Illegal substances in anaesthetic and intensive care practices

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Key points
The National Poisons Information Service provides expert advice through Toxbase http://www.toxbase.org or +44 844 892 0111. Consult them in all cases of severe poisoning.

Resuscitate to conventional guidelines but treat arrhythmias with magnesium and bicarbonate. Anti-arrhythmics are used only after expert advice.

Death results from hyperthermia, rhabdomyolysis, or arrhythmias; vigilance for these is crucial. Serial ECGs may predict malignant arrhythmias.

Blood tests should always include urea, electrolytes, bone profile, liver function, paracetamol level, glucose, creatine kinase, full blood count, and clotting profile.

Slang terms should not be used to identify drugs; this language evolves rapidly and regional variations exist.

General overview of illegal substances
Misure of drugs for recreational purposes is common in the UK. The use of some drugs, for example, ethanol and nicotine, are legal, while others are regulated under the Misuse of Drugs Act 1971. This defines a controlled drug as any substance or product for the time being specified in Part I, II, or III of Schedule 2 to this Act and there may be a delay before substances are added to the list. Similarly, as evidence accumulates, a drug may be moved from one schedule to another. Parts I, II, and III are lists of Class A, B, and C drugs, respectively, which carry varying penalties for production, supply, or possession. The number of deaths directly attributed to drug misuse is increasing and was 1608 in England and Wales in 2005. Similarly, the number of adults admitting illicit drug use during that year increased, equating to 10.5% of the population with 3.4% using Class A drugs.1 However, the actual incidence of drug-related deaths may be higher, as drug abusers are at increased risk of suicide and may choose non-toxic methods of self-harm. Users of illegal substances may be reluctant to admit their habit and careful questioning is required.

If not recorded in the initial history, clinicians may discern the situation retrospectively as patients withdraw or develop other complications of their drug misuse during their admission.

Although a history may not be forthcoming initially, clearly the type and pattern of use is important as patients may have developed tolerance or dependence with chronic use or may be acutely intoxicated. This has a bearing on their pharmacology, psychology, and changes in pharmacodynamics and pharmacokinetics. In addition to adverse effects directly related to the pharmacology of each drug of abuse, users may also suffer ill health arising from the circumstances of use. These include complications arising from the route of abuse and those associated with malnutrition and lifestyle (e.g. tuberculosis). The route of administration of the most addictive drugs is often parenteral. Inhalation and i.v. routes are often used which minimize onset time and first-pass metabolism. I.V. injection can be the cause of infections, including local abscess formation and infective endocarditis which usually involves the right side of the heart. Cutting agents are relatively inexpensive chemicals added to street drugs to dilute them and maximize profit. They are increasingly sophisticated, for example, cocaine can be cut (mixed) with lidocaine, capitalizing on the similar effect of lidocaine at least on the nasal mucosa. Other cutting agents include sugars, vitamins, and over-the-counter drugs. Cutting later in the supply chain by inexperienced dealers, for example, with tale can cause ventilation–perfusion mismatch on injection of solubilized product; this in turn is associated with pulmonary hypertension.

Venous thrombosis is a common complication of i.v. drug abuse and this may make vascular access difficult, particularly in chronic abusers. Inhalation induction of anaesthesia or central venous access may be required if peripheral veins have thrombosed. If this is the case, then the central line should be removed as soon as the patient is ambulant or unsupervised to minimize the risk of air embolism, infection, or overdose if the venous catheter is abused.

All patients should have their nutritional status assessed and vitamin supplementation should be considered, for example, in those with chronic alcohol abuse and susceptible to developing a withdrawal syndrome. Similarly, the risk of refeeding syndrome should be considered.

Drug interactions are common with illegal substances and include volatile anaesthetic agents. For example, sedating substances reduce minimum alveolar concentration (MAC)
and stimulants will increase it. Serotonergic drugs may involve interactions producing raised 5-hydroxytryptamine and a serotonin syndrome. Features of serotonin syndrome are shown in Table 1.

Tolerance to opioids arising from chronic abuse can result in substantially increased dosing requirements should these drugs be administered therapeutically. Drug withdrawal, for example, from opioids or alcohol is a risk factor for delirium and increased length of stay in hospital. It is best managed by anticipating the problem and carefully observing the patient, rather than facing the avoidable challenges of managing agitated patients who may be distressed, tachycardic, and hypertensive. Opioid withdrawal may be managed either by symptomatic treatment or by preventing withdrawal by administration of substitute opioids or clonidine. Scoring systems, for example, the Clinical Institute Withdrawal Assessment alcohol withdrawal scale, have been used successfully for patients with alcohol addiction and may enable smaller overall doses of benzodiazepines to be administered. Consideration should be given to vitamin substitution and control and prevention of seizures with benzodiazepines.

