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Injecting drug use, the skin and vasculature

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Abstract

Damage to the skin, subcutaneous tissues and blood vessels are among the most common health harms related to injecting drug use. From a limited range of early reports of injecting-related skin and soft tissue damage there is now an increasing literature relating to new drugs, new contaminants and problems associated with unsafe injection practices. Clinical issues range from ubiquitous problems associated with repeated minor localised injection trauma to skin and soft tissue and infections around injection sites, to systemic blood infections and chronic vascular disease.

Limited availability and access to sterile injecting equipment, poor injecting technique, compromised drug purity, drug toxicity, and difficult personal and environmental conditions, interplay to give rise to injecting related health harms. We provide a review to inform clinical practice in the care of people who inject drugs.

Introduction

Injection drug use, if practiced unsafely, can be an extremely harmful mode of non-medical drug use. Once the skin has been damaged or breached problems can arise at the site of injection, in and beneath the skin, in the blood vessel which has been penetrated, in the subcutaneous fascia and muscle tissue, and at remote sites in distant organs in the body. Blood vessels form part of the structure of all tissues and organs in the body and are therefore the entry point for contaminated products or foreign bodies to be introduced into organs such as the lungs, kidneys, the heart, brain, or liver but also into muscle and bone tissue. Many subsequent problems are due to bacterial, viral, or fungal infections but drug toxicity, irritants and contaminants can also cause aseptic damage to all these organs and structures. Repeated trauma to vessels gives rise to superficial or deep damage.

Description of blood borne viruses, bacterial sepsis and contamination, endocarditis, and rarer infectious conditions such as candidal endophthalmitis, deep infections in end organs and internal toxic effects of micro organisms and contaminants will be explored elsewhere in this series. In this article we will address injecting-related skin and soft tissue and vascular infections (SSTVI) and other issues affecting blood vessels, with a focus on identification and treatment of common presentations

and their sequelae, as well as issues related to engaging marginalised populations with care.

We shall overview SSTVIs and other vascular damage, with a focus on epidemiology and causation, clinical examination and investigation, treatment, and prevention.

Epidemiology

Blood vessel and vascular damage can be relatively superficial but can also lead to severe infections distal to the injection site.

Soft tissue and vascular infections (SSTVIs), sometimes referred to as cutaneous injection related infections (CIRI), are infections of the surface of the skin or subcutaneous tissues causing damage. These problems are the most reported injection related injury with wide geographical variation in lifetime prevalence. Due, in part, to a policy and practice focus on blood borne viruses such as HIV and Hepatitis C among people who inject drugs (PWID), they have been described as a 'hidden epidemic of suffering' (1).

Reports of injecting related injury show a range of problems and frequencies in different geographical localities (2). Lifetime prevalence is reported to range from 6% (Australia) to 69% (Ireland) (3). Hospitalisation for related complications are high with 49% of hospital admissions in people who inject drugs being related to an SSTVI, over a four year period in Vancouver and up to 10% Of PWID in the UK reporting SSTVI related admissions per year (4-8). Other studies show a lifetime prevalence of injecting complications among PWID ranging from (0.5-12%) including sepsis (2-10%), bone and joint infections (0.5-2.0%), and thrombosis and emboli (3-27%) (3, 4). The majority of hospital admissions may be avoidable and are often related to delays in access to simple interventions in the community and suboptimal health care facilities targeted at PWIDs (3).

SSTVIs among PWID costs the National Health Service, in England, an estimated £47 million annually and intensive care admission is common (5). Severity and frequency of an SSTVI is variable in geographical location and individual situation depending upon multiple factors and associated health and social problems (6-10). Differences in drug markets, administration practices, service availability and other local factors may all influence the appearance and patterns of SSTVIs. Examples of other situations exacerbating vascular problems are, fragmented drug supply chains, limited provision of injecting equipment

and environments hostile to drug use such as custody situations.

The nature of the drug and material injected is important. Preparations differ in their solubility and consequently their suitability for injection. Types of heroin used vary from country to country. Powder heroin from SE Asia is most common in the UK and Europe whereas black tar heroin, a resinous low grade type from Mexico and South America, is more common in the part of USA and white “Chinese” heroin is common in Australia. The heroin common in Oceania is easily dissolved and prepared for injection but less used as a smoked product. The USA seems to be divided into East and West when it comes to availability and quality of heroin, powder from Columbia being the most available type in the east side and Black tar from Mexico in the west (11, 12). These variations in injecting materials have implications for the methods of injection solution preparation and the associated impact on vascular sites (13).

Skin and vascular problems tend to impact the most marginalised, those who are homeless or unstably housed, people living with multi morbidities and those who are economically insecure. Women who inject drugs are disproportionately impacted with power relations playing an influence (women may be less likely to be in control of the injection preparation and administration process) (14). The stigma, shame, pain, unpleasant odour, and mobility restrictions associated with complications such as chronic leg ulcers, can restrict social integration, access to care and the possibility of accumulating recovery capital, thus exacerbating and entrenching social exclusion. Homelessness, lack of safe or private injecting spaces, limited access to harm reduction information and equipment or hygiene and cleaning facilities can all exacerbate risks of contamination and unsafe injecting technique. In this way, injecting practices, and the environments and social relations in which they take place interplay to determine injecting related health harms.

