

Lecture Notes

Drugs & Drug Related Deaths



Definitions & Terminology

Legal Aspects: Misuse of Drugs Act, 1971, Misuse of Drugs Regulations, 1985, Medicines Act, 1968
The Addictive process

Exercises in recognising drug intoxication

There is a spectrum of drug use, mis-use and abuse. The 6 main classes of misused drugs are :

1. Opiates (morphine, heroin, methadone, dihydrocodeine)
2. Depressants (alcohol (see separate lecture notes), barbiturates)
3. Minor tranquilisers (benzodiazepines, e.g. Diazepam (Valium), Temazepam)
4. Stimulants (cocaine, amphetamines, Ecstasy, ADAM, EVE, ICE)
5. Hallucinogens (LSD, magic mushrooms, mescaline)
6. Others (cannabis, nicotine, volatile solvents)

Local terminology and patterns of drug use are detailed at the [Tayside Police Web Site](#)

Current terminology:

Appropriate use is that for which the drug was prescribed.

Drug Misuse (Royal College of Psychiatrists, 1987) "is the taking of a drug which harms or threatens to harm the physical or mental health or social well-being of an individual, of other individuals, or of society at large, or which is illegal". This definition includes:

1. Dangerous use of licit substances such as alcohol and tobacco
2. Deleterious and prolonged use of prescribed medications, e.g. benzodiazepines (Valium), barbiturates, methadone, analgesics, antidepressants.
3. Illicit drug use

Drug Dependence (WHO, 1964):

"a state, psychic and sometimes physical resulting from the interaction between a living organism and a drug, characterised by behavioural and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence. Tolerance may or may not be present. A person may be dependent on more than one drug."

Note: 1. *Drug misuse can occur in the absence of dependence*

LSD is often misused but has little potential to cause dependence

Alcohol misuse (intoxication) is more dangerous than dependence (alcoholism)

2. *Drug dependence can occur in the absence of misuse*

dependence is not always immediately harmful, eg diazepam

3. *Drug misuse and dependence often go hand-in-hand*

Older terminology:

Drug abuse is a term usually reserved for misuse of illicit drugs such as marijuana, cocaine,

amphetamines, hallucinogens and opiates.

Habituation results from continued consumption of a drug, resulting in an intense desire to continue taking the drug (psychological dependence). There is little tendency to increase the dose (i.e. no tolerance). Habituation may be detrimental to the individual.

Addiction is a state of chronic intoxication characterised by an overpowering desire, need or physical compulsion to continue taking more drug. This results in psychological and physical dependence (withdrawal syndromes on stopping). The individual becomes pre-occupied with the drug. Detrimental to both the individual and society.

MISUSE OF DRUGS ACT, 1971

Provides the legal framework for the control of drugs with respect to their potential for misuse. The act details the specific requirements for prescription, safe custody and record-keeping. Section 2 classifies drugs and provides the penalty framework for trafficking offences (section 4) and possession (section 5).

Class A: Major natural & synthetic opiates

Cocaine

LSD

Injectable forms of amphetamines

Cannabinol (the active ingredient separated from the cannabis plant)

Penalty for trafficking is up to life imprisonment.

Penalty for possession is up to life imprisonment

Class B: Oral amphetamines,

Cannabis plant material & resin

Codeine & Dihydrocodeine

Pentazocine

Penalty for trafficking is up to 14 years imprisonment.

Penalty for possession is up to 5 years imprisonment

Class C: Benzodiazepines

Buprenorphine

Dextropropoxyphene

Penalty for trafficking is up to 5 years imprisonment.

Penalty for possession is up to 2 years imprisonment

MISUSE OF DRUGS REGULATIONS, 1985

Defines who may produce, possess, supply, prescribe and administer certain drugs.

Schedule 1: Prohibited except with Home Office authority

e.g. cannabis, LSD, raw opium, Ecstasy

Schedule 2: Controlled drug

Specific requirements for prescribing, safe custody, registering

e.g. diamorphine (heroin), pethidine, cocaine, amphetamine

Schedule 3: Barbiturates, Pentazocine

Schedule 4: Benzodiazepines

Schedule 5: Preparations containing small amounts of controlled drugs

e.g. Co-proxamol, Co-codamol

MEDICINES ACT, 1968

Controls the production and supply of drugs.