Patients who have concealed substantial quantities of illicit drugs by ingestion may be a particular challenge in the intensive care and anaesthetic setting. ‘Body stuffers’ are individuals who hastily ingest wrapped packets of illegal substances in order to evade detection by the authorities. These have often already been divided into ‘single doses’. The drugs may not be wrapped well and may result in early leakage. The body stuffers may also be regular users and may have developed a tolerance to the effect, for example, heroin. ‘Body packers’ ingest carefully wrapped packages of illegal substances in order to evade border security checks as in Figure 1. Substantial numbers of packets may be ingested and each package may contain several lethal doses of a drug. They may also coingest anti-diarrhoeal agents, for example, loperamide, to decrease gut motility. If the packaging is breached in either circumstance, then a potentially life-threatening dose of a drug of abuse may be received, with rupture of packages from body packers posing a greater risk. The diagnosis should be considered in patients who present with a decreased level of consciousness, particularly after plane flights from parts of the world where the export of illicit drugs is common. A urine drug screen may be positive if packets have started to leak. Although the effects of heroin leakage may be antagonized with very large doses of naloxone, it should be noted that those who are not regular users are at particular risk as regular users may have developed a degree of pharmacological tolerance. Initial i.v. naloxone dose is 0.4–2 mg in severe heroin intoxication, repeated within 2 min if there has been no response. Rupture of packages containing cocaine may be more troublesome, producing refractory hypertension and cardiovascular effects.

### General management of poisoned patients

The general management of these cases is anticipatory and supportive and the importance of assessing airway, breathing, and circulation cannot be overemphasized. If the airway can be protected, activated charcoal may be indicated to decrease absorption if the patient presents within 1 h of ingestion. Whole-bowel irrigation is rarely performed and occasionally endoscopic retrieval may be indicated for body stuffers. Urgent surgery may be required for body packers or stuffers and these cases should be discussed with surgeons early.

For some drugs, including some sustained release preparations, multiple doses of activated charcoal are indicated as a method to enhance elimination. In severe poisoning with drugs of a low volume of distribution, extracorporeal elimination techniques including haemodialysis or haemofiltration may be considered. These cases must be discussed with the National Poisons Information Service. The particular investigations required for a poisoned patient will depend upon the substances which are thought to have been ingested. The threshold for measuring paracetamol is low, it is commonly ingested, and the consequences of failing to give antidote are serious. Supporting investigations must include urea and electrolytes, bone profile, liver function, glucose,

| Table 1 | Features of serotonin syndrome: a triad of symptoms and signs occurring as a result of ingestion of compounds, alone or in combination, with activity at serotonin receptors or inhibition of serotonin metabolism or reuptake. The differential diagnosis must include neuroleptic malignant syndrome |
| --- | --- | --- |
| Neurornuscular excitability | Autonomic disturbance | Mental changes |
| Tremor | Mydriasis | Headache |
| Stiffness | Tachycardia | Poor concentration |
| Hyperreflexia | Hypertension | Agitation |
| Clonus | Flushing | Confusion |
| Myoclonus | Hyperthermia | Coma |

![Fig 1](https://academic.oup.com/bjaed/article-abstract/13/2/42/283618) CT reconstruction of a suspected body packer taken in by police after he exhibited strange behaviour at an airport. It clearly demonstrates concealed packages; smaller packets are harder to discern from faecal matter on plain films. Image courtesy of Dr Frank Gaillard, Radiopaedia.org.
creatinine kinase, full blood count, and a clotting profile. Urine can be tested for urinary myoglobin. Other investigations will include ECGs to determine conduction and repolarization defects and arrhythmias. Consideration must be given to other possible causes for the patient’s condition, for example, head injury or intracranial infection. Conditions including rhabdomyolysis, disseminated intravascular coagulation, and serotonin syndrome must be considered if their consequences are to be minimized. Fasciotomies have been used in the management of compartment syndrome secondary to rhabdomyolysis, and dantrolene can be used as an adjunct to cooling in the management of hyperthermia when neuromuscular excitability in serotonin syndrome is a prominent feature.

**Cannabis**

Cannabis is the most commonly used drug of abuse in the UK. The Cannabis sativa plant produces more than 60 cannabinoids and modern strains contain higher concentrations than older varieties. Cannabis can be ingested or inhaled. Absorption after inhalation is rapid, whereas ingestion may produce erratic absorption; the effects may have a delayed onset and be prolonged for several hours. Acute toxicity is low, producing mood changes of anxiety and excitement progressing to calmness and a decreased level of consciousness. Rarely, cannabis psychosis may occur. Ingestion by children has produced hypotonia and coma. Dysphoric reactions are common in new users and may result in the drug not being used again. Vasodilatation is common and may result in hypotension. Agitation should be treated by reassurance, particularly in children, and if pharmacological intervention is required, benzodiazepines are the drugs of choice.

