

2

Injection of drugs

Hypodermic injections should be prepared extemporaneously. In most cases they are plain solutions of alkaloidal or other salts in water. All utensils used should be sterilised by thorough washing and drying in an oven at 220 degrees Fahrenheit. The distilled water must also be sterilised by boiling.

Instructions for preparation of injections, in
'Pharmaceutical Formulas', 1911

Heroin, cocaine and amphetamine are drugs that are commonly administered intravenously. The majority of injectors begin by taking other non-parenteral psychotropic drugs, or by taking their first intravenous drug in a non-parenteral form. Many chronic drug users eventually prefer to inject rather than administer by other routes and there are a number of reasons for this. Intravenous administration provides the quickest access to the circulation, resulting in rapid passage of the drug to the brain. This produces the fastest possible onset of intoxication, and usually a 'rush' or 'buzz' of initial euphoria occurs when a bolus of drug reaches the brain. This effect is particularly sought after. Other methods of administration generally provide a slower onset and a less intense 'rush'. Non-parenteral methods often involve a degree of wastage as well: when given orally a proportion of the dose may not be absorbed or may be metabolised by the liver before reaching the brain; smoking or vaporisation usually destroys some of the drug; nasal inhalation wastes the percentage of the drug that passes down the throat to be absorbed more slowly later.

Apart from these considerations, injecting forms an important ritual for many individuals and, for those who become dependent, abandoning the ritual of preparation and administration is often a difficult part of stopping. The process of injecting may also be tied to a particular social setting, environment or time. The importance of ritual is seen in other areas of substance dependence – for example, tobacco smokers may prefer to smoke at specific times of the day, or to use particular techniques for preparation, and feel discontent if unable to do this.

Injection equipment (needle and syringe) is often referred to at street level by terms such as ‘works’ and the process of injection is called ‘main-lining’, ‘fixing’ or ‘shooting up’. The typical sites chosen for injection in the beginning are the veins of the forearms, but users may switch to the lower leg, back of the hand, groin or neck if forearm veins are difficult to access. If intravenous access is severely restricted (as may occur in chronic users because of venous damage), the subcutaneous or intramuscular routes may be employed. Some users may actually prefer these routes.

Despite the many problems connected with injecting drugs at street level, most injectors generally do not seek medical assistance. A study of 112 injectors in Glasgow identified 107 with current injection-related medical problems.¹ There was a mean of 2.3 problems per patient. However, 73% of subjects had not sought medical assistance, mainly because such problems were perceived as normal or not serious. The remainder had had unpleasant previous experiences with healthcare professionals, feared discrimination, or did not want to be seen as wasting healthcare resources.

The dangers arising from the process of intravenous injection of street drugs are discussed below.

Infection

Injecting drug users are prone to infections from bacteria, viruses and fungi. The most serious infections associated with intravenous drug abuse arise from the transfer of blood-borne infections between individuals as a result of the sharing of needles, syringes and filters. These infections include human immunodeficiency virus (HIV) and viral hepatitis (see below).

However, the drugs themselves and the process of administering them can also give rise to infections. Street drug injections are usually prepared by dissolving a non-sterile powder or crushed tablet in tap water, as illustrated in Figure 2.1. Occasionally other sources of non-sterile water are used, such as bottled mineral water. The preparation may be prepared in a spoon or bottle cap. When injecting heroin in countries where the drug is supplied as base heroin (e.g. Europe), intravenous drug users commonly heat the mixture and use citric, ascorbic or other weak acids to aid heroin dissolution (see Chapter 3); sometimes readily available acidic liquids are used such as vinegar or lemon juice. Oral liquid preparations such as methadone mixture are also injected but this is rare in countries such as the UK where a viscous dilute formulation is used. Once a solution has been prepared, a filter may then be

