

# RECREATIONAL DRUGS AND THEIR NEUROLOGICAL CONSEQUENCES

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This article deals with neurological problems following the use of recreational drugs and substances as they present to neurologists. The effects of alcohol and the details of neuropsychiatric and neuropharmacological effects of recreational drugs are not considered.

## CLINICAL FEATURES

It is sometimes difficult to attribute a particular clinical syndrome to a particular drug type. Certain common features emerge which may be related directly and specifically to the drug (as outlined later) but other clinical features may arise in a non-specific way from complications of injection and/or coma. Furthermore addicts may use more than one drug (wittingly or unwittingly), each of which they may describe by a variety of “street” names which are far from standard (table 1). Moreover, the dose and the constituents of what they actually take (in terms of contaminants and other substitutes) may vary according to the source, batch, etc. Lastly the effects of the drug may vary considerably according to the method of intake (orally, nasally, inhalation/smoking or by intravenous, intramuscular, or subcutaneous injection), and they may be intensified by coincidental alcohol use.

All these factors may produce a variable clinical picture which cannot be relied upon to indicate that drug abuse is the cause. Conversely and on a more practical note, the recognition of drug addiction should raise suspicion that the presenting neurological syndrome may have an unusual aetiology and pathogenesis, and be a warning for the neurologist that there is the potential for more than one pathology, and that future management may have predictable difficulties. Certain common clinical themes are useful (table 2), partly because their recognition may act as a “red flag” for drug abuse (marked with an asterisk in table 2).

### WHY THINGS GO WRONG

Obviously in almost all instances of drug misuse, the effects of the drug wear off without mishap. However, problems may arise directly due to the drug, under the influence of a number of interacting factors, or indirectly by other mechanisms (table 3). Identifying these in individual cases is very difficult.

### “WHERE IS THE LESION AND THEN WHAT IS THE LESION?”

Any level of the nervous system may be affected, from the cortex to the neuromuscular junction, and this old adage is even more pertinent than usual. There is a tendency to take the initial clue of drug misuse and to jump to conclusions about pathologies, and thence location. It is essential that the location(s) of the lesion(s) is worked out first in the normal way, with the history of drug addiction *then* being introduced to bring in any “extra” pathologies which might explain this lesion, over and above those in non-users.

### PARTICULAR NEUROLOGICAL SYNDROMES

Some of the more common neurological syndromes in drug addicts are outlined in table 4. However, it should always be remembered that drug addicts are at much greater risk of having alcohol abuse problems and/or HIV infection, both of which are associated with their own blend of neurological syndromes and which may co-exist or subsequently develop (for example, alcohol withdrawal fits). Once their drug addiction is recognised, addicts often deny alcohol abuse, just as they often claim that they have never injected, or no longer do so. I *always* regard such assertions with great scepticism, and allow for these possibilities.

### CLINICAL EFFECTS OF RECREATIONAL DRUG GROUPS

There are five broad groups of recreational drugs:

- ▶ The stimulants
- ▶ The sedatives
- ▶ The hallucinogens
- ▶ The organic solvents
- ▶ Drugs used to enhance athletic performance

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**Table 1** Common street names of common drugs

▶ Cannabis	Marijuana, Pot, Puff, Resin, Hash, Hashish, Dope, Ganja, Hemp, Weed, Whacky backy, Gunk, Smoke, Spliff
▶ Cocaine	Coke, Charlie, Lady, Percy, Snow, Toot
▶ Crack (alkaloidal cocaine)	Base, Gravel, Pebbles, Rocks, Stones, Wash
▶ Amphetamines	Speed, Base Ice, Crystal, Billy, Whiz, Dexies
▶ Metamphetamine	Crystal Meths, Ice, Krank, Tina, Tweak
▶ Ecstasy	E, X, XTC Brownies, Eckies, Hug drug, M & Ms, Sweeties
▶ $\gamma$ Hydroxybutyrate	GHB, GBH, Liquid Ecstasy, Midnight blue, Blue nitro
▶ Heroin	H, Horse, Smack, Skag
▶ Ketamine	Green, K, Special K, Supa K and Vitamin K
▶ LSD	Acid, Lucy, Tabs
▶ Poppers (amyl nitrate, etc)	Liquid Gold, Ram, Rock hard, Thrust and TNT
▶ Magic Mushrooms	Shrooms, Mushies, Happies, Silties, Liberties

## THE STIMULANTS

Examples of the stimulants include cocaine/crack, amphetamine, 3,4-methylene, dioxymethylamphetamine ("Ecstasy"), ephedrine, phenylpropanolamine, and methylphenidate.

