

JULY 2007  
QUESTION 3

Pharmacological effects and principles of management of a TCA overdose

### TCA Mechanism

Inhibition of presynaptic neurotransmitter reuptake  
    norepinephrine  
    serotonin  
Blockade of cardiac fast sodium channels  
Antagonism  
    central and peripheral muscarinic acetylcholine receptors  
    peripheral alpha-1 adrenergic receptors  
    histamine (H1) receptors  
    CNS GABA<sub>A</sub> receptors

### Physiological Response

#### Cardiovascular

Sinus tachycardia most common (vagolytic)  
Hypertension or refractory hypotension  
Na Channel blockade causes  
    Dose related QT prolongation  
    Widened QRS  
    RBBB

#### CNS

Brief excitement/restlessness  
Myoclonus, tonic clonic seizures, dystonia  
Coma, respiratory depression

#### PNS

Antimuscarinic - atropine like reaction  
Mydriasis, flushed skin, dry mucosae, absent bowel sounds, urinary retention

### Pharmacokinetics

Highly protein bound, lipophilic and with a large volume of distribution  
    Haemoperfusion, dialysis and diuresis are not indicated  
Metabolised in the liver, half life can be prolonged (days)

### Treatment

Airway, Breathing, Circulation  
Baseline bloods, including paracetamol levels  
Gastric lavage and activated charcoal should be initiated early  
    TCAs have high absorption through the gut  
Hypotension resuscitation with isotonic crystalloids (alpha adrenergic vasoactives if needed)  
Increasing arterial pH to > 7.45 reduces available free drug reducing cardiotoxicity  
    sodium bicarbonate should be initiated in all pts with ECG abnormalities  
Arrhythmias best treated with 1a antiarrhythmics (action potential lengthened) eg Lignocaine  
Seizures managed by benzodiazepines