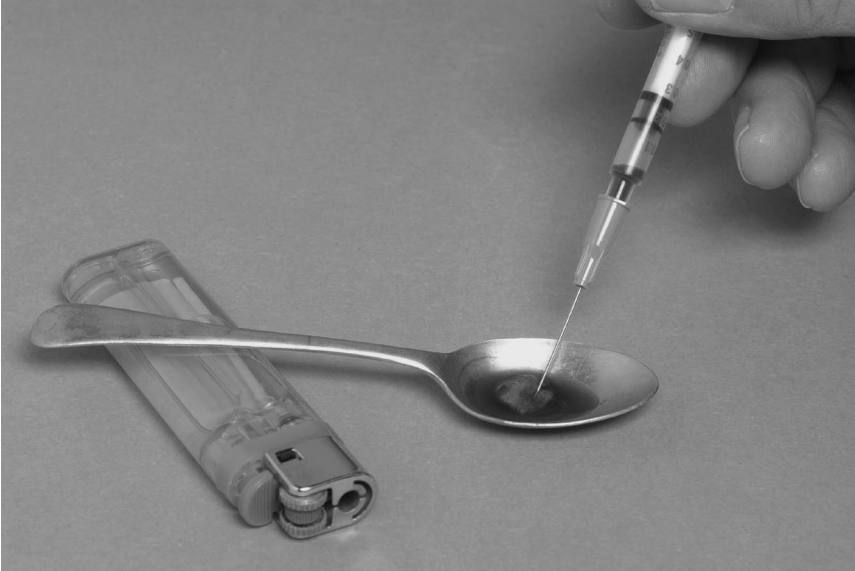


Figure 2.1 The preparation of powdered heroin base for injection involves heating the powder with water and a weak acid to create a solution of a heroin salt. In countries where heroin is supplied as the hydrochloride, the drug is freely soluble and neither heating nor a weak acid are required (Photo courtesy of Multimedia Research Partners Ltd).

used to remove any solid particles. Although in certain countries sterile medical filters are supplied via needle exchange schemes, at street level a variety of non-sterile filters are commonly used, such as cigarette filters, or a piece of permeable fabric, cotton wool or blotting paper.

Finally, the preparation is injected with a needle and syringe through the skin and into a vein. The injection equipment may be shared with another person, or used by the same individual on numerous occasions, and may or may not be washed between injections. Even if washing does take place it is impossible to guarantee that this will prevent contamination.

All of these steps in the injection process are clearly a potential source of contamination with pathogenic organisms: the drug itself and anything non-sterile added to it, the solvent, the receptacle it is made up in, the needle and syringe if not sterile, the filter, and the skin of the patient. By conveying a contaminated solution directly into the bloodstream, the individual bypasses all of the body's normal safeguards against the entry of micro-organisms. For this reason, the infections seen in intravenous drug users are frequently well-known conditions but with atypical pathogens, or they may occur in unusual body locations.

The likelihood of infection occurring, and of atypical organisms being responsible for them, is further increased if the individual is also suffering immunodeficiency due to HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome).

Infections can be difficult to diagnose, because of the wide range of micro-organisms that are potentially responsible. However, not all fevers or infections in injecting drug users are caused by the injection of contaminated drug solutions. Many (but by no means all) users have generally poor health due to inadequate nutrition, unsuitable living conditions and deficient personal hygiene, amongst other considerations. In this environment, certain infections are likely to be more common anyway, for example chest infections, ‘coughs and colds’ and urinary tract infections. Tuberculosis and other contagious infections can be spread by affected individuals associating with others. Another important point is that withdrawal from some drugs, most notably opioids, can cause fever without any underlying infection.

Attempts at harm reduction include methadone maintenance programmes, counselling, supplying clean equipment, and educating users to try to minimise the risk of infection. Harm reduction in all its forms seeks to reduce the risk of infection, but it does not eliminate it. Needle and syringe exchange schemes aim primarily to prevent users sharing injection equipment or using the same equipment more than once themselves. In countries such as the USA, which have been slow to introduce needle exchange schemes, injecting drug users represent a comparatively high proportion of HIV/AIDS cases compared to countries such as the UK, where needle exchange schemes were implemented at an early stage. The supply of sterile needles and syringes also gives the drug user the opportunity to return used equipment for safe disposal and to interact with a healthcare professional. An extension of the idea of opportunistic interactions with a professional is to provide supervised injecting rooms where intravenous drug users can inject safely, knowing that medical assistance is available in case of overdose, accident or side-effects, and that advice can be offered on injection technique.^{2,3}

