Ecstasy

ECSTASY is the street name generally applied to 3,4-methylenedioxymethamphetamine or MDMA. However, other drugs are sold as ecstasy, and ecstasy tablets often contain a range of drugs (including amphetamine, various amphetamine derivatives, caffeine, aspirin, paracetamol, or ketamine) in addition to, or in place of MDMA (Wolff et al., 1995).

Ecstasy is usually sold as a tablet or capsule. The tablets are typically identified by a symbol impressed on the surface. This leads users to refer to them as 'white doves', 'love hearts', etc. Other common street names are 'E', 'Eccy', 'Adam' and 'XTC'.

PHARMACOLOGY

MDMA initially enhances the extracellular brain concentrations of serotonin but eventually serotonin becomes depleted. MDMA also induces a rapid and substantial elevation of dopamine. Serotonin has a role in regulation of aggression, mood, sexual activity, sleep, sensitivity to pain, memory and body temperature (Schloss & Williams, 1998). Dopamine plays a role in the control of movement, cognition, motivation and reward (Rawson, 1999). It is probably the mechanism underlying the stimulant properties of MDMA (Daws et al., 2000).

MDMA is well absorbed from the gastrointestinal tract (Mas et al., 1999). Effects become apparent about 20 minutes after administration and last about 4 hours. Dose and blood concentration relationship may not be linear (de la Torre et al., 2000), and small increases in dose may produce disproportionate increases in effect, possibly contributing to toxicity. Some of the metabolic products of MDMA are themselves bioactive and may also contribute to toxicity (Mas et al., 1999).

MDMA is metabolised in the liver. Some people have low activity of CYP2D6, one of the enzymes involved (Tucker et al., 1994). It has been suggested (but not validated) that, due to reduced metabolism, these individuals are at greater risk of MDMA toxicity (O'Donohoe et al., 1998; Schwab et al., 1999).

Drug interactions may influence MDMA toxicity by altering elimination of MDMA from the body, or through an additive effect. Reported cases of adverse reactions involving ecstasy in combination with fluoxetine (Bingham et al., 1998; Coore, 1996) and ritonavir (Henry & Hill, 1998) support this as a possibility.

PATTERNS OF USE

In the 2001 Australian National Drug Strategy Household Survey, lifetime use of ecstasy or other designer drugs was reported by 6.1% of people aged 14 and over, while 2.9% reported using ecstasy in the previous 12 months (AIHW, 2002). The current trend is one of increasing prevalence of use.

Ecstasy is almost exclusively taken in a social setting (McKetin et al., 1999; Topp et al., 1997b) usually as part of youth culture centred on dance music. Use of ecstasy by friends is a significant factor in initiation and continuation of ecstasy use.

The quantity of active ingredient in one tablet is usually in the range 75–100 mg. Normally one or two tablets are taken at a time but there are reports of greater doses being used, especially by experienced users (Topp et al., 1997b).

Ecstasy is mainly taken orally, but there may be a trend of increasing use by injection (Humeniuk, 2000; Topp et al., 1997b). Most users appear able to regulate their use of ecstasy but some progress to problematic use (Topp et al., 1997b). Whether such problematic use constitutes dependence is an area of debate (Jansen, 1999; Topp et al., 1997a).

PHYSICAL AND PSYCHOSOCIAL COMPLICATIONS

MDMA produces immediate positive psychological effects of euphoria, increased energy, and a feeling of closeness to others, and (less commonly) negative psychological effects of paranoia, anxiety and depression.

Physical Effects of Ecstasy

The incidence of serious acute adverse events arising from ecstasy use is low. It is the unpredictable nature of those adverse events and the risk of mortality and substantial morbidity in young people that make the health consequences of ecstasy significant.

Table 7–1 lists the short- and long-term physical effects of ecstasy.

Hyperthermia

The most significant adverse effect of ecstasy use is hyperthermia. It can quickly become life threatening The degree of hyperthermia is predictive of mortality.

It is typically accompanied by a number of clinical problems, including:

- seizures
- disseminated intravascular coagulation
- rhabdomyolysis
- renal and liver impairment which may be induced or exacerbated by the hyperthermia (Green et al., 1995)

Clinical signs and symptoms are consistent with malfunction of normal temperature control and water balance. MDMA can produce hyperthermia in quiet surroundings, but in the setting of 'raves' or dance parties, toxicity appears to be enhanced. It is probably a combination of:

- the direct effects of MDMA
- high ambient temperature
- sustained physical activity; and
- inadequate fluid replacement

All impair temperature regulation (Green et al., 1995; Henry et al., 1992).

Hyponatraemia ('water intoxication')

Ecstasy use has also been associated with hyponatraemia. Cases are marked by:

- features of confusion
- reduced consciousness; and
- in some cases, seizures or convulsions

In general symptoms resolve as sodium levels are normalised, with full recovery achieved within a few days. However, fatalities have been reported, apparently due to cerebral oedema associated with excess fluid.

In most cases of hyponatraemia, copious amounts of water were consumed. This may be a response to a sensation of thirst induced by MDMA. Alternatively, behavioural disturbance, including stereotyped repetitive actions such as water consumption, may arise from MDMA ingestion (White et al., 1997). The administration of MDMA is associated with inappropriate release of antidiuretic hormone, arginine vasopressin (Henry et al., 1998). This would reduce

Table 7–1
Physical effects of ecstasy

Short-term effects	Long-term effects
• pupil dilation • increased jaw tension and grinding of teeth • loss of appetite • dry mouth • tachycardia • hot and cold flushes • sweaty palms • hyperthermia • hyponatraemia or 'water intoxication'	• insomnia • depression • headaches • muscle stiffness

urine formation and the body's capacity to excrete excess fluid.

First reports of hyponatraemia occurred after dance club owners encouraged users to take dance breaks in a cool room and drink water. This advice is still sound for prevention of hyperthermia, but:

- an upper limit of 500 ml per hour is considered the amount able to be handled by the body

Drug screening undertaken in cases of acute adverse effects commonly indicate the presence of a range of drugs in addition to MDMA. However, the reporting of cases of hyperthermia or disturbances of salt or water balance where MDMA was the only drug detected, demonstrate that MDMA alone can produce adverse effects. Given that hyperthermia and disturbances of salt or water balance generally occur when MDMA is used in nightclub or dance party settings, these data also suggest that the acute adverse effects of MDMA arise primarily from the way it is used.

Dose–response relationship

The dose of MDMA is not predictive of severity of outcome (Gowing et al., 2002). In the absence of a dose–response relationship, it has been suggested that some form of metabolic myopathy or individual variability in metabolism of MDMA may underlie adverse effects. However, instances of muscle abnormality or impaired MDMA metabolism have not been identified in any cases of severe reactions and there appears to be a mix of first time and experienced MDMA users affected, making this explanation unlikely, or at least uncommon.

Severe reactions might be due to contaminants in the preparation taken. However, reports of affected persons taking from the same supply as others, who did not experience severe reactions, means that contaminants are an unlikely explanation (Hall, 1997). The combination of dose, setting and individual behaviour most likely determines outcome.

Liver damage

Severe liver damage can occur shortly after ingestion of ecstasy, typically in conjunction with hyperthermia. However, liver damage, apparently unrelated to hyperthermia, can also occur days or weeks after single or multiple episodes of ecstasy use (Jones & Simpson, 1999). Most reported cases resolved spontaneously over weeks to months, but a minority progressed to full liver failure requiring transplantation, with some cases being fatal.

It appears that those who resume ecstasy use after recovery are at risk of recurrence of liver damage and development of chronic hepatitis (Andreu et al., 1998). The mechanism of ecstasy-related liver damage is uncertain and, relative to other causes, ecstasy use remains a minor contributor to the incidence of liver failure (Andreu et al., 1998; Jones & Simpson, 1999).

Neurotoxicity

Animal studies show administration of MDMA produces damage to serotonin axons in the brain (McCann et al., 2000). Brain imaging techniques have found persisting abnormalities in brain morphology in ex-users of ecstasy, even with moderate use (Gamma et al., 2000; Kish et al., 2000; Reneman et al., 2000). Psychological tests in current and former ecstasy users compared to non-using controls have consistently found impairment in short-term memory function in ecstasy users (Gouzoulis-Mayfrank et al., 2000; Parrott et al., 2000; Rodgers 2000; Wareing et al., 2000).

These studies constitute mounting evidence of ecstasy having a neurotoxic effect.

Psychological Effects and Complications

Depression, or low mood, and concentration and/or memory problems are commonly reported in the week following ecstasy use (Curran, 2000). Cases of persistent depression, panic disorders, 'flashbacks' and delusions have been related to ecstasy use (Benazzi & Mazzoli, 1991; Cohen & Cocores, 1997).

The risk of psychiatric sequelae is probably greater when:

- other drugs, particularly cannabis, are used in addition to ecstasy
- ecstasy is used repeatedly and at high doses over a period of months
- there is a family or personal history of psychiatric disorders (Schifano et al., 1998)

MANAGEMENT AND INTERVENTION STRATEGIES

Strategies for Different Levels of Use

Acute adverse effects

Reassurance, observation and monitoring for several hours in a subdued environment until symptoms subside, is appropriate in most ecstasy intoxication cases (Williams et al., 1998).

Hyperthermia and hyponatraemia are the most significant complications necessitating intervention. In both conditions the treatment response needs to be rapid and intense to avert significant morbidity and mortality. In the case of hyperthermia, the patient may deteriorate rapidly towards multiple organ failure, requiring intensive support of cardiovascular, respiratory and renal systems (Hall, 1997). This requires admission to an intensive care unit.

Many cases of ecstasy-induced liver damage will resolve without intervention, and simply require monitoring. However, patients developing jaundice, or with evidence of hepatic failure, require specialist care.

It is also important to educate users about the importance of controlling body temperature and fluid intake, early signs of adverse effects, and the need to seek medical assistance promptly.

Treatment for Ecstasy Use

Those who use ecstasy more frequently (monthly to weekly) and/or use larger amounts, and those who use by injection are likely to be at increased risk of harm and hence constitute targets for intervention.

Pharmacological interventions

There is currently very little information on pharmacological interventions for ecstasy users. Selective serotonin reuptake inhibitors (SSRIs), if taken concurrently with MDMA, have been shown to block usual subjective effects of MDMA (Stein & Rink, 1999). However, administration of SSRIs (e.g. fluoxetine, citalopram) subsequent to MDMA may potentiate the effects of released serotonin, worsening any adverse effects (Green et al., 1995) and limiting their value as a treatment agent.

Non-pharmacological interventions

See Chapter 13 Psychosocial Interventions

Non-pharmacological interventions (also see Chapter 13) which have demonstrated most efficacy in treating psychostimulant users are:

- relapse prevention
- cue exposure/response prevention
- multifaceted behavioural therapy

Contingency management approaches may also be of value.

Attracting users into treatment and intervening prior to development of problematic use is a priority. An approach well suited to these purposes is early and brief intervention (Barry, 1999), administered opportunistically when possible ecstasy use is identified.

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Ecstasy

Cocaine

COCAINE is a stimulant derived from the South American coca plant. It is imported in the form of a salt, cocaine hydrochloride, a white odourless crystalline powder with a bitter taste. Cocaine base can be extracted from the powder to form rocks or crystals known as 'freebase' or 'crack' that are smoked and produce strong subjective effects almost immediately.

Although it is relatively easy to make crack from cocaine hydrochloride, and some Australian cocaine users report doing this, there is little evidence of widespread or problematic crack cocaine smoking in Australia to date.

PHARMACOLOGY

Cocaine blocks the reuptake of dopamine (DA), noradrenaline and serotonin at presynaptic locations, thus increasing the concentration of these transmitters at postsynaptic receptor sites (Chesher, 1993). DA concentration is particularly increased, and is thought to be the basis for cocaine's abuse potential. Cocaine also stimulates the sympathetic nervous system, which accounts for its activating effects.