General sales List (GSL)

Drugs which can be purchased from supermarkets and shops without the advice of a pharmacist

Paracetamol, Aspirin, Cough syrups.

Pharmacy Medicines (PM)

Drugs which can only be sold under the supervision of a pharmacist. Mostly symptomatic drugs:

Painkillers such as non-steroidal anti-inflammatory drugs (NSAID) such as Nurofen, Co-codamol (paracetamol + codeine)

Cough & cold remedies (often contain paracetamol, codeine, pseudoephedrine)

Antacids such as Gaviscon & Maalox, Cimetidine

Travel sickness, Laxatives, Antihistamines, Antiemetics

Prescription Only Medicines (POM)

Must be prescribed by a doctor, dentist or approved professional

Mostly therapeutic drugs:

Stronger painkillers, most NSAID, Co-proxamol, dihydrocodeine, opiates

Ulcer healing drugs

Antidepressants, Tranquillisers

Antibiotics

Drugs for heart & lung disease

Oral contraceptives

Drugs can be used and misused by several routes; orally, sublingually, rectally, vaginally, smoking, snorting and injection (into muscle, veins and into or beneath the skin).

Drug misusers are typically in the age group 20 - 35 years and males outnumber females by approximately 3 to 1. Students and high achievers will usually confine their drug use to marijuana and stimulants by smoking or the oral route. The unemployed and low achievers tend to abuse a wider spectrum of drugs and more often resort to intravenous drug abuse. An unstable family background and poor social circumstances are common. Abnormal personality, characterised by inability to deal with stress is a common predisposing factor. Reasons for first experimenting with drugs include curiosity, bravado, peer pressure and a search for excitement, pleasure or relief of anxiety. Severe drug addiction is closely linked to crime, most commonly petty theft and burglary, in order to pay for a regular supply of expensive drugs.

THE ADDICTIVE PROCESS

Addictive or dependency inducing drugs have two features in common:

1. An initial pleasurable effect (high or relaxation)
2. A subsequent rebound unpleasant effect (low or tension, later withdrawal)

The initial stimulation or high of amphetamine or cocaine use is followed later by the opposite effect, an unpleasant low. The initial relaxation and euphoria of Valium or heroin use is followed later by the opposite effect, unpleasant tension.

The following describes how dependence on stimulant drugs such as amphetamines and cocaine develops,

but the same principles can be applied to most other drugs.

The various normal needs and drives and needs of the body (hunger, thirst, friendship, sex, achievement) are normally in balance and controlled by the brain. Satisfaction in each area causes certain brain cells (monitor cells) to make and release chemicals (neurotransmitters) which stimulate the nerve cells within the REWARD CENTRE of the brain, causing a feeling of well-being.

This is analogous to placing coins (satisfying the body's natural needs) in a vending machine (monitor cell) to dispense chocolate (stimulate the reward centre).

Use of the drug stimulates the monitor cells artificially causing it to release its neurotransmitters which then stimulate the reward centre, causing the same feeling of well-being. The individual utilises the immediate, predictable effect of the drug on the reward centre which then replaces the need to satisfy life's normal desires for reward. The drug is lying to the monitor cells and reward centre.

This is analogous to using counterfeit coins to dispense chocolate from the vending machine.

The first pleasurable effect of the drug becomes firmly implanted in the memory and there is a powerful desire to regularly repeat drug use in order to recapture that experience. Such repetition reinforces memory and drug use replaces the desire to seek life's normal rewards. People, places and activities involved with using drugs become increasingly important at the expense of 'normal' activities. Heavy users will come to resent people, places and activities which do not fit with drug use. More confidence is placed in these false feelings of well-being and life's normal rewards are bypassed and ignored.

With repeated, regular use the nerve cells of the brain adapt to the artificial drug stimulation by reducing production of the normal neurotransmitter chemicals. This **neuroadaptation** is responsible for the development of **tolerance**, whereby increased doses are required to achieve the same pleasurable effects.

