outcome |
|---------|--------|---|------------------------------------|
| 1 | 250mls | <ul style="list-style-type: none"> • GCS 3/15, respiratory arrest; <ul style="list-style-type: none"> ➢ <i>Intubation and ventilation. Extubated day 4.</i> • Hypotension (BP 61/40) <ul style="list-style-type: none"> ➢ <i>vasopressin, noradrenaline, dopamine</i> • Tachycardia (HR 155) • vomiting | Sequelae (aspiration pneumonia) |
| 2 | 400mls | <ul style="list-style-type: none"> • GCS 3/15, Respiratory depression <ul style="list-style-type: none"> ➢ <i>Intubation and ventilation. Extubated day 3.</i> • pH 7.28 <ul style="list-style-type: none"> ➢ <i>IV fluids; no sodium bicarbonate required</i> • Hypotension (BP 57/28) <ul style="list-style-type: none"> ➢ <i>IV fluids; no inotropes required</i> • Haematemesis | Complete recovery |
| 3 | 250mls | <ul style="list-style-type: none"> • GCS 3/15 <ul style="list-style-type: none"> ➢ <i>Intubation. Extubated day 2.</i> • pH 7.21 <ul style="list-style-type: none"> ➢ <i>IV fluids; no sodium bicarbonate required</i> • BP "low" <ul style="list-style-type: none"> ➢ <i>IV fluids; no inotropes required</i> • Hyperglycemia (BM 10.8) | Complete recovery |



TOXBASE® is the toxicology database of the the UK Poisons Information Service. It provides advice on the features and management of many different types of poisons and is currently available on request to all Emergency Departments and Intensive Care Units in Irish Hospitals.

Recently a new TOXBASE® app has been produced for iphones/ipads and android devices. It is available on a subscription basis for users based outside the UK and provides access to more than 1000 of the most frequently used information pages.



Further information is available under NPIS SERVICES on the **TOXBASE®** homepage at www.toxbase.org

Focus on **ATYPICAL ANTIPSYCHOTICS**

Poisons enquiries involving the second generation or **atypical antipsychotics** are now 5 times more common than cases involving the older **typical** antipsychotics like chlorpromazine and haloperidol.

Mechanism of action

The primary physiological effect of all the antipsychotics is antagonism at the D₂ dopamine receptor. Competitive antagonism at a range of other neuroreceptors also occurs and the severity of symptoms seen in overdose varies according to the varying affinity for these receptors.

Atypical Antipsychotics; antagonism at neuroreceptors-

| Neuroreceptor: | α -adrenergic | Muscarinic | Histamine | Serotonin 5-HT |
|-------------------------|----------------------|----------------------------|------------|--------------------------|
| Clinical effect: | » Hypotension | » Anticholinergic symptoms | » Sedation | » Lower incidence of EPS |
| Amisulpride | ++ | ++ | + | + |
| Aripiprazole | ++ | - | + | ++ |
| Clozapine | +++ | +++ | ++ | ++ |
| Olanzapine | ++ | +++ | +++ | +++ |
| Quetiapine | +++ | +++ | ++ | + |
| Risperidone | ++ | - | + | +++ |
| Sertindole | + | - | + | + |

Features

The atypical antipsychotics usually cause features of toxicity within 4-6 hours after ingestion. Symptoms can be prolonged and can include drowsiness, coma and respiratory depression. Tachycardia is commonly seen due to competitive binding at the muscarinic receptors. Other anticholinergic effects can include dilated pupils, agitation, delirium, dry mouth and urinary retention.

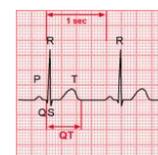
Treatment is symptomatic and supportive. Do an ECG and observe all patients until at least 6 hours post-ingestion. Quetiapine can cause delayed convulsions so observe symptomatic patients until 24 hours post-ingestion.

Further reading

Thomas SHL. **Cardiotoxicity of newer antipsychotics** [abstract 103] Clin Toxicol 2013; 51(4): 299-300

Joy JP, Coulter CV, Dufful SB et al. **Prediction of torsade de pointes from the QT interval: analysis of a case series of amisulpride overdoses.** Clin Pharmacol Ther 2011; 90: 243-5

QT prolongation can occur particularly with amisulpride and sertindole.



Torsade de pointes appears to be less common but has been reported with amisulpride. It should be treated by administration of IV magnesium sulphate over 30-120 seconds: adults 2g (8mmol); children-25-50mg/kg. Repeat twice if necessary at intervals of 5-15 minutes.

Unlike the typical antipsychotics, the atypical antipsychotics bind to the serotonin 5-HT receptors. This may reduce the incidence of extrapyramidal effects.

SEROTONIN SYNDROME

Caused by excessive stimulation of serotonin receptors by serotonergic agents such as:

- Drugs that enhance serotonin release (eg amphetamines, cocaine, lithium)
- Drugs that block serotonin reuptake (eg SSRIs, cocaine, venlafaxine)
- Drugs that inhibit serotonin breakdown (eg MAOIs)
- Drugs that are precursors of serotonin (e.g L-tyrophan)

Features:

Onset of symptoms is usually rapid. In all cases there must be recent exposure to a serotonergic agent. Most features resolve within 24 hours once the offending drug has been stopped.

Autonomic instability: hyperthermia can be severe and life-threatening. It should be treated promptly with cooling methods and benzodiazepines. Dantrolene may be considered if these measures fail (1mg/Kg by rapid intravenous injection to a maximum of 10mg/Kg). Additional features may include tachycardia, hypertension or hypotension, sweating, diarrhoea.

Neuromuscular effects: The presence of **clonus** (spontaneous, inducible or ocular) is strongly associated with serotonin syndrome. Tremor together with hyperreflexia is also highly suggestive of serotonin syndrome. There may be shivering and teeth grinding. Muscle rigidity contributes to hyperthermia. In severe cases, intubation and muscle paralysis may be required.

NB: many of the features of serotonin syndrome overlap with neuroleptic malignant syndrome. The presence of lead pipe rigidity and bradykinesia may suggest neuroleptic malignant syndrome rather than serotonin syndrome.

Mental status changes: agitation, confusion, delirium and hallucinations.

Treatment:

Stop all serotonergic drugs. Initiate active cooling and sedation with benzodiazepines.

Cyproheptadine has non-specific antagonist properties at 5-HT_{1a} and 5HT_{2a} receptors. It has been shown in animal studies and case reports to reduce symptoms of serotonin syndrome but there are no controlled trials assessing its use for this purpose. Suggested protocols for moderate toxicity include an initial dose of 12mg followed by 4-8mg every 6 hours *or* 2mg every 2 hours. This dose may cause sedation which can be beneficial.

Cyproheptadine is only available in oral form. In cases of severe toxicity or when oral dosing is not possible **chlorpromazine** may be useful. Give 12.5-25 mg iv followed by 25 mg orally every 6 hours. Chlorpromazine can cause hypotension so ensure sufficient volume loading.

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.



www.facebook.com/NPICDublin