Clinical presentation, acute and chronic conditions

Injecting related medical problems can be related to several factors: lack of skin and hand hygiene, trauma to the skin or subcutaneous tissues, the use of non-sterile or shared equipment and contamination and toxicity of the substances injected.

Damage can occur during or after intravenous injection causing phlebitis, inflammation, or infection, such as a localised sore or abscess. These problems are characterised by swelling, irritation and pain, or, if clotting or thrombosis occurs, by hard tender swellings. Long term persistent injecting into superficial vein can cause fibrosis of the vein leading to subcutaneous, palpable, swellings at the sites of valves or around injection sites leading to subsequent loss of patency. Skin lesions such as hypodermatitis are indurated chronic ulcerated lesions related to venous insufficiency. "Puffy hands" result from longstanding injecting into veins on the dorsum of the hand and chronic lymphatic damage (15, 16).

Folliculitis, cellulitis, and abscesses are sometimes comparatively trivial and self-limiting but not infrequently require medical and hospital interventions and occasionally lead to septicaemia, tissue sepsis and infection such as endocarditis (17).

Chronic venous insufficiency or unresolved infection can lead to ulceration at, and distal to, injection sites such as the groin. These can be extensive penetrating and frequently become infected and can be difficult to heal.

Subcutaneous bacterial infections leading to superficial erysipelas or deeper cellulitis present as painful, swollen, red areas often spreading by the lymphatic system. This can be associated with fever, rigors and systemic symptoms of irritability confusion and vomiting (18, 19).

Untreated, dehydration can lead to sepsis, shock, acute renal injury, and the requirement for admission to hospital and occasionally to intensive care treatment.

Localised bleeding from an injection site or into soft tissues can arise from traumatic injecting practice or indicate an underlying condition such as liver failure or, rarely, a bleeding disorder. Penetration of an artery by accident may result in more serious haemorrhage manifesting as bright red blood, soft tissue swelling and pain at, or distal to, the injection site.

While injecting into a vein in the hand or upper limb may result in damage and introduction of infection, injection into muscle or deeper vein is potentially more damaging. Femoral or neck veins are used preferentially in some places (20, 21). Longer term injecting into a femoral vein can give rise to a sinus formation, establishing a track with new skin lining (figure 1).

Insert Figure 1 here

Damage or trauma to a deep vein such as the femoral vein can result in a deep vein thrombosis causing swelling of the limb and general pain in the area. Dislodgement and movement of a clot or part of a clot, known as an embolus, from the original site might allow transmission of this material to the heart and from there to the lungs causing a pulmonary infarction manifested by sharp chest pain, breathlessness, or sudden death. Injecting into subcutaneous tissues or muscle is also common and damage, when it occurs at these sites, maybe locally problematic or lead to systemic problems. More dangerous and rare infections include necrotising fasciitis manifesting as a dramatic, painful, swollen ulcerated area caused by contamination of injecting materials with a combination of anaerobic and aerobic organisms (22, 23).

Arterial problems are less frequent than venous but have, potentially, more damaging consequences. Variations in injecting behaviours such as injecting into open wounds or use of unusual site for the injection exist and may complicate recovery and obscure causation.

Arterial spasm and stroke due to stimulants may occur due to haemorrhage or thrombosis or vasospasm. The drug type may be important, cerebral haemorrhage being implicated more with methamphetamine and cocaine and stroke caused by vasospasm with ecstasy (24-29)

Causal mechanisms

The most prominent and available sites for injection into a vein are usually in the cubital fossa or on the dorsal surface of the hands. Surface markings and visibility of veins are more variable than the arterial system but conform to a roughly familiar pattern throughout the body. Females have the same vascular architecture but less surface visibility due to greater subcutaneous soft tissue adipose tissue due in part to physiology. BMI and gender maybe significant factors in accessing veins (30, 31).

In both sexes difficulty in identifying and accessing a suitable vein for injection can lead to the use of other sites such as the femoral vein and veins on the legs or foot and the external jugular vein.

Less commonly, often in desperation, veins in other parts of the body

such as the scalp, breast or penis can be used. Choice of injecting site is determined by multiple factors but with care, a single vessel can sometimes be used for many years. Over a prolonged period of injecting, however, peripheral veins may become thrombosed, painful, or obstructed leading to the use of sites in areas other than the arm. The need for covert use may result in use of a choice of a lower limb vein and the femoral vein is the largest and most easily identified by its proximity to the pulsation of the femoral artery, which can usually be palpated in the groin.