With regular use of some drugs, the body's natural neurotransmitter chemistry can become so suppressed and disturbed that the nerve cells cannot function without the artificial stimulus of the drug, and **physical dependence** results. At this stage stopping or reducing drug use leads to a **withdrawal syndrome**. Withdrawal syndromes represents a rebound effect comprising the opposite clinical effects to those of the drug itself. Hence withdrawal from nervous system stimulants (amphetamines, cocaine) is characterised by depression and fatigue whilst withdrawal from nervous system depressants is characterised by nervous excitability and fits. Physically dependent drug misusers will continue to use drugs in order to avoid the unpleasant effects of withdrawal. By now the drug is *needed* "for relief" and "just to make it through the day", and not merely *wanted* in "seeking pleasure".

Drugs vary considerably in their potential to produce dependence, tolerance and withdrawal syndromes.

CANNABIS (pot, dope, blow, grass, marijuana, ganga, weed, skunk, hash, draw, puff)

Acute Effects:

Talkative, hilarity, well-being, self-confidence, appreciation of sound & colour

Poor concentration

Impaired driving

Anxiety, agitation, paranoia

Cannabis psychosis (high doses)

Dry mouth, red conjunctivae

Tachycardia, increased blood pressure, postural hypotension

Chronic effects:

Cannabis psychosis with long term heavy use

Amotivational syndrome

Reduced sperm count in men

Reduced fertility in women
Bronchitis & emphysema
? Lung cancer

In comparison to tobacco, cannabis is poorly combustible and burning results in production of abundant tars and hydrocarbons which are particularly toxic to the lungs. The particles in the smoke are deposited throughout the lungs and are subsequently taken up by the lung's scavenger cells (alveolar macrophages). This results in numerous microscopic pigment-laden macrophages being scattered and grouped throughout the lungs. Scarring results in chronic degenerative lung disease (emphysema). There is a higher incidence of cancer in comparison to tobacco smoking.

Withdrawal: Irritability, restlessness, decreased appetite, weight loss

BENZODIAZEPINES (Tranx, benzos)

Main drugs:

Diazepam (*ValiumTM*, vallis)

Temazepam (*NormisonTM*, jellies, eggs, temazzies)

Lorazepam (*AtivanTM*), Nitrazepam (*MogadonTM*), Chlordiazepoxide (*LibriumTM*)

These are tranquilliser (sedative or hypnotic) drugs which depress the central nervous system and are used for treatment of anxiety, insomnia and muscle spasms. They are mostly presented as tablets but Temazepam capsules (recently withdrawn) were filled with a gelatinous centre which many drug misusers injected. Injectable and gel suppository forms of Diazepam are available for the emergency treatment of convulsions.

Temazepam & Lorazepam are short acting (6-12 hours) and are taken 3-4 times daily.
Diazepam, Nitrazepam & Chlordiazepoxide are longer acting and usually taken once daily.

Acute intoxication:

Psychological:

Relief of anxiety, relaxation

Impaired memory

Paradoxical aggression

Uncharacteristic criminal behaviour (shoplifting & indecent exposure)

Uncontrollable emotions (giggling & weeping)

'Hangover' with drowsiness, inability to concentrate & impairment of skilled tasks

Effects are potentiated by alcohol

Physical:

Dizziness, sedation, incoordination

Sexual dysfunction, weight gain

Hypotension & coma with high dose

Chronic effects:

Tolerance

Physical & psychological dependence

A state of **chronic intoxication** with slurred speech, poor concentration, impaired comprehension, impaired memory, emotional lability, irritability and depressed mood.

Withdrawal syndrome commences within 2-3 days in 20-40% of long term users (4-6 months): anxiety, insomnia, sweating, headache, tremor, nausea, disordered perceptions, hypersensitivity to stimuli, psychosis and convulsions.

AMPHETAMINES

Main drugs:

Amphetamine (*Benzedrine*TM, uppers, 'A', speed, whizz, cranks, wake-up, sulph, hearts)

Dextroamphetamine (*Dexedrine*TM, dex, dexy, dexies)

Methamphetamine (ICE, crystal, glass, meth)

Methylenedioxyamphetamine (MDA, EVE)

3,4, Methylenedioxymethamphetamine (MDMA, ADAM, Ecstasy, 'E', doves, Dennis)

Amphetamines are synthetic stimulants. Their use is popular in rave culture. Amphetamines act by stimulating the release of catecholamines, particularly adrenaline within the body.

