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Recreational drug toxicity

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Introduction

In 2005–6, 10.5% of people aged 16–59 years who lived in England and Wales had used at least one illicit drug in the previous year and 3.4% had used a class A drug (Table 1), so it is not surprising that presentations to hospital with toxicity are common.¹ The age-standardised mortality associated with drug misuse increased between 1993 and 2000 but has declined since then. Most deaths involve men and people who are using opioids/opiates, especially heroin, methadone and dihydrocodeine, but deaths associated with cocaine and codeine have been increasing (Fig 1).² Recreational drug toxicity occurs in the

context of other health and social problems that may also need to be addressed – for example, social and criminal justice issues, mental health problems and alcohol and tobacco abuse, as well as bloodborne virus infection, thrombosis and infections in intravenous users.

Cannabis

Smoking or ingestion of cannabis, which is derived from the plant *Cannabis sativa*, is common, but it is unusual for users to require hospital treatment. They occasionally present with disorientation, anxiety or tachycardia, and arrhythmias such as atrial fibrillation have been reported. Long-term use has been connected with psychosis and chronic lung disease.³

Stimulants

Sympathomimetic amines – for example, amfetamines, ecstasy, piperazines and cocaine – act by enhancing central release and inhibiting reuptake and metabolism of catecholamines and serotonin. This results in increased concentrations of norepinephrine, epinephrine, dopamine or serotonin, or their combination, within the synaptic cleft.

These substances share a number of clinical effects, although their precise mode of action and potency for causing each differs. The effects produced

Key Points

Toxicity associated with recreational drug use is a common reason for presentation to hospital

Most deaths are associated with heroin, methadone, benzodiazepines and cocaine. Deaths due to cocaine are increasing in the UK

Stimulants (for example, amfetamines and cocaine) have adrenergic effects. Serious complications of toxicity are most common with cocaine and include metabolic acidosis, convulsions, rhabdomyolysis, myocardial infarction and stroke

Toxicity from opiates and opioids is exacerbated by co-ingestion of alcohol and other sedatives and those with recent abstinence. Opioid effects can be reversed by the competitive antagonist naloxone

Treatment of benzodiazepine toxicity with the antidote flumazenil can increase the level of consciousness but may cause convulsions and acute benzodiazepine withdrawal

KEY WORDS: cocaine, ecstasy, gamma hydroxybutyrate, heroin, poisoning

Table 1. Examples of potential drugs of misuse and their classification under UK Misuse of Drugs legislation.

Schedule ¹		Class ²		
		A	B	C
		Most harmful	Intermediate	Least harmful
1	No recognised medical use Possession prohibited without licence from Home Office	Ecstasy LSD		Cannabis
2	Recognised medical use Subject to special prescription and safe custody requirements and the need to maintain registers	Morphine Diamorphine Methadone Cocaine	Amfetamines Methylamfetamine Dihydrocodeine Codeine	
3	Subject to special prescription although not to safe custody requirements		Barbiturates	Temazepam Flunitrazepam
4 (Part 1)	Subject to neither special prescription nor safe custody requirements			Other benzodiazepines Zolpidem GHB Ketamine
4 (Part 2)				Anabolic steroids
5	Preparations that, because of their strength, are exempt from most of the controlled drug requirements			Cough medicines Antidiarrhoeals

GHB = gamma hydroxybutyrate; LSD = lysergic acid diethylamide.
¹Misuse of Drugs Regulations, 2001.
²Misuse of Drugs Act, 1971

include a feeling of wellbeing, increased energy, increased self-esteem and alertness. At higher doses, adrenergic effects, such as anxiety, sweating, tachycardia,

hypertension and dilated pupils, are common. Subsequently, confusion, hallucinations, agitation, vomiting and abdominal pain may occur. Serious com-

plications include metabolic acidosis, tachyarrhythmias, convulsions, chest pain, hyperpyrexia, cerebral infarction or haemorrhage (Fig 2), rhabdomyolysis, disseminated intravascular coagulation, renal failure and myocardial infarction.^{4,5} Severe effects are more common after intravenous use or overdose.