The anatomy of the femoral vein is important as it is closely situated next to the femoral artery and nerve (figure 2). This proximity leads to some of the more serious complications of injecting such as bleeding, thrombosis or, when material is injected into an artery by mistake to arterial insufficiency, arterio-venous fistula, aneurysm formation and damage to the supply of oxygenated blood to the limb. Rarely, injecting into a nerve can result in acute or longer standing neuropathic pain.

Insert Figure 2 here

Poor hygiene when preparing the injection site is commonly the cause of skin irritation and the introduction of infection. When infection is present the bacteria involved are, most commonly, a variety gram positive bacteria such as streptococcus and staphylococcus (and occasionally the resistant variety MRSA) (32-35). These can be the cause of folliculitis, cellulitis, sepsis, and septicaemia.

Less common, and usually occurring in clusters due to contaminated batches of heroin, are the gram positive gas and toxin producing bacteria varieties such as *clostridium* and the spore forming *bacillus anthracis* which are encountered when there is gross contamination of materials from soil or animal materials. These outbreaks tend to be severe and are associated with considerable morbidity and mortality but are usually self-limiting and geographically quite localised (22, 23, 36-38).

Unusual infections such as anthrax and clostridial types might initially appear to be a comparatively trivial skin or subcutaneous problem but can rapidly escalate to systemic sepsis, necrotising fasciitis, tissue, or organ damage.

Injection sites contaminated with anaerobic organisms are more likely to become a problem when the injection is subcutaneous or intramuscular where oxygen levels are lower and anaerobic infections flourish.

As injected materials are introduced into the venous system in the body drugs and contaminants, sterile or septic, either soluble or in particulate form, will be transmitted first to the right side of the heart and then to the lungs where the blood goes for reoxygenation. The lungs can act as a filter for insoluble materials larger than microorganisms and form a locus for any foreign material introduced into the circulation. Oral preparations consist largely of fillers such as talc or starch and this insoluble particulate matter accumulates in the pulmonary capillaries. These can provoke a foreign-body giant cell reaction, potentially causing thrombosis and fibrosis and at longer term pulmonary hypertension. (39) Thrombosis can occur in femoral, iliac and, more rarely, inferior vena cava veins.

While the most common drugs of injection are opiates and stimulants there are reports of damage caused by injection of prescription drugs not manufactured for injection. These include pharmaceuticals such as benzodiazepines, methadone tablets, oxycodone, morphine sulphate, methylphenidate and antidepressants (27, 40). Drugs prepared in pill, powder or capsule form for oral use are likely to increase vascular damage if used by injection without adequate filtration to remove large particulates. There are some drugs such as such as mephedrone and methadone injectable solution which can cause vein damage because of their irritant quality. Cocaine is damaging to blood vessels when injected, through its irritant, anaesthetic, vasoconstrictive effects and the increased frequency of its use. Crack cocaine requires acidification to render it soluble for injection – overuse of acidifier can cause additional venous problems (41).

Superficial infections can be a commonplace experience among people who inject drugs. Considerable barriers to medical care access, normalisation of pain and limited perceptions of severity mean that self management is common (42).

Contaminated drug preparation and reused injecting equipment are important factors informing skin and tissue damage. Widespread low-threshold availability of sterile needle and syringes is critical to reduce injecting related risk practices and infections. Service restrictions and

closures due to the COVID-19 pandemic highlight the need to invest and support innovative modes of distribution, including street outreach, vending machine provision and secondary supply through peer networks (43).

Injecting culture and practice are geographically variable. Brown 'Afghani' powder heroin available in most of Europe is not water soluble without the addition of an acidifying agent such as lemon juice, vitamin C or citric acid. The solution requires heat, which can kill contaminating bacteria although may encourage spores from clostridial infection to germinate (35). Citric acid and vitamin C are provided by most needle and syringe programmes (NSP), given the risk of systemic candidiasis infections from use of lemon juice(44). It is crucial however, that minimal acidifier is used in injection preparation, as excess citric acid use has been identified as a causal factor in venous sclerosis and subsequent SSTI risk (41). Clean water to prepare injection solutions with can be difficult to access when injecting in constrained circumstances; reports of saliva used as a water alternative in injection preparation are concerning, given potential for severe systemic infection (45). The environment in which drugs are injected has significant effects on frequency of sharing equipment, materials used and infection risk. Injection in public places for example, can increase risk of venous trauma through hurried injections, and transitions to injecting in the femoral vein to expediate ease of injection and hide injection sites. A dearth of sterile injection equipment in most custodial settings places individuals at risk of viral and bacterial infections by necessitating equipment sharing. Hospitals have also been identified as environments where risky injection practices can take place, due to a lack of timely opiate replacement therapy provision (42).

Assessment

Examination of infection sites is a crucial part of management. Serious or unresolving injury to skin or infection in tissue surrounding a vein or artery can present as local pain, swelling, warmth and discolouration. Abscesses, at an injection site or in surrounding tissue, can be comparatively superficial and easily observed as a hot red swelling or deeper in subcutaneous tissue or muscle. Here the diagnosis might be more difficult and general signs such as fever and nausea can require further investigations such as ultrasound or soft tissue MRI scanning.