Long-term use has similar effects on the cardiovascular and respiratory systems as does smoking. Cannabis users have a tendency to maximize the inhaled dose by taking large breaths and then breath holding. This results in an associated increase in tar, carbon monoxide, and other carcinogens when compared with normal cigarette smoking.

The conduct of anaesthesia is little different from that of tobacco smokers, except that in acute intoxication, the effects of agitation and sedation need to be addressed. If withdrawal symptoms occur, they are generally mild, predominantly irritability and anorexia. They do not generally require any treatment. Anxiolytics may be given; however, little evidence favours their use. Nicotine patches can lessen the withdrawal effects from nicotine.

**Cocaine**

Cocaine has a long history, having been used by civilizations where the coca bush is native in South America. The local anaesthetic effect is largely irrelevant to current users who experience euphoria from its central inhibition of catecholamine and serotonin reuptake, although it may predispose to arrhythmias. However, ‘street cocaine’ may be contaminated with other local anaesthetic agents, including those that predispose to methaemoglobinemia. The effects of cocaine are predominantly sympathetic: tachypnoea, tachycardia, hypertension, chest pain with myocardial ischaemia or infarction, and arrhythmias. Vascular complications occur anywhere as a result of vasospasm, infarction, or dissection. Neurological features include anxiety, paranoia and psychosis, mydriasis, headache, subarachnoid haemorrhage, stroke, seizures, and coma. The serotonin syndrome may occur. This includes the triad of central nervous system effects, including agitation or decreased level of consciousness, autonomic instability, including raised temperature, and neuromuscular excitability (Table 1) which may be associated with an increased serum creatine kinase. Death is usually associated with hyperpyrexia and multiorgan failure.

General supportive care for these patients includes the use of benzodiazepines to treat agitation and seizures. Hypertension is best treated initially with benzodiazepines and subsequently with nitrates if it does not settle. Calcium channel blockers are an alternative if these measures prove ineffective. The use of β-blockers is controversial as they may produce an unopposed α-action and paradoxical hypertension. For this reason, it may be prudent to first achieve α-block with phentolamine if their use is considered; labetalol has not been shown to abolish coronary artery spasm. A more practical solution is the use of central sympatholytics such as dexmedetomidine or clonidine to provide anxiolytic and anti-hypertensive effects with a single agent. Dexmedetomidine may be a more feasible option in the management of cocaine overdose and general withdrawal effects now that it is available in the UK. Chronic cocaine use predisposes to accelerated atheroma, although in a small study of cocaine users presenting for elective surgery, this was not found to be associated with increased risk. This together with cocaine induced coronary vasospasm, and increased cardiac oxygen demand predisposes these patients to myocardial infarction. The diagnosis of cocaine abuse should be considered in young patients presenting with chest pain. Broad complex tachycardias should be treated with sodium bicarbonate.

**Ecstasy**

3,4-Methylenedioxymethamphetamine (MDMA) or ecstasy rapidly became popular during the late 1980s as the rave scene expanded. Users intend to achieve euphoria with added feelings of empathy, forgiveness, and increased energy and self-confidence. MDMA is profoundly serotonergic and can precipitate serotonin syndrome whether the user is on other serotonergic drugs or not. Sudden death can occur with ecstasy use; it is rare and of unclear cause. It may be due to arrhythmias from sympathetic stimulation or prolongation of the QT interval. Hyperthermia and rhabdomyolysis seen in severe serotonin syndrome in combination with exertional dehydration carries a high risk of death. Dantrolene can be used in conjunction with other cooling measures, resuscitation, and neuromuscular block. Severe hyponatraemia has led to cerebral oedema and death in some cases. This is thought to be as a result of overenthusiastic water ingestion after warnings about dehydration, repetitive behaviour, and to combat dry mouth. Given that this is due to
a rapid change in sodium concentration, it can be reversed quickly with hypertonic saline, give 100–200 ml (3%), recheck, and re-assess. Allow the patient to self-correct once the plasma sodium has increased by 6 mmol litre$^{-1}$ unless cerebral oedema persists. Manage the patient appropriately for raised intracranial pressure.

Other amphetamines such as methamphetamine (crystal meth) may have subtle differences in their desired effects and addictive properties, but the risks of serotonin syndrome, hyperthermia, and rhabdomyolysis remain.