Tolerance to the acute effects develops extremely rapidly, before the depletion of plasma levels. Most of the active drug is metabolised in the liver, but some is acted on by plasma esterases, and a small amount is excreted unchanged in the urine (Schuckit, 1995). Cocaine metabolites may be detected in urine for three days or longer following use.

Australian Street Names

Most common:

- cocaine
- coke
- charlie

Less common:

- okey doke
- nose candy
- toot
- blow
- snow
- white lady

PREVALENCE AND PATTERNS OF USE

Darke et al., 2000

Lifetime

The proportion of the Australian population who reported having used cocaine at some time increased from 2.5% in 1993 to 4.4% in 2001 (AIHW, 2002).

Past Year

The proportion who had used cocaine in the past year increased from 0.5% in 1993 to 1.3% in 2001 (AIHW, 2002).

Gender

In 1998, males were more likely than females to report lifetime (5.3% versus 3.3%) and past year (1.9% versus 0.9%) cocaine use.

Age

Cocaine use is most common amongst young people. In 1998, 8% of Australians aged 20–29 years reported having used cocaine in their lifetime, and 3% in the past year.

AVAILABILITY

Since the late 1990s there has been a marked increase in cocaine availability and use, especially in Sydney (Darke et al., 2002a). Although cocaine is available in other jurisdictions it is harder to get and more expensive than in Sydney (Topp et al., 2002).

The late 1990s saw an increase in use in Sydney. It was most apparent amongst committed heroin injectors, who administered the two drugs simultaneously in a 'speedball' or 'CC' (cocaine cocktail) or sequentially. In 2001, when the availability and use of heroin decreased substantially, the frequency of injection of cocaine amongst former primary heroin users in Sydney increased markedly (Darke et al., 2002b).

ROUTES OF ADMINISTRATION

In Australia, cocaine is generally administered intranasally (snorted) or intravenously (injected). Onset of action is rapid via either route of administration: within eight minutes when snorted and within two minutes when injected. Peak blood levels develop within five to 30 minutes. Duration of action is relatively brief: the half-life of cocaine's active metabolites is typically 15 to 30 minutes when the drug is injected and 60 minutes when snorted (Chesher, 1993; Platt, 1997).

Those who inject cocaine tend to have a higher quantity and frequency of use, and experience more associated harm, than those who snort it (Kaye et al., 2000).

BINGEING

A substantial proportion of those who use cocaine heavily do so in 'binges', i.e. where it is administered at short intervals repeatedly until either the supply or the user is exhausted. This destructive pattern of use appears to arise because tolerance to the rewarding effects of cocaine develops extremely quickly, as a result of rapid neuroadaptation (i.e., where the neurons on which cocaine exerts its effects attempt to restore normal function) (Chesher, 1993). Thus, the intense pleasure experienced after cocaine injection is of only short duration and is followed by either an absence of euphoria or even a dysphoria. Such rapid mood changes seem to stimulate the need for more cocaine.

TYPES OF USERS

Most Australians who use cocaine snort small amounts infrequently and with few problems.

People who use cocaine more heavily tend to fall into two groups:

- middle-class, well-educated professionals who generally snort the drug; and
- injecting drug users who inject cocaine, often (but not always) in association with heroin

POLYDRUG USE

Cocaine users tend to be extensive polydrug users; other drugs are used both in conjunction with cocaine as well as to medicate the 'come down' (aversive recovery period following use).

Snorters

Those who snort cocaine tend to do so in a social context such as at dance parties, and tend to use other party drugs such as ecstasy, methamphetamine, ketamine, and/or GHB, as well as alcohol and cannabis, and may use benzodiazepines to come down (Topp et al., 2000). A small proportion of this group progress to problematic cocaine use, in which large amounts of the drug are snorted frequently.

Injectors

Those who inject cocaine tend to be either:

- former heavy cocaine snorters who have developed nasal problems and/or a high level of tolerance and so make the transition to injecting; or
- committed injecting drug users who have added cocaine to their injection repertoire, and will usually inject other drugs including heroin and methamphetamine, and use a wide range of other drugs including alcohol, cannabis, benzodiazepines and methadone (Kaye et al., 2001)

It is estimated that the latter group constitutes a higher proportion of cocaine injectors than the former.

Cocaine and Alcohol

- a common pattern of polydrug use
- with repeated administration, alcohol sensitises the body's reaction to cocaine, and cocaine attenuates the development of tolerance to alcohol
- the combination produces a third active substance, cocaethylene (Schuckit, 1995), which has a half-life of two hours (as opposed to about 30 minutes for cocaine alone)
- concurrent use of cocaine and alcohol leads to a significantly elevated risk for sudden cardiac deaths

EFFECTS OF COCAINE

Factors Influencing the Effects

- form (powder versus crack)
- dose (influenced by purity as well as quantity)
- route of administration
- intensity and duration of use
- concurrent polydrug use

Desired Effects

- euphoria
- sociability, gregariousness and talkativeness
- increased confidence and feelings of control
- energy
- decreased need for sleep
- temporary increase in functional activity or efficiency
- suppressed appetite

Other Acute Effects of Low Doses

- local anaesthesia
- pupillary dilation
- vasoconstriction
- increased respiration
- increased heart rate
- increased blood pressure
- increased body temperature

Acute Effects of High Doses ('Toxic Reactions')

See p. 111
'Treatment of Toxic Reactions'

Toxic reactions are cocaine 'overdoses'. They occur after excessive doses. Any of the following signs and symptoms may be expected as part of a toxic reaction to cocaine:

- stereotyped, repetitive behaviour
- anxiety/severe agitation/panic
- aggression/hostility
- muscle twitches/tremors/loss of coordination
- heightened reflexes
- respiratory failure
- markedly elevated blood pressure
- chest pain/angina
- pulmonary oedema
- acute renal failure
- convulsions
- blurred vision
- acute stroke
- pallor
- confusion/delirium
- hallucinations, most often auditory or tactile, e.g. formication (the feeling of bugs crawling under the skin)
- dizziness
- muscle rigidity
- weak, rapid pulse
- cardiac arrhythmias including malignant arrhythmias
- myocardial ischaemia and infarction
- sweating/very high body temperature (up to 41°C rectally)
- headache
- stomach pain/nausea/vomiting

Effects of Chronic Use

- insomnia
- depression
- aggression or violence
- loss of appetite and concomitant weight loss
- muscle twitching
- anxiety
- psychosis — paranoid delusions, hallucinations
- loss of libido and/or impotence
- heightened reflexes
- increased pulse rate

PHYSICAL AND PSYCHOSOCIAL COMPLICATIONS

Physical Problems Relating to Route of Administration

Intranasal users

Intranasal users may suffer from:

- runny nose
- blood nose
- nasal ulcers
- sinusitis
- epistaxis
- perforated nasal septum
- slight risk of hepatitis C transmission due to sharing of straws or other equipment used to snort cocaine which may contain traces of blood

Injecting users

Injecting users may suffer from:

- systemic and local infections which may be viral, bacterial, fungal or parasitic
- local inflammatory and infection complications can be more common than with heroin due to the vasoconstrictive and anaesthetic properties of cocaine
- injection-related abscesses, cellulitis, phlebitis
- bacterial endocarditis
- transmission of blood borne viral infection such as hepatitis C, hepatitis B and HIV

Other Physical Problems

Other physical problems may be experienced regardless of route of administration, particularly cardiovascular complications.

Cocaine-related Death

Death is relatively rare, but is associated with:

- muscle rigidity
- delirium
- agitation
- a stroke-like CNS vascular picture
- cardiac arrhythmias
- elevated body temperature

Psychological Problems

Psychological complications are the most common cocaine-related problems. See ‘Acute Effects of High Doses’ and ‘Effects of Chronic Use’ above.

Social Problems

Intensity of cocaine use may incur:

- interpersonal problems
  - heightened discord in significant relationships
  - paranoia leading to irrational jealousy
  - alienation from social support networks
- occupational problems
  - impaired productivity
  - absenteeism
  - job loss

- financial problems
  - cocaine is expensive and use can escalate rapidly
  - debt to dealers and/or others may grow
  - dealing or other criminal activity may appear a viable financial option
  - financial problems may be compounded by job loss
- legal problems
  - may be directly drug-related
  - may be the result of criminal activity designed to support use

Cocaine Dependence

Key criteria for diagnosing drug dependence are:

- continued use of a drug despite knowing that it causes significant harm
- loss of control over use manifest by using more or for longer than intended
- repeated relapse despite resolving to reduce or eliminate use

(APA, 1994)

Some cocaine users clearly develop such symptoms of dependence, along with others including tolerance.

Cocaine Withdrawal Syndrome

The existence of cocaine withdrawal is contentious because the syndrome is dominated by symptoms rather than clinical signs. The aversive nature of the experience for users, and the strong motivation to resume use to alleviate withdrawal, however, is well documented.

DSM–IV (APA, 1994) describes withdrawal after several days of heavy cocaine use as consisting of:

- dysphoric mood (anhedonia or sadness rather than depression) and at least two of the following symptoms:
  - fatigue
  - insomnia or hypersomnia
  - psychomotor agitation or retardation
  - craving
  - increased appetite
  - vivid, unpleasant dreams
- withdrawal reaches its peak in 2–4 days
- dysphoric symptoms persist for up to 10 weeks (Lago & Kosten, 1994). Some suggest that cocaine craving and a desire to resume use may persist indefinitely, even after withdrawal is complete and normal mood and the ability to enjoy experiences have returned (Gawin & Kleber, 1986)

Foetal Effects

Exposure to cocaine during pregnancy has been associated with:

- shorter gestation
- premature delivery
- abruption of placenta
- retardation of growth
- behavioural problems

However, many of the perinatal and postnatal adverse effects commonly attributed to cocaine may be caused by multiple confounders

that can occur in a cocaine using mother, rather than by cocaine itself (Addis et al., 2001), such as:

- polydrug use, including alcohol and cigarettes
- poor prenatal care
- single motherhood
- poverty
- poor quality postnatal environment

MANAGEMENT AND INTERVENTION STRATEGIES

Clinical Screening

The most common clinical problems associated with cocaine use are anxiety conditions, temporary psychosis and cardiovascular problems.

Acute toxic reactions

Possible cocaine use should be considered in individuals who manifest:

- dilated pupils
- dry mouth
- increased reflexes
- elevated temperature
- sweating
- increased heart rate
- a restless, hyperalert state
- an anxiety-like attack (usually nervousness plus rapid pulse)
- emotional lability or irritability
- aggressive or violent outbursts
- paranoia or suspiciousness
- hallucinations, especially auditory or tactile
- confusion or an organic brain syndrome
- behavioural abnormalities
- acute ischaemic events

If the clinician suspects cocaine use, blood or urine toxicological analysis will confirm the diagnosis.

Chronic Cocaine Use

Chronic cocaine users who do not disclose their use may manifest:

- depression/anxiety
- suicidal ideation
- paranoia/hallucinations
- lethargy
- insomnia
- loss of libido
- social problems (as outlined above)
- evidence of IV drug use (track marks, abscesses)
- abnormalities in the nasal lining or mucosa
- worn teeth (from tooth grinding during intoxication)
- missed appointments and other signs of chaotic lifestyle
- seeking of medications such as benzodiazepines, antidepressants or opioids to relieve withdrawal, medicate side effects or to sell for profit

Treatment of Toxic Reactions

The treatment chosen will depend on the condition of the patient at the time of presentation. Priorities are:

- emergency care to ensure a clear airway, circulatory stability and treatment of shock
- control of elevated body temperature with hydration, sedation, cold water, ice packs or in extreme cases, a hypothermic blanket
- control of seizures with doses of IV diazepam of 5 to 20 mg injected very slowly and repeated as required
- diazepam will also reduce agitation
- vigorous treatment of a sustained elevation in blood pressure with phentalomine (5–10 mg IV) to prevent CNS haemorrhage

- CT scans and lumbar puncture in the confused or unconscious patient will rule out the possibility of cerebral haemorrhage
- excretion of cocaine can be hastened through acidification of the urine with 500 mg ammonium chloride orally every 3–4 hours. The goal is a urinary pH under 6.6
- low doses of an antipsychotic such as haloperidol may be required to manage psychotic patients when benzodiazepines are insufficient. Such patients should be closely monitored as haloperidol can reduce the seizure threshold and may increase the risk of seizures (Nathan et al., 1998)
- once the patients start to recover, they should be reassured and comforted, preferably by supportive friends or relatives, and placed in a quiet room with minimal stimulation to be closely monitored

Management of Withdrawal

There is, as yet, no generally accepted, effective pharmacotherapy for cocaine withdrawal. Management of withdrawal is largely supportive.

