Infections in people who inject drugs on the acute medical take

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ABSTRACT

People who inject drugs are disproportionately affected by acute/chronic bacterial and viral infections that are a cause of significant morbidity. Clinical presentations to the acute medical take vary from skin and soft tissue infections to complications of bacteraemias, and can be challenging with difficulties in adherence, pain management, early self-discharges and loss to follow-up.

This review summarises the most recent UK epidemiology of injecting drug use and infection as well as clinical presentation and management.

Introduction

People who inject drugs (PWID) are vulnerable to a wide range of viral and bacterial infections with significant morbidity and mortality.

Psychoactive substances that can be injected are heroin, cocaine, methamphetamine, ketamine and fentanyl. Polysubstance use is common. Injecting psychoactive substances often takes the course of a chronic, relapsing disease such as diabetes or cardiovascular disease.

Epidemiology

According to the *World Drug Report 2021*, 35 million people are estimated to be suffering from drug use disorders.[1] Around 1.2% of global population used opioids for non-medical purposes with the highest prevalence in North America (3.6%).[1]

The UK has 0.82% of the adult population who are high-risk opioid users: the highest prevalence in Europe.[1] Heroin (94%) and cocaine (58%) are the most injected psychoactive drugs in the UK.[2]

In an anonymous survey in 2020, 65% of PWID had a history of imprisonment; 49% had been homeless in the previous year; 16% had ever traded sex for money, goods or drugs; 43% had indirect sharing of needles, syringes, mixing containers or filters; and 24% had direct sharing of needles and syringes.[2]

Systematic reviews have shown mortality rates that are 10–15 times higher than in the general population with significantly lower life expectancy in PWID. The most common causes of death were drug poisoning followed by chronic obstructive pulmonary disease and suicide.[3]

Morbidity is due to sharing of injecting equipment with risk of blood-borne virus acquisition, contaminated injecting sites resulting in skin and soft tissue infections (SSTIs), vascular complications from thromboembolism to amputation, and systemic infections (eg infective endocarditis (IE); Fig 1).[4,5]

In 2020, a UK survey found that 20% of PWID had chronic hepatitis C (HCV) infection, 12% had hepatitis B (HBV) and 1.1% had HIV.[6] The pandemic has resulted in decreased uptake of the HBV vaccine and missed opportunities for diagnosis persist. It has also challenged continuity of care in drug and alcohol services, with effects that are slowly becoming visible.[6]

Key points

People who inject drugs are a group who may have physical and/or mental health issues as well as social vulnerabilities; all putting them at risk of a wide range of infections with significant morbidity and mortality.

Common infections are due to blood-borne viruses (mainly hepatitis C), skin and soft tissue infections, and deep-seated bacterial infections.

Substance use disorder often takes the course of a relapsing and remitting disease that needs a multidisciplinary, non-judgemental approach, linking inpatient care with community care.

It is important to talk about injection practice to understand risk factors and explore prevention measures.

Prescribing opioid substitution therapy is an evidence-based intervention to reduce morbidity and mortality, it can also facilitate adherence to medical care and reduce infectious risks.

KEYWORDS: infectious diseases, people who inject drugs, skin and soft tissue infections, substance use disorder, opioid substitution therapy

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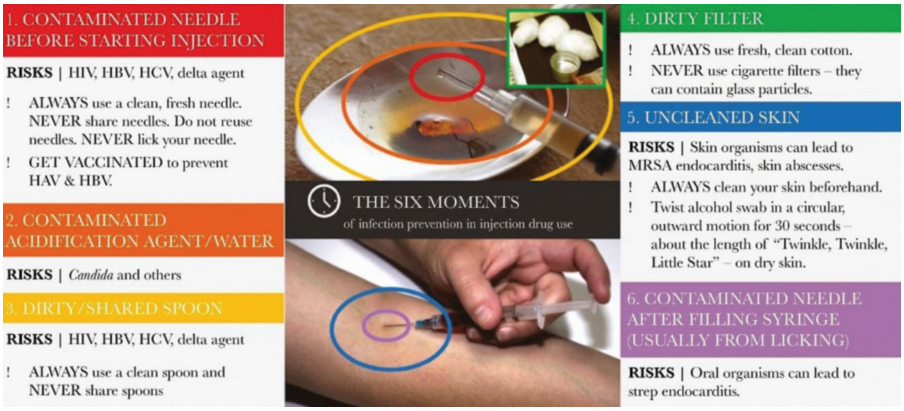