Visual examination may be enough to identify the need for treatment, but caution is needed to prevent progression to more serious conditions. Superficial skin infections and infestations should be carefully diagnosed and actively treated.

More general symptoms such as malaise, fever, nausea and vomiting, and rigors caused by transient bacteraemia, may indicate sepsis or generalised septicaemia. The presence of gangrene, or deep sepsis maybe suspected clinically when there are skin changes, crepitus indicating gas under the skin and a characteristic smell of a wound, associated with clinical deterioration, high temperature toxicity, and signs of systemic disease such as rigors, shock and renal failure. The organism responsible may be identified and confirmed by bacteriological sampling of material at the site or by blood culture. As with other complications of drug use, simple tests to detect anaemia, white cell count, impaired renal function and blood borne virus screening are part of any assessment.

The presence of swelling or groin pain in PWIDs raises the clinical suspicion of thrombosis in a femoral vein (46). Preliminary investigations to exclude deep vein thrombosis include a Well's score and positive D-dimer test, to assess the presence of thrombosis, followed by venography, ultrasound scanning and intra vessel angiography to demonstrate deep vein thrombosis or soft tissue scanning to measure the extent of abscess or deep seated infection (47-49).

More severe consequences such as critical limb ischaemia from intra-arterial injection may be more common than reported (48). Femoral artery aneurysms result from damage to the wall of the blood vessel. Symptoms and signs of vascular insufficiency in the lower limb include pain on walking, or even at rest, loss of hair, mottling of the skin, absent pulses, and skin ulceration. Urgent assessment by vascular specialist is required. Acute arterial insufficiency can lead to tissue necrosis and in extreme cases gangrene and limb amputation.

Treatment and prognosis

Although most skin and vascular complications are common and relatively easily managed there are situations which because of late presentation are likely to make diagnosis more difficult, treatment more complicated and the outcome less favourable. As infected injections sites are common, they are usually self-managed and, in most cases,

resolve with minimum adverse consequences. Knowledge among PWID about SSTVI care and complications can be poor. Coupled with barriers to care this can result in practices such as lancing abscesses, obtaining antibiotics from informal sources and poor adherence to treatment (33, 50). Self management is not always as protective as medical interventions and progressive and cumulative damage to the vein is common.

The mainstay of treatment of SSTVIs is local hygiene and dressing care combined with broad spectrum antibiotics. Cleaning injecting sites with alcohol pads or soap and water is protective against skin infections. Adequate provision of swabs and wipes for people who are street injecting and/or unstably housed is important, as access to clean water cannot be guaranteed (45). Deeper infections which show signs of spread beyond the original site are usually treated with fluid and intravenous antibiotics.

Skin ulceration due to unresolved infection and exacerbated by chronic venous insufficiency requires careful management. Early nursing and medical care might avert more serious consequences of infection. Complications associated with delayed SSTVI care include septicaemia, sepsis, gangrene, endocarditis, chronic venous ulcers leading to surgical debridement, limb amputation, renal failure and death.

Recurrence of SSTVIs among PWID is associated with repeat hospital visits, poor antibiotic adherence, the need for surgical intervention and hospital discharge against medical advice. Primary care and community based interventions have been shown to reduce SSTVI-related hospital admissions by as much as 35% and operating room procedures by 70% (51).

Treatment of vein thrombosis may be by surgical removal of the clot in the leg or, more commonly anticoagulation with low molecular weight heparin or warfarin in the acute phase of treatment, following on during recovery a shorter or longer period of daily injections to prevent a return of clotting in a traumatized vein (52-55). In some cases where the problem has been recurrent ongoing treatment with an anticoagulant may be necessary for as long as injecting continues. This should be weighed against the increased risk of anemia and prolonged bleeding after injection.

Incision and drainage are the most common surgical interventions in treatment of injection site abscesses. The diagnosis or suspicion of vasospasm may suggest a diagnosis of temporary damage to blood flow

rather than thrombosis or endarteritis and indicate a non-invasive treatment (56).

The presence of cellulitis at an injection site may initially seem something to be treated with oral antibiotic but diagnosis of a more invasive infection may lead to necrotising fasciitis and clearly requires early and urgent intervention.

For arterial problems anticoagulation may be required and surgical drainage of abscess or infection may be necessary.

Complications such as necrotising fasciitis may require urgent surgical interventions. Operative treatment employs procedures such as wide incision, subfascial examination, aggressive debridement and excision of necrosed tissue. In more critical infections or when irreversible limb ischaemia is present, amputation of part or all of the limb.

Rarely contamination with gas and organisms such as *Clostridium Perfringens* or *novyii* again requires urgent tissue excision.

Additional clinical management includes oral or intravenous broad spectrum antibiotics, critical care support, and reconstructive procedures (57, 58).