Other materials can be issued with needles and syringes via formalised programmes.⁴ Sterile alcoholic swabs enable users to clean the injection site immediately before drug administration to decrease the likelihood of skin commensal bacteria being injected into the body. Sterile water may be supplied as an alternative to the tap water that is typically used. Those injecting base heroin, ‘crack’ cocaine or crystal metamfetamine may be supplied with sachets of weak acids (e.g. citric acid). These acids convert the base form of the drug to a more soluble

salt, enabling preparation of a solution for injection. Supplying an acid prevents use of more inappropriate alternatives such as lemon juice (see below). Sterile containers for mixing drugs, and filters, can also be made available. If all of these materials are supplied and used appropriately, the principal remaining source of infection is the street drug itself. While widespread prescribing of sterile pharmaceutical heroin (diamorphine injection) to dependent users has not been advocated, prescribing for those who have failed first-line treatments has been evaluated within supervised injectable maintenance clinics.^{3,5}

A variety of specific infections can occur in injecting drug users and some of these are discussed in more detail below.

Skin and injection site infections

The skin is a common source of pathogenic bacteria in intravenous drug users, and so the risk of causing superficial infections is increased when injections are given without first cleaning the surface of the skin with an alcohol swab. The risk is further increased when injection occurs through parts of the skin that carry a particularly high population of commensal bacteria (e.g. groin) and when injections are deliberately given subcutaneously or intramuscularly. Nonetheless, infection is a common complication after repeated non-sterile injection by any route and tends to initially occur local to the sites of injection. Abscesses and cellulitis are the most frequently recognised presentations.

In one US study of 242 consecutive injection drug users presenting to an emergency department with soft tissue infections, 72% suffered from abscesses, and 23% had cellulitis.⁶ For the total cohort, the median length of time for which participants had tolerated symptoms before seeking medical attention was 4 days; by the time they were seen in the emergency department 40% required hospital admission. Infections were most frequently seen on the arms (50%), legs (23%), buttocks (20%) and deltoid area (14%). Several studies suggest that skin and soft tissue infections are the most common reason for injecting drug users to be admitted to hospital.⁷

The organism most commonly identified as causing skin infections is *Staphylococcus aureus*, reflecting its widespread presence on the surface of the skin itself. *Streptococcus* species are probably the next most common. However, polymicrobial infection or the involvement of atypical pathogens is well known. These skin infections can develop into more severe local infections (e.g. cervical abscess, necrotising fasciitis or myonecrosis), but can also metastasise to other areas (e.g. bone, heart

valves, septicaemia). The importance of local infection as a potential source of more serious harm is illustrated by an outbreak of infections with *Clostridium novyi* and other *Clostridium* species in Scotland, England and Ireland in injecting drug users in 2000.^{8,9} It is believed that initial clostridium infection at injection sites, perhaps facilitated by soft tissue damage secondary to use of citric acid, enabled the spread of infection and the release of bacterial toxins, which led to the death of many injectors. Clostridia are anaerobic species and infections in injecting drug users may arise due to heroin contamination with soil or faeces.

Infected ulcers occur as a consequence of impaired blood flow in the limbs of chronic injectors.^{4,7} The lower leg is the most common site. They may initially arise due to infection at the site of a venous injury caused by injecting, or they can develop from minor trauma sustained by other means that becomes infected. The fact that local veins have become occluded leads to a reduced blood supply, which in turn hinders healing of these small wounds. From this beginning the damage may increase to form deeper and larger ulcers, which are painful and difficult to heal.

Endocarditis

In the USA, the incidence of infective endocarditis in intravenous drug users has been quoted as 2–5% per year, and is responsible for up to 20% of hospital admissions and 5–10% deaths in this patient group.¹⁰ More than half of the intravenous drug users presenting with this condition are found to have *Staphylococcus aureus* endocarditis. It is assumed that this organism is derived largely from skin infections. Most infections are of the tricuspid valve (i.e. right side of the heart), especially in HIV-positive patients.^{10,11} However, *Streptococcus viridans* and other *Streptococcus* species, enterococci, or fungal micro-organisms (especially *Candida* species) are more likely to be responsible if the endocarditis affects the left-hand side of the heart. A variety of theories have sought to explain why the right side of the heart seems more prone to endocarditis in injecting drug users.¹² It has been suggested that insoluble particles in injected drugs or the drugs themselves could damage heart valves, enabling them to act as a focus for the adherence of platelets and then micro-organisms, and because venous blood drains to the right side of the heart first it would be exposed to a more concentrated effect. Another theory suggests that after intravenous injection any blood contaminated with micro-organisms will drain into the right

side of the heart first, predisposing it to infection. However, neither of these theories alone, or others that have been put forward, seem to adequately explain the phenomenon, which may be caused by a number of factors acting in concert.¹²