Fig 1. Six moments of infection prevention in injection drug use model. HAV = hepatitis A virus; HBV = hepatitis B virus; HCV = hepatitis C virus; MRSA = methicillin-resistant *Staphylococcus aureus*. Reproduced from Harvey L, Boudreau J, Sliwinski SK *et al*. Six moments of infection prevention in injection drug use: an educational toolkit for clinicians. *Open Forum Infect Dis* 2022;9:ofab631.

Severe bacterial infections disproportionately affect PWID. Group A *Streptococcus* (GAS) and *Staphylococcus aureus* (methicillin-sensitive and -resistant (MSSA and MRSA, respectively)) infections have been increasing in the UK since 2013. The reason is not clear, but several factors have been postulated including homelessness, poor hygiene, and injecting in the groin and other high-risk sites.

In 2020, 7% of all invasive GAS isolates, 19% of MRSA and 11% of MSSA bacteraemia in the UK were associated with injecting drug use. Information on risk factors was missing in many cases so this is likely an underestimate.[6,7]

Increased SSTIs are related to the drug itself (black tar heroin and speedball (a combination of heroin and cocaine)), injection practices (eg skin-popping (subcutaneous or intramuscular use), frequency of use per needle, injection frequency and inguinal injection as opposed to antecubital injection), needle-licking (a practice aimed at cleaning, enjoying the taste and avoiding drug wastage) and necrosis secondary to excipients (eg citrate and levamisole).[4,8,9]

In 2020, a survey found 38% of PWID had symptoms of an injection site infection during the preceding year.[2] Of these, 55% did not seek healthcare treatment.[2] A study of 455 PWID in London found that 46% did self-care for their worst SSTI and 43% waited for more than 10 days before seeking medical care or did not seek it at all, which is a concern for potentially more severe infections and complications.[10]

PWID have a higher risk of IE due to the direct inoculation of bacteria into the bloodstream and direct mechanical damage due to impurities present in injected drugs. In an international cohort of 7,616 patients with IE, the 591 PWID were much younger patients and had higher rates of systemic emboli.[11]

Poor oral health with dental caries, tooth erosions/loss and periodontal disease is commonplace in PWID and can be a risk factor for invasive bacterial infections. Multiple predisposing factors include alcohol and tobacco use, heroin use (which itself causes xerostomia), high sugar-containing methadone use, poor nutrition, and infrequent dental follow-up.[12]

The most common microbiological organisms associated with intravenous substance use are MSSA, MRSA and GAS, which are part of the normal skin flora. Organisms that are a part of the normal oral flora (such as viridans streptococci, *Eikenella corrodens* and *Candida* species) have been isolated. They can all cause wound-related and systemic infections. Polymicrobial infections have also been described.

In the USA, candidaemia rates have been increasing among PWID, on a background of historical descriptions of outbreaks related to contaminated lemon juice used in the preparation of the injected drug.[13] Sporadic outbreaks of tetanus, botulism and anthrax are also ongoing in this population and likely due to contamination of the drug, diluents and excipients with spores.[6]

The prevalence of tuberculosis in PWID is higher than in the general population. They are more likely to have pulmonary involvement and PWID have higher risk overall of severe outcomes (critical care / death) compared with the general population, partially due to the high prevalence of chronic diseases.[14]