Pseudoaneurysm formation is a serious consequence of injecting into an artery and are most common in the femoral artery where proximity to the femoral vein makes it a common adverse risk. Pseudoaneurysms are less common, but not unknown, in the upper limb (59). For femoral aneurysms vessel ligation is reported as the safest option with a low amputation risk. A high proportion of patients have subsequent longer term symptoms of circulation problems such as venous insufficiency (60).

The complexity and extent of wound care may require prolonged nursing care. This contact may allow the opportunity to engage the patient and build trust (61). Engagement is frequently associated with other interventions such as medically assisted prescribing (opiate agonist treatment) and syringe equipment programmes (62, 63). Advice can also include alternative, and potentially less damaging, ways of using the substance such as smoking, sniffing or by rectum (“plugging”).

Technical opportunities for identifying veins for injection should be used at safer injecting facilities. This can prevent unnecessary trauma and vein damage. Figures 2-5 illustrate the device used and demonstrates the illumination of the veins in the hand. This can be used to identify veins in other parts of the body and is available in injecting room and heroin assisted treatment clinics.

Insert figures 3,4,5 here

Where injection cessation is required to obtain improvement, it is important to recognize how difficult this may be for the individual involved. Support in switching to other routes of administration, including though equipment provision, can be helpful (64). In case of a completely deficient venous system, an extreme measure such as insertion of a central venous catheter (CVC) to facilitate drug intake has been tried but this poses several practical and ethical questions for the care givers. Such an intervention in an exceptional situation still lacks data on long-term effects and cost-benefits (Broers, personal communication).

Outcomes for skin and soft tissue infections are, inevitably, variable and depend upon a variety of factors and circumstances. Treated promptly and with proper expertise recovery is usually achieved and damage minimised. Poor outcomes depend upon factors such as the constituency of the infectious or toxic agent present, the delay before intervention and the recurring nature of the traumatic process. Access to sterile drugs and clean injecting equipment has, in many localities, made a significant impact on the problems described in this article.

Other considerations relating to assessment and management

Outreach services recognise the importance of early intervention and support with injecting practices and access to equipment. Limited access to injection supplies and experiencing withdrawal are frequently reported barriers to utilizing risk reduction interventions (65). Engaging marginalized people in care is increasingly recognized as an area of policy and management importance (66, 67). People from more supported backgrounds with added personal resources are likely to be able to avoid some of these risk factors. Required initiatives include comprehensive support for wound care, including provision of bandages and dressings, education and equipment to support injection site hygiene, safe injection preparation practices and transitions from injecting, where desired. Initiatives to reduce stigma toward PWID in hospital and other care settings are crucial to enhance engagement. These can include employment of peer workers and cultural safety informed training for health care

professionals (68).

Among these newer initiatives are educational programmes on wound care, injection site hygiene, equipment provision and measures to be taken when problems arise and early hospitalization for infection and sepsis (69-73). Needle and syringe availability are critical to the prevention of vasculature problems either from inappropriate equipment or contamination and tissue trauma from reuse and sharing. Training of health care workers is likely to help in conveying correct messages to drug users.

The political and structural framework of drug control and legislation has considerable impact on many substance use related problems including vascular problems. Attention has been drawn to neglect of political and policy interest into the causes and solutions for skin and soft tissue infections and the importance of supportive interventions such as safe injecting environments (62). The rapid rise in opiate use and overdose in the USA and the inadequate response to this “epidemic” has contributed to an increase in use of illegal opioids, injecting and subsequent sepsis complications (74-76).

The impact of HIV/AIDS and Hepatitis C infection has had a significant effect on injection practices and the delivery of services for people who inject drugs highlighting the importance of harm reduction (77).

Safer injecting facilities in sites such as Vancouver, Geneva, Amsterdam, and a new heroin assisted treatment clinics in Glasgow and Middlesbrough are important to engage people with care, including through implementation of the broader programmes of health and social care interventions recommended by WHO (78). In the USA state laws have a significant impact on NSP availability, with subsequent collateral damage when this is restricted ((75).

The need for integrated and robust support for people who inject drugs includes mental and physical health and a non-judgemental approach to essential delivery of opiate agonist treatment and injecting equipment. This is available in several countries around the World but often with a limited range of services (66).

In conclusion, skin and vascular problems are frequent in people who inject drugs and vary widely in severity in a constantly changing

environment. The impact of Covid 19 remains to be seen but is likely to impact on service access, particularly in relation to NSP access.

Prevention includes access to harm reduction measures such as sterile injection equipment, a safe consumption environment, and education on safe drug use and alternative ways of using drugs, and access to drug treatment.

Clinical examination for PWID should include a respectful request to discuss safe injection practices and to inspect injection sites including the groin and the neck.

Treatment of skin and vascular problems occurs in the community and in specialist care facilities. All social and medical care workers have a role to play in reducing vascular harms. Engaging out of treatment and marginalised populations remains an important priority.