Issues to be considered include:

Assessment

- careful neurological and physical examination
- detailed psychiatric history
- detailed drug use history
- concomitant use of other drugs, licit and illicit
- reasons for withdrawal

Management

- the patient should be placed in quiet surroundings for several days and allowed to sleep and eat as much as is needed
- benzodiazepines may be prescribed on a short-term basis for agitation
- if the patient is markedly despondent, (temporary) suicide precautions may be necessary
- severe and persistent depression may require antidepressants. Antidepressants are not effective in reducing cocaine use itself, but can be effective in the management of major depressive episodes associated with cocaine use
- care should be taken in prescribing SSRIs if cocaine use is continued, as toxic interactions have been described (Barrett et al., 1996), and, in mice, SSRIs have facilitated cocaine-induced convulsions (O'Dell et al., 2000)

Treatment of Cocaine Dependence

Pharmacotherapy

There is no widely effective pharmacotherapy for cocaine dependence:

- disulfiram as an adjunct to buprenorphine or methadone maintenance may reduce cocaine use in opioid-dependent clients (George et al., 2000; Petrakis et al., 2000)
- however, there is a potential interaction between disulfiram and cocaine that increases cocaine associated cardiovascular responses and consequently may increase cocaine toxicity (McCance-Katz et al., 1998)

Behavioural and psychosocial therapies have produced better results.

Cognitive-behavioural therapy

- aims to reduce cocaine use by helping the client master an individualised set of coping strategies as effective alternatives to cocaine use (Carroll, 2000)
- typical skills taught include:
  - identifying high-risk situations for relapse
  - identifying the functions of cocaine use
  - developing skills for coping with craving

- has been shown to be more effective than control treatments for more severely dependent cocaine users and those with comorbid mental disorders
- is more effective than less intensive approaches
- effects are durable, with clients continuing to reduce their cocaine use even after they leave treatment (Carroll, 2000)

Contingency management

- has shown promise in increasing cocaine abstinence and treatment retention in research-based treatment programs
- uses an escalating reward system in which violations are punished both by denying the immediate reward and taking away the benefits of an escalated payment (Sindelar & Fiellin, 2001)
- different types of rewards have been used, including money and vouchers which can be exchanged for retail goods

Enhancement of psychosocial skills

- an adjunct to conventional therapy associated with better treatment outcome is the enhancement of social skills through training programs (Volpicelli et al., 2000)

Acupuncture

- may be useful for some cocaine dependent clients, particularly those maintained on methadone (Avants et al., 2000)

General approaches

Given the lack of generally accepted, effective treatments for cocaine dependence in Australia, efforts aimed at rehabilitation of cocaine users should follow the same general supportive and commonsense approaches used for those dependent on other drugs.

Clinicians should:

- *not* judge the user and should not insist on abstinence
- seek to engage and retain the user in treatment for as long as possible, as retention is associated with better outcomes (Simpson et al., 1999)
- ensure understanding of the client/patient's treatment goals (e.g., to make it through an acute crisis; to reduce frequency and/or quantity of cocaine use; to achieve long-term abstinence)
- tailor the treatment where possible to meet those goals, including referral when appropriate to:
  - treatment programs
  - individual counsellors
  - family counsellors
  - self-help groups such as NA
- remember the need for flexibility of service delivery; as goals and outcomes change throughout the course of treatment, the treatment program should be adjusted to reflect these changes
- provide as multifaceted and intensive a program as possible, as more intensive psychosocial treatment programs are associated with better outcome (Crits-Cristoph et al., 1999)

NIDA has produced a manual for an individual counselling approach for cocaine dependence that consists of 36 sessions designed to take place over six months (Merder & Woody, 1999).

Comorbid disorders

Cocaine users often have multiple psychiatric and psychosocial problems. It is estimated that 30% of cocaine treatment presentations suffer with anxiety disorders, 20% with bipolar disorders, and 5% with attention deficit disorders (Tutton & Crayton, 1993). Programs that assess and address these issues

have better outcomes than those which do not (McLellan et al., 1997, 1998).

Readiness to change

In patients who do not wish to become abstinent despite significant impairment related to cocaine use, the clinician should attempt to:

- establish an empathetic, respectful relationship
- retain contact with the client
- maximise physical and mental health, as clients will find it difficult to achieve long-term abstinence if chronic medical problems have not been adequately treated
- enhance motivation toward abstinence by educating clients and their significant others about the usual course of cocaine dependence and the relationship between cocaine use and current and/or future problems
- emphasise the client's responsibility for their own actions
- help clients rebuild a life without cocaine through:
  - vocational counselling
  - family counselling
  - helping them develop a network of non-drug using peers
  - showing them how to use free time appropriately

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Cocaine

Heroin and Other Opioids

OPIOID drugs mainly act on the opioid receptor system to produce a range of effects which may be considered therapeutic or adverse (side effects). Opioids affect the nervous, gastrointestinal, endocrine and other physical systems as listed in Table 9–1.

PATTERNS OF HEROIN USE

The use of prescribed opioids and illicit heroin has been steadily increasing in Australia since the 1980s. Most people who use illicit psychoactive drugs such as heroin do so on an irregular basis. However, it is estimated that about one in three heroin users develop dependence.

OPIOID DRUGS

Heroin

Heroin is a potent opioid derived from morphine. Heroin is an illegal drug in Australia, and is usually available in the form of a water-soluble, white crystalline powder:

- heroin is usually injected intravenously, although increasing numbers of Australians smoke or snort the drug. Oral heroin is largely metabolised by the liver before exerting

its main effects (high first-pass metabolism), so that few users take heroin orally

- heroin is a short acting drug with rapid onset of effects. Onset of effects occur within minutes of smoking or injection, with significant effects lasting up to 3–6 hours in regular users

Morphine

Morphine is prescribed for a range of medical conditions, most notably as an analgesic.

- it has variable but significant first-pass liver metabolism (the bioavailability of oral morphine is about 25% of injected doses)
- it has a similar duration of action to heroin, with significant effects for 3–6 hours
- slow-release oral morphine preparations are available allowing once or twice a day dosing for chronic pain

Methadone

Methadone is a long acting opioid used in the management of chronic pain (methadone tablets) and for the treatment of opioid dependence (methadone syrup or solution).

See Tables 9–2 & 9–8

Table 9–1
Opioid effects

Physical system	Effect
Nervous system	• analgesia (pain relief) • euphoria • sedation, drowsiness, respiratory depression • reduced cough reflex • pupillary constriction
Gastrointestinal actions	• nausea and vomiting • constipation • biliary spasm (elevated tone of Sphincter of Oddi)
Endocrine actions	• changes in sex hormones in women (low follicle-stimulating hormone (FSH) and leutenising hormone (LH); raised prolactin) resulting in menstrual changes, reduced libido, galactorrhoea • reduced testosterone in men with reduced libido • elevated anti-diuretic hormone (ADH), reduced ACTH
Other	• itching, sweating, flushed skin (histaminic reaction) • dry mouth, skin and eyes • difficulty passing urine • low blood pressure

Buprenorphine (Subutex®)

Buprenorphine is registered as an analgesic (low dose sublingual tablets), and for the management of opioid dependence (high dose sublingual tablets). Buprenorphine is a partial opioid agonist (i.e. low activity) and binds tightly (high affinity) at the mu opioid receptors. This means that:

- buprenorphine generally produces typical opioid effects
- buprenorphine binds in preference and more tightly to receptors than other opioids such as heroin or methadone. It can therefore precipitate opioid withdrawal if taken by individuals who have recently used other opioids (e.g. within 6–8 hours of heroin use or within 24 hours of even low methadone doses)
- it reduces (blocks) the effects of other opioids. This can complicate efforts to achieve additional opioid analgesia in clients on buprenorphine
- onset of effects approximately 30 to 60 minutes after a dose. Peak effects occur 3 to 8 hours after a dose
- duration of effects are dose related:
  - ☐ low doses (e.g. 0.2 to 0.8 mg used for analgesia): 4–12 hours
  - ☐ medium doses (e.g. 4 to 8 mg): 12–24 hours
  - ☐ high doses (e.g. 12 mg or more): 24–72 hours (this allows some clients to be dosed every 2 or 3 days)
- buprenorphine appears to have a milder withdrawal syndrome than withdrawal from equivalent amounts of morphine or methadone

 See Table 9–7

Table 9–2
Methadone effects and duration

Effect	Timing
Onset of action	30–90 minutes after oral dose
Peak effects	3–8 hours after dose
Duration of effects in substitution treatment of opioid dependence	20–30 hours, allowing once a day dosing
Duration of analgesic effects in pain management	8–12 hours, and is usually taken two or three times a day for pain management
Half-life	Approximately 15–30 hours. It takes approximately 5 half lives to achieve steady-state equilibrium after a dose change. This is important when starting methadone — during the first few days of treatment the client will experience increasing opioids effects after each dose. Hence caution is required when starting methadone treatment.

Naltrexone

Naltrexone is an opioid antagonist. It binds to opioid receptors but produces no opioid effects, and importantly prevents other opioids from binding to receptors. This blocks the effects of other opioids (e.g. heroin) and relapse to heroin use is prevented as long as naltrexone is taken. There is no withdrawal on ceasing naltrexone. Naltrexone is registered in Australia for the prevention of relapse in heroin and alcohol dependence.

See Chapter 3 Alcohol

Table 9–3
Common symptoms and time frames of opioid withdrawal

Time since last heroin use	Common symptoms
6 to 12 hours	• runny eyes and nose, sneezing, yawning • sweating
12 to 24 hours	• agitation and irritability • goosebumps • sweating, hot and cold flushes • loss of appetite
more than 24 hours	• strong urges (cravings) to use heroin • stomach cramps, diarrhoea • poor appetite, nausea, vomiting • back pain, pain in joints, legs or arms, headache • poor sleep • lethargy, fatigue • restlessness, irritability, agitation • poor concentration • hot and cold flushes, increased sweating
2nd to 4th days	• symptoms reach their peak
5th to 7th days	• most physical symptoms begin to settle down. Appetite returns
second week	• 'physical' discomfort subsiding. May have ongoing problems with poor sleep, tiredness, irritability, cravings
weeks to months	• return of normal sleep, levels of activity and mood. Improvement in general health, and cravings reduce

TOLERANCE

The body adapts to the repeated use of opioid drugs so that a higher dose is required to produce the same effect that was once obtained at a lower dose. The process is called neuroadaptation and results in the phenomenon of tolerance. Tolerance results in a reduction in response to opioids after regular use.

WITHDRAWAL

A withdrawal syndrome is the emergence of characteristic signs and symptoms upon the reduction or cessation of heavy and prolonged opioid use. Opioid withdrawal is very unpleasant, but not life-threatening. Table 9–3 shows the characteristic features and time frames for short acting opioids such as heroin and morphine.

