

26.5.5 Substance misuse

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SECTION 26 Psychiatric and drug-related disorders 6490 Disulfiram (Antabuse) is a commonly used drug, but is only moderately effective. It works by inhibiting aldehyde dehydrogenase, which prevents the metabolism of acetaldehyde, alcohol's main metabolite. The build-up of acetaldehyde leads to flushing, tachycardia, nausea, vomiting, and sympathetic overactivity. This sympathetic overactivity can also lead to acute hypertension and potential cardiovascular or cerebrovascular harm. Patients must therefore be counselled on the effects of drinking alcohol while on disulfiram, on the need to avoid topical alcohol products, and about the potential for hepatotoxicity. It is most effective when professionals or a supportive partner or family supervises its use. Acamprosate reduces short-term and long-term (more than six months) relapse rates in patients with alcohol dependence when combined with a talking treatment. It is thought to work by modulating hyperactive glutamatergic N-Methyl-D-aspartic acid (NMDA) receptors. It is also only moderately effective. Naltrexone is an opioid antagonist, which competitively binds to opioid receptors and blocks the effects of endogenous opioids such as β -endorphin. It reduces cravings for alcohol and has a moderate effect on the risk of a return to heavy drinking in the short term.

FURTHER READING Day E, Copello A, Hull M (2015). Assessment and management of alcohol use disorders. *BMJ*, 350, h715. Mann K (2004). Pharmacotherapy of alcohol dependence. *CNS Drugs*, 18, 485-504. Room R, Babor T, Rehm J (2005). Alcohol and public health. *Lancet*, 365, 519-30. Wood A, et al. (2018). Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *Lancet*, 391, 1513-23.

26.5.5 Substance misuse Stephen Potts ESSENTIALS Many chemical substances are taken for their psychoactive properties, even if prescribed for other purposes. Such use and misuse of psychoactive substances is so highly prevalent that it inevitably impinges on medical practice. All physicians therefore need a general understanding of the ways in which substance misuse may interrelate with medical needs, as well as a specific understanding of the interrelationships most relevant to their own area of medical practice. Use of psychoactive substances may lead to acute intoxication and its consequences, or the effects of chronic use and dependence. Acute intoxication is associated with accidents and with acute psychiatric and medical illness. Chronic misuse may cause medical harm, which is often linked to the route of administration. Injection of

substances poses particular hazards. Drug dependence may lead to great difficulties in the delivery of medical care. Clear policies and communication with drug misuse services are an important part of managing patients who are dependent on drugs such as opioids. Introduction When the recreational or dependent use of psychoactive substances inflicts harm, it becomes misuse. The incidence and prevalence of use varies by substance, setting, culture, and country, and it changes over time. No area of medicine is unaffected by the physical and other harms caused by substance misuse. This chapter aims to provide a framework to guide physicians, rather than providing a list of specific medical harms by substance. The illustrative examples are drawn mainly from acute general medical inpatient settings. Substances that are misused Table 26.5.5.1 provides a pragmatic classification of drugs of misuse. Many of these agents and their effects are familiar to physicians. The class 'novel psychoactive substances', also known as 'clubbing drugs', includes many agents which have recently become easily available in the United Kingdom and elsewhere (United Kingdom law has made the alternative term 'legal highs' inaccurate). Drugs that are usually prescribed can also be misused, such as opioid analgesics or steroids for bodybuilding. In ICD-10, the physical problems caused by substance misuse are divided into: (a) acute intoxication, (b) harmful use, and (c) dependence. Physicians also see cases of acute poisoning, and of regular use that is hazardous but not harmful. Medical services are increasingly being encouraged to screen for hazardous substance misuse when seeing patients for other reasons, and to offer advice or refer on as appropriate. Table 26.5.5.2 lists harm from substance misuse and Table 26.5.5.3 lists harms by drug type. Acute poisoning and intoxication Emergency departments and acute medical admission units are familiar with the presentation of acute opioid poisoning. This can arise from deliberate overdose, or a recreational user's misjudgement of the potency of an unreliable illicit supply. Respiratory depression, aspiration of stomach contents through an impaired cough reflex, hypotension, and the consequences of prolonged immobility can all arise, and may be fatal. The direct effect of the opioid Table 26.5.5.1 Pragmatic classification of psychoactive substances (other than alcohol and tobacco) Group Examples Sedative/hypnotics Benzodiazepines, barbiturates Opioids Heroin, morphine, methadone, tramadol Stimulants Cocaine, amphetamine, methamphetamine Hallucinogens/ euphoriant Cannabis, ecstasy, MDMA, LSD, ketamine Novel psychoactive substances ('legal highs', 'club drugs') Multiple types, sold by brand name (e.g. 'Ivory Wave') Solvents GHB, GBL, volatile solvents Other Anabolic steroids