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References

1. Harris M, Brathwaite R, McGowan CR, Ciccarone D, Gilchrist G, McCusker M, et al. 'Care and Prevent': rationale for investigating skin and soft tissue infections and AA amyloidosis among people who inject drugs in London. *Harm reduction journal*. 2018;15(1):23-.
2. Rahimi-Movaghar A, Noroozi A, Page K, Mohraz M, McFarland W, Malekafzali H, et al. Transition to and Away from Injecting Drug Use among Young Drug Users in Tehran, Iran: A Qualitative Study. *Iran J Psychiatry Behav Sci*. 2017;11(1):e4561.
3. Larney S, Peacock A, Mathers BM, 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.
4. Dahlman D, Berge J, Björkman P, Nilsson AC, Håkansson A. Both localized and systemic bacterial infections are predicted by injection drug use: A prospective follow-up study in Swedish criminal justice clients. *PLoS One*. 2018;13(5):e0196944.
5. Hope V, Kimber J, Vickerman P, Hickman M, Ncube F. Frequency, factors and costs associated with injection site infections: findings from a national multi-site survey of injecting drug users in England. *BMC infectious diseases*. 2008;8:120-.
6. Hope V. Neglected infections, real harms: A global scoping of injection-related bacterial infections and responses. 2010. p. 89-96.
7. Hope VD, Hickman M, Parry JV, Ncube F. Factors associated with recent symptoms of an injection site infection or injury among people who inject drugs in three English cities. *Int J Drug Policy*. 2014;25(2):303-7.
8. Lipsky BA, Silverman MH, Joseph WS. A Proposed New Classification of Skin and Soft Tissue Infections Modeled on the Subset of Diabetic Foot Infection. *Open Forum Infect Dis*. 2016;4(1):ofw255-ofw.
9. Ciccarone D, Bourgois P. Explaining the Geographical Variation of HIV Among Injection Drug Users in the United States. *Substance Use & Misuse*. 2003;38(14):2049-63.
10. Lewer D, Jayatunga W, Aldridge RW, Edge C, Marmot M, Story A, et al. Premature mortality attributable to socioeconomic inequality in England between 2003 and 2018: an observational study. *Lancet Public Health*. 2020;5(1):e33-e41.
11. Summers PJ, Struve IA, Wilkes MS, Rees VW. Injection-site vein loss and soft tissue abscesses associated with black tar heroin injection: A cross-sectional study of two distinct populations in USA. *Int J Drug Policy*. 2017;39:21-7.
12. Mars SG, Bourgois P, Karandinos G, Montero F, Ciccarone D. The Textures of Heroin: User Perspectives on "Black Tar" and Powder Heroin in Two U.S. Cities. *J Psychoactive Drugs*. 2016;48(4):270-8.
13. Mars SG, Ondocsin J, Ciccarone D. Toots, tastes and tester shots: user accounts of drug sampling methods for gauging heroin potency. *Harm Reduct J*. 2018;15(1):26.

14. Murphy EL, DeVita D, Liu H, Vittinghoff E, Leung P, Ciccarone DH, et al. Risk Factors for Skin and Soft-Tissue Abscesses among Injection Drug Users: A Case-Control Study. *Clinical Infectious Diseases*. 2001;33(1):35-40.
15. Rowe L, Cantwell A, Jr. Hypodermatitis Sclerodermiformis: Successful Treatment With Ultrasound. *Archives of Dermatology*. 1982;118(5):312-4.
16. Andresz V, Marcantoni N, Binder F, Velten M, Alt M, Weber JC, et al. Puffy hand syndrome due to drug addiction: a case-control study of the pathogenesis. *Addiction*. 2006;101(9):1347-51.
17. Lewer D, Harris M, Hope V. Opiate Injection-Associated Skin, Soft Tissue, and Vascular Infections, England, UK, 1997-2016. *Emerg Infect Dis*. 2017;23(8):1400-3.
18. Swartz MN. Clinical practice. Cellulitis. *N Engl J Med*. 2004;350(9):904-12.
19. Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. *Cochrane Database of Systematic Reviews*. 2010(6).
20. Karimi M, Ghaheri H, Assari S, Moghani Lankarani R, Moghani Lankarani M, Rafiey H, et al. Drug Injection to Sites other than Arm: A Study of Iranian Heroin Injectors. *Frontiers in Psychiatry*. 2014;5(23).
21. Maliphant J, Scott J. Use of the femoral vein ('groin injecting') by a sample of needle exchange clients in Bristol, UK. *Harm Reduction Journal*. 2005;2(1):6.
22. Mc GC, Penrice GM, Gruer L, Ahmed S, Goldberg D, Black M, et al. Lethal outbreak of infection with *Clostridium novyi* type A and other spore-forming organisms in Scottish injecting drug users. *J Med Microbiol*. 2002;51(11):971-7.
23. Ramsay CN, Stirling A, Smith J, Hawkins G, Brooks T, Hood J, et al. An outbreak of infection with *Bacillus anthracis* in injecting drug users in Scotland. *Eurosurveillance*. 2010;15(2):19465.
24. Lappin JM, Darke S, Farrell M. Stroke and methamphetamine use in young adults: a review. *J Neurol Neurosurg Psychiatry*. 2017;88(12):1079-91.
25. Huang MC, Yang SY, Lin SK, Chen KY, Chen YY, Kuo CJ, et al. Risk of Cardiovascular Diseases and Stroke Events in Methamphetamine Users: A 10-Year Follow-Up Study. *J Clin Psychiatry*. 2016;77(10):1396-403.
26. Darke S, Ross J. The use of antidepressants among injecting drug users in Sydney, Australia. *Addiction*. 2000;95(3):407-17.
27. Darke S. The use of benzodiazepines among injecting drug users. *Drug and Alcohol Review*. 1994;13(1):63-9.
28. Sordo L, Indave BI, Barrio G, Degenhardt L, de la Fuente L, Bravo MJ. Cocaine use and risk of stroke: a systematic review. *Drug Alcohol Depend*. 2014;142:1-13.
29. Reneman L, Habraken JB, Majoie CB, Booij J, den Heeten GJ. MDMA ("Ecstasy") and its association with cerebrovascular accidents: preliminary findings. *AJNR Am J Neuroradiol*. 2000;21(6):1001-7.
30. Kröger K, Ose C, Rudofsky G, Roesener J, Weiland D, Hirche H. Peripheral veins: influence of gender, body mass index, age and varicose veins on cross-sectional area. *Vasc Med*. 2003;8(4):249-55.
31. Vuylsteke ME, Colman R, Thomis S, Guillaume G, Degrande E, Staelens I. The influence of age and gender on venous symptomatology. An epidemiological survey in Belgium and Luxembourg. *Phlebology*. 2016;31(5):325-33.
32. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: A review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. *Can J Infect Dis Med Microbiol*. 2008;19(2):173-84.