DEPENDENT HEROIN USE

The Dependence Syndrome

- dependence has *grades* of severity — it is not an 'all or nothing' phenomenon
- the most salient feature of the syndrome is the loss of control over the use of a drug, with persistent use despite significant harms
- physical dependence is not a requisite of drug dependence, nor is physical dependence alone sufficient for a diagnosis of dependence

Natural History of Dependent Heroin Use

Most dependent heroin users describe first using heroin in their late teens to early twenties, with regular use usually commencing several years later.

Table 9–4
Factors impacting upon severity of withdrawal

Factor	Impact
Opioid type	Withdrawal from longer acting opioids (e.g. methadone) is typically slower in onset and lasts longer (weeks to months). Withdrawal from partial agonists (e.g. buprenorphine) appears to be less severe.
Opioid dose	Higher doses are generally associated with greater withdrawal severity.
Duration of regular opioid use	A short history of regular use (e.g. < 6 months) is generally associated with a milder withdrawal syndrome.
Prior experience of withdrawal and expectancy	Individuals who are particularly anxious about withdrawal often experience greater discomfort.
Concomitant medical or psychiatric conditions	May increase the severity of withdrawal, or decrease the individual's capacity to cope with symptoms.
Setting	The environment in which withdrawal is undertaken impacts upon the experience.

Heroin dependence is a chronic, relapsing–remitting condition. Long-term follow-up of those entering treatment suggests:

- 10% of heroin users will become and remain abstinent in the first year after treatment
- approximately 2–3% of users will achieve and remain abstinent in each subsequent year

Features of Dependent Heroin Use in Australia

- dependent heroin use is difficult to sustain for most people
- heroin is a *short acting* drug: 2 to 4 injections a day is common
- illicit heroin has variable concentration and adulterants, and is expensive (costing $50 to $200 per day in 2001)
- stigma associated with heroin use can deter people from seeking treatment or disclosing their drug use to family, friends, work colleagues and health workers
- polydrug use is common: over half of dependent heroin users use cannabis regularly, and approximately one third used benzodiazepines within last month

HARMS ASSOCIATED WITH HEROIN USE

Side effects associated with opioids are described above. Other harms include:

Overdose

- the estimated mortality rate (from all causes) for heroin users is approximately 1–2% per annum (10 to 20 times greater than age and gender matched controls). More common in male heroin users over age 25
- most opioid-related deaths occur following use of opioids with other drugs (alcohol, benzodiazepines)

Harms Related to Injecting

- trauma and/or infection of injection sites: scarring, thrombosis, thrombophlebitis, cellulitis
- systemic bacterial or fungal infections: septicaemia, infective endocarditis, pneumonia, osteomyelitis, and renal complications (glomerulonephritis)
- blood borne viruses (HIV, HCV and HBV)
  - HIV: has been contained in Australian IDUs thus far (prevalence rates of 0.8%)
  - HCV: Prevalence (HCV Ab +ve) 64% of IDUs; incidence rate approximately 5 to 15% — an area of increasing concern
  - HBV: Estimated 17% from self-report

(National Seroprevalence Study of Users of Needle Exchange Programs, 2001)

Psychological Harms

Dependent heroin users have a greater incidence of depression, anxiety, suicidal ideation and poor self-esteem. This relationship is often complex and causality difficult to establish. Psychological problems can subside following management of heroin dependence (e.g. methadone maintenance) without the need for psychiatric treatment; however, psychiatric assessment should be sought for clients with severe or persistent problems.

Social and Community Harms

- financial, legal problems
- impaired functioning/retraction from other activities (work, parenting, friendships)
- stigma for individuals, families, friends
- economic cost to the community

MANAGEMENT AND INTERVENTION STRATEGIES

There are two treatment pathways available for dependent heroin users as illustrated in Figure 9–1 overleaf.

WITHDRAWAL SERVICES

Objectives

Withdrawal can temporarily alleviate much of the stress of heroin dependence; however, withdrawal alone rarely results in long-term changes in drug use. Heroin dependence is a chronic condition, requiring long-term interventions for lasting benefits.

Withdrawal services are short-term interventions with the following objectives:

- alleviate the discomfort of heroin withdrawal
- prevent the development of complications (e.g. overdose)
- interrupt a pattern of heavy and regular drug use
- facilitate linkages to post-withdrawal services

Key Components

Assessment

Referral to or consultation with a specialist is recommended for patients with complex presentations (e.g. polydrug dependence, psychiatric or complex medical presentations).

Setting

Withdrawal can usually be attempted at home (outpatient or home based withdrawal services). Clients with unsuitable home environments or repeated failure at outpatient withdrawal may require residential support (e.g. community withdrawal unit). Clients with significant medical or psychiatric comorbidity require more intensive residential withdrawal settings (e.g. inpatient detoxification units, general or psychiatric hospital).

Supportive care

Supportive care can significantly reduce anxiety which, in turn, may reduce the severity of somatic complaints. Provide:

- information regarding the nature and duration of withdrawal symptoms, strategies for coping with symptoms, and the role of medication
- supportive counselling aimed at helping patient cope with symptoms, cravings and to maintain motivation. Defer addressing complex personal, emotional or relationship issues until after withdrawal

- crisis intervention addressing accommodation, personal safety, or other urgent welfare issues may be required

Frequent monitoring and review

Patients should be reviewed by a health worker at least daily during the first few days, monitoring:

- general progress, ongoing motivation, complications or difficulties encountered
- severity of withdrawal (can be facilitated by the use of withdrawal scales)
- use of heroin and other drugs, and reasons identified by the patient for drug use
- use of, and response to, medication(s) including side effects

Medication

Medication can be a useful adjunct to reduce withdrawal symptoms and cravings. Contemporary approaches for management of heroin withdrawal include:

- medications to manage somatic complaints such as analgesics, anti-emetics, anti-anxiolytics, benzodiazepines, clonidine
- partial opioid agonists — buprenorphine
- reducing doses of an opioid agonist, usually methadone
- opioid antagonists, such as naltrexone which aim to accelerate the withdrawal period

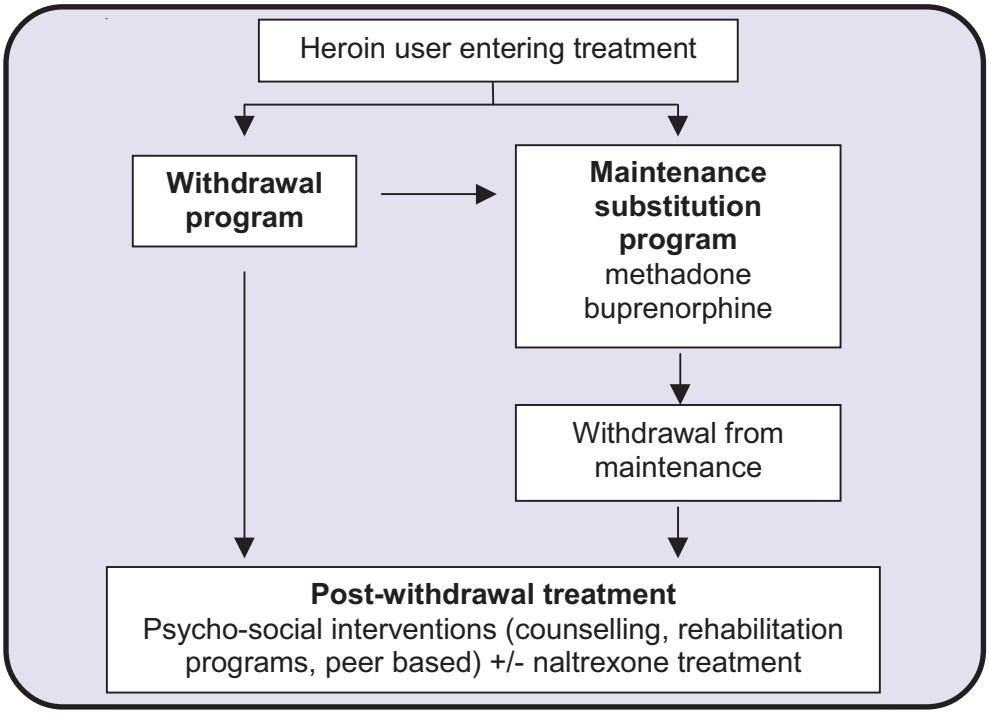

Figure 9–1
Treatment pathways for dependent heroin users

Medication Regimes for Opioid Withdrawal

See Tables 9–5 & 9–6
Medications offering symptomatic relief

See Table 9–8
Methadone for heroin withdrawal

See Table 9–7
Buprenorphine for heroin withdrawal

See Table 9–9
Accelerated withdrawal using opioid antagonists

Table 9–5
Symptomatic medications for opioid withdrawal

Other symptomatic medications	
Benzodiazepines	For sleep, anxiety. Concerns regarding abuse (overdose, intoxication, intravenous use, dependence) and/or delayed return of normal sleep pattern. Recommend: • limit access to medication (regular dispensing/responsible carer) • beware of multiple sedatives (e.g. clonidine, heroin, alcohol) • do not continue beyond 7 to 10 days. Diazepam 10 mg to 30 mg per day (to maximum 40 mg / day), in 2 or 3 divided doses; or temazepam 10 to 30 mg (tablets not capsules) nocte. Higher doses may be used in inpatient settings with experienced staff.
Antiemetics	Use reducing doses over 3 to 7 days (e.g. metoclopramide 10 mg t.d.s.)
Antidiarrhoeal agents	These may be useful during the first two to three days. Diphenoxylate i-ii b.d. p.r.n. for up to 5 days.
Antispasmodic agents	May help severe abdominal cramps. Hyoscine butylbromide 10 mg t.d.s. p.r.n. (up to 7 days).
Quinine	For skeletal muscle cramps. Potentially toxic in high doses (blindness, severe liver disease). 300 mg i-ii nocte p.r.n.
NSAIDs	For muscle and joint pains. Ibuprofen 200-400 mg t.d.s. with food p.r.n.

Table 9–6
Symptomatic medications for opioid withdrawal: clonidine

Clonidine		
Clonidine (α-adrenergic agonist) effective in reducing 'autonomic' features (diarrhoea, nausea, abdominal cramps, sweating, rhinorrhoea); but less effective for sleep disturbances, aches, cravings. Limit access to large amounts of medication (risks of overdose/abuse).		
Precautions, contraindications	Use only if patient closely monitored (e.g. daily) — unsupervised use not recommended. Use with caution in depression, cerebrovascular disease, renal disease, or with other CNS sedatives. Safety in pregnancy and lactation not established. Contraindications: severe bradyarrhythmia, hypersensitivity.	
Side effects	Hypotension (experienced as dizziness, fainting, light-headedness), fatigue, lethargy, sedation, dry mouth. Severe arrhythmias (bradycardia) following clonidine overdose.	
Dosing regimes	Treatment requires upward dose titration according to the patient's withdrawal severity and adverse events. A recommended outpatient regime is shown below. Higher doses (to maximum 15 mcg / kg / day) can be used in inpatient settings. Omit/reduce dose if patient is experiencing hypotension.	
	The maximum daily dose of clonidine = 12 mcg / kg / day, given in 3 or 4 divided doses.	
	Days 1–3:	Titrate dose of clonidine according to clinical response: • for patients < 60 kg (body weight): 1 x 100 mcg 3 or 4 times / day (300–400 mcg / day) • for patients > 60 kg (body weight): 1 x 150 mcg 3 or 4 times / day (450–600 mcg / day).
	Day 4:	The total dose is reduced to 75% of the day 3 dose and given in 3 or 4 divided doses.
	Day 5:	The total dose is reduced to 50% of the day 3 dose and given in 2 or 3 divided doses.
	Day 6:	The total dose is reduced to 25% of the day 3 dose and given in 1 or 2 doses.
	The maximum daily dose of clonidine = 12 mcg / kg / day, given in 3 or 4 divided doses	

Table 9–7
Buprenorphine for heroin withdrawal

Buprenorphine is a partial opioid agonist useful in managing heroin withdrawal, either in short-term regimes (e.g. 3 to 10 days); or in gradual reduction regimes over several weeks (similar to methadone reduction programs). Issues include:

- opioid-like side effects (usually mild and tolerable) are common during first few days. The initial buprenorphine dose can precipitate opioid withdrawal in a person who has recently used heroin — first dose should be delayed until patient has features of opioid withdrawal (or at least 6–8 hours after last heroin use).
- an authorised medical practitioner requires a permit to prescribe buprenorphine, and it is dispensed under supervision at an authorised pharmacy.
- other medications for opioid withdrawal are not routinely required.
- some patients will experience 'rebound' withdrawal on stopping buprenorphine — this is generally greater with longer durations of buprenorphine treatment.
- a range of post-withdrawal treatment options available, including (a) transfer to maintenance buprenorphine, (b) naltrexone treatment or (c) 'drug-free' rehabilitation.