There are many other organisms that have caused endocarditis in intravenous drug users, including other *Staphylococcus* species, *Pseudomonas* species, *Serratia*, respiratory organisms and anaerobes. A particular micro-organism can predominate in a specific geographical location, and at a specific time.¹³ This is most often linked to the fact that non-staphylococcal endocarditis is likely to be caused by contaminants of the drug itself. Polymicrobial infection can occur in an estimated 2–5% of cases.¹⁰

Infective endocarditis often responds favourably to antimicrobials once the causative organism has been identified. However, long courses of treatment (4–6 weeks) are often needed and prognosis is worst for patients with left-sided infection, certain infective micro-organisms (e.g. *Candida*), and severe immunosuppression due to HIV/AIDS.^{10,11}

Viral infection

When injecting street drugs intravenously, it is common practice to pull on the plunger of the syringe during injection to check that the needle has entered a vein. This results in blood being drawn into the syringe, together with any micro-organisms. If the injection equipment is then shared, the second user will inject any pathogenic organisms in the blood of the donor directly into his or her own bloodstream. This is a very important method by which blood-borne viruses are transferred from one person to another – especially HIV and hepatitis B and C.

HIV can remain viable inside blood-contaminated needles and syringes for more than 4 weeks.¹⁴ However, the tip of the needle is contaminated whether or not the individual actually draws blood into the barrel of the syringe, so any sharing of injection equipment should be discouraged. Once an injecting drug user has become HIV-positive, the infection can spread beyond the injecting community via sexual contacts of the injector. A full discussion of the implications of HIV status is outside the scope of this book, but those who become immunocompromised as a result of their HIV status are more prone to a whole range of other infections, some of which are diagnostic for AIDS, e.g. *Pneumocystis carinii* pneumonia.

Injecting drug users should be encouraged to seek vaccination against the hepatitis B virus, which is thereby a preventable infection.

Unfortunately there is no hepatitis C vaccine. Hepatitis C infection, like HIV infection, can remain largely asymptomatic for many years so persons carrying the disease can pass it on to others before becoming ill themselves. Some carriers seem never to develop overt liver disease, but about a quarter develop serious chronic liver disease (including cirrhosis and liver cancer).

Fungal infections

One review has estimated that fungal infections represent 5–50% of serious infections in intravenous drug users.¹⁵ *Candida* species are most commonly involved, causing disseminated candidiasis, endocarditis, CNS infections and endophthalmitis. In the 1980s, an outbreak of severe candida infections in Australia and Europe was found to have arisen because of the use of lemon juice to dissolve heroin before injection. This is a known growth medium for fungi.¹⁶ Aspergillosis and mucormycosis have also been described in the injecting population.

Bacterial septicaemia

This usually occurs secondary to wider dissemination of an infection from elsewhere (e.g. the skin). *Streptococcus* species are typically responsible. Tetanus has only rarely been encountered since the widespread adoption of prophylactic vaccination.

Joint and bone infections

Septic arthritis and osteomyelitis have been described in intravenous drug users. In 1987, a study of 37 heroin users with septic arthritis revealed that the joints involved were somewhat atypical. In 39% of patients sacroiliac joints were affected and in 37% chondrosternocostal unions.¹⁷ Diagnosis can be difficult because infection has an insidious onset, the joint is often painless, and there may be no systemic signs of infection.¹⁸ However, without prompt treatment, chronic incurable infection may result.

Irritant effects

Most drugs that are injected are not themselves irritant. Temazepam and dextropropoxyphene are notable exceptions as they both cause irritation of tissues or veins after injection, leading to abscesses, tissue

necrosis, venous fibrosis and phlebitis.¹⁹⁻²¹ These areas of damaged tissue can then act as foci for infection or thrombosis.