Absorbed by GIT, clinical effects commence within 20 minutes, last 4-6 hours.

Previously used for weight reduction and still used to treat narcolepsy and overactive children.

Manufactured in illicit laboratories as tablets, capsules, powder.

May be taken orally, sniffed, snorted, smoked or injected.

Tolerance and psychological dependence occur

Acute intoxication:

Psychological

Euphoria, self-confidence and self-esteem

Feeling of calm, peace and friendliness towards strangers (the 'hug drug'),

Heightened sense of awareness & concentration

Increased energy, desire and ability to dance for long periods

Irritability & restlessness

Irrational behaviour, confusion

Hallucinations

Delusions, paranoia, psychosis

Psychological dependence

Physical

Tachycardia (fast pulse), hypertension (high blood pressure), tachypnoea (breathing)

Loss of appetite

Dilated pupils

Brisk reflexes

Dry mouth, sweating, blurred vision, dizziness, flushing or pallor

Teethgrinding (bruxism), repetitive actions (stereotypy)

Pyrexia

Acute adverse affects

Disturbances in the electrical rhythm of the heart (cardiac arrhythmias)

Stroke due to elevated blood pressure bursting a blood vessel

within the brain itself (intracerebral haemorrhage)

on the surface of the brain(subarachnoid haemorrhage).

Severe disturbance in the blood clotting mechanisms (DIC)

Acute paranoid psychosis

Hyperpyrexia): heat production by amphetamines and reduced heat loss by the skin result in a dangerous rise in body temperature This is particularly dangerous when dehydration and heavy sweating coexist following prolonged dancing.

Chronic adverse effects

Chest pains & muscle spasms

Anorexia, malnutrition & weight loss

Diarrhoea & vomiting

Damage to the heart muscle (cardiomyopathy)

Aggression, fatigue & insomnia

Depression
Chronic paranoid psychosis, schizophrenia

Psychological dependence leads to anxiety, depression, disturbed sleep and irritability on cessation

COCAINE

Main drugs:

Cocaine hydrochloride (coke, 'C', charlie, wash, nose-candy, snow)
Crack cocaine (rock)
Benzoylmethylecognine

Cocaine is a naturally occurring plant alkaloid stimulant derived from the coca leaf of South America. Refined in illegal factories from leaves, through paste, to cocaine HCl powder. Powder can be snorted up a straw, smoked, rubbed on mucous membranes of mouth, rectum or vagina, or injected. Cocaine HCl is used rarely medically as a surface (local) anaesthetic and terminal pain relief. The powder when heated with baking soda forms 'crack', a very pure form which is smoked.

Acute intoxication:

Short acting & dose dependent. It causes the body to secrete adrenaline in a similar fashion to amphetamines but the detrimental and pleasurable effects are more florid.

Physical:

Tachycardia, hypertension, tachypnoea
Dilated pupils,
Increased mental excitement
Hyperpyrexia,

Psychological:

Euphoria & well-being
Irritability & confusion
Hallucinations, formication (sensation of insects crawling under the skin)
Depression, paranoia as effects wear off

Cessation induces withdrawal ('crash') with both **psychological dependence** (intense craving and drug-seeking behaviour) & **physical dependence** (muscle pains, tremor, hunger, fatigue, prolonged sleep)

Chronic effects & External signs of cocaine abuse:

Intense psychological dependence
Chest pains, muscle spasms
Weight loss
Male impotence & female orgasm problems
Nasal septum may become ulcerated and perforated due to ischaemia and blood vessel spasm.
Eyes may exhibit "crack keratitis" due to the local anaesthetic effect allows excessive rubbing of the eyes.

Teeth may show acid erosion of the surface enamel
Hands may show 'crack callus' of the fingers due to repeated use of lighter.

Cocaine has serious detrimental effects both acutely and chronically on the coronary arteries, heart muscle and central nervous system.

