



# Poison HOTLINE

1-800-222-1222

November 2015



## Did you know .....

In an overdose, the half-life of a drug will probably be altered.

The half-life of a given medication is how long it takes the body to get rid of half of the dose. The half-life is commonly used in routine therapeutic drug monitoring to facilitate drug dosing.

In an overdose, the half-life of the drug is not the same as with routine therapeutic dosing. Drug half-life will be affected by changes in drug absorption, protein binding, elimination, and renal and liver function which occur in an overdose.

In general, there is no relationship between therapeutic half-life and duration of the drug's effects in a significant overdose.

## Tricyclic Antidepressants

Tricyclic antidepressants (TCA's) play an important role in the treatment of a wide range of disorders such as depression, panic disorder, social phobia, bulimia, narcolepsy, attention deficit disorder, obsessive compulsive disorder, childhood enuresis, and chronic pain syndromes. Some of the more commonly prescribed TCAs include amitriptyline, desipramine, imipramine, nortriptyline, doxepin, and clomipramine.

TCA's are structurally similar to the phenothiazine class of antipsychotics. The toxic dose of TCA's may be only three to four times the normal therapeutic dosing and is even less in children. These drugs block the reuptake of norepinephrine, serotonin, and dopamine in the brain. The toxic effects of TCA's in overdose include anticholinergic effects, alpha-adrenergic blocking effects (vasodilation), and blockade of cardiac fast sodium channels (quinidine-like effect) which can cause significant cardiac conduction abnormalities and depress cardiac contractility.

EKG changes can predict possible complications from a TCA overdose: seizures are seen in 33% of patients with a QRS >100 mSec; ventricular arrhythmias are seen in 14% of those with QRS >100 mSec and in 50% of those with QRS >160 mSec. Severe cardiac toxicity usually develops within six hours, although EKG changes may persist for 48 hours or more.

Treatment of TCA toxicity focuses on airway management, benzodiazepines for seizures, sodium bicarbonate for QRS >100 mSec or hypotension, and IV fluids or norepinephrine for hypotension. Serum alkalization with sodium bicarbonate is an important treatment for EKG changes and hypotension because it increases the amount of protein-bound TCA (i.e. decreases free TCA in the serum) and helps reverse the sodium channel blockade effects. Hemodialysis is unlikely to be effective in removing TCA's due to the high protein binding and large volume of distribution. For treatment advice concerning TCA overdose, contact the IPCC at **1-800-222-1222**

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