Dosing regimes		
Short outpatient regimes	Proposed regime	Recommended lower and upper limits
Day 1	6 mg	4 to 8 mg
Day 2	8 mg	4 to 12 mg
Day 3	10 mg	4 to 16 mg
Day 4	8 mg	2 to 12 mg
Day 5	4 mg	0 to 8 mg
Day 6		0 to 4 mg
Day 7		0 to 2 mg
Day 8		0 to 1 mg
Short inpatient regimes	Proposed regime	Recommended lower and upper limits
Day 1	4 mg at onset of withdrawal, & additional 2 to 4 mg evening dose p.r.n.	4 to 8 mg
Day 2	4 mg mane, with additional 2 to 4 mg evening dose p.r.n.	4 to 8 mg
Day 3	4 mg mane, with additional 2 mg evening dose p.r.n.	4 to 6 mg
Day 4	2 mg mane p.r.n.; 2 mg evening p.r.n.	0 to 4 mg
Day 5	2 mg p.r.n.	0 to 2 mg
Day 6	no dose	
Day 7	no dose	

Post-withdrawal Interventions

Psychosocial interventions

These aim to prevent relapse back to dependent heroin use following withdrawal from heroin or maintenance substitution treatment. The evidence regarding their efficacy suggests:

- outpatient counselling programs are more effective for those individuals with good social support systems (e.g. relationships, employment), good cognitive functioning and higher levels of education
- those without good community supports or cognitive functioning may benefit from more structured interventions such as long-term residential rehabilitation (including therapeutic communities), self-help groups

Outpatient counselling

Counselling can be individual, group or family based, and may be structured upon principles of supportive counselling; cognitive-behavioural or psychodynamic theory. Relapse prevention is a common approach used by drug treatment agencies aiming to:

- enhance commitment to abstinence
- identify environmental and psychological factors associated with relapse to drug use
- develop cognitive-behavioural coping skills to deal with these risk factors

As in most forms of counselling, the quality of the relationship between client and counsellor is critical.

Therapeutic communities

These are usually long-term (e.g. 6 month to 3 year) residential programs in which drug

Table 9–8
Methadone for heroin withdrawal

Methadone can be used in short regimes (e.g. 7 to 14 days), or longer regimes with gradual reduction over weeks. Issues include:

- opioid-like side effects (usually mild and tolerable) are common during first few days.
- an authorised medical practitioner requires a permit to prescribe methadone, and it is dispensed under supervision at an authorised pharmacy.
- withdrawal discomfort generally increases as the patient reduces their methadone dose, with greatest discomfort experienced when/soon after the patient ceases their methadone, and can continue for several days. This limits the use of methadone in inpatient settings.
- other medications for opioid withdrawal are not routinely required until the patient has reduced their methadone dose, when short courses of symptomatic medication may be of value. Caution about using other sedating drugs (benzodiazepines, alcohol).

Dosing regimes	Commence with doses between 20 and 30 mg (depending upon level of physical dependence and concomitant medical conditions). Dose is reduced according to proposed duration of regime (e.g. start 25 mg, reduce by 2.5 mg per day for 10 day regime).

users move into a highly structured, isolated environment, with varying approaches to counselling and rehabilitation. Therapeutic communities tend to attract individuals with highly entrenched drug using lifestyles, few community supports or resources, often with legal conditions. This is an effective approach for those prepared to remain in treatment long-term; although rates of relapse on community re-entry are high.

Self-help groups

Narcotics Anonymous (NA) is the main self-help group for opioid dependent individuals in Australia. It operates on a 12-step abstinence philosophy and is attractive for some drug users as it provides a support structure and 'community', but does not appeal to all.

Naltrexone Treatment

Naltrexone is registered in Australia for the prevention of relapse for heroin or alcohol dependent patients. Naltrexone is an opioid antagonist that blocks the actions of other opioids.

Clinical aspects

- clients should complete opioid withdrawal (at least 5 to 7 days without heroin use, 10 days without methadone) prior to starting naltrexone. Premature naltrexone treatment results in severe withdrawal — a naloxone challenge test is recommended prior to starting naltrexone
- recommended dose is 50 mg daily. Blockade effects wear off within 2 to 3 days of ceasing such a dose
- treatment outcomes can be optimised by:
  - participation in a comprehensive psychosocial treatment program
  - supervision of doses (e.g. by a family member) and close monitoring by treatment team

Adverse events

- mood and sleep disturbances, abdominal cramps, nausea are common during the commencement of treatment, but usually subside with time
- overdose: overdose on opioids cannot occur whilst a client is taking naltrexone, however, there appears to be an increased risk of overdose upon stopping naltrexone, due to loss of opioid tolerance and possible increased opioid sensitivity following naltrexone treatment
- barriers to analgesia: naltrexone blocks the effects of opioids for analgesia

Outcomes associated with naltrexone treatment

Naltrexone treatment generally has poor retention rates - trials of 'street heroin users' suggest:

- 40% are retained in naltrexone treatment beyond one month
- 10–20% are retained in naltrexone treatment at 6 months

Higher success rates can be achieved by carefully selecting clients for treatment — those who are employed, have good social support networks, are in relationships with non-drug users, and have strong motivation for abstinence (e.g. professionals, court-ordered individuals).

SUBSTITUTION MAINTENANCE TREATMENT WITH METHADONE OR BUPRENORPHINE

Rationale, Objectives and Outcomes

The rationale is to supply dependent heroin users with a long-acting opioid (methadone or buprenorphine) that substitutes for heroin thereby preventing withdrawal, reducing cravings and reducing the euphoric effects of

Table 9–9
Accelerated withdrawal using opioid antagonists

Naloxone and naltrexone accelerate the onset and reduce the duration of opioid withdrawal. Rapid detoxification involves the use of naltrexone and symptomatic medications (clonidine, benzodiazepines, anti-emetics). Ultra-rapid detoxification involves inducting the patient onto antagonists using general anaesthesia or heavy sedation in highly supervised (hospital) setting. It is postulated that more rapid withdrawal and early induction onto naltrexone enhances long-term outcomes, although research is yet to establish such benefits. Naltrexone is not registered in Australia for this indication, and specialist consultation is recommended.

continued heroin use. This enables clients to stop using heroin, and to disassociate themselves from a drug-using lifestyle. The specific objectives are:

- to reduce heroin and other drug use by clients
- to improve the general health and well-being of clients
- to reduce mortality
- to reduce the transmission of blood borne viruses
- to improve the social functioning of clients, including a reduction in criminal activity

This is an effective treatment modality for most heroin users in reducing mortality, heroin use and criminality, and in improving psychosocial functioning. Australian research suggests that approximately 50–70% of heroin users commencing methadone treatment are retained in treatment at 1 year. Of these:

- approximately half will no longer be using heroin
- approximately one third will continue to use heroin at a markedly reduced frequency (e.g. weekly)
- approximately one sixth will continue to use heroin regularly (e.g. daily)

Treatment outcomes are enhanced in maintenance programs when:

- clients remain in treatment for long periods of time (> 12 months). Clients should be encouraged to remain in treatment until they have distanced themselves from heroin use and associated lifestyles
- clients are on adequate doses of methadone (e.g. 60–120 mg daily) or buprenorphine (e.g. 12–24 mg daily)
- there is a good therapeutic relationship between the client and service providers; and
- where the client participates in counselling and other psychosocial interventions

Methadone and buprenorphine are of comparable efficacy when used in equivalent doses.

Delivering Substitution Treatment in Australia

- maintenance substitution treatment is restricted to medical practitioners, pharmacies or clinics specially authorised by state or territory governments. This generally requires a training program for medical practitioners
- doctors must receive a permit to treat individual clients with methadone or buprenorphine

- the administration of methadone and buprenorphine is usually supervised at a clinic or pharmacy. Stable clients can receive a number of take-away doses after a period of time (policies vary in each jurisdiction)
- treatment is increasingly being delivered by general practitioners and community pharmacies, thereby normalising treatment and increasing its accessibility. Public clinic programs are being oriented towards managing clients with more complex presentations

Problems with Maintenance Substitution Treatment

- the inconvenience of daily/regular dispensing
- the cost to clients of supervised dispensing
- withdrawal syndrome and high relapse rates upon the cessation of treatment
- a minority have persistent side effects
- stigma associated with methadone treatment

Buprenorphine can be better tailored to the needs of the individual client.

Principles of Safe and Effective Methadone/ Buprenorphine Treatment

- comprehensive assessment and informed consent is required prior to commencing treatment. Methadone/buprenorphine treatment are only suitable for opioid dependent people
- commence with low doses, review client frequently during induction and titrate dose accordingly:
  - starting doses of methadone are usually between 20 to 30 mg (and never > 40 mg). Beware of accumulation of methadone during induction — in general only increase dose after every 3–4 days
  - starting doses of buprenorphine are usually between 4 and 8 mg (never greater than 8 mg), and delay first buprenorphine dose until client is in opioid withdrawal. Beware of precipitated withdrawal on starting buprenorphine, especially in clients transferring from methadone
  - only increase dose after review by an experienced treatment provider
- beware of combined use of other sedatives (e.g. alcohol, benzodiazepines), due to an increased overdose risk
- an experienced treatment provider should review clients who have missed multiple (> 3) consecutive methadone/buprenorphine doses prior to recommencing treatment — risk of overdose from drop in tolerance
- clients who are not responding to treatment (e.g. continued high risk drug use) require increased monitoring, psychosocial interventions and referral to specialist services

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Volatile Substances

VOLATILE substances are central nervous system (CNS) depressants and are chemical compounds that rapidly change from a liquid, or semisolid state to vapour when exposed to air.

Volatile substance use is the deliberate inhalation of vapour given off from a substance at ambient temperature to alter consciousness or cause intoxication.

Volatile substance use may be:

- experimental — using out of curiosity
- recreational — frequently a group practice
- chronic — an habitual and dominant activity

COMMONLY USED VOLATILE SUBSTANCES

The most commonly used volatile substances include petrol, lacquers and varnishes containing benzene and adhesives, spray paints, glues and paint thinners containing toluene. Table 10–1 lists the major volatile substances and their sources. Also used are amyl nitrite and nitrous oxide found in canisters.

Table 10–1
Major volatile substances and their sources

Major volatile substances	Sources
• benzene	• petrol, varnish, resins, lacquer
• toluene	• adhesives, spray paints, glues, paint thinners
• xylene	• lacquer, thinner, wood glues
• propane	• bottled fuel
• butane	• cigarette lighter fluid
• acetone	• nail polish remover
• n-hexane	• model glues, rubber cement
• trichloroethane	• dry cleaning agents, degreasing agents
• trichloroethylene	• dry cleaning agents, stain removers, degreasing agents
• trichlorofluoromethane	• aerosol propellant
• dichloromethane	• paint stripper
• butyl nitrite	• room air freshener

MODES OF ADMINISTRATION

There are three major modes of volatile substance administration:

- *sniffing*: Vapours inhaled directly from a container. Lowest vapour concentration, with a significant quantity dissipated into the surrounding air
- *huffing*: A piece of saturated material (commonly a piece of clothing) held against the mouth or nose. In extreme cases may be held *in* the mouth. Spraying aerosol vapours directly into the mouth
- *bagging*: Vapours inhaled from a plastic or paper bag held firmly over the mouth and nose

Chronic users generally begin with sniffing and progress to huffing and bagging to increase vapour concentration availability and achieve and maintain euphoria (Henretig, 1996; Linden, 1990).