33. Roose RJ, Hayashi AS, Cunningham CO. Self-management of injection-related wounds among injecting drug users. *J Addict Dis.* 2009;28(1):74-80.
34. Morrison A, Elliott L, Gruer L. Injecting-related harm and treatment-seeking behaviour among injecting drug users. *Addiction.* 1997;92(10):1349-52.
35. Seaton RA. Skin and soft tissue infection: Diagnosis and management. *Clinical Pharmacist.* 2009;1:13-22.
36. Brett MM, Hood J, Brazier JS, Duerden BI, Hahné SJ. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. *Epidemiol Infect.* 2005;133(4):575-82.
37. Talan DA, Moran GJ, Talan DA, Moran GJ, Pinner RW. Update on Emerging Infections: News from the Centers for Disease Control and Prevention: Tetanus Among Injecting-Drug Users—California, 1997. *Annals of Emergency Medicine.* 1998;32(3):385-6.
38. Wound botulism--California, 1995. *MMWR Morb Mortal Wkly Rep.* 1995;44(48):889-92.
39. Corrin B, Nicholson AG. Occupational, environmental and iatrogenic lung disease. *Pathology of the Lungs.* 2011:327-99.
40. Scott RN, Going J, Woodburn KR, Gilmour DG, Reid DB, Leiberman DP, et al. Intra-arterial temazepam. *Bmj.* 1992;304(6842):1630.
41. Harris M, Scott J, Wright T, Brathwaite R, Ciccarone D, Hope V. Injecting-related health harms and overuse of acidifiers among people who inject heroin and crack cocaine in London: a mixed-methods study. *Harm Reduction Journal.* 2019;16(1):60.
42. Harris M. Normalised pain and severe health care delay among people who inject drugs in London: Adapting cultural safety principles to promote care. *Social Science & Medicine.* 2020;260:113183.
43. Craine N, Hickman M, Parry JV, Smith J, McDonald T, Lyons M. Characteristics of injecting drug users accessing different types of needle and syringe programme or using secondary distribution. *Journal of Public Health.* 2010;32(3):328-35.
44. Servant JB, Dutton GN, Ong-Tone L, Barrie T, Davey C. Candidal endophthalmitis in Glaswegian heroin addicts: report of an epidemic. *Trans Ophthalmol Soc U K.* 1985;104 (Pt 3):297-308.
45. Harris M, Scott J, Hope V, Wright T, McGowan C, Ciccarone D. Navigating environmental constraints to injection preparation: the use of saliva and other alternatives to sterile water among unstably housed PWID in London. *Harm Reduction Journal.* 2020;17(1):24.
46. Anand SS, Wells PS, Hunt D, Brill-Edwards P, Cook D, Ginsberg JS. Does this patient have deep vein thrombosis? *Jama.* 1998;279(14):1094-9.
47. Schulz S, Beckenbach C, Philipp M, Hengstmann J. Color coded duplex sonography of inguinal vessels in i.v. drug addicts. *Vasa.* 2002;31(1):7-13.
48. Woodburn KR, Murie JA. Vascular complications of injecting drug misuse. *Br J Surg.* 1996;83(10):1329-34.
49. Chong LY, Fenu E, Stansby G, Hodgkinson S. Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance. *BMJ : British Medical Journal.* 2012;344.
50. Smith ME, Robinowitz N, Chaulk P, Johnson KE. Self-care and risk reduction habits in older injection drug users with chronic wounds: a cross-sectional study. *Harm Reduct J.* 2014;11(1):28.