The coronary arteries

Proliferation and thickening of the inner lining reduces blood flow.
Premature hardening and narrowing (atherosclerosis).
Coronary artery spasm may result in a heart attack (myocardial infarction)

Increased incidence of coronary artery thrombosis & myocardial infarction).

The heart muscle

Acutely damaged by catecholamine excess with subtle microscopic damage (contraction band necrosis). Repeated use over several weeks causes a mild form of heart muscle inflammation (myocarditis). Repeated use over several months will result in patchy scarring of the heart muscle (cardiomyopathy).

As a result of this myocardial damage there is a risk of sudden death due to cardiac arrhythmia which is most likely to occur during acute intoxication.

Brain:

Stroke, due to hypertensive blood vessel rupture within the brain (intracerebral haemorrhage) or on the surface of the brain (subarachnoid haemorrhage). In addition blood vessels may undergo spasm, causing ischaemic infarction of the brain.

In summary the common causes of cocaine-induced death are convulsions, respiratory arrest, cardiac arrhythmia and coronary artery spasm and stroke.

Although cocaine itself is quite short lived in the body it can be detected in the brain and blood within a short time of a hit and its metabolites are detectable for longer periods in nasal swabs, urine, hair and saliva.

LSD (Lysergic Acid diethylamide) (Acid, dots, microdots, tabs, the cube, pellets, trips)

Nicknames are also derived from the paper designs into which tiny amounts (25-150 μ g) of the drug are impregnated (blue star, smiley). Also presents as tablets.

LSD is a semi-synthetic hallucinogen first synthesised in 1938 and was formerly used to treat psychiatric disorders. It is derived from the alkaloid lysergic acid, which is found in ergot, a fungus which grows on rye grains.

Following oral intake effect commence within 1 hour, peak at 4 hours and last 12 hours.

Acute effects:

Psychological:

Effects vary widely between individuals & on different occasions
Effects depend on to mood & environment (good & bad trips)
Hallucinations (visual & auditory)
Distorted perception of time, distance & speed
Mood swings, paranoia & violence

Physical:

Hypertension, tachycardia
Dilated pupils
Pyrexia
Tremor & Inco-ordination
Flushing & nausea

Chronic effects:

Tolerance develops but not dependence
Abortion in pregnant women
Anxiety & psychosis
Later flashbacks

OPIATE ABUSE (Smack, skag, horse, 'H', gear, shit)

Main drugs:

Morphine

Heroin (Diamorphine)

Methadone

Dipipanone (*DiconalTM*), Pethidine, Pentazocine (*FortralTM*), Buprenorphine (*TemgesicTM*)

Medical uses are pain relief (analgesia), cough suppressants & antidiarrhoeal agents.

Illicit heroin is a white or brown powder, and other opiates are tablets or injection ampoules. Abuse of opiates is typically by intravenous injection (mainlining) for the immediate 'rush' but heroin can also be smoked ("chasing the dragon") or sniffed. The stereotype 'junkie' is typically an intravenous abuser of opiates.

Methadone comes as a green linctus intended for oral use as a substitute for iv heroin use (damage limitation). It is frequently sold for heroin or itself injected.

Acute intoxication:

Psychological:

Rush of euphoria & contentment

Relief of anxiety, inability to concentrate

Physical:

Constricted pupils

Suppression of cough reflex

Nausea & vomiting

Decreased heart & breathing rate

Unconsciousness, respiratory arrest and death

Fatal reaction to impurities

Reversal with Naloxone(*NarcanTM*) may be necessary

Chronic effects:

Tolerance

Physical & psychological dependence

Constipation

Loss of libido

Complications of intravenous injection

Interruption of an addict's supply of opiates will result in typical **withdrawal syndrome** ("cold turkey") due to 'rebound' with clinical effects opposite to those of intoxication.

Withdrawal typically commences 8 - 15 hours after stopping the drug, peaks at 36 - 48 hours and subsides over 5 - 10 days.