These drugs share the ability to enhance transmission at the catecholaminergic (including dopaminergic) synapses and so share some common pharmacological effects and adverse effects in excess. Cross-tolerance may be seen. Those with greatest central action produce elation and increased alertness, with increased motor activity in the short and longer term (increased endurance). The motor manifestations of excess include tremor, myoclonus, and seizures, while the neuropsychiatric manifestations include restlessness, irritability, violence, and a psychotic state, which is

**Table 2** Common features in neurological patients with drug misuse

1. In the UK, the vast majority of drug addicts seen by neurologists will be seen as ward referrals, not as outpatients
2. \*Patients are usually young, and often remarkably so for the type of pathology (for example, stroke)
3. \*Drug addicts usually present very late, with severe neurological deficits, often waiting for an extraordinary time before seeking medical attention
4. \*The history from the patient or from relatives/friends is often inconsistent and unreliable, and may sound either incredible or misleading
5. Drug misuse is usually not volunteered though generally (but not inevitably) admitted on direct questioning
6. \*Looking at previous A&E notes is often a good source for the clue to drug misuse
7. \*Once drug addicts are mobile, or even sometimes before, they will often abscond from the ward and/or hospital for periods. The nursing staff are the best ones to question, since they are usually the first to notice this, and the altered behaviour before and after these periods, let alone the nature of the "friends" who come to visit them
8. If in doubt, request a urinary drug screen, as early as possible after admission
9. Multiple pathologies are possible, and it is important not to jump to the rare ones, since in my experience the common and mundane are more likely (see below)
10. Always remember the possibility of infective endocarditis: it can produce or mimic so much, and is devastating if missed
11. Management is frequently complicated by poor compliance and/or by poor follow up attendance
12. Be prepared for an up-hill struggle, not only with the patient but also with other health care staff who you will have to rely on to help get investigations done promptly

\*Clinical "red flags" for drug misuse.

**Table 3** Factors which may influence adverse effects with recreational drugs

<b>Directly due to drug</b>	
▶ A high dose	—sometimes because of an unusual source
▶ The speed of entry	—especially intravenous or when smoked
▶ Individual sensitivity	
▶ Chronic/repeated use	—for example, cocaine, leads to longer half life
▶ Interaction with other compounds in the drugs	
▶ Interaction with other drugs, including alcohol	
▶ Interaction with pre-existing pathologies	—hypertension, AVM, aneurysm, right to left cardiac shunt
<b>Indirectly due to drug</b>	
▶ Secondary effects of coma or fits	—especially if aspiration occurs
▶ Infection risks	—easy portal of entry for pathogens —impairment of the immune system —exposures to pathogens such as HIV
▶ Accompanying lifestyle changes	—alcoholism —homelessness —prostitution —trauma*

\*In my practice, the most common single neurological adverse effect of drug addiction is head trauma (for example, from baseball bats or gunshot wounds).  
AVM, arteriovenous malformation.

often paranoid. Temperature and blood pressure rise, and cardiac arrhythmias and/or sudden death may occur. In the case of cocaine, at least, there is an interaction with alcohol that increases risk of sudden death.

Acute abstinence from these stimulants is not associated with the autonomic or life threatening problems seen with alcohol and opiate dependence, but rather with disturbances of sleep, low mood and anxiety, and a craving for the drug.

Stroke is the most common lasting adverse neurological event associated with the use of these stimulant drugs. Headache and/or seizures may accompany onset. The association is temporal, often very close, and this is the main evidence for a causal link, though there are also very plausible mechanisms for causation. Details are listed for each drug below. However, several potential mechanisms may apply in individual patients, and it may be impossible to disentangle the many possibilities, particularly in infarction.

Seizures may occur, particularly with the more rapid and higher levels achieved when cocaine is injected or smoked as "crack". In patients with pre-existing enhanced risk of seizures (for example, those with epilepsy or taking other epileptogenic drugs), intranasal cocaine may apparently precipitate fits. When they do occur, seizures may be prolonged and fatal, not only through the secondary consequences of prolonged seizures but also perhaps through the direct effect of the high drug levels.

Hyperpyrexia may develop because of direct effects on the hypothalamus and also the agitation and hyperactivity that these stimulant drugs tend to produce. These may contribute along with muscle vasoconstriction, central rigidity, and seizures to the rhabdomyolysis that sometimes occurs in more sick patients. In addition, cocaine may have a direct toxic effect on skeletal muscle (as it does on cardiac muscle). These problems have been emphasised in patients dying after the use of Ecstasy.