Patients who present with toxicity should undergo cardiovascular and ECG monitoring. A 12-lead ECG should be performed and blood should be taken for measurement of electrolytes, bicarbonate and hepatic and renal function. Blood gases and creatinine kinase should be obtained when severe poisoning is suspected. Activated charcoal may reduce absorption after ingestion, but most patients present with established clinical effects, at which point this treatment is unlikely to affect outcome. Further management is directed at complications (Table 2).

Amfetamines

Recreational use of amfetamines is usually via ingestion, nasal inhalation of powder ('snorting') or injection. The

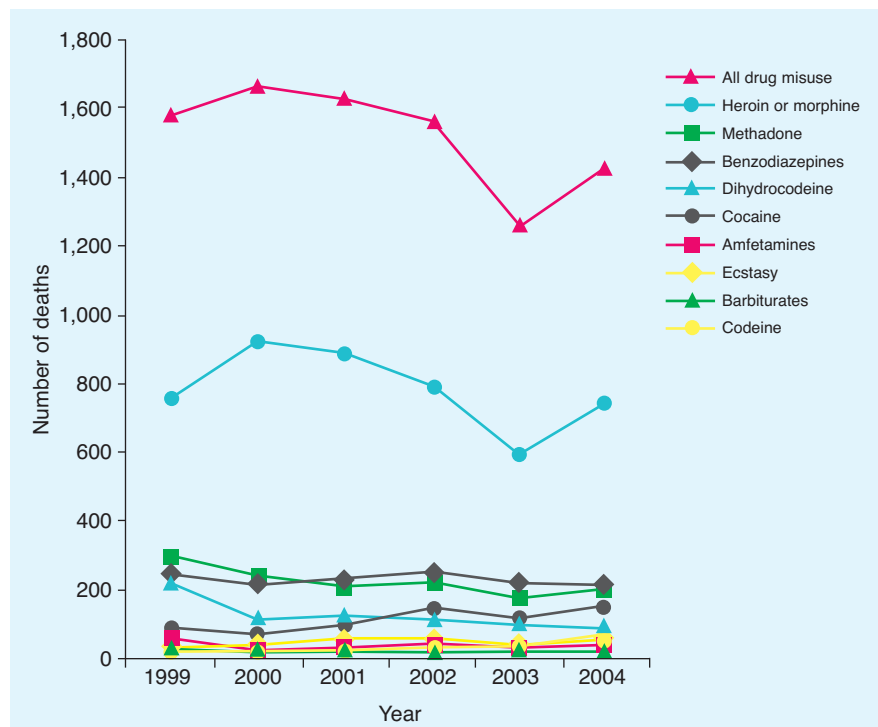


Fig 1. Number of deaths for some specific substances involved in deaths related to drug misuse, 1999–2004. Data sourced from Reference 2.

latter two routes give more rapid and intense effects. There is considerable individual variation in response, and tolerance develops in habitual users. Use of methamphetamine has been increasing in some countries.

Adrenergic clinical effects are common and may be associated with increased appetite and headache. As these effects wear off, restlessness, fatigue and depression may ensue, which encourages the user to take further doses. Chronic use is associated with aggressive behaviour, delusions and paranoia ('amphetamine psychosis').

Ecstasy

Ecstasy (3,4 methylenedioxyamphetamine (MDMA)) is a semi-synthetic amphetamine-like drug that is usually taken by ingestion. It increases central concentrations of serotonin and, to a lesser extent, dopamine. The half-life is about eight hours; clinical effects occur within about 20 minutes of ingestion and may last six hours or more. Ecstasy commonly causes adrenergic effects similar to, although generally less intense than, those seen with other sympathomimetic amines. Nausea and trismus are common.