Symptoms (easily fabricated by the addict wanting more drugs):

Craving for the drug,

Anxiety, restlessness, irritability, insomnia

Alternate sweating and shivering

Generalised aches

Pains and cramps in the back, legs and abdomen

Nausea & vomiting

Physical signs:

Dilated pupils

Watering of the eyes (lacrimation),
Yawning,
Tachycardia, hypertension
Cold clammy skin with goose flesh
Loudly audible bowel sounds (borborygmy)
Diarrhoea.

Treatment with regular Diazepam & *Lomotil*TM (Diphenoxylate & Atropine) is often necessary.

A similar withdrawal syndrome is seen on stopping benzodiazapines.

Methadone treatment programs are aimed at reducing intravenous opiate abuse. Methadone is an opiate preparation in the form of a sticky green liquid for oral use. It is taken once daily and has longer duration of action than heroin, keeping the individual free of withdrawal symptoms for up to 24 hours. However, it fails to give the "rush" associated with iv heroin use and is therefore often traded for other drugs. Many addicts even inject the methadone!

Methadone is itself a very potent opiate and numerous methadone-related deaths occur every year in non-tolerant new users and previous users whose tolerance has diminished (e.g. after a period of imprisonment)

Injection marks are found at numerous sites on the body beginning with the hands, the forearms and elbows and moving on to the groin, thighs, toes and even the neck. In desperation the addict will seek veins in the genital regions. When the veins are scarred and no longer accessible injections will be instead given into the muscles (intramuscular) or into the skin and subcutaneous fat ('skin popping'). Tattoos are frequent, often depicting drug paraphernalia, and are strategically placed to conceal injection marks.

Local complications of injecting

Skin abscesses and ulceration
Skin scarring and the needle track marks
Fat necrosis due to injection beneath the skin
Myositis (inflammation of the muscle)
Thrombosis following repeated injection into veins
Lymph channels become blocked and lymph nodes enlarged resulting in swelling or oedema of the limb.

General complications of injecting

Gradual lung scarring in relation to injected foreign material (foreign body granulomas).
Liver granulomas.
Blood vessel and nerve cell damage in the brain.

Infections are frequent in intravenous drug abuse due to the impossibility of maintaining aseptic technique. Injection of bacteria into the blood stream will result in septicaemia. Bacteria may settle on the heart valves causing inflammation (endocarditis), valve destruction and acute heart failure. Fragments of infected blood clot may break off and travel via the bloodstream to the organs, including the brain and kidney with serious peripheral effects (embolic phenomena). **Hepatitis B infection** and **HIV** (human immunodeficiency virus) may result from needle sharing.

Many of the local and general effects of drug abuse are due to other inert substances present in the drug preparation (adulterants). These tend to be insoluble white powders which are added to the drug to increase its bulk during cutting and dealing. Typical substances include caffeine, quinine, cocaine, starch, salt, lactose, manitol and dextrose.

Microscopic examination of the lungs and liver of intravenous drug addicts will reveal chronic scarring in relation to injected foreign bodies such as starch, talc and cellulose (foreign body granulomas). These materials are typically abundant in those who crush, dissolve and inject medications intended for oral use.

Post Mortem Toxicology

Interpretation of the results of toxicological analysis of post mortem blood samples is problematic. Heroin related deaths present the greatest practical difficulties since heroin is such a commonly abused drug, its supply is illegal and abuse is frequently fatal. However, prosecution is never straightforward since interpretation of both the circumstances & post mortem drug levels is difficult and fraught with uncertainty.

When an addict dies suddenly with the needle still protruding from the arm, it is reasonable to presume death was indeed the result of intravenous heroin abuse and toxicology will usually confirm the presence of morphine in the bloodstream. After injection Heroin is metabolised in the body within a matter of minutes to an intermediate metabolite called 6-Mono-Acetyl-Morphine (6-MAM). This is in turn rapidly metabolised further to Morphine. The presence of 6-MAM indicates death occurred within about 2 hours of injection and that it was Heroin and not morphine which was injected. However, the absence of 6-MAM does not exclude rapid death.

Most Heroin related deaths occur several hours after taking the drug (either by injection or smoking). The victim is typically active for a period before lapsing into sleep and is often heard snoring by family or witnesses. Under these circumstances PM toxicology usually reveals a relatively low level of morphine (& no 6-MAM). Other drugs, particularly Diazepam, Methadone & Alcohol are often also present.