PREVALENCE

There is a lack of good epidemiological data on the prevalence of use amongst general community groups and subgroups. However some trends in using volatile substances are emerging:

- there is a higher prevalence amongst the 14–17 year old age group than older adults (White, 2001)
- the trend for use is greatest amongst younger teenagers, aged 12 and over (White, 2001)
- male adolescents use more than female adolescents (AIHW, 1999)
- amongst recreational drug users volatile substances and cannabis were most commonly combined with ecstasy, amphetamine or LSD at rave scenes (Boys et al., 1997)

- compared with non-Indigenous counterparts, young Indigenous users
  - show greater habitual use
  - use more frequently
  - use over a longer period

  (Carroll et al., 1998)

APPEAL

Volatile substances:

- are relatively inexpensive
- are readily available from supermarkets, hardware stores, homes, building sites, cars and offices, despite legislation in a number of Australian States to preclude their sale to minors
- can be packaged in small and discrete containers (e.g. cans or bottles) and easily concealed
- create rapid intoxication and rapid disappearance of intoxication. The user can indulge and then go home or to other venues in a sober state

PHYSICAL COMPLICATIONS

Acute Effects

Following use, blood levels peak within minutes then rapidly decrease as the drug is absorbed into fat, including the central nervous system (CNS).

Common initial effects are:

- euphoria
- excitation
- exhilaration
- a sense of invulnerability

Negative Acute Effects

Users may also experience:

- nausea
- vomiting
- headaches
- diarrhoea
- abdominal pain

These effects commonly resolve within two hours (Liira et al., 1988).

Effects at Higher Doses

Central nervous system depression leads to:

- slurred speech, disorientation, confusion, delusions, weakness, tremor, headaches, visual distortions and visual hallucinations; then
- ataxia; followed by
- stupor
- final stages associated with seizures, coma, cardiopulmonary arrest and death (Linden, 1990)

In the novice, or infrequent user, desired effects are achieved after a few breaths. However, tolerance develops rapidly and within several days of repeated use the user requires a significant increase in dose to achieve the desired effect. Withdrawal symptoms commonly include headache, nausea and muscle and abdominal cramps.

Specific Physical Effects

Central Nervous System

The majority of solvents are fat soluble and readily absorbed from the blood into high fat tissue including nerve cells. This results in generalised reduction of nerve membrane functioning, which causes CNS depression (Lolin, 1989).

Of the commonly abused substances, toluene causes the most CNS damage. White matter damage, cortical atrophy and cerebellar damage are observed in long-term chronic users. Destruction of nerve cells also results in peripheral neuropathy (Lolin, 1989), optic atrophy and hearing loss (Fornazzari et al., 1983; Williams, 1988).

Maternal and neonatal

Given their fat solubility, volatile substances readily cross the placenta. Neonatal toluene exposure is associated with malformations including:

- oral clefts and microcephaly
- spontaneous abortion
- foetal growth retardation
- low birthweight
- prematurity
- developmental delays

(Arnold et al., 1994; Jones & Balster, 1998)

Heart

Sudden death associated with ventricular fibrillation and cardiac arrhythmia is a major concern. Hydrocarbons contained, for example, in aerosols, petrol and substances containing benzene and toluene, sensitise the myocardium to adrenaline. When the user is 'startled', the resulting sudden serge of adrenaline causes ventricular fibrillation (Shepherd, 1989). Approximately 20% of those who die from 'sudden death' in these circumstances have no prior history of volatile substance use (Ramsey, Anderson et al., 1989).

Lung

Volatile substances displace oxygen and can directly damage lung tissue resulting in loss of consciousness.

It is not uncommon for asphyxiation or suffocation to occur from aspiration of vomit in plastic bags used for bagging. Asphyxiation can also be caused by material placed in the mouth during huffing (Linden, 1990).

Kidneys, liver and bone marrow

Compounds containing toluene cause renal tubular acidosis that interferes with functioning of the distal tubule and collecting ducts (Marjot & McLeod, 1989). Complete kidney and liver failure have been associated with toluene use (Dinwiddie, 1994). Chloroform and chlorinated hydrocarbon vapours result in toxic hepatitis with liver dysfunction associated with trichloroethane and trichloroethylene use (Hutchens & Kung, 1985).

Chronic use of benzene is associated with suppressed functioning of bone marrow production, aplastic anaemia and related morbidity and cancers such as myeloma, leukaemia and lymphoma (Rosner & Grunwald, 1980).

Other Morbidity and Mortality

The sense of invulnerability associated with volatile substance use results in impulsive high risk behaviours that can cause accidents, injury, brain damage, trauma and death. Morbidity and mortality are also associated with fires resulting from combustion of inhalants.

PSYCHOSOCIAL COMPLICATIONS

Adolescents who chronically use volatile substances are more likely than non-users to report poor family relations, family history of alcohol and other drug problems and unstable living environments, school absenteeism and academic problems, criminal activity, low self-esteem and associated depression and suicidal thoughts (Howard & Jenson, 1999). There are reports of violence amongst adolescent chronic volatile substance users, both towards other users and non-users (Dukarm et al., 1996).

MANAGEMENT AND INTERVENTION STRATEGIES

Detection and Assessment

To detect and assess volatile substance use:

- look for indicators of recent or chronic use
- obtain a comprehensive history
- conduct a thorough physical examination by a medical practitioner

Clinical signs and symptoms

Recent use may be indicated by the identification of solvent containers, or bags, bottles and cans with solvent residue or residual odour on breath, skin or contaminated clothing.

Mucous membrane irritation may result in increased sputum production, cough, wheeze, salivation, sneezing, or conjunctival injection (McHugh, 1987). Chronic use can lead to drying of mucous membranes and facial skin which causes irritation and may permit bacterial infections to become established. The resulting patchy redness of skin (erythematous spots) or pus producing skin lesions around the mouth and nose are commonly referred to as 'sniffer's or huffer's rash'. Recent use may also be associated with decreased reflexes and oscillatory movement of the eyes.

Excessive mood swings, disinhibition or inappropriate aggression coupled with one or more of the above physical symptoms may also indicate use.

Symptoms associated with polysubstance use may mask those of volatile substances.

Urine drug screening is not designed to detect volatile substances or metabolites.

Toluene use is confirmed by elevated levels of hippuric and benzoic acid in urine.

Intoxication

In most instances, acute volatile substance intoxication resolves spontaneously. Clothing and skin should be decontaminated, and the user placed in a well ventilated, safe environment and observed. Cardiopulmonary function should be monitored until intoxication resolves.

There is no significant way to enhance the rate of volatile substance elimination. Cardiopulmonary assessment, stabilisation and monitoring is required. Electrocardiography is indicated in the presence of cardiac abnormalities. Hydration with saline may be required. Laboratory tests include complete blood count and oxygen saturation. Urine or blood screening may be indicated where polysubstance use is suspected.

Experimental, Recreational and Chronic Use

Experimental

Volatile substance use is usually a transitory event amongst a kaleidoscope of experimental activities. It commonly resolves without intervention or major incident. Patterns of use in this group preclude the development of tolerance and associated excessive toxicity, and morbidity is low. Mortality from 'sudden death' is of concern. Education initiatives provided in early school years (late primary) as part of an integrated general curriculum may reduce the prevalence and frequency of use. However, any educational programs should be undertaken with care as they can inadvertently increase use.

Recreational

Similar to experimental use, volatile substance use is commonly an optional activity amongst recreational users. Social status, for example, in those attending rave dances, is more likely to be associated with body image and rave activities, than volatile substance use per se. Information on the relationship

between use, tolerance and morbidity and mortality will likely decrease the frequency and quantity of use in this group. Sudden death is a real possibility and information on the avoidance of use and co-activities that raise adrenaline levels (e.g. exertion and co-stimulant use), both popular activities amongst 'rave' users, is necessary. For both experimental and recreational users, the portrayal of volatile substances as a low class of drugs may reduce the prevalence and frequency of use.

Long-term management — the chronic abuser

Management is difficult and lacks rigorous empirical evaluation. The objectives here are to:

- assess and care for medical complications
- minimise harm associated with use
- move the user away from chronic use patterns and associated lifestyles

Assess and care for medical complications

Mental state, organ and neurological examination are necessary. Chest x-rays are required where there is evidence of pulmonary morbidity. Laboratory tests include complete blood count, oxygen saturation, serum electrolytes, and blood urea, nitrogen and creatinine. Additional tests may be required to assess the presence of metabolic disturbances and morbidity to other organs (e.g. kidneys).

Minimise harm associated with use

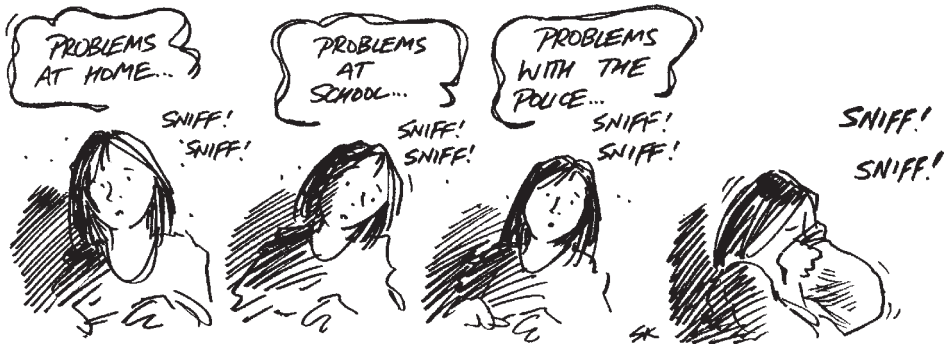
Although total abstinence may be the optimal objective, this may be initially impractical in high risk communities, short of removal of the user. Here harm minimisation to reduce morbidity and mortality is required. For example, non-use of plastic bags that cause asphyxia, removal of lead-based petrol and education about the development of tolerance to reduce overall acute and chronic tissue toxicity and damage.

Move the user away from habitual and chronic use patterns

Exposure to those with significant morbidity, resulting from volatile substance use has been identified by chronic users as a significant factor in reducing use (Carroll, Houghton et al., 1998). Overall, initiatives should focus on the community and environment in which volatile substance use takes place (e.g. urban or Indigenous communities).

Use in these environments is often closely associated with:

- a lack of alternative social activities and poor economic prospects
- the conferring of greater status within the group upon those who consume the greatest quantities of volatile substances



Providing both desirable social activities and social status outside the user group are essential. Initiatives should be acceptable to and developed in collaboration with local communities. Community and family counselling and support may be required.

Primary Prevention Strategies

Many volatile substance users commence use in early or pre-teen years, so early prevention initiatives at primary schools should be considered. Limited available information suggests that mass media, fear tactics and factual education programs are *not* hugely effective. Some modest success has been reported with programs utilising peer support initiatives and targeting social skills and healthy lifestyle acquisition (CDH, 1985).

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Benzodiazepines

BENZODIAZEPINES are minor tranquillisers widely used in clinical practice for sedation and relief of anxiety. They are also widely used for illicit or non-prescribed purposes. The first benzodiazepine (chlordiazepoxide) was marketed in 1959 as a safe alternative to barbiturates. This was followed by the introduction of many related compounds that achieved immense popularity to become the most commonly prescribed class of drugs in the 1970s and 1980s.

Benzodiazepines are CNS depressants. They have antianxiety, anticonvulsant, hypnotic and muscle relaxant properties. Their use results in performance deficits (including memory impairment, motor incoordination, decreased reaction time and ataxia).