Irritant reactions such as phlebitis from most other injectable preparations may be attributed to adulterants or additives, local infection, or other forms of poor injection technique. Areas of phlebitis are sometimes called 'track marks' when they appear as inflamed red lines on the surface of the skin following a vein. Base forms of heroin, cocaine or metamfetamine are often deliberately mixed with acidic substances such as citric acid to aid dissolution; this can be irritant and cause local tissue damage (so-called citric acid 'burns'). It has also been reported that ammonia may contaminate 'crack' or 'freebase' cocaine as a result of the manufacturing procedure. This can be very caustic if injected.²² Other potentially irritant adulterants in street drugs include quinine and sodium bicarbonate. Clearly, irritant effects local to the injection site are more likely to occur if the offending preparation is administered subcutaneously²³ or if there is extravasation during venous injection. Those who inject cocaine may be at particular risk because this drug has local anaesthetic properties that can mask the pain of impending damage.

The repeated intravenous administration of injections at the same location eventually destroys the normal pliable nature of the vein because of the accumulated effects of fibrosis around numerous puncture marks, episodes of phlebitis, local thrombosis, irritation and swelling, venous collapse, infection and the actions of impurities. Veins may block temporarily or permanently, but once scar tissue forms it tends to be irreversible. This requires injectors to seek alternative intravenous access sites and eventually, sometimes, to use subcutaneous or intramuscular injection instead.

Emboli, blood vessel occlusion and thrombosis

Most injections given at street level are prepared by mixing an impure powder, or a crushed tablet, with water. Consequently, injectors typically attempt primitive filtration to try to remove non-soluble particles, with varying degrees of success. Those that are not removed, or which arise from the filter itself, will become microemboli in the bloodstream. In some cases the drug itself may form microemboli if it is very insoluble in plasma (e.g. temazepam²⁰). When injected intravenously, these particles can form granulomas in the lung that may impair gaseous diffusion across alveoli (pulmonary granulomatosis), ultimately giving rise

to dyspnoea, hypoxia, pulmonary hypertension or emphysema. Microembolisation of temazepam to the lungs causing death has been reported.²⁴

Embolicisation of insoluble particles can also cause retinopathy. This has been particularly reported in those injecting crushed methylphenidate tablets, but other crushed tablets and heroin have also been cited as potential causes. In many cases visual acuity is not affected, despite the obvious accumulation of obstructive particles in retinal blood vessels. However, impairment of sight can occur. In one study, five out of 23 patients with retinopathy had reduced visual acuity.²⁵

Occlusion of veins as a direct result of particulate contamination may occur, but embolisation to other parts of the body is frequently undetected because it is asymptomatic. In many cases particulate emboli probably dissolve over a period of time leaving no trace.

Certain risk factors increase the chance of venous blockage by blood clots. These include the presence of phlebitis (see above), injecting into the groin, lack of exercise, smoking, and taking oral contraceptives. Subsequent to the development of a deep vein thrombosis (DVT), thromboembolism may also occur, giving rise, for example, to pulmonary embolus (PE). DVTs are reported quite commonly in the injecting population and those injecting temazepam in any form may be more at risk because of the irritant nature of the drug. Moreover, in response to the widespread abuse of temazepam liquid-filled capsules, a gel-filled capsule was introduced with the intention of making injection more difficult. However, injectors learned to heat the gel and/or mix it with water to enable injection. This had the unfortunate consequence of causing DVTs, probably as a result of the gel solidifying within veins.^{21,26}

Intra-arterial injection is particularly likely to give rise to serious forms of blood vessel occlusion. For example, the intra-arterial injection of temazepam has been widely reported as it can result in severe damage to many parts of the body. Often the femoral artery or a forearm artery is involved, the patient having missed a vein and punctured an artery by mistake. As with intravenous administration, the gel capsule formulation may solidify in blood vessels after injection causing ischaemia. The irritant nature of temazepam might also cause arteries to go into spasm, or damage the arterial wall (e.g. vasculitis) and so act as a focus for thrombus formation. Temazepam itself is very insoluble and solid particles of it may cause vascular blockade downstream of the injection site via microembolism;²⁰ the common practice of filtration through a cigarette filter may introduce further microemboli. The gel

capsule formulation in particular can cause severe tissue damage distal to the site of intra-arterial injection, especially muscle necrosis, necessitating fasciotomy or limb/digit amputation.^{26–30} Rhabdomyolysis and renal failure may subsequently ensue, as may secondary DVT or PE.