The effective therapeutic concentration of morphine is usually less than 0.1 mg/l. The levels of morphine reported in fatalities range from 0.2 -2.3 mg/l (average 0.7 mg/l) (reference : R. C. Baselt, Disposition of Toxic Drugs & Chemicals in Man, 5th edition, Chemical Toxicology Institute, California, 2000). However, similar levels are often found in tolerant, living drug addicts.

The presence of morphine post mortem may reflect administration of morphine itself but more commonly represents use of heroin, which is rapidly broken down (via 6-MAM) to morphine in the body.

The interpretation of post mortem morphine levels is complicated by the phenomenon of “tolerance”, whereby a regular heavy user may survive high blood morphine levels. Conversely, deaths have been reported even at low morphine levels, particularly when the individual is a naïve or irregular user or has survived for a period of time following drug administration. Tolerance is unpredictably variable, both between individuals and within the same individual. For these reasons there is considerable overlap between the published therapeutic and fatal levels. In practice this means that the levels found in dead drug addicts are often no different from those found in living addicts. Interpretation of drug levels is further complicated by post mortem changes within the body which may artefactually change the level of the drug.

Taking the history, circumstances and findings as a whole, death is often attributed to the acute and chronic adverse effects of heroin use. Acute adverse effects include the expected dose-related toxic effects, any dose independent collateral side effects, any idiosyncratic or allergic type reactions to impurities, or complications arising in relation to the method of drug administration, intravenous injection being potentially the most hazardous route. It is also well recognised that the chronic adverse effects of drug abuse (particularly its effects on the heart, lungs, liver and brain) may also cause or contribute to death, although the precise mechanisms involved are poorly understood.

Acute alcohol intoxication is known to potentiate the toxic effects of heroin and is therefore often viewed as a significant contributory factor.

Although the level of each individual drug may be below its own expected fatal level, it is well recognised that taking drugs together has an additive or “Cocktail Effect” and that this may result in a fatal combination, particularly when taken with alcohol.

POST MORTEM DRUG REDISTRIBUTION

Artefactual elevation of measured post mortem drug concentrations caused by the drug passively re-

distributing itself around the body after death.

During life, drugs and metabolites will accumulate in various organs and tissues (especially the liver). After death, when cell membranes lose their functional integrity, drug will pass from these areas of high concentration to areas of low concentration by the passive process of diffusion. Blood within nearby blood vessels will thus contain an elevated drug level compared to that present in life. Many drugs accumulate in the liver and some in other organs such as heart muscle, lung tissue or kidneys. The central vessels in and around these organs will contain spuriously elevated drug levels after death. This process continues over a period of hours and days after death.

The most commonly encountered practical difficulties arise from taking a central blood sample from the heart or neighbouring great vessel (aorta, pulmonary artery, pulmonary vein, inferior vena cava or superior vena cava). Blood from these sites is often spuriously elevated by PM drug redistribution from the liver, the most metabolically active organ in the body and the site of much drug metabolism in life.

Drug levels in peripheral blood samples, such as blood returning from the legs via the femoral vein or from the arms via the subclavian veins, is less vulnerable to this artefact. Drug levels should be measured in peripheral blood since these levels are much more likely to represent the level circulating around the body during life.

Reference:

Pounder DJ, Jones GR. Post-mortem drug redistribution—a toxicological nightmare. *Forensic Sci Int* 1990;**45**:253–63

VOLATILE SUBSTANCE ABUSE (VSA, 'glue sniffing')

Responsible for over 100 deaths in UK per year since 1985

Between 3.5 and 10 % of adolescents have at some time experimented.

Between 0.5 and 1 % are current users.

Experimental, one-off experience or a recreational group activity.

Approximately 20 chemical solvents are commonly abused. These are cheap, readily available and their possession is not illegal. Recent legislative procedures limit the sale of solvents to young people.

The acute toxic effects of all the commonly abused solvents are similar and are due to the central nervous system depressant effects which resemble of alcohol intoxication.