**Table 4** Neurological syndromes associated with drug abuse

	Syndrome	Cause
Peripheral nerves	Femoral/median neuropathy	Direct trauma from needle
	Mononeuropathies and multiple mononeuropathies	Compressive neuropathies arising from prolonged coma, especially lateral popliteal and ulnar nerves, but also the sciatic nerves
	Botulism	"Skin-popping" (deep intradermal injections) addicts using "black tar" heroin
	Guillain Barré	Consider HIV and n-hexane abuse
Spinal cord	Plexopathy	?Compressive, ?ischaemic
	Compression	Osteomyelitis/discitis and extradural abscess
	Anterior cord syndrome	Cord infarction (infective endocarditis, vasospasm, vasculitis)
Brain	Intrinsic cord lesion	Haemorrhage (infective endocarditis, arteriovenous malformation, vasculitis), abscess
	Encephalopathy	Direct effect of drug (especially heroin or barbiturate), or Post-anoxic (secondary to respiratory depression, cardiac arrhythmia or airway obstruction—for example, with aspiration of vomit)
		Meningo-encephalitis (must exclude early, do lumbar puncture)
		Metabolic: especially sodium or glucose
		Head injury
		"Vasculitis" (diagnosis of "exclusion" and then biopsy)
	Meningitis	Remember atypical organisms, and possibility of infective endocarditis, or HIV
	Subarachnoid haemorrhage	Hypertensive surge and co-existent vascular malformation/aneurysm
		Mycotic aneurysm with or without infective endocarditis
		Vasculitis
	Stroke: cerebral infarct(s)	Vasospasm
		Cardiac embolism (infective endocarditis, cardiomyopathy, arrhythmias or paradoxical embolism)
		Dissection
		Vasculitis
	Intracerebral haemorrhage	Hypertensive surge (especially with underlying AVM)
	Septic arteritis and/or mycotic aneurysm	
	Haemorrhagic transformation of infarct	
	Vasculitis	
Subacute focal deficit	Abscesses (infective endocarditis or right to left cardiac shunt)	
	Subdural empyema	
	Progressive multifocal leucoencephalopathy (PML) if also AIDS	
Seizures	Direct effect of drugs (cocaine and amphetamines, and "look alikes"), including hypertensive crisis	
	Indirectly caused by metabolic complications, including alcohol withdrawal	
	Abscess or empyema	
	Stroke (infarction/intracerebral haemorrhage/subarachnoid haemorrhage)	
	Meningo-encephalitis	
Trauma	Closed or from gunshot	
Confusion, nystagmus, ataxia	Directly drug effects (organic solvents and "Angel Dust")	
	Posterior fossa abscess/infarct/haemorrhage	
External & internal ophthalmoparesis, with fasciobulbar and limb weakness	Botulism from "skin-popping" (subcutaneous injections) heroin addicts, especially "black tar"	
Tetanus	"Skin-popping" (deep intradermal injections) heroin addicts	

Movement disorders have been reported with these drugs—for example, tics and acute dystonic reactions with cocaine and acute chorea with metamphetamine.

Long term cocaine abuse has been associated with cognitive dysfunction and cerebral atrophy, and with multiple focal perfusion defects on single photon emission computed tomography (SPECT) and positron emission tomography (PET) studies. These effects may all persist despite abstinence. Of course, there are often other confounders in the lifestyles of these individuals which may also be implicated, not just the drug.

Chronic amphetamine (and to a lesser extent cocaine) use may be complicated by a psychosis with visual and auditory hallucinations, often with paranoia, though without the sympathomimetic effects of these drugs.

### Strokes occurring with stimulant use Cocaine

About 70% of strokes arising with intranasal and intravenous use are caused by haemorrhage rather than infarction. However, the pattern of stroke may depend upon the preparation used and upon its mode of administration, since infarcts are as likely as haemorrhages when alkaloidal cocaine, "crack", is smoked. This may be due to a complex

interplay of pharmacokinetic and pharmacodynamic factors, as well as the concentration and type of contaminants, and whether there has been coincidental alcohol use (which more commonly accompanies intranasal cocaine use). These factors may all change the half lives of cocaine metabolites, their metabolic pathways, and their effects on the blood vessels. The liver metabolises cocaine with a half life of only about one hour, but its major metabolites last much longer, sometimes days, and they too have vasoconstrictive actions. The pharmacokinetics of cocaine and its metabolites show large inter-individual variation and there is evidence for prolongation of action in chronic cocaine abusers, which may also occur when alcohol is consumed simultaneously. This may explain why most strokes occur in chronic users and/or with alcohol use.