PHARMACOLOGY

Benzodiazepines enhance the effects of gamma-aminobutyric acid (GABA) which is the main inhibitory neurotransmitter in the CNS. Benzodiazepines bind to receptors on the GABA–A receptor complex (Cape et al., 2002).

ABSORPTION

Benzodiazepines are relatively lipophilic (fat soluble) and most are poorly water soluble with the exception of midazolam (used in anaesthetic practice but also as a ‘date rape’ drug). They are

generally rapidly and fully absorbed orally with peak plasma concentrations from ½ to 2 hours after ingestion. The more lipophilic agents e.g. diazepam are absorbed faster than the relatively more hydrophilic agents e.g. oxazepam (Cape et al., 2002).

DISTRIBUTION

Benzodiazepines rapidly enter the CNS and are then distributed to less vascular adipose tissue. They all cross the placental barrier and can result in neonatal drowsiness, respiratory depression, hypotonicity and withdrawal (Therapeutic Guidelines Ltd., 2000).

METABOLISM

Benzodiazepines must be converted to water soluble compounds before renal excretion. They are metabolised by both oxidation, which may produce active compounds, and by glucuronidation which inactivates them. Active metabolites may have longer half-lives than the parent drug resulting in prolonged effects (especially with chronic dosing).

PATTERNS OF USE

- in 2001, 1.1% of Australians aged 14 years or over reported use of tranquillisers or sleeping pills in the previous 12 months for non-medical purposes, with peak use reported amongst those aged 20–29 years
- while there is little overall difference in prevalence of tranquilliser or sleeping pill use between men and women (M: 1.2%; F: 1.0%), men aged 20–29 were more likely than women of the same age to use these drugs (3.0% and 2.2% respectively)
- across age groups, people aged 40 years or over had the highest proportion of people who reported use of prescription drugs for non-medical purposes every day, or every week (AIHW, 2001)
- according to the Australian Statistics on Medicines (PBS, 1998), a total of 8.89 million prescriptions for benzodiazepines were dispensed through Australian pharmacies in 1998 (including PBS/RPBS, private and under co-payment prescriptions)
- the use of night-time sedation with benzodiazepines increases markedly with age
- long-term use of benzodiazepines remains common

EFFECTS OF BENZODIAZEPINES

All are sedating, anxiolytic and anti-convulsant.

Short-term Effects

- drowsiness, lethargy, fatigue
- motor incoordination, decreased reaction time and ataxia
- impaired cognition and memory (especially anterograde amnesia)
- confusion
- muscle weakness or hypotonia
- depression
- nystagmus, vertigo
- dysarthria, slurred speech
- blurred vision, dry mouth
- headaches
- paradoxical euphoria, excitement, restlessness, hypomania and extreme disinhibited behaviour (especially high dose, users may feel 'invulnerable, invincible and invisible')
- potentiation of other CNS depressants e.g. alcohol and opioids increasing likelihood of respiratory depression

(Victoria Police, 2002; Cape et al., 2002)

Long-term Effects

Similar to short-term effects (with no known organ toxicity) plus:

- tolerance to sedative/hypnotic and psychomotor effects (conflicting evidence whether tolerance develops to anxiolytic actions and effects on memory)
- emotional blunting (inability to feel normal highs or grief due to inhibition of arousal)
- menstrual irregularities, breast engorgement
- dependence (may develop after 3–6 weeks at therapeutic doses)

(Cape et al., 2002)

USES AND PROBLEMS

Uses

Clinically useful in the treatment of anxiety and insomnia because of their efficacy, at least in the short-term, and relative safety compared to the barbiturates or tricyclic antidepressants.

Other uses in clinical practice include the treatment of alcohol withdrawal (to prevent delirium tremens), epilepsy, tremor and agitation in psychiatric disorders.

Problems Associated with Benzodiazepines

- short- or long-term patterns of benzodiazepine use is associated with excess sedation, cognitive impairment, and increased risk of accidents (Oster et al., 1990). Advise patients of risks when driving or operating machinery
- adverse sleep effects. Studies amongst people with sleeping disorders have demonstrated that insomnia sufferers who use benzodiazepines have a similar quantity but poorer quality of night-time sleep compared with normal subjects. Rebound insomnia frequently occurs on cessation of benzodiazepines
- polydrug use, or concurrent use of benzodiazepines, alcohol or opioids, increases the risk of overdose
- dependence and withdrawal can occur even when recommended doses are used (Busto et al., 1986) (i.e., within 3–6 weeks)
  - withdrawal symptoms may be apparent while the patient is still taking medication, possibly because the patient avoids increasing the dose to cover increased tolerance (Ashton, 1991) or due to the short half-life of some drugs
- adverse mood effects with inability to experience emotions or unwanted stimulation or aggression

HIGH RISK GROUPS

- elderly:
  - higher risk of falls and fractures amongst the elderly (Leipzig et al., 1999). Through long-term use, many elderly patients have become dependent on benzodiazepines as a sleep aid and therefore find cessation very difficult. Accumulation of doses can readily cause oversedation and increase the risk of accidents
  - are higher users of prescribed medications for the management of chronic disease. Use of benzodiazepines in combination with some medications places the patient at increased risk of negative side effects and/or dependence
- polydrug and injecting users:
  - high-dose use, particularly amongst polydrug users, may result in extremely disinhibited, or uncharacter-

istic behaviour. Described as the 'Rambo syndrome', a person may engage in assaults, shoplifting or other activities, in full view of witnesses, and be unable to recall any events related to the offence

- benzodiazepine use appears to be increasing amongst injecting drug users, and is associated with a higher rate of HIV risk-taking behaviour (Darke et al., 1992)
- risk of overdose in people using heroin is increased when other CNS depressants, such as alcohol and benzodiazepines, are used (Zador et al., 1996)

PRESCRIBING BENZODIAZEPINES

Rational Use of Benzodiazepines

The following guidelines (RACGP, 2000) are recommended when prescribing benzodiazepines:

- avoid prescribing benzodiazepines to people suspected of using other psychoactive drugs
- advise all patients prescribed benzodiazepines of the risk of dependence
- to prevent inadvertent dependence, encourage patients to see the same doctor for repeat prescriptions
- prescribe benzodiazepines in the lowest possible dose for the shortest possible time
- reduce benzodiazepine dose only with the patient's consent and cooperation
- rely on non-pharmacological approaches to manage anxiety and insomnia
- before writing a repeat prescription for benzodiazepines, undertake a review of all medications (and ask about visits to other general practitioners)

To reduce access and harm resulting from the prescribing of multiple, single, high-dose prescriptions, write short-term prescriptions and encourage regular review. There is a high risk associated with prescribing large quantities of benzodiazepines (and other drugs of dependence).

Precautions

Benzodiazepines should be used with caution in patients:

- with renal failure
- with liver disease
- with respiratory disease
- in late pregnancy
- who are breastfeeding

Drug Interactions

Refer to Table 11–1.

Use in Management of Anxiety and Insomnia

Benzodiazepines are effective for relief of anxiety symptoms and will induce sleep if given in sufficient doses (Therapeutic Guidelines Ltd., 2000). Research has questioned the efficacy of prescribing benzodiazepines for symptom reduction in anxiety management, with studies demonstrating that counselling alone has similar, if not greater efficacy (Catalan et al., 1984).

Benzodiazepines have demonstrated efficacy in the short-term management of insomnia, however similar results have not been demonstrated for periods longer than two weeks (NHMRC, 1991). Insomnia should be regarded as a symptom requiring assessment and evaluation, rather than a diagnosis per se. A sleep–wake history may reveal the patient to:

- be functioning normally on the amount of sleep obtained

- have unrealistic expectations of the requirements for sleep
- have a disorder of the sleep–wake schedule (including problems associated with shift work) which is not improved with hypnotics
- have a specific sleep disorder such as sleep apnoea or narcolepsy, in which case hypnotics are contraindicated

Finally, many patients who have taken benzodiazepines for periods in excess of 4–6 months have unwittingly become, dependent and experience withdrawal insomnia (Busto et al., 1986; Therapeutic Guidelines Ltd., 2000).

MANAGEMENT AND INTERVENTION STRATEGIES

Reviewing Benzodiazepines in Long-term Users: A Staged Approach

- advise the patient you want to review their benzodiazepine medication with them
- assess dosage and pattern of use
- assess use of alcohol and other psychotropics
- assess withdrawal symptoms
- assess reported and observed side effects

Table 11–1
Drug interactions

Interacting drug	Mechanism of interaction	Clinical effect
Alcohol or other CNS depressants	additive effect	increased sedation
Antacids, anticholinergics	decreased absorption	delayed onset of acute clinical effects of benzodiazepines
Oral contraceptives, isoniazid	reduction in metabolism	prolongation of elimination half-life and effect of benzodiazepine
Cimetidine	inhibition of metabolism	increased toxic effects due to elevated plasma concentrations of diazepam
Rifampicin	increased metabolism	elimination half-life of benzodiazepine shortened
Digoxin	protein binding diazepam altered	increased digoxin levels
L-dopa	unknown	exacerbation of parkinsonian symptoms
Disulfiram	decreased metabolism	increased effects of benzodiazepine

Source: Norman et al. (no date, p. 37)

- assess history of depression
- assess other medical problems (e.g. pain)
- discuss long-term use with the patient
- discuss withdrawal symptoms with the patient
- finalise the management plan

(Mant & Walsh, 1997; NPS News, 1999)

Dependence and Withdrawal

- tolerance and withdrawal from benzodiazepines can occur in individuals who have been taking therapeutic doses of benzodiazepines for two or more weeks
- it is estimated that symptoms may occur in up to 45% of patients discontinuing low therapeutic doses and up to 100% of patients for high doses
- there is a significant risk of withdrawal if benzodiazepines are discontinued abruptly, particularly in the sick and elderly.

Symptoms of withdrawal

Commonly include:

- insomnia
- anxiety
- irritability
- restlessness
- agitation
- depression
- tremor
- dizziness

Less common but medically serious:

- seizures (high dose ± alcohol)
- delirium

Other symptoms include:

- muscle twitching and pains
- anorexia, nausea
- metallic taste
- fatigue
- tinnitus
- hyperacusis, photophobia, perceptual disturbances
- depersonalisation, derealisation
- blurred vision

Principles when helping the patient withdraw from benzodiazepines

- withdrawal must be gradual (e.g. 10–20% per week, slowing reduction at lower doses e.g. < 15 mg diazepam)
- a reducing regime will generally take 6–8 weeks (or longer especially with higher doses)
- make a contract with the patient
- gradually reduce the patient's dose using a set reducing dosage over a set time period (e.g. reduce the most important dose of the day by ¼ of the tablet)
- consider converting the patient to a benzodiazepine with a long half life e.g diazepam, to reduce the severity of withdrawal symptoms (see benzodiazepine equivalence table below)

Table 11–2
Benzodiazepine equivalence table

5 mg diazepam	=	0.5–1 mg alprazolam
	=	3–6 mg bromazepam
	=	10 mg clobazepam
	=	0.5 mg clonazepam
	=	1–2 mg flunitrazepam
	=	1 mg lorazepam
	=	5–10 mg nitrazepam
	=	15–30 mg oxazepam
	=	10–20 mg temazepam
	=	0.25 mg triazolam

- titrate the dosage reduction according to patient symptoms
- discuss sleep and stress management, diet and exercise
- review regimen weekly
- provide support, reassurance and explanation

(NPS News, 1999)

Dose equivalents are approximate, some drugs at higher doses may be more potent.

Aged Care Residential Facilities

Prescribing for residents in aged care facilities (and other residential facilities) presents special difficulties. Accreditation of aged care facilities has heightened awareness of responsibilities of the facility for quality use of medicines (Australian Pharmaceutical Advisory Committee, 1997). This responsibility includes drug utilisation review by an accredited pharmacist. The use of benzodiazepines is lower where staff have received education in geriatric care and where the organisational culture is supportive (Roberts et al., 1998).

