ABC of Poisoning

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GLYN VOLANS

PSYCHOACTIVE DRUGS

Tricyclic antidepressants

Amitriptyline

Related tricyclic antidepressants:

- Butriptyline
- Dothiepin
- Doxepin
- Nortriptyline
- Protriptyline

Imipramine

Related tricyclic antidepressants:

- Clomipramine
- Desipramine
- Dibenzepin
- Opipramol
- Trimipramine

Most of the drugs used to treat psychiatric disorders are relatively toxic, and since suicidal behaviour is often a feature of these conditions the risk of overdose, often with potentially serious consequences, is real. Those prescribing psychoactive drugs should ensure not only that the diagnosis is correct and the treatment appropriate but that the proper use and possible side effects of the medication are carefully explained to the patient. If suicide is thought to be a risk the least toxic of the available drugs should be chosen.

Tricyclic antidepressants have a three ring structure, hence their name.

Clinical features

Symptoms of tricyclic antidepressant poisoning.

Anticholinergic:

- Sinus tachycardia
- Mydriasis
- Urinary retention

Central nervous effects:

- Hallucinations
- Coma
- Brisk tendon reflexes
- Extensor plantar reflexes
- Respiratory depression
- Convulsions

Cardiac

- Electrocardiographic changes
- Ventricular arrhythmias
- Hypotension

Metabolic

- Hypothermia
- Hypoxia
- Metabolic acidosis
- Hypokalaemia

Self poisoning with tricyclic antidepressants accounts for about 300 deaths a year in adults in England and Wales. Patients prescribed tricyclic antidepressants should be told that the drug will not fully reverse their depression for some weeks and that they should persevere with their treatment. These drugs are also the major cause of fatal accidental poisoning in children in the United Kingdom, causing about 5 deaths a year.

Although the antidepressant activity of these drugs probably relates to their effects on the neurotransmitter systems in the brain, their toxic effects are largely due to anticholinergic and cardiodepressant effects. Symptoms include dilated pupils, sinus tachycardia, hallucinations, urinary retention, and ileus. Cerebral toxicity may result in deepening coma, convulsions, brisk tendon reflexes, and extensor plantar responses. In severe poisoning tendon reflexes and muscle tone may be lost, and brain stem reflexes may be absent. Respiratory or cardiac depression may lead to hypoxaemia. Metabolic acidosis is common, and hypokalaemia can also occur. Death is usually due to cardiotoxicity or respiratory depression. The most frequent cardiac effect is sinus tachycardia without impairment of cardiac output. Further electrocardiographic abnormalities may, however, occur, with wide bizarre QRS complexes, heart block, and sometimes ventricular ectopic beats or ventricular tachycardia. A cardiac depressant effect can produce hypotension, which may accentuate the hypoxaemia and metabolic acidosis. Sudden death has been reported up to six days after overdose but is very rare.

Other antidepressants

Other antidepressants	
Lofepramine	
Tryptophan	
Maprotiline	
Mianserin	
Nomifensine	
Trazodone	
Viloxazine	

Maprotiline is a bridged tricyclic antidepressant. It has anticholinergic effects and the toxic symptoms are similar to those of the tricyclic antidepressants. Convulsions should be expected in overdose and have been reported during therapeutic use.

Mianserin does not have anticholinergic effects and is less cardiotoxic than the tricyclic antidepressants. Drowsiness is the main clinical feature. Deaths from overdose are rare and are usually clearly attributable to a number of problems including mixed overdose and underlying disease.

Nomifensine—Toxicity is generally mild. Drowsiness and tremor sometimes occur, and coma is rare.

Trazodone. Toxicity is usually mild. Trazodone can cause drowsiness, dizziness, and occasionally coma.

Lofepramine is metabolised to the tricyclic antidepressant desipramine and might be expected to show the same effects in overdose. Claims have been made for increased safety, but there is not yet enough information to support this.

Lithium

Lithium toxicity	
Nausea, vomiting, diarrhoea	
Tremor, weakness, ataxia, rigidity	
Stupor, convulsions, coma	

Lithium salts are widely and effectively used to treat bipolar or manic-depressive disorders. This metal is eliminated by the kidneys, and reduced renal function can lead to accumulation. The therapeutic range is narrow (plasma concentrations between 1.0 and 1.4 mmol/l (6.9-9.7 g/l)), and toxicity in therapeutic use can be caused by changes in fluid or electrolyte balance (particularly due to reduction in fluid intake or increased fluid loss from diarrhoea or vomiting or diuretic therapy). Deaths from lithium poisoning are rare, but the fact that lithium toxicity usually resolves completely should not lead to complacency.

Clinical features

Chronic lithium toxicity usually presents with nausea, vomiting, diarrhoea, and tremor. Nephrotoxicity also occurs during chronic treatment. In acute overdose neurological features are the rule, with tremor, rigidity, nystagmus, and convulsions starting within hours of ingestion as the lithium enters brain tissue. Plasma concentrations correlate poorly with toxic effects, and patients are often asymptomatic with plasma lithium concentrations as high as 4 mmol/l (28 g/l). Lithium preparations are usually formulated for sustained release, so that toxic features may be delayed even in acute overdose.

Management of lithium poisoning

- (1) Gastric lavage should be carried out up to six hours after ingestion to remove any lithium remaining in the stomach.
- (2) A plasma or serum sample should be obtained for measuring lithium concentration. Remember that blood should not be collected into a lithium heparin tube.
- (3) Lithium is excreted by the kidneys, and a good urine output should be ensured. Forced diuresis does not greatly

increase excretion of lithium, however, and should not be used. Likewise, peritoneal dialysis is not recommended.