Haemorrhages may be intracerebral (basal ganglia, thalamic, lobar, or brainstem), intraventricular or subarachnoid. They may occur especially in individuals with pre-existing vascular malformations such as aneurysms and arteriovenous malformations (accounting for up to 50% of intracranial haemorrhage with cocaine). Most strokes tend to occur within an hour of use, especially for crack and intravenous cocaine, and most of the others within three hours. The surge in blood pressure is thought to be to blame for acute rupture.

Blood pressure may no longer be elevated by the time of presentation, or alternatively, the hypertension may be wrongly attributed at presentation to the haemorrhage itself. Vasospasm has also been postulated to contribute to aneurysm rupture. In injecting addicts, with or without demonstrable infective endocarditis, septic arteritis and/or mycotic aneurysms need consideration as alternative causes of intracranial haemorrhage. Haemorrhagic transformation of infarcts is another cause. The possibility of cerebral vasculitis is often mentioned, but this is usually because of irregularity of arteries seen on angiography (see below). However histological proof is very seldom provided (a handful of cases only), especially in cases involving abuse of cocaine alone. No cases of vasculitis were found in several larger postmortem series of patients dying of intracranial haemorrhages. If vasculitis does occur in pure cocaine abuse, it must be very rare. Cerebral biopsy specimens examine only small vessels but in the few cases that have revealed vasculitis at postmortem, it is limited to these small vessels and spares the larger ones and would not be seen on angiography.

Infarction of brain, cord (usually anterior spinal artery syndromes) or retina is less common than haemorrhage, but may be particularly associated with smoking crack cocaine. There may be preceding transient ischaemic attacks (TIAs) in 10% of crack related infarcts. Patients tend to develop their infarct within a few hours of use, or wake up with a deficit the morning after. Imaging usually shows infarcts involving cortical or deep penetrating arteries. They often occur in individuals without conventional risk factors and through a variety of potential mechanisms, though again proof is seldom possible (table 5).

Cocaine and its metabolites do undoubtedly have major effects on cerebral (and other) arteries. The acute vasospasm has been demonstrated in animals, and by magnetic resonance angiography (MRA) and transcranial Doppler in human volunteers, and occurs in large and medium sized arteries, probably mediated by endothelin 1. In patients, angiography may show beading and focal stenosis, and there may also be associated large vessel occlusion. Such abnormalities may arise through vasospasm caused by the drug itself but the possibility of additional subarachnoid haemorrhage needs excluding. Postmortem specimens in a few patients have shown that arteries may sustain damage to the media and elastic lamina, but no abnormality has been detectable in most studies and in some patients no vasculopathy can be

demonstrated (other than aneurysms and AVMs in cases with intracranial haemorrhage).

In half the cases of cocaine infarcts, angiography is unremarkable and does not show the above abnormalities. Occasionally intraluminal clot is seen in the internal carotid artery, perhaps possibly because of "stasis" distant to extracranial carotid artery spasm. Artery-to-artery embolism is therefore another possible mechanism for vessel occlusion, in addition to spasm, in situ thrombosis, and embolism from the heart.

### Amphetamine

Amphetamine causes the same range of strokes as cocaine, with similar characteristics and mechanisms. They usually occur in the first few hours after ingestion in a chronic heavy abuser, presenting with headache, an evolving focal deficit and impaired conscious level. Haemorrhages are the most common type of stroke, but even in these patients TIA-like episodes may have occurred previously. Infarction may also occur, particularly with crystal methamphetamine, which is the smoked form.

Angiography may be normal but amphetamines may also be associated with beading of large arteries, or focal narrowing of arteries. This may be diffuse or affect just one or two major vessels. At least acutely, "vasospasm" may be the mechanism responsible, but since it may persist for weeks, there must sometimes be other pathogenesis for this vasoconstriction. Superimposed thrombosis may contribute to vessel occlusion and infarction.

Especially when used chronically and intravenously, amphetamines are the drugs most commonly associated with a vasculitic/angiitic picture histologically. This may just affect smaller calibre vessels and may be associated with normal angiography. This may be an acute hypersensitivity reaction, perhaps caused by contaminants. In some cases, a frank necrotising vasculitis may involve many organs and may be clinically evident elsewhere in the body and pathologically similar to polyarteritis nodosa.

Cases in the literature of proven vasculitis with cocaine (only a few) and amphetamines (much more common) are less likely to present with clear cut strokes. They seem to have a more diffuse neurological picture, often with a subacute progressive time course, including headache, encephalopathy and/or bilateral clinical and radiological abnormalities (often ischaemic as well as haemorrhagic). The erythrocyte sedimentation rate (ESR) is often greatly raised (but such patients may have other reasons for this, especially if intravenous injectors). Treatment with high dose steroids and sometimes cyclophosphamide has been reported, but with no convincing evidence of any change in the natural history.