Presentation and diagnosis

Assessment of patients' injection practices gives the opportunity to understand risks and facilitate discussions on prevention. This includes how often they share needles and injection equipment with others; how much they re-use needles, cookers and filters; which water they use; and if they rotate sites and disinfect skin before every use.[4]

The most common SSTIs are cellulitis, abscesses, ulcers, necrotising fasciitis and thrombophlebitis. These are a result of local trauma to the skin, the direct inoculation of bacterial skin flora, sharing of unsterile equipment, using contaminated drugs or the local effects of the injected drugs themselves (tissue necrosis).[9]

Long-term complications of SSTIs are chronic venous disease and ulcers; repeated femoral injections can cause deep venous thrombosis, sinus formation and pseudoaneurysms. Septic arthritis and osteomyelitis are common complications acquired via haematogenous or contiguous spread. Severe systemic sepsis, bacteraemia and IE can develop further to complications such as spondylodiscitis and epidural abscess, deep seated infection in any organ, musculoskeletal abscesses, septic pulmonary emboli, endophthalmitis etc.

Investigations

Based on the history, risks and thorough clinical examination (including inspection of injection sites), essential investigations should include blood cultures, wound swabs, tissue or fluid for microbiological investigations, and serology for HIV, HBV and HCV.

The following should be considered: pregnancy testing; sexual health screening (syphilis, chlamydia, gonorrhoea and *Mycoplasma*); drug testing on saliva, blood or urine; and imaging as required (Table 1).[4]

Table 1. Screening and treatment for people who inject drugs[4]

Screening	Vaccines	Medications
Hepatitis C	Hepatitis A and B	Opioid substitution therapy (methadone and buprenorphine)
Hepatitis B	Tetanus (Tdap: 10 years update)	HIV pre-exposure prophylaxis
HIV	Pneumococcus and meningococcus (homelessness)	Naloxone
Gonorrhoea/ chlamydia	Influenza (yearly)	
Syphilis	COVID-19	

Treatment

There is very limited literature for treatment of bacterial infections in PWID. These patients are usually younger, have fewer comorbidities and have more mental health issues, which affects adherence to medical treatment.[15] A multidisciplinary approach and a supportive network in hospital in conjunction with the community is key. Flexibility from medical staff and setting achievable goals with patients can reduce the risk of early self-discharge or loss to follow-up.

Opioid substitution therapy with methadone or buprenorphine is an evidence-based intervention to reduce use, cravings and death. In-hospital initiation or continuation is an important action to improve compliance and reduce risk of blood-borne virus acquisition and recurrent injection-related SSTIs.[16,17]

The long course of antimicrobial treatment necessary for IE, osteomyelitis or septic arthritis is often difficult to adhere to in unstable social circumstances. Two large trials, OVIVA and POET, have shown non-inferiority of oral versus intravenous antibiotics, but had very few PWID in the study groups.[18,19] The use of long-acting lipoglycopeptides (dalbavancin) licensed for SSTIs has been increasingly used off label for bone/joint infections and bacteraemia, as they reduce inpatient stay. Outpatient parenteral antibiotics are rarely given due to issues with indwelling line care and the risk of overdose or reinfection.[20]

Source control with surgery or interventional radiology for SSTIs and deep collections should always be considered. Cardiac surgery for IE has been associated with improved survival but tend to be less frequently performed given concerns about follow-up.[11]

Management of acute pain can be paramount; for example, in cases of deep abscesses or spondylodiscitis. Poor acute pain management can result in self-discharge, self-medication, sedation and overdose, especially when tolerance to opioids is uncertain and when patients are using additional centrally active medications.