Acute toxic effects

Feeling of well being and euphoria due to disinhibition

Higher levels cause changes in perception, hallucinations

Impaired co-ordination (ataxia) and confusion

Aggressive and risk-taking behaviour

Solvents most commonly abused

Toluene (adhesives and paint stripper)

111 trichloroethane and other chlorinated solvents (correction fluid, household dry cleaning agents)

acetone (nail varnish remover),

dichloromethane (paint stripper),

butane (cigarette lighter fuel),

propane (camping gas fuel),

halons (aerosol propellant, paint),

petrol and fire extinguishers.

Mortally results chiefly from the use of gas fuels (30%), adhesives (24%), aerosols (18%) and other volatile solvents (29%).

Chronic toxicity affects the central nervous system (peripheral nerve damage, encephalitis and dementia), the heart, liver and kidneys.

The **methods of volatile substance abuse** depend on the physical characteristic of the solvent involved

Viscous adhesives are usually poured into a plastic crisp packet which is gripped around the neck and the vapours are re-breathed from the bag.

Fluid solvents are poured onto a cloth or handkerchief or a plastic bottle and sniffed directly.

Aerosols may be sprayed into a large plastic bag placed over the head.

Lighter fuel and aerosols are sometimes sprayed directly into the mouth and throat.

External signs of volatile solvent abuse are minimal. Apart from the smell of solvents on the clothes and breath the presence of a minor rash around the nose and mouth is said to be characteristic.

In fatal cases **autopsy findings** are typically minimal with mild tracheitis, bronchitis and occasionally a fatty liver. However, the solvents can be detected in the blood urine and in some tissues, including the brain.

Deaths due to volatile substance abuse may be immediate or delayed.

Immediate deaths due to

1. The direct toxic effects of the solvents
2. The indirect effects, such as trauma or accidents whilst intoxicated.

Direct toxic deaths fall into four main categories:

1. Critical reduction in the amount of oxygen reaching the brain and tissues (**hypoxia**). This can be the result of airway obstruction caused by an unfavourable position of the upper airways and head or, more often, lack of oxygen in the inspired air (plastic bag over the head)
2. **Respiratory centre depression**. All solvents are central nervous system depressants. When their concentrations in the blood rise too high the depressant effects on the brainstem may result in loss of consciousness and death.
3. "**Vagal inhibition**". The spraying of cold or cooling gases such as butane and aerosols directly into the mouth may stimulate the nerves of the larynx and trigger a nervous reflex with nerve impulses passing up to the brain via one set of nerves, connecting in the brain and relaying impulses down to the heart via the vagus nerves, resulting in cardiac arrest (vagal inhibition).
4. Disturbance in the electrical rhythm of the heart (**cardiac arrhythmia**). VSA results in the heart muscle (myocardium) becoming oversensitised to the effects of adrenaline (the body's flight of fight hormone which is normally synthesised by the adrenal glands). Adrenaline is a catecholamine hormone which causes a rise in blood pressure, pulse rate, breathing rate and mental awareness to enable a 'fight or flight' response. However, when the heart becomes oversensitised to these effects there is a risk of arrhythmia which can be triggered by vivid hallucinations at the time of intoxication. This risk persists for several hours and many deaths have been reported following some subsequent burst of physical activity such as during a chase by police or other figure of authority or in subsequent sexual activity. An arrhythmia occurring on the basis of volatile substance abuse is often unresponsive to cardiac massage and normal resuscitation.

Restraint asphyxiation in excited delirium

In America there has been a recent upsurge in deaths of acutely intoxicated drug addicts following their arrest and restraint. This phenomenon has been called restraint asphyxiation in excited delirium and is most often seen following use of stimulant or hallucinogenic drugs.

The main features are

1. Acute drug induced excited delirium and police confrontation results in excessive catecholamine stress on the heart.
2. Pronounced hyperactivity, restraint and a struggle against restraint, result in increased oxygen demand by the tissues (an oxygen debt builds up).
3. Following arrest the hog-tied position (wrist and ankles cuffed together behind the back) impairs the breathing movements of the diaphragm and chest wall.

Thus, at a time when oxygen demand is at its highest, breathing is impaired resulting in a state of hypoxia. It is likely that the final mechanism of death in these cases is a disturbance in the electrical rhythm of the heart.