### Amphetamine "look-alikes" (other sympathomimetics)

These drugs share many of the potential adverse effects of amphetamines, particularly those involving the cerebral circulation. For example, the beading of large arteries has also been reported with phenylpropanolamine, ephedrine, and pseudoephedrine. Although the risks of adverse effects occurring are less, this may be outweighed by the more widespread use of some of these drugs in the community. Individuals may vary in their susceptibility, partly because of pre-existing medical conditions (for example, hypertension).

**Table 5** Potential mechanisms for infarction after cocaine and other stimulant misuse

- ▶ Vasoconstriction (seen on acute or subacute angiography), with or without superimposed thrombosis/occlusion, either as direct drug effect or secondary to subarachnoid haemorrhage
- ▶ Cardiac arrhythmias and/or cardiomyopathy (especially with cocaine) causing infarction by embolism or even by hypoperfusion in cases of transient ventricular tachyarrhythmias
- ▶ Embolism from infective endocarditis\*
- ▶ Cerebral vasculitis
- ▶ Embolism of venous thrombus or particulate contaminant matter (for example, talc or corn starch) in injecting users, presumably with cardiac right to left shunts\*
- ▶ In the case of cocaine, it may also lead to enhanced thrombus formation due to effects on platelets and depletion of coagulation control proteins (anti-thrombin III and protein C)

\*Intravenous injecting patients.

Doses may vary between different sources and the effects may be increased by coincidental caffeine intake.

“Ecstasy” (3,4-methylene, dioxymethylamphetamine) has a hallucinogenic effect at low doses, but at higher doses has amphetamine-like stimulant effects. Toxicity may present with hyperpyrexia, seizures, hypertonia, and coma leading to rhabdomyolysis and/or death. The drug has also been associated in small numbers of patients with both intracranial haemorrhage and cerebral infarction.

Phenylpropranolamine and pseudoephedrine have been constituents of over-the-counter nasal decongestants for many years and these compounds have also been used as appetite suppressants. In both situations the drugs are open to abuse, mostly in young and middle aged adults. In chronic female users, phenylpropranolamine and pseudoephedrine have been associated with increased risk of haemorrhagic strokes, and this may also apply to first time users of phenylpropranolamine. As a result the US Food and Drug Agency issued a warning about these compounds; however, in 2000 the UK Committee for the Safety of Medicines were less convinced and noted that appetite suppressants containing phenylpropranolamine were not available in the UK, and that in all over-the-counter cold and “flu” preparations in the UK the maximum daily doses were less (100 mg) than in the USA (150 mg). Nowadays, these restrictions may not apply to medications easily available through the internet.

Ephedrine may cause a similar picture, and has been linked with haemorrhagic and ischaemic strokes. Tolerance and dependence have been reported in those using it for appetite suppression and dieting and as a “stimulant”. It is easily available on the internet.

Ephedra alkaloids are included in some Chinese herbal medicines which purport to “increase energy” or help weight loss, often in preparations also containing caffeine. In high doses, they have been associated with haemorrhage and seizures.

Methylphenidate is a drug which is of course increasingly available because of its use in hyperactive children with attention deficit disorder. It has a “street value” and is essentially amphetamine-like, though with greater central than peripheral effects. It tends, therefore, to cause more problems by causing seizures, though has also been associated with intracerebral haemorrhage. It is usually taken orally, though occasionally crushed tablets are injected intravenously.

## THE SEDATIVES

### Heroin and other opiates

Heroin is rather different from the above drugs in two major ways. Firstly it is mainly used intravenously. It can also be sniffed, smoked or injected subcutaneously (“skin-popping”, which has recently been associated with cases of botulism and tetanus). Its intravenous use involves non-sterile needles, syringes etc, and leads to the well recognised infective complications (see below). Not only are the entry and dissemination of organisms into the blood stream facilitated, but also intravenous addicts have an altered immune system (humoral, cell mediated, and phagocytic defects), even if they have not yet contracted HIV infection.

Secondly the direct effects of the drug are very different. Initially there is a euphoric effect with drowsiness, though in some there will be anxiety and increased alertness. There may be nausea and vomiting. Autonomic effects (such as small pupils, difficulty passing urine, flushing, and dry mouth) may occur, but it is the suppression of respiration and coughing

which are potentially the most serious, especially if vomiting occurs. With excess (and such is the variation in purity of the preparations that the dose taken is very variable), coma and deep respiratory depression are produced, along with hypotension and sometimes non-cardiogenic pulmonary oedema. Cardiorespiratory arrest may occur, especially if vomiting and aspiration are superimposed. Post-anoxic encephalopathy is therefore one of the more frequent effects of heroin abuse seen by the neurologist. Even without this, some patients may awake from their coma with more focal central deficits, presumably caused by more focal ischaemia.

