THE MEDICAL MANAGEMENT OF INTOXICATION

GENERAL PRINCIPLES

Intoxication with central nervous system (CNS) depressant drugs (alcohol, opiates, sedative-hypnotics, solvents) may cause death either directly through depression of brainstem centres responsible for maintaining essential bodily functions such as respiration, or indirectly through accidental injury or inhalation of vomit. The effects of such drugs are additive, and thus although an overdose of a benzodiazepine is rarely fatal in itself, it may well cause death if taken together with another CNS depressant drug. Intoxication with central nervous system stimulant drugs such as cocaine and amphetamine may cause death directly through cardio- and cerebro-vascular complications, or indirectly through accidental or self-inflicted injuries sustained while psychotic. The regular use of all substances is associated with an increased risk of suicide and deliberate self-harm. (*See appendix 3*, page 117 for characteristic intoxication syndromes).

- Intoxication with any substance of misuse is potentially life-threatening either through direct pathophysiological effects or/and through an increased risk of suicide, violence and accidents.
- Baseline management will include supportive measures (maintenance of airway and circulation), taking a history from informants paying special attention to the possibility of polydrug use, and collecting urine (or blood) for toxicological analysis.
- Immediate transfer to hospital should be arranged where there is marked CNS depression or marked behavioural disturbance.

ALCOHOL INTOXICATION

Acute intoxication with alcohol progresses from euphoria to incoordination and ataxia, to confusion, stupor and coma. The blood level of alcohol at which these stages occur is lower in women and children but higher in those physically dependent on alcohol. In all cases other causes for apparent intoxication should be sort including head injury and hypoglycaemia. Toxicological analyses and careful observation are essential together with a strong awareness of the risk of accidental or intentional overdose. Parenteral thiamine should always be given **before glucose** if hypoglycaemia is to be treated, to prevent precipitation of Wernicke's Encephalopathy.

ALCOHOLIC COMA

This serious disorder has a mortality rate of 5%. Admission to hospital is essential to maintain vital functions and counteract other conditions that may threaten. Inhalation of vomit and resulting acute respiratory distress due to Mendelson's syndrome is frequently fatal. It is necessary to monitor vital functions to avoid metabolic complications such as lactic or keto-acidosis, hypoglycaemia, hyponatraemia etc. Many interventions may be necessary including haemo- and peritoneal dialysis, to prevent death.

OPIATE INTOXICATION

Severe intoxication or overdose with opiate drugs is a **medical emergency**. 'Overload' of central nervous system (CNS) mu (μ) receptors may lead to respiratory depression and death. Many such deaths occur in longer-term injecting opiate misusers who have recently lost their tolerance through a period of abstinence, and fail to account for this when re-starting use of opiates, often following release from prison. However, opiate overdose and death may occur with any route of delivery and also involves individuals who have not lost their tolerance; for example an exceptionally pure batch of heroin may become available which is not recognised as such by the user.

SEDATIVE-HYPNOTIC INTOXICATION

Mild to moderate toxicity presents in a similar way to intoxication with alcohol, with slurred speech, ataxia and incoordination. Delirium may supervene with relatively small doses in the elderly. With more severe intoxication stupor and coma develop. To this point the effects of intoxication are similar for all sedative drugs. Significant differences are present between sedative classes when very high doses are consumed.

BARBITURATES

Toxicity may progress to fatal respiratory arrest or cardiovascular collapse. An additional danger is presented by the potential of some barbiturates to induce tolerance to their therapeutic effects but less so to their lethal effects. The maintenance dose may then approach the lethal dose, and only small increases above the individual's regular dose can lead to death.

BENZODIAZEPINES

Benzodiazepines virtually never lead to death when ingested by themselves. The several deaths that have occurred involved the newer, short-acting high potency benzodiazepines such as alprazolam and triazolam (Litovitz, 1987). However, benzodiazepines are often implicated in deaths associated with polydrug misuse, when used in combination with alcohol, opiates, major tranquillisers or sedative antidepressants due to their synergistic CNS-depressant action (*see appendix 9*, page 129 for illicit drug/drug interactions).

INTOXICATION WITH SOLVENTS

Intoxication with solvents presents with a picture similar to that of intoxication with alcohol. Behavioural changes together with signs such as nystagmus, incoordination, slurred speech may progress to lethargy, psychomotor retardation and stupor or coma. Death ('sudden sniffing death') may occur from respiratory or cardiovascular depression, acute arrythmias, hypoxia or electrolyte abnormalities. Distinguishing signs include an odour of paint or solvents, conjunctival irritation, 'glue sniffer's rash' around the mouth or nose. Signs of chronic solvent use may be present including jaundice (hepatitis), peripheral and cranial nerve neuropathies, pyramidal tract signs, and signs of chronic renal failure.