Methadone and buprenorphine are prescribed once daily as treatment for substance use disorders but the analgesic effect lasts only 6–8 hours. The Faculty of Pain Medicine recommends continuation of the baseline opioid but splitting the dose into two or three times a day and titrating additional analgesia to effect, with multimodal non-opioid analgesic strategies followed by incremental doses of opioids. Non-opioid analgesics that can be useful are non-steroidal anti-inflammatory drugs, ketamine, lidocaine, glucocorticoids and gabapentinoids. Opioid cross-tolerance may be present so that PWID typically require higher doses of opioids than naive patients. Initially, regular short-acting opioids need to be promptly up-titrated and then tapered after the acute pain phase.[21]

Table 2. Drug interactions and toxicity of antimicrobials with methadone and buprenorphine[22]

Antimicrobial agent	Potential toxicity	Recommendation
Fluoroquinolones (eg ciprofloxacin, levofloxacin or moxifloxacin)	> Increasing concentration of methadone > Prolongation of QT interval (methadone)	Avoid
Macrolides (eg clarithromycin or erythromycin)	> Increasing concentration of methadone or buprenorphine > Prolongation of QT interval (methadone)	Avoid
Oxazolidinones (eg linezolid)	> Increasing risk of serotonin syndrome (methadone)	Avoid
Rifampicin	> Decreasing concentration of methadone or buprenorphine	Monitor and increase dose of methadone or buprenorphine while on rifampicin then decrease at the end of the course
Antiretrovirals (eg efavirenz, nevirapine, abacavir or some protease inhibitors)	> Increasing/decreasing concentration of methadone or buprenorphine	Consult Liverpool HIV Drug Interactions checker
Direct agents against hepatitis B and C (eg some NS5A inhibitors)	> Increasing concentration of buprenorphine	Avoid
Antifungals (eg amphotericin B or fluconazole)	> Increasing risk of hypokalaemia and torsade de pointes (methadone) > Fluconazole increases concentration of methadone or buprenorphine	Avoid
Antimalarials (eg arthemether, mefloquine or quinine)	> Prolongation of QT interval (methadone)	Avoid
Antiprotozoal (eg pentamidine)	> Prolongation of QT interval (methadone)	Avoid
Antimycobacterial (eg bedaquiline or delamanid)	> Prolongation of QT interval (methadone)	Avoid

Table 3. Six moments of infection prevention in injection drug use

Moment	Potential pathogens	Intervention
Contaminated needle (prior to filling)	HIV, HCV, HBV, delta agent	> Use new needle for every injection > One needle for each person injecting > Vaccination against HBV > HIV PrEP
Contaminated water or acid	*Candida* and other fungal infections	> Use sterile water > Use single-use sachet of citric or ascorbic acid
Contaminated cooker	HIV, HCV, HBV, delta agent	> Use clean cooker > One cooker for each person injecting > Vaccination against HBV > HIV PrEP
Contaminated filter	'Cotton fever': endotoxin from Gram-negative bacteria	> Use clean, single-use cotton filter > One cotton for each person injecting
Unclean skin	MRSA and skin flora	> Wash hands > Wash area to be injected
Contaminated needle (after filling)	*Streptococcus* and oral flora	> Avoid contact with mouth or other surfaces after needle filled > Use of sharps bin

HBV = hepatitis B virus; HCV = hepatitis C virus; MRSA = methicillin-resistant *Staphylococcus aureus*; PrEP = pre-exposure prophylaxis. Reproduced from Harvey L, Boudreau J, Sliwinski SK *et al*. Six moments of infection prevention in injection drug use: an educational toolkit for clinicians. *Open Forum Infect Dis* 2022;9:ofab631.

Opioid substitution therapy can interact with many pharmaceutical agents (including antimicrobial agents) as methadone and buprenorphine are both metabolised by cytochrome P450 (Table 2).[22]

Prevention and patient education

The inpatient stay may provide a suitable opportunity to vaccinate a patient or encourage to engage in vaccination or treatment programmes (eg hepatitis C treatment; Table 1).[4]

In a survey among healthcare providers in the USA, 59% reported being uncomfortable or neutral in educating PWID about reducing risk of infection during the injection process. More than half reported no or low knowledge of harm reduction strategies. The educational toolkit by Harvey *et al* helps address this effectively (Table 3; Fig 1).[5] ■