Coma may also result in a patient awakening with compressive nerve palsies, especially of the lateral popliteal and ulnar nerves. Characteristically they may present for attention many days later, a clue to the diagnosis in itself. The presence of bilateral synchronous sciatic nerve palsy is almost always explained by the patient passing out while sitting on the toilet, or having slid down the wall or off a seat and come to rest sitting or crouching on the floor. Compartment syndromes may also be seen after such periods of prolonged coma. Sometimes it is not immediately clear why certain peripheral nerve injuries occur, especially some of those involving the brachial or lumbar plexuses. In other cases, direct damage to a nerve may occur during an addict’s attempt to gain access to a vein, and the median nerve in the antecubital fossa and femoral nerve in the groin are particularly prone.

Strokes may occur by a variety of mechanisms, but heroin does not elevate blood pressure and so haemorrhages should be assumed to be caused by infective arteritis/mycotic aneurysm until proven otherwise. Infarction is commonly due to infective endocarditis or paradoxical embolism. Rarely angiography may reveal “beading”, but the mechanism of this is unclear and the possibilities of unrecognised subarachnoid haemorrhage or coincidental stimulant abuse should be considered.

Although the infective complications may all be seen in patients injecting other drugs such as amphetamines or cocaine, they are much more common in heroin addicts, who form the vast bulk of drug injectors. They may occur with obvious infective endocarditis and embolic infarcts, but the following may also be seen in patients without obvious endocarditis:

- ▶ meningitis (including with atypical organisms)
- ▶ cerebral abscess
- ▶ septic arteritis and mycotic aneurysm, causing intracranial haemorrhage (mostly intracerebral)
- ▶ osteomyelitis, and discitis, causing extradural abscesses and cord involvement
- ▶ HIV infection and AIDS, with its own neurology.

In addition, contaminants within the injection, often talc or corn starch, may embolise and may sometimes be seen in retinal arteries and/or cause infarction in the spinal cord or brain.

### Barbiturates and other sedatives

These orally taken preparations of course may also lead to coma and similar complications to those described from heroin comas, including cardiorespiratory depression (especially after barbiturates), aspiration, anoxic encephalopathy, and peripheral nerve palsies/compartment syndromes.

## THE HALLUCINOGENS

### Phencyclidine (“Angel dust”)

This drug, originally used as an anaesthetic agent, may be taken orally, nasally, or by inhalation (commonly by

smoking). It produces a mixture of effects, some stimulant, some more depressant, but abuse arose from its heightened sensory perception with eventual hallucinogenic effects. It affects many neurotransmitter systems, including those involving dopamine and acetylcholine. It produces perceptual changes, decrease in pain sensations, and autonomic effects with flushing, sweating, raised blood pressure, and tachycardia. In higher doses, an acute confusional state develops, with ataxia, dysarthria, and prominent nystagmus. Convulsions or dystonic posturing may occur and the patient may progress to coma. The patients may complain of numbness, and with the combination of the anaesthesia and mental changes, they may self mutilate. These adverse effects and risk of psychosis led to it falling from popularity in the 1980s. Strokes were reported in some patients.

### LSD (lysergic acid diethylamide)

This hallucinogenic drug alters perception, mood, and thought, and may have mild sympathomimetic effects. However, it seems not to be associated with neurological problems. There are a few reports of cerebral infarcts with large vessel occlusion but polydrug abuse makes interpretation difficult. However, the bizarre behaviour has resulted in fatal accidents and suicide. The same is also true of “magic mushrooms”.

### Ketamine

Ketamine is a dissociative anaesthetic, which has hallucinogenic properties and has become a drug of abuse, both “on the street” and in a few veterinary surgeons. The drug is still used as an anaesthetic in veterinary practice and large doses can certainly produce coma in humans.

### Marijuana

There is no convincing association with stroke in marijuana users. Very high doses may cause a toxic psychosis with hallucinations and paranoia. Recently the possible precipitation of more long term psychoses has been highlighted with frequent use.