Benefits for the elderly in aged care accommodation following successful reduction in rates of benzodiazepine use include:

- increased mobility
- increased alertness
- reduced incontinence
- improved wellbeing (Gilbert et al., 1993)

BENZODIAZEPINE MISUSE

Habitual Drug Users ('Doctor Shoppers')

Almost all GPs come across patients who may be obtaining prescriptions from several doctors.

The following may help in responding effectively (Mant et al., 1997):

- do not prescribe a benzodiazepine on the first visit
- there is rarely a valid indication for benzodiazepines in young people
- say 'no' from the start to the patient's requests for the prescription, whilst offering your help as a doctor
- take the opportunity to discuss risks associated with drug use and consider referral to a specialist agency

Drug Dependent Patients

The RACGP (2000) has endorsed the following protocol for prescribing benzodiazepines in high doses on a regular basis the definition of which is 'more than three occasions per month for more than two months in any one year.' There are high risks with patients seeking large quantities of benzodiazepines (and other drugs of dependence) from one prescriber or from multiple prescribers. Most high dose users cannot be managed with an ordinary script.

The protocol aims include the support of quality medical practice, reducing overdose deaths and indiscriminate prescribing to polydrug users while reducing barriers to doctors seeing drug-dependent patients.

A protocol for prescribing benzodiazepines in high doses on a regular basis (RACGP, 2000) follows.

Where relevant and appropriate the following should be undertaken and adequately documented in the medical record:

- a full history, including use of alcohol and other drugs and psychiatric comorbidity
- adequate physical examination
- problem/diagnosis list
- management plan, which should include the following:
  - consultation with another medical practitioner with experience in management of drug dependence
  - communication with other prescribers, notably methadone prescriber
  - supply of specified small quantities (e.g. daily), whether at the surgery or, if applicable, at a community pharmacy.
  - communication with the Health Insurance Commission to clarify whether the patient is seeing multiple doctors for prescriptions for benzodiazepines and/or narcotic analgesics
  - monitoring of consumption where applicable by the Health Insurance Commission, with agreement by the patient to attend only one doctor and one pharmacy and signed consent to the doctor receiving feedback on actual consumption for the period of the contract

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Other Drugs

THERE are some substances not covered in earlier chapters that are used in non-medical contexts. These drugs do not share a common pharmacology or pattern of effects and are used for different purposes in a variety of contexts. They include:

- hallucinogens
- 'party drugs'
- anabolic steroids
- over the counter drugs

It is important that use of non-prescription and complementary medicines is included in any drug use screening program.

HALLUCINOGENS

While a range of drugs have potential to produce hallucinations (e.g. cannabis, amphetamines), the label 'hallucinogenic' indicates that this is the major purpose for which the drug is consumed. These drugs are normally administered orally, on an irregular basis. Harms are likely to arise from acute drug effects (especially behavioural and psychiatric sequelae) rather than regular or dependent use.

The most common hallucinogens include:

- lysergic acid diethylamide (LSD or acid)
- magic mushrooms (containing psilocybin and other active compounds)
- anticholinergics (pharmaceuticals and plant sources e.g. datura, angels' trumpet)

Physical and Psychological Effects

The irregular use of hallucinogens means that most problems that arise are due to acute toxicity. While the exact symptoms vary, a common presentation is a person who is actively hallucinating, and is disturbed by the experience.

This can result from:

- an overdose (the strength of effect is greater than the person is accustomed to); or
- a 'bad trip' (the experience has become dysphoric rather than euphoric)

Management and Intervention

Agitation and feelings of panic and loss of control may be prominent. The best response is to try and calm and reassure the person. A quiet, non-threatening environment is important. If this is not successful, administration of a benzodiazepine (e.g. diazepam) may be required.

In isolated cases the symptoms do not completely subside when the drug effect has ceased. Some patients report daily recurrence of the unpleasant episode and may need psychiatric referral.

Other signs and symptoms depend on the drug consumed. LSD and psilocybin produce sympathomimetic effects including tachycardia, tremor, hyperreflexia. These are not usually problematic, but can be if the person has overdosed. Anticholinergic overdose is life-threatening and the effects may persist for many hours and even days. Physostigmine has been used, but treatment is usually conservative.

PARTY DRUGS

Party drugs is a term used to describe substances taken in the context of 'raves', nightclubs or similar situations. Two of the main party drugs, amphetamines and ecstasy, have been discussed in earlier chapters in this Handbook.

See Chapters 6 & 7
Amphetamines; Ecstasy

Other drugs used as party drugs include:

- LSD (see above)
- GHB (gamma hydroxybutyrate)
- ketamine

Party drugs (sometimes known as '*club drugs*' or '*dance drugs*') are frequently taken in combination with other drugs, including alcohol. This practice increases the risk of intoxication, overdose and other harms.

See Chapter 1
Overview and Introduction
'Polydrug Use', p. 5

GHB

Gamma hydroxybutyrate (GHB) is a clear, odourless and fairly tasteless powder usually taken in the form of a solution.

Street names include:

- liquid ecstasy
- fantasy
- GBH (grievous bodily harm)

GHB occurs naturally in some mammalian cells and is structurally similar to gamma aminobutyric acid (GABA). A synthetic form was initially developed as a hypnotic agent and is easy to manufacture.

Physical effects

GHB is absorbed rapidly and reaches peak plasma concentrations in 20–60 minutes. Common effects include:

- placidity
- mild euphoria
- pleasant disinhibition

Unpleasant side effects may include:

- drowsiness
- dizziness
- nausea
- vomiting

GHB has a steep dose response curve and consequent narrow therapeutic index. There is wide interpersonal variation in tolerance and metabolism. It is easy to overdose. Adverse effects usually subside within 12 hours.

Detection and assessment

GHB is very difficult to detect or measure in body fluids. Taking an oral history is the best method for assessing GHB use.

Management and intervention

In milder cases of intoxication, supportive treatment ensuring adequate respiratory function should be provided.

GHB overdose is a real danger, usually occurring within 15–20 minutes of ingestion. Most fatalities associated with GHB occur when it is taken with other substances, most notably alcohol. It may present as:

- nausea and vomiting
- seizures
- aggressive outbursts
- respiratory depression
- coma

Table 12–1 outlines the features of the management of GHB intoxication, as described by McDowell (1999).

Ketamine

Ketamine is a dissociative anaesthetic and n-methyl-d aspartate (NMDA) receptor antagonist. It has recently become popular amongst party drug users. It may be sold as ketamine or as a constituent of pills sold as ‘ecstasy’.

Its street names include:

- K
- super K
- vitamin K
- special K

Ketamine is usually snorted but may also be injected or taken orally.

Physical effects

Ketamine has a rapid onset but short duration (1–2 hours) of action. Dosage titration is difficult and the effects are highly sensitive to setting.

Table 12–1
Management of GHB intoxication

For spontaneously breathing patients:

1. Maintain oxygen supplementation and intravenous access
2. Maintain comprehensive physiological and cardiac monitoring
3. Attempt to keep the patient stimulated
4. Use atropine for persistent symptomatic bradycardia
5. Admit the patient if he or she is still intoxicated after 6 hours
6. Discharge the patient if he or she is clinically well in 6 hours

Patients whose breathing is laboured should be managed in an intensive care unit.

Ketamine can cause:

- thought disorders, out of body experiences, aphrodisiac effects, hallucinations and other perceptual distortion (psychedelic effects)
- stimulant effects

Adverse effects can include:

- anxiety
- agitation
- 'bad trips' (known as the 'K hole')
- nausea and vomiting (especially if taken with alcohol)
- tachycardia
- chest pain
- hypertension
- temporary paralysis
- analgesia and sensory dissociation thereby creating a high risk of accidental injury
- coma

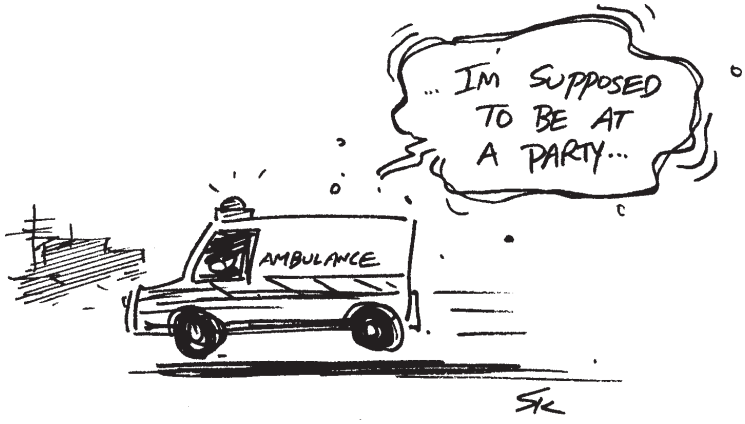
Ketamine can create dependency in some individuals (McDowell, 1999, p. 301).

Management and intervention

Most clinical presentations are short lived and require symptomatic relief and observation. An environment with low lighting and stimulation should be provided. Levels of patient anxiety should be closely monitored.

ANABOLIC STEROIDS

Anabolic steroids are synthetic variations of the male sex hormone testosterone. Traditionally, they have been associated with enhancing sporting performance but are now widely used for cosmetic reasons to modify body shape. Anabolic steroid use is currently dominated by males but a growing number of women use these drugs.



They are primarily taken orally or by intramuscular injection, generally in cycles with a period of use followed by a period of abstinence. The length of a cycle can vary widely but an average would be 6 to 8 weeks with a small number of people using continuously.

Anabolic steroids are commonly used in 'stacks', that is, a number of anabolic steroids or other drugs are taken at the same time.

A vast array of side effects have been associated with anabolic steroids. These range from relatively minor cosmetic changes such as acne, lowering of the voice and baldness to potentially life threatening complications involving the cardiovascular system, liver and kidneys.

OVER THE COUNTER DRUGS

A number of over the counter drugs have psychoactive effects. Drugs in the following medication groups can cause concern:

- analgesics
- antihistamines
- sympathomimetics
- cough suppressants

Non-prescription Medication

Few data are available on the extent of intentional misuse of non-prescription pharmaceuticals. However anecdotal accounts (and some monitoring by State authorities) indicate cause for concern in the following medication groups:

Analgesics

Paracetamol, codeine

Concern for codeine-containing products:

- codeine is an opioid and can be used to make home-bake heroin
- need to be aware of the potential for abuse and sale as a street drug
- abuse of paracetamol/codeine/doxylamine succinate combinations, i.e. analgesic plus antihistamine
- combination products (e.g. codeine plus paracetamol) increase the likelihood of hepatic damage from high dose paracetamol

Antihistamines

Chlorpheniramine, dexchlorpheniramine, diphenhydramine, pheniramine, promethazine hydrochloride, trimeprazine

- used alone or in combination with analgesics or sympathomimetics. There is little therapeutic justification for these combination products and recommendation should be avoided
- use of older style antihistamines for sedative effects
- the combination with alcohol increases sedation
- paradoxical stimulation, including hallucinations, can occur, particularly at higher doses

Sympathomimetics

Pseudoephedrine, phenylpropanolamine, phenylepherine

- potential for misuse by people dependent on stimulants
- high potential for diversion into manufacture of amphetamines
- concern for use in pregnancy
- overdose causes tachycardia, palpitations, and more rarely arrhythmias and seizures

Cough suppressants

Codeine, dihydrocodeine, dextromethorphan, pholcodeine

- often available in combinations with antihistamines and many other drugs

Injecting Drug Users

Dose form is cause for extreme caution; in particular requests for liquid preparations (e.g. cough and cold mixtures) or preparations in soft gelatin caps (e.g. diphenhydramine gel caps, ibuprofen/codeine gel caps).

Other

Anecdotal reports of experimentation with use of a wide range of products including eye drops and complementary medicines are not uncommon.

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Other Drugs