### Opioids

An unconscious patient with pinpoint pupils, bradypnoea, and bradycardia should prompt a trial of naloxone. This is given i.v., although i.m. route is a good alternative, while venous access is sought. Doses up to 4 mg may be required in serious cases with an infusion of 60% of the initial dose per hour titrated to effect.$^7$ Naloxone is safe; however, bolus doses should be avoided in patients with suspected ischaemic heart disease as the rapid return of sympathetic activity could induce myocardial ischaemia. Rhabdomyolysis and compartment syndrome is a risk, even in the absence of a history of unconsciousness.$^3$ Hyperkalaemia should be managed conventionally with sodium bicarbonate. Hypocalcaemia should be permitted, provided that there are no ECG changes suggestive of hyperkalaemia and managed according to laboratory results rather than arterial blood gas machine analysis. Infusions of calcium should not be used as hypercalcemia and calcium deposition in tissues can occur in the recovery period.

Withdrawal from opioids is characterized by dysphoria, rhinorrhea, myalgia, and gastrointestinal symptoms such as diarrhoea 24–48 h after abstinence. The patient is likely to inform staff that they are withdrawing and they should make efforts to liaise with the coordinator of their care to establish the maintenance regime. This should be re-established quickly or methadone can be used at its starting dose of 10–40 mg in the interim. Other adjuncts are diazepam, clonidine, and loperamide, and β-blockade if tachycardia requires treatment. Heavy opioid users presenting for surgery should continue their maintenance and use adjuncts such as clonidine and regional blocks. They will require massive doses of opioids intraoperatively. They are at high risk of sepsis; therefore, non-steroidal anti-inflammatory drugs should be considered very carefully before use.

### Gamma hydroxybutyrate

Gamma hydroxybutyrate (GHB) is a metabolite of GABA and may act on GABA and GHB receptors. Large enough doses lead to a brief period of euphoria followed by coma and rapid recovery in 2–3 h. It is metabolized to carbon dioxide and water which favours its use as a ‘date rape’ drug.$^8$ Other central nervous effects are myoclonus which could be mistaken for fits were it not for miosis. Agitation and delirium can complicate emergence, and sweating is also a feature. Management is along conventional resuscitation guidelines, loss of airway, and bradycardia is a feature that responds to anti-muscarinics. Self-extubation is common and is a result of rapid emergence.$^5$

Withdrawal from GHB in chronic users produces an unexpected and startling syndrome. It is characterized by autonomic instability, aggressive delirium, psychosis, seizures, hyperthermia, and rhabdomyolysis. Massive doses of diazepam are often required, with phenobarbitial or an infusion of propofol to combat the central nervous effects and cooling and bicarbonate to reduce the risk of rhabdomyolysis.$^9$ Neuroleptics may lower the seizure threshold and are not recommended.

### Anabolic steroids

Anabolic steroids were developed as performance-enhancing drugs for athletes. Since they have been banned, detection techniques have markedly reduced their use in professional athletes and members of the armed forces. The use is now seen in bodybuilders, amateur athletes undergoing weight training, and occupations such as bouncers and security guards. The most common adverse effects are psychological and endocrinological. Cardiovascular effects are hypertension, thrombosis, and ventricular hypertrophy.$^{10}$ Focal areas of myocardial fibrosis are seen in cases of sudden death and these may represent a substrate for malignant arrhythmias. Liver dysfunction with raised transaminases and cholestasis occurs with risk of hepatocellular carcinoma in longer term use.$^{10}$ Preoperative evaluation should focus on accurate drug history and excluding cardiac disease. Physical signs in a muscular patient such as acne, striae, gynaecomastia, and needle marks or hirsutism in a female should prompt suspicion. Liver function should be added to routine blood tests; an ECG and echocardiogram are mandatory.$^{10}$ Increased muscle mass causes decreased thoracic compliance, increased oxygen requirement, work of breathing, and carbon dioxide production warranting a tracheal tube in preference to a laryngeal mask airway for most procedures. Resistance to non-depolarizing neuromuscular blocking agents has been attributed to an increase in nicotinic receptors; succinylcholine is not contraindicated but will result in more energetic fasciculations.$^{10}$

### New agents and hallucinogens

Mephedrone entered the news in early 2010 and this prompted a Department of Health alert. Although there have not been any reported deaths from its use in isolation, it has amphetamine-like effects and should be managed in large doses according to MDMA as above. Hallucinogens such as lysergic acid diethylamide or the legal hallucinogen, Salvinorin A derived from *Salvia divinorum* do not present a serious problem, meriting little more than symptomatic treatment if taken in isolation.

### Summary

Illegal substances are commonly used and carry a high risk of medical and surgical complications. They can impair judgement...
and attract the possibility of trauma. An awareness of the effects and management of intoxication are important because resuscitative surgery may have to progress in conjunction with treatment of acute intoxication. Adequate knowledge will avoid basic errors such as the use of indirectly acting sympathomimetics in the presence of serotonin syndrome. Withdrawal syndromes occurring in the post-operative period must be recognized and appropriate therapy instituted in order to rehabilitate the patient and reduce length of stay.

**Declaration of interest**

None declared.

**References**


Please see multiple choice questions 5–8.