### GHB ( $\gamma$ hydroxybutyrate)

The dose varies considerably among different preparations of this drug, which is taken orally. Euphoria and disinhibition are the desired effects, but in excess sedation ensues, with disorientation and vomiting. Muscle twitching and seizures can occur. These effects are more likely if alcohol is also consumed. It is therefore all the more dangerous that the compound (usually as a liquid, but sometimes a powder) is odourless, tasteless, and readily slipped into others’ drinks, with a variety of intentions (so also is flunitrazepam, Rohypnol).

### ORGANIC SOLVENTS

“Glue sniffers” are usually young teenage boys and the rash and/or inflammation which often develops around the mouth and nose is an additional clue to the cause of their condition. They will experiment with all sorts of substances (lighter fluids, varnishes, paint thinners, etc) based upon organic solvents such as toluene, hexane, and benzene. Acutely these may produce a feeling of exhilaration, associated with some light headedness and giddiness, and sometimes auditory and visual hallucinations. Vomiting, tinnitus, and a later headache are additional features. The effects are short lived (for example, half an hour), often leading to repetitive use to

maintain the “buzz”. Toxicity becomes manifest with repeated or prolonged exposure, producing impairment of coordination and cognition, with double vision, ataxia, dysarthria, and nystagmus. With increasing exposure, there is worsening disorientation, confusion, and respiratory depression that may evolve to coma. The confusional state may last for some days, and during it only supportive treatment is possible. With chronic abuse, at least of toluene, the cognitive changes, cerebellar features, ocular motor abnormalities, and pyramidal features are unlikely to fully resolve.

Abuse of n-hexane may cause a symmetrical sensory motor peripheral neuropathy. Symptoms start insidiously with a symmetrical numbness of toes and fingers. Touch, pain, temperature, and vibration loss occur, accompanied by a loss of ankle jerks. Hand weakness may develop. With more intense or prolonged exposure, more severe and proximal weakness may develop. Autonomic disturbances in the hands and feet may occur. The time course of this neuropathy may be subacute, even leading to a differential diagnosis of Guillain-Barré syndrome. It is important to realise (diagnostically and prognostically) that progression may continue for 1–4 months after cessation of exposure, and that recovery may take many months and even then be incomplete.

### ATHLETIC PERFORMANCE ENHANCING DRUGS

This is a very murky area with relatively little science and a proliferation of claims, which may be readily appreciated by using the internet. The claims include uses that do not immediately spring to mind—for example, bodybuilders may use opiates before very heavy weightlifting sessions on the legs, to dull pain and enable greater lifts. They may also use GHB to promote sleep between training sessions, during which there is supposedly enhanced release of (endogenous) growth hormone (according to animal work).

Athletes, bodybuilders, and other gym users may use a variety of drugs for a variety of purposes:

- ▶ anabolic effects (steroids, insulin, growth hormone)
- ▶ stimulants to heighten alertness, reduce fatigue, and prolong endurance (amphetamines, cocaine)
- ▶ erythropoietin to increase haemoglobin and oxygen delivery in endurance sports
- ▶  $\beta_2$  agonists for supposed “fat-burning” effects.

Drugs are often obtained from “underground” sources or via the internet with little or no quality control and with obvious risks. Some preparations have to be injected because of significant first pass effects, with the same infection risks as for heroin addicts (needles and syringes are often shared).

Fortunately, neurological sequelae are uncommon (table 6), and the clinical clue is in the history (prompted by the occurrence of the clinical syndrome in an unusual age or setting) or in the physique. However, getting the patient to admit to it is, in my experience, rather more difficult than for other recreational drugs.

Lastly, it is worth remembering that patients with (undiagnosed) myotonia congenita may be falsely accused of being abusers of anabolic drugs (B Lecky, personal communication).

### INVESTIGATIONS

Patients obviously need investigating neurologically in the usual way according to their clinical presentation with appropriate imaging and/or neurophysiology.

**Table 6** Adverse effects of "performance enhancing" drugs

Drug	Relevant adverse effects
Anabolic steroids	Cardiovascular, including hypertension and presumably strokes
Growth hormone*	Carpal tunnel
Insulin	Hypoglycaemia
Erythropoietin	Headaches, encephalopathy, strokes, seizures
Clenbuterol	Tremor, headaches
Cocaine and amphetamines	As earlier

\*Growth hormone obtained through internet sources may include human pituitary derived growth hormone, and so there is the theoretical risk of Creutzfeldt-Jacob disease.

Urine toxicology screens are helpful, and have been shown to greatly increase detection rate compared to history alone. They become positive early, within hours after ingestion, and should remain so for periods which may depend on many factors, including coincidental alcohol use and whether the user is a novice or chronic abuser. For example, for cocaine the metabolites may be detectable in the urine of a novice user for about 48 hours, but this may extend up to three weeks following chronic heavy abuse. A number of other stimulants may give false-positive results for amphetamine testing in the urine and local laboratory guidance should be sought.