- (4) In a symptomatic patient with high plasma lithium concentrations after an acute overdose haemodialysis should be considered. Although well removed by haemodialysis, lithium has a large volume of distribution and repeated dialyses may be necessary.

Antipsychotic agents

Antipsychotic agents	
Phenothiazines	Thioxanthenes
Chlorpromazine	Cloperithixol
Fluphenazine	Flupenthixol
Methotrimeprazine	Butyrophenones
Oxypertine	Benperidol
Pericyazine	Droperidol
Perphenazine	Haloperidol
Pipothiazine	Trifluoperidol
Prochlorperazine	
Promazine	Diphenylbutylpiperidines
Thioridazine	Fluspiriline
Trifluoperazine	Pimozide

Chlorpromazine has been used to treat psychotic disorders for over 30 years, and many other phenothiazines and related drug groups are now also used.

In therapeutic use parkinsonian rigidity and tremor are common and often require treatment with anticholinergic drugs such as orphenadrine, which can themselves be toxic in overdose. Excessive doses in therapeutic use may cause drowsiness, tremor, or convulsions. Patients may die suddenly while under treatment: the reason for this is not clear ("phenothiazine sudden death"). The neuroleptic malignant syndrome is another complication which may occur at any time in patients under treatment, hours or months after initial exposure to the drug. It consists of muscular rigidity, hyperthermia, rapid pulse and respiration, lethargy, and coma. Mortality is 30%.

In overdose the antipsychotic agents can cause drowsiness, hypotension, tachycardia, supraventricular and ventricular tachyarrhythmias, and convulsions. Acute dystonic reactions sometimes occur after overdosage.

Management of poisoning with antipsychotic drugs

- (1) Gastric lavage should be performed up to six hours after ingestion.
- (2) Activated charcoal should be given.
- (3) Supportive care is the mainstay of treatment.
- (4) Dystonic reactions normally respond rapidly to procyclidine 5-10 mg or orphenadrine 20-40 mg given intramuscularly or intravenously.
- (5) Dantrolene is the drug of choice in the neuroleptic malignant syndrome.

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What are the merits of the implant operation for cataract? What are the contraindications for this procedure, and what are the complications over and above other cataract operations?

Most patients undergoing cataract extraction are elderly, and many find their thick glasses or contact lenses difficult to see through and to handle. But patients receiving an intraocular lens at the time of their cataract operation enjoy almost immediate improved sight. Intraocular lens implantation is therefore becoming an increasingly popular surgical option, and world wide over one million intraocular lenses have now been implanted. An intraocular lens offers patients permanent correction of their aphakia, and with newer techniques the surgeon can now decide which power of lens a particular patient needs, although spectacles are usually necessary to focus the vision exactly for distant and near objects. As to whether the lenses are safe, the early problems of design were that they were too heavy and the materials and methods used were of poor quality or toxic.¹ These problems have been virtually solved and with microsurgical techniques an intraocular lens implantation is tolerated by almost every eye. Large clinical studies in the United States and smaller studies in the United Kingdom underline the safety of intraocular lenses when inserted by orthodox techniques and with approved materials.² As experience with lenses has expanded so too have the number of cases when the use of an intraocular lens is considered acceptable. In particular many younger patients with cataracts now receive intraocular lens implantations routinely. Their use is controversial and probably contraindicated in children, adolescents, patients with glaucoma or active uveitis, and diabetic patients with retinopathy.³

Many complications are directly related to the style of lens as well as to the anatomical site chosen for the fixation of the lens. There are three basic

positions in which a lens may be supported within the eye: the anterior chamber lens that spans the anterior chamber from drainage angle to drainage angle, the iris clip lens that is supported by the tissues of the iris, and the posterior chamber lens that lies behind the iris. Anterior chamber lenses have caused recurrent haemorrhages from the iris, damage to the drainage angle (sometimes with the formation of adhesions), uveitis, and glaucoma; during implantation of anterior chamber lenses it is possible to damage the corneal endothelium with the development of chronic corneal oedema. Nevertheless, anterior chamber lenses are widely and safely used and are particularly useful for secondary lens implantations. Lenses that clip on to the iris enjoyed a vogue in the 1970s and early 1980s but are less popular now because they are relatively unstable, moving continuously and causing chronic irritation of the iris, and releasing prostaglandins that are thought to lead to chronic macular oedema. Lenses placed in the posterior chamber of the eye, behind the iris, are occasionally unstable but on the whole their use seems to be the safest of the three lens types, though an extracapsular technique of cataract extraction is required. The arguments about technique and lens design will continue, but it is increasingly clear that intraocular lens implantation is a safe adjunct to good cataract surgery, and the improvements in the quality of vision enjoyed by patients receiving such an implant is much better than that offered by any of the other methods for correcting aphakia.—B A NOBLE, consultant ophthalmic surgeon, Leeds.

1 Drews RC. Quality control, and changing indications for lens implantation. *Ophthalmology* 1983;90:301-10.

2 Stark WJ, Worthen DM, Holladay JT, et al. The FDA report on intraocular lenses. *Ophthalmology* 1983;90:311-20.

3 Straatsma BR, Pettit TH, Wheeler N, et al. Diabetes mellitus and intraocular lens implantation. *Ophthalmology* 1983;90:336-43.