References

1 United Nations Office on Drugs and Crime. *World Drug Report 2021*. UN, 2021.
2 Public Health England. *Unlinked Anonymous Monitoring (UAM) Survey of HIV and viral hepatitis among PWID: 2021 report: Preliminary data*. PHE, 2021.
3 Lewer D, Brothers TD, van Hest N *et al*. Causes of death among people who used illicit opioids in England, 2001–18: a matched cohort study. *Lancet Pub Health* 2022;7:e126–35.
4 Saldana CS, Vyas DA, Wurcel AG. Soft tissue, bone, and joint infections in people who inject drugs. *Infect Dis Clin North Am* 2020;34:495–509.
5 Harvey L, Boudreau J, Sliwinski SK *et al*. Six moments of infection prevention in injection drug use: an educational toolkit for clinicians. *Open Forum Infect Dis* 2022;9:ofab631.
6 UK Health Security Agency. *Shooting Up: infections and other injecting-related harms among people who inject drugs in the UK, 2020*. UK Health Security Agency, 2021.
7 European Monitoring Centre for Drugs and Drug Addiction. *Drug-related infectious diseases in Europe: Update from the EMCDDA expert network, 2020*. EMCDDA, 2021.
8 Larney S, Peacock A, Mathers B, Hickman M, Degenhardt L. A systematic review of injecting-related injury and disease among people who inject drugs. *Drug Alcohol Depend* 2017;171:39–49.
9 Brunt TM, Lefrançois E, Gunnar T *et al*. Substances detected in used syringes of injecting drug users across 7 cities in Europe in 2017 and 2018: The European Syringe Collection and Analysis Project Enterprise (ESCAPE). *International Journal of Drug Policy* 2021;95:103130.
10 Wright T, Hope V, Ciccarone D *et al*. Prevalence and severity of abscesses and cellulitis, and their associations with other health outcomes, in a community-based study of people who inject drugs in London, UK. *PLoS ONE* 2020;15:e0235350.
11 Pericàs JM, Llopis J, Athan E *et al*. Prospective cohort study of infective endocarditis in people who inject drugs. *J Am Coll Cardiol* 2021;77:544–55.
12 Department of Health. *Drug misuse and dependence: UK guidelines on clinical management*. DoH, 2017. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/673978/clinical_guidelines_2017.pdf
13 Zhang AY, Shrum S, Williams S *et al*. The changing epidemiology of candidemia in the United States: injection drug use as an increasingly common risk factor—active surveillance in selected sites, United States, 2014–2017. *Clin Infect Dis* 2020;71:1732–7.
14 UK Health Security Agency. *Tuberculosis in England: 2021 report*. UK Health Security Agency, 2021.
15 Serota DP, Chueng TA, Schechter MC. Applying the infectious diseases literature to people who inject drugs. *Infect Dis Clin North Am* 2020;34:539–58.
16 Weaver VK, Kennedy MC. Importance of opioid agonist therapy to reduce injection-related infections. *Open Forum Infect Dis* 2022;9:ofac145.
17 Platt L, Minozzi S, Reed J *et al*. Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database Syst Rev* 2017;9:CD012021.
18 Bejon PA, Li HK, Rombach I, Walker S, Scarborough M. The OVIVA trial. *Lancet Infect Dis* 2019;19:1058.
19 Pries-Heje MM, Wiingaard C, Ihlemann N *et al* Five-year outcomes of the Partial Oral Treatment of Endocarditis (POET) Trial. *N Engl J Med* 2022;386:601–2.
20 Serota DP, Chueng TA, Schechter MC. Applying the Infectious Diseases Literature to People who Inject Drugs. *Infect Dis Clin North Am* 2020;34:539–58.
21 Faculty of Pain Management. *Opioids Aware: Substance misuse: acute pain management*. Faculty of Pain Management.
22 British National Formulary. *Interactions A to Z*. National Institute for Health and Care Excellence.

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