Some form of angiography is appropriate after any sort of stroke. After any intracranial haemorrhage, this is necessary to look for an arteriovenous malformation or aneurysm, including mycotic aneurysms which are usually more distally located. Digital subtraction angiography (DSA) is still necessary in these patients. CT or MRA may be adequate after infarction, where the "vasospastic" and multiple occlusive abnormalities may help establish the relation of the infarct to drug abuse, although these non-invasive tests are probably less sensitive than DSA (though more easily repeated).

Even in patients who do not admit to intravenous injection, let alone those who do, blood cultures should be taken and serological tests for syphilis and HIV also considered. Echocardiography is required for all those patients with fever, any suggestion of abscesses or meningitis, or with any type of stroke, looking for any evidence of infective endocarditis, even in those who deny injecting intravenously. It is also appropriate for those who have been exposed to the cardiac effects of cocaine and amphetamines. Especially in injecting addicts with otherwise unexplained infarcts, there should be a low threshold for transoesophageal echocardiography, looking for evidence of a right-to-left shunt which may be a passage for paradoxical embolism of venous thrombi or particulate matter.

Assuming radiology does not suggest it will be dangerous, cerebrospinal fluid (CSF) examination is also advised with any stroke occurring in patients suspected of being drug abusers. On the one hand, this is looking for evidence of

infection or inflammation, and on the other it also looks for subarachnoid haemorrhage which may co-exist with any form of stroke in these patients—for example, with heroin, cocaine, or amphetamine.

If a vasculitis appears likely on clinical grounds (see sections on amphetamines above), cerebral and meningeal biopsy should be considered. As in non-drug abuse patients, the purpose of this is not only to diagnose a vasculitis but also to exclude other sometimes treatable and often unexpected pathologies which may give rise atypically to similar clinical syndromes with similar radiological and CSF abnormalities.

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## REFERENCES

- 1 Sanchez-Ramos JR. Effects of drugs of abuse on the nervous system. In: Bradley WG, Daroff RB, Fenichel GM, et al, eds. *Neurology in clinical practice: vol II. The neurological disorders*, 2nd ed. Oxford: Butterworth-Heinemann, 1996:1402–14.
- 2 Ricarte GA, Langston JW. Neurological complications of substance abuse. In: Aminoff MJ, ed. *Neurology and general medicine: the neurological aspects of medical disorders*. New York: Churchill Livingstone, 1989:549–57.
- 3 Sloan MA. Toxicity/substance abuse. In: Welch KMA, Caplan LR, Reis DJ, et al, eds. *Primer on cerebrovascular diseases*. London: Academic Press, 1997:413–16.
- 4 Levine SR, Brust JCM, Futrell N, et al. A comparative study of the cerebrovascular complications of cocaine; alkaloidal versus hydrochloride—a review. *Neurology* 1991;**41**:1173–7.
- 5 Levine SR, Brust JCM, Futrell N, et al. Cerebrovascular complications of the use of the "crack" form of alkaloidal cocaine. *N Engl J Med* 1990;**323**:699–704.
- 6 Konzen JP, Levine SR, Garcia JH. Vasospasm and thrombus formation as possible mechanisms of stroke related to alkaloidal cocaine. *Stroke* 1995;**26**:1114–18.
- 7 Kaufman MJ, Levin JM, Ross MH. Cocaine-induced cerebral vasoconstriction detected in humans with magnetic resonance angiography. *JAMA* 1998;**279**:376–80.
- 8 Daras M, Tuchman AJ, Marks S. Central nervous system infarction related to cocaine abuse. *Stroke* 1991;**22**:1320–5.
- 9 Fredericks RK, Lefkowitz DS, Challa VR, et al. Cerebral vasculitis associated with cocaine abuse. *Stroke* 1991;**22**:1437–9.
- 10 Aggarwal SK, Williams V, Levine SR, et al. Cocaine-associated intracranial hemorrhage: absence of vasculitis in 14 cases. *Neurology* 1996;**46**:1741–3.
- 11 Heye N, Hankey GJ. Amphetamine-associated stroke. *Cerebrovasc Dis* 1996;**6**:149–55.
- 12 Kernan WN, Viscoli CM, Brass LM, et al. Phenylpropanolamine and the risk of hemorrhagic stroke. *N Engl J Med* 2000;**343**:1826–32.
- 13 Anon. Medical aspects of drug use in the gym. *Drug and Therapeutics Bulletin* 2004;**42**:No 1.