Occasional patients may develop severe apparently idiosyncratic adverse

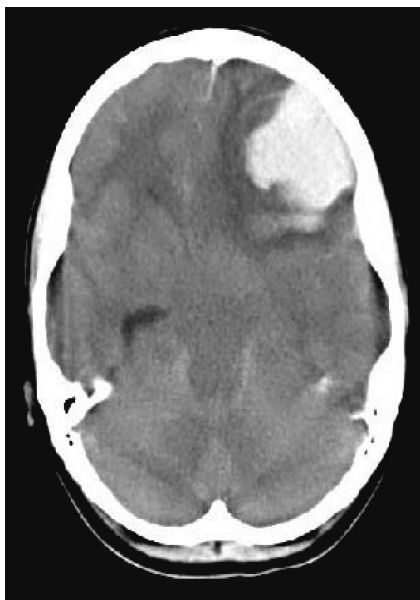


Fig 2. Intraparenchymal cerebral haemorrhage in an intravenous user of amphetamines.

Table 2. Complications and management of sympathomimetic amine toxicity.

Complication	Notes on management
Confusion, behavioural disturbances	Diazepam or lorazepam
Tachyarrhythmias	Avoid treatment unless cardiovascular compromise Correct pH and electrolytes Diazepam or lorazepam if supraventricular and associated with agitation β blockade may be effective but risks hypertension due to unopposed alpha stimulation Calcium channel blockade may also be considered
Hypertension	Diazepam or lorazepam. Consider infusion of glyceryl trinitrate (GTN) if diazepam/lorazepam ineffective and hypertension is severe
Seizures	Diazepam or lorazepam
Acidosis	Correct with sodium bicarbonate
Hyperpyrexia	Physical cooling methods Consider dantrolene if cooling ineffective
Rhabdomyolysis	Intravenous fluids Urinary alkalisation Monitor renal function and potassium Dialysis for renal failure or severe hyperkalaemia

effects, including fulminant hepatic failure, aplastic anaemia or a syndrome similar to neuroleptic malignant syndrome. Hyponatraemia may also occur because of inappropriate antidiuretic hormone action. This is worsened if users drink large amounts of fluids.⁶

Management is as for poisoning with other sympathomimetic amines. Hepatic failure should be treated conventionally. Liver transplantation has been performed successfully for patients with fulminant hepatic failure.

Cocaine

Cardiovascular complications are particularly common with cocaine and include arrhythmias, myocardial ischaemia or infarction, aortic or coronary dissection,⁷⁻⁹ intracerebral or subarachnoid haemorrhage and cerebral infarction.⁴ Management is supportive (Table 2). If adequate sedation or glyceryl trinitrate infusion fail to control hypertension, a calcium channel blocker may be effective. Ventricular arrhythmias may respond to lidocaine, but this should be used only once the pH has been corrected.

Chest pain may herald coronary ischaemia or infarction in cocaine intox-

ication. Initial treatment should be with diazepam and nitrates. Aspirin and intravenous nitrates should be given to patients with features of ischaemia on ECG. Conventional thrombolysis should be considered if there are no contraindications. Troponin I should be measured after an appropriate interval.

Hyperpyrexia with cocaine may be life-threatening and must be treated aggressively – for example, using ice baths and possibly dantrolene.

Piperazines

A variety of piperazine-based recreational drugs are emerging, including benzylpiperazine, phenylpiperazine (trifluoromethylphenylpiperazine, TFMPP) and 1-(meta-chlorophenyl)piperazine (mCPP). These are usually taken as tablets, but intravenous use has occasionally been reported. These drugs stimulate release of dopamine and norepinephrine and inhibit reuptake of serotonin, dopamine and norepinephrine. Clinical effects are similar, although usually less marked, than those of the amphetamines. Cerebral oedema and convulsions have been reported.^{10,11} Management is as for other sympathomimetics (Table 2).