26.5.5 Substance misuse 6491 is readily reversed by the antagonists naloxone or naltrexone, but care must be taken to avoid subsequent deterioration if the drug taken has a long half-life and the dose was high. Aspiration pneumonia, rhabdomyolysis, compartment syndromes, and other consequences need medical or surgical treatment in their own right. Paradoxical excitation, where benzodiazepines cause disinhibited behaviour, and thereby increase agitation, is less familiar. The problem arises more often with recently prescribed administration than with illicit use, especially when treating acute alcohol withdrawal. If unrecognized, a vicious circle of escalating behavioural disturbance and increasing doses can occur. Treatment involves stopping all benzodiazepines and using instead antipsychotics such as chlorpromazine or haloperidol. Novel psychoactive substances can also cause serious acute medical and psychiatric effects, which may be fatal. These include rhabdomyolysis, acute kidney injury, seizures, hyperpyrexia, acute psychotic states, and severe agitation. The sheer number of such agents, uncertainty about what any given branded package actually contains, and the absence of specific antidotes, means that management is symptomatic and pragmatic. Some of these agents have a long half-life and may therefore require treatment over a period of days. Harmful use In chronic use, most psychoactive substances are less directly

toxic than alcohol. A notable exception is the bladder damage associated with the euphoriant drug ketamine. Mucosal inflammation and petechial haemorrhage cause symptoms of pain, frequency and haematuria, and can progress to bladder fibrosis and renal failure. Many harmful effects arise from the route of use, rather than from the toxicity of the drug itself. Examples include perforation of the nasal septum due to snorting cocaine, and the effects on the airways of smoking cannabis. Repeated injection can lead to local vascular problems through direct irritation (thromboembolism, phlebitis); soft tissue problems through poor injection hygiene (cellulitis, abscesses); and the familiar consequences of interpersonal transmission of blood-borne viruses (hepatitis C, HIV) or bacteria (infectious endocarditis). There are many psychiatric and neurological consequences of the sustained use of psychoactive substances. Some solvents are directly neurotoxic, with chronic use leading to cognitive deficits. Stimulants can cause panic attacks, sustained anxiety, isolated psychotic symptoms (such as tactile hallucinations) and a paranoid psychosis resembling schizophrenia. Cannabis too can cause a schizophreniform psychosis with heavy use. Emerging evidence links it to the development of schizophrenia itself, especially when use begins at an early age and consequently acts on the developing brain. This relationship appears to be dose-related, so that the heavier and more prolonged the use, and the more potent the cannabis consumed, the higher the risk.

Table 26.5.5.2 Types of medical harm arising from the use of psychoactive substance

Type of harm	Subtype	Examples
Acute Physical poisoning	Respiratory depression—opioids, benzodiazepines	stroke, MI—cocaine
Intoxication	Oversedation—opioids, benzodiazepines	Paradoxical excitation—benzodiazepines
Psychotic symptoms—novel psychoactive substances, hallucinogens, disturbed behaviour	Hazardous use	Regular use which has not yet caused harm but risks doing so
Harmful use	Direct toxicity	Bladder damage due to ketamine
Local consequences of route of use	Nasal septum—cocaine (inhaled)	Airways—cannabis (smoked)
Thrombophlebitis	Abscesses—anything injected	Cellulitis
Systemic consequences of route of use	Infective endocarditis, hepatitis C, HIV—anything injected	Mental/behavioural/ neurological effects
Anxiety—stimulants	Psychosis—stimulants, novel psychoactive substances, cannabis	Depression—stimulants
Cognitive deficits—solvents	'Flashbacks'—hallucinogens	Dependence see Table 26.5.5.3

Table 26.5.5.3 Severity and frequency of harm by drug type

Drug type	Acute effects	Chronic effects	Dependence	Physical	Psychiatric	Direct	Route-related	Psychiatric	Overall
Sedative/ Hypnotics	+	+	-	+	_	+++	+++	+++	+++
Opioids	+++	+	-	+++	+	+++	+	+++	++
Stimulants	++	++	+	++	+++	++	+	Hallucinogens/ euphorians	+
Hallucinogens/ euphorians	+	+++	+	+	++	-	-	Novel psychoactive substances	+++
Novel psychoactive substances	+++	+++	?	++	+++	?	?	Solvents	++
Solvents	++	+	+++	++	+++	+++	+++	Steroids	-
Steroids	-	-	+++	-	+++	-	+++	Major harm; ++, Moderate harm; +, Minor harm; -, Minimal/no harm; ?, Uncertain.	