The injection of temazepam represents an extreme example of the potential consequences of intra-arterial injection of irritant substances or those containing solid particles. Similar effects have been reported after intra-arterial administration of most other parenteral street drugs.^{31–34} The general symptoms are swelling distal to the injection site, pain, discolouration, and sensory and/or motor deficit. The subsequent pattern of events will depend on the site of injection and the tissues affected. Muscle ischaemia will cause rhabdomyolysis and its sequelae. Vasculitis is common and this can result in thrombosis leading to gangrene and amputation; it can also trigger secondary thromboembolism, which may manifest as DVT or PE. Gangrene may occur if blood supply to an area is blocked by restrictive jewellery during swelling, or if a tight tourniquet is inadvertently left *in situ* by an injecting drug user for very long periods.

In long-term injectors the cumulative effects of blood vessel occlusion, venous irritation and damage, and infections commonly results in impaired blood flow to the legs. This is called chronic venous insufficiency and can reduce mobility.³⁵ Symptoms include swelling, pain, an itching or burning sensation, changes to skin colour, dermatitis, and persistent ulcers.

Air embolus is a potential hazard when large volumes are injected intravenously. A substantial amount of air in the heart causes blood to froth in the chambers during pumping, leading to inefficiency and heart failure. It has been estimated that 10 mL of air would be required in the heart to cause failure;³⁶ this would be very difficult to achieve after injection with a hand-held syringe and is unlikely to occur at street level.

Pharmacological effects

Compared to oral administration, the pharmacological effects of street drugs appear much more rapidly after intravenous injection. The effects may in some cases also be more dramatic. For example, large doses of intravenous opioids are known to cause sudden respiratory depression and death. Usually this occurs because a sample of heroin is more potent than the user anticipated, or because of a lowering of tolerance due to a reduction in heroin usage (e.g. those leaving prison and returning to illicit drug use). Fentanyl analogues are particularly powerful drugs that

are known to have caused death so rapidly that individuals have died with the needle still in place (see Chapter 3).

One reasonably common reaction that can occur after intravenous administration of most street drugs is fainting. In one study of 13 methylphenidate users, 12 reported fainting immediately after injection;³⁷ in a study of 23 temazepam users, 12 reported 'blackouts' after injection.²¹

Adulterants, diluents and impurities

At street level no drugs are pure; even prescription medicines that are injected, such as tablets, contain excipients.

A variety of cheap, inert or pharmacologically active adulterants are used to dilute or bulk out ('cut') illicit drugs, including glucose, paracetamol, mannitol and lactose. The active adulterants are often those considered appropriate to the illicit drug in question. For example, amphetamine and cocaine powders may include other stimulants such as amphetamine derivatives, pseudoephedrine and caffeine. Cocaine may be adulterated with other local anaesthetics.³⁸ The pharmacological effects of adulterants may be important. Thrombocytopenia has been reported in intravenous heroin users and is believed to be an immune reaction to an unknown toxin.^{39,40} Thrombocytopenia explicitly caused by quinine in street drugs has been identified.⁴¹ Quinine can also be a venous and dermal irritant. Two deaths associated with strychnine contamination of street drugs have been described.⁴² Strychnine has been found in heroin and cocaine. Arsenic can be an adulterant of opium in some areas.⁴³ Finally hyoscine (scopolamine) has been included in some batches of cocaine and heroin in sufficient quantities to require emergency hospital admission for antimuscarinic poisoning.^{44,45}

It should be noted that a wide range of chemicals are used to synthesise, transform and purify street drugs, and data are often lacking on the effects in humans of these chemicals and of the intermediate products that arise from the various manufacturing processes.

'Stigmata'

Repeated intravenous injection over a prolonged period frequently results in certain characteristic changes around veins that mark the individual as an intravenous drug user. These are most frequently seen in the

forearm. These may include needle marks, scarring caused by abscesses, phlebitis, granulomas, bruising, and discolouration of the skin along the line of veins due to insoluble particles accumulating within the skin.

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32 Injection of drugs

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