STIMULANT INTOXICATION

The acute psychomotor stimulant effects of cocaine, amphetamine and methylamphetamine, including restlessness, irritability, talkativeness, anxiety, panic attacks, lability of mood, headache, chills, vomiting and sweating, are principally attributable to increases in CNS catecholamine neurotransmitter activity. Enhanced catecholamine activity occurs through stimulant-mediated blockade of the neurotransmitter presynaptic reuptake pumps (cocaine) and by presynaptic release of catecholamines (amphetamine). Behaviourally, disinhibition, hypervigilance, compulsive or stereotyped behaviour, paranoia and acute psychosis may supervene. The occurrence of hyperthermia is associated with misuse of Ecstasy.

In very high doses, an acute organic brain syndrome (delirium) may supervene, characterised by clouding of consciousness and disorientation in time and place, with or without delusional thinking and hallucinations. Such reactions are usually self-limiting and should be treated symptomatically, having excluded an underlying acute neurological lesion (see below). Chronic, frequent use of stimulant drugs may lead to the development of a chronic paranoid perspective or fully formed psychosis that is difficult to differentiate from schizophrenia.

Medical complications of stimulant intoxication may be serious and life-threatening; cocaine intoxication is the commonest cause of myocardial infarction in young males presenting to A&E departments. The medical aspects of cocaine intoxication can be divided into three phases (Weiss, Greenfield & Mirin, 1994). The first phase presents with the psychological/behavioural effects described above and mild physiological effects, usually not requiring specific treatment. The second phase is characterised by myocardial ischaemia or infarction, seizures, malignant encephalopathy, incontinence and ventricular dysrhythmias. The third (premorbid) phase is characterised by coma, paralysis, and fixed, dilated pupils. Other complications include hyperthermia (which may suggest a more severe prognosis (Weiss, Greenfield & Mirin, 1994)) leading to reversible coagulopathy and renal failure, cerebral and pulmonary oedema, cerebral haemorrhage, rhabdomyoloysis, myoglobinuria, nephrotoxicity and hyperkalaemia (Callaway & Clark 1994).

INTOXICATION WITH OTHER SUBSTANCES

CANNABIS

Intoxication is characterised by behavioural changes such as euphoria and impaired motor coordination but in some individuals social withdrawal, anxiety and panic. Conjunctival injection, tachycardia, dry mouth and increased appetite occur frequently. The course is self-limiting to several hours and is never directly life-threatening. Intoxication may occasionally precipitate a psychotic reaction in vulnerable individuals.

HALLUCINOGENS (LSD, MAGIC MUSHROOMS)

Intoxication is characterised by a mild to moderate stimulant reaction with pupillary dilation, tachycardia and sweating, leading onto intense perceptual and mood changes. Intoxication is only very rarely directly life-threatening (see stimulant intoxication), although death may occur through suicide or accidents.

PHENCYCLIDINE (PCP)

Behavioural changes and physical signs such as nystagmus, hypertension, tachycardia, diminished responsiveness to pain, ataxia, slurred speech occur after moderate doses. Higher doses may progress to cardiorespiratory depression, coma and death. Psychosis may supervene in vulnerable individuals.

NICOTINE

Intoxication occurs only very rarely and has been poorly studied.

THE MEDICAL MANAGEMENT OF INTOXICATION

1 Institute general supportive management – maintain airway, support breathing and cardiac function as required.

2 Treat hyperthermia (over 102°F) aggressively with ice packs, cold water and hypothermic blankets if available.

3 Treat seizures with parenteral or per rectal diazepam.

4 If respiratory depression due to opiate overdose is suspected, administer naloxone hydrochloride 0.4 to 0.8mg IV (IM if venous access not immediately obtained). Repeat as required.

5 Arrange emergency transfer to A&E if indicated by baseline physical examination or behavioural disorder.

6 If history is available from relatives or friends establish the amount and type of drug used as well as time of last use.

7 Ask about poly-drug misuse – death associated with opiate overdose is often complicated by concurrent misuse of benzodiazepines which adds to generalised CNS depression – this has immediate implications for acute management as administration of flumazenil may reverse the benzodiazepine-induced component of the CNS depression (although this may cause seizures in benzodiazepine-dependent subjects).

8 Confirm the presumptive diagnosis on physical examination.

9 Collect urine (or if not possible blood) for toxicological analysis, bearing in mind the possibility of poly-drug misuse.

10 Following arrival at hospital and confirmation of toxicology, behavioural disorder may be treated with a combination of a high potency neuroleptic (typically haloperidol) and a benzodiazepine. It is **essential to use a high potency neuroleptic (such as haloperidol)** to avoid exacerbation of stimulant-induced anticholinergic effects.

11 Patients treated for opiate overdose must be observed for a period of hours – if a longer-acting opiate such as methadone is responsible for the overdose, the effects of naloxone may 'wear off' before those of the methadone, leading to re-occurrence of respiratory depression.