SECTION 26 Psychiatric and drug-related disorders 6492 the risk. Continued use after the development of psychosis or other mental disorder also makes treatment more difficult. Depression typically arises more from the nonmedical (i.e. educational, social, financial, and legal) harms associated with sustained substance misuse than from the drugs themselves, but depressive symptoms are common in the 'come-down' period after stimulant use. Steroids have many psychiatric consequences, including depression and psychotic episodes, which can be florid. Dependence Dependence on psychoactive substances constitutes a cluster of physical, psychological, and behavioural characteristics associated with sustained use. The key features seen in a medical context are listed in Table 26.5.5.4, together with their main manifestations and the implied roles for medical services. Tolerance and loss of tolerance This can be notable with opioids and sedative/hypnotic drugs, such as the benzodiazepines. Since these drugs are used as analgesics or as sedation for medical and surgical procedures, a dependent user's tolerance can

present problems in judging the correct doses, routes, and frequency of administration when prescribing for medical use. This is especially the case if the dependence is not recognized, or the need to adjust doses insufficiently appreciated. 'As required' analgesia is not recommended in a dependent user and patient-controlled analgesia regimens need carefully set limits. Loss of tolerance occurs after prolonged periods of abstinence from a dependogenic substance such as an opioid while in hospital (or prison). It confers risk, as a usually tolerated dose may become fatally toxic. Patients should consequently be warned not to resume consumption at previous levels on discharge.

Withdrawal syndromes These can be problematic in medical settings. This is particularly the case for opioids and benzodiazepines, although the severe withdrawal associated with the anaesthetic agent γ -hydroxybutyrate is becoming more common. Withdrawal from opioids causes sleeplessness, agitation, and autonomic effects (sweating, nausea, vomiting, and diarrhoea). While intensely unpleasant, it carries a low mortality. Withdrawal from benzodiazepines has physical and psychological manifestations similar to those of anxiety, but also brings a risk of death from withdrawal seizures. This risk is higher when the agent used has a short half-life (such as lorazepam) or when there is abrupt cessation of intake on entering a nonmedical environment (e.g. after arrest and imprisonment). γ -hydroxybutyrate withdrawal is similar in nature to alcohol withdrawal, though often much more severe in degree. It too carries a risk of withdrawal seizures. Withdrawal states may present with medical manifestations such as isolated seizures or a state resembling delirium tremens. The primary management aim is treatment via standardized dosage regimens. These take two main forms: reducing fixed dose schedules, and symptom-triggered scales. In these regimens, long-acting substitutes such as diazepam and methadone are reduced in dose over a period of days or occasionally weeks, together with agents to provide symptom relief (e.g. loperamide for diarrhoea). Baclofen has recently been found to be effective in managing γ -hydroxybutyrate withdrawal. Withdrawal syndromes may also present incidentally, when patients admitted for unrelated medical or surgical problems have unrecognized dependence. The main management aim here should be prevention, by screening and taking proactive action for those at risk. Early decisions may be required about substitute prescribing and withdrawal regimens. These should be guided by a detailed history of the user's normal daily and weekly levels of consumption, as well as previous episodes of withdrawal. 'As required' prescriptions should be minimized, and strict daily limits set on the total doses of dependogenic prescribed drugs. These limits should be explicitly discussed with the patient. It is important that there is clear communication across nursing shifts and ward transfers to ensure the all-important consistency of management. This is best ensured via explicit, hospital-wide protocols. Dependent users of illicitly acquired drugs should be advised that the use of substitute prescribing to treat or prevent withdrawal syndromes in medical settings is normally a temporary measure. It does not commit service providers to continued prescription on discharge and referral to specialist drug service should be offered instead.

Medically enforced withdrawal Dependent users who have an established regimen of substitute drugs, prescribed by drug treatment agencies, should generally have those prescriptions respected. Medical teams treating seriously ill patients may be tempted to impose opportunistic withdrawals from long-established prescriptions of opiates while the patient is 'captive'. This is rarely wise, as it often leads to destabilization on discharge, and a return to illicit use with associated social disruption. Communication with drug misuse prescribing services is therefore required in order to agree management plans both during and after medical admission.

Rapid reinstatement after abstinence This is a well-established phenomenon, especially for opioids. Patients who become abstinent during a medical admission, and

Table 26.5.5.4 Medically relevant features of dependence on psychoactive substances	Feature	Manifestation	Medical role
Tolerance	Lack of response to normal doses of analgesia and sedation	Adjust doses	Withdrawal syndrome
As			

cause of medical admission Treatment Accompanying medical admission Prevention, screening, early intervention Substitute prescribing Rapid reinstatement after abstinence Rapid escalation from single use to full dependence after abstinence Relapse prevention Salience and craving Desire for drug outweighs need for healthy lifestyle Proactive follow up via community services Desire for drug outweighs need for medical treatment Manage nonconcordance Legal measures Substitute prescribing Desire for drug outweighs need for healthy lifestyle in pregnancy Substitute prescribing Liaison with obstetric services, primary care, and substance misuse specialists

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