Opiates and opioids

Heroin (diacetylmorphine) is highly addictive. Although absorbed rapidly when taken by mouth, inhaled as a powder or smoked, serious toxicity is less common via these routes, and most deaths occur after intravenous injection.¹² Methadone is widely available, and misuse is common, with effects similar to heroin but much more prolonged. In addition, the drug may cause delayed ventricular repolarisation, QT interval prolongation and torsade de pointes ventricular tachycardia.¹³ Life-threatening poisoning is well recognised after oral ingestion. Oxycodone can also produce prolonged and severe toxic effects. Illicit use of codeine, dihydrocodeine and tramadol is also common, but these are less potent agents and serious poisoning is uncommon unless large doses are taken. Abuse of dextropropoxyphene, as a constituent of co-proxamol, is becoming less common now that this preparation is being phased out.

Characteristic clinical features of intoxication include nausea, vomiting, confusion and hallucinations, which progress to miosis, hypotension, tachycardia, central nervous system and respiratory depression or arrest. Rhabdomyolysis, renal failure, aspiration pneumonia and non-cardiac pulmonary oedema may occur. The presence of needle tracks may be a clue as to aetiology in a patient who presents with unconsciousness. Life-threatening intoxication is more common after a period of abstinence (for example, after release from prison) and with co-ingestion of sedatives, including alcohol and/or benzodiazepines.¹²

The short-acting, lipid-soluble, competitive opiate receptor antagonist naloxone penetrates the central nervous system rapidly to reverse the features of toxicity after intravenous injection. It may also be given effectively via the intramuscular or subcutaneous routes. The aim of naloxone treatment is to ensure that the patient is sufficiently conscious to maintain their airway and ventilation, and doses should be titrated carefully to achieve this. Although substantial doses may be required for seriously poisoned patients, excessive doses

may precipitate acute withdrawal syndromes associated with confusion or aggression. Patients may then leave hospital and subsequently develop recurrent opiate toxicity. Patients should not be discharged from hospital until at least six hours after the last dose of naloxone is given. Other reported adverse effects of naloxone are seizures, pulmonary oedema and arrhythmias, although these seem to be uncommon.¹²

Pending treatment with naloxone, patients should be given supportive management including adequate oxygenation and attention to the airway. Before and after naloxone treatment, frequent monitoring of the pulse, blood pressure, oxygen saturation and level of consciousness should be performed. Otherwise, treatment is supportive and symptomatic

Benzodiazepines

Benzodiazepines, including diazepam and temazepam, are commonly misused and frequently implicated in intentional or accidental poisoning. Clinical effects include drowsiness, unsteadiness, nystagmus and slurred speech. Coma associated with reduced tendon reflexes may occur, especially in those with underlying respiratory or neurological disease or when alcohol or other sedative agents have been co-ingested.

Management is supportive. Activated charcoal may be beneficial if given within one hour of ingestion. The level of consciousness can be improved by administration of the specific antagonist flumazenil, but this may be at the expense of adverse effects, including convulsions (especially in those with a history of seizures or co-ingesting proconvulsant agents) and acute withdrawal. Current guidelines in the UK suggest that flumazenil may be used for patients who would otherwise require intubation and ventilation provided there are no contra-indications. Small initial doses should be used by staff who have appropriate training.¹⁴

Gamma hydroxybutyrate

Gamma hydroxybutyrate (GHB) is an endogenous neurotransmitter and

gamma aminobutyric acid (GABA) agonist originally developed as an anaesthetic agent. The related compounds gamma butyrolactone (GBL) and 1,4-butanediol (1,4-B) are prodrugs of GHB and have similar actions.

The principal clinical effects of these compounds are neurological and include headache, agitation, ataxia, progressive confusion and drowsiness, which are often associated with tremor and myoclonus. Nausea, vomiting and diarrhoea are also common. In severe cases, coma with reduced tendon reflexes and respiratory depression develop, especially if alcohol or other sedatives are involved. Bradycardia and hypotension, metabolic acidosis, electrolyte disturbances and hyperglycaemia may occur.¹⁵ Coma may be prolonged but with a characteristic abrupt recovery.

Treatment is supportive. Appropriate airway and respiratory management are essential.

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