51. Fernandez R, Griffiths R, Ussia C. Effectiveness of solutions, techniques and pressure in wound cleansing. *JBI Libr Syst Rev.* 2004;2(7):1-55.
52. Sampson FC, Goodacre S, Kelly AM, Kerr D. How is deep vein thrombosis diagnosed and managed in UK and Australian emergency departments? *Emerg Med J.* 2005;22(11):780-2.
53. Russell M, Dawson D. Best evidence topic report. Low molecular weight heparin for intravenous drug users with deep vein thrombosis. *Emerg Med J.* 2004;21(6):711.
54. Mackenzie AR, Laing RB, Douglas JG, Greaves M, Smith CC. High prevalence of iliofemoral venous thrombosis with severe groin infection among injecting drug users in North East Scotland: successful use of low molecular weight heparin with antibiotics. *Postgrad Med J.* 2000;76(899):561-5.
55. Russell M, Dawson D. Low molecular weight heparin for intravenous drug users with deep vein thrombosis. *Emergency Medicine Journal.* 2004;21(6):711-.
56. Silverman SH, Turner WW, Jr. Intraarterial drug abuse: new treatment options. *J Vasc Surg.* 1991;14(1):111-6.
57. Chen JL, Fullerton KE, Flynn NM. Necrotizing Fasciitis Associated with Injection Drug Use. *Clinical Infectious Diseases.* 2001;33(1):6-15.
58. Callahan TE, Schechter WP, Horn JK. Necrotizing Soft Tissue Infection Masquerading as Cutaneous Abscess Following Illicit Drug Injection. *Archives of Surgery.* 1998;133(8):812-8.
59. Siu WT, Yau KK, Cheung HY, Law BK, Tang CN, Yang GP, et al. Management of brachial artery pseudoaneurysms secondary to drug abuse. *Ann Vasc Surg.* 2005;19(5):657-61.
60. Coughlin PA, Mavor AI. Arterial consequences of recreational drug use. *Eur J Vasc Endovasc Surg.* 2006;32(4):389-96.
61. Nuttall R. Holistic care of a drug-related wound: a case study from a clinic for homeless people. *Nurs Times.* 2009;105(27):18-21.
62. Phillips KT, Stein MD, Anderson BJ, Corsi KF. Skin and needle hygiene intervention for injection drug users: results from a randomized, controlled Stage I pilot trial. *J Subst Abuse Treat.* 2012;43(3):313-21.
63. Robinowitz N, Smith ME, Serio-Chapman C, Chaulk P, Johnson KE. Wounds on wheels: implementing a specialized wound clinic within an established syringe exchange program in Baltimore, Maryland. *Am J Public Health.* 2014;104(11):2057-9.
64. Harris M. An urgent impetus for action: safe inhalation interventions to reduce COVID-19 transmission and fatality risk among people who smoke crack cocaine in the United Kingdom. *International Journal of Drug Policy.* 2020:102829.
65. Strathdee SA, Patrick DM, Currie SL, Cornelisse PG, Rekart ML, Montaner JS, et al. Needle exchange is not enough: lessons from the Vancouver injecting drug use study. *Aids.* 1997;11(8):F59-65.
66. Ho IS, Holloway A, Stenhouse R. What do HIV-positive drug users' experiences tell us about their antiretroviral medication-taking? An international integrated literature review. *Addiction.* 2020;115(4):623-52.
67. Kalk NJ, Robertson JR, Kidd B, Day E, Kelleher MJ, Gilvarry E, et al. Treatment and Intervention for Opiate Dependence in the United Kingdom: Lessons from Triumph and Failure. *European Journal on Criminal Policy and Research.* 2018;24(2):183-200.

68. Pauly BB, McCall J, Browne AJ, Parker J, Mollison A. Toward cultural safety: nurse and patient perceptions of illicit substance use in a hospitalized setting. *ANS Adv Nurs Sci*. 2015;38(2):121-35.
69. Koester S. Copping, Running, and Paraphernalia Laws: Contextual Variables and Needle Risk Behavior among Injection Drug Users in Denver. *Human Organization*. 1994;53(3):287-95.
70. Ng J, Sutherland C, Kolber MR. Does evidence support supervised injection sites? *Can Fam Physician*. 2017;63(11):866-.
71. Macpherson D. A Four-Pillar Approach to Drug Problems in Vancouver. 2001.
72. Gershon RR. Infection control basis for recommending one-time use of sterile syringes and aseptic procedures for injection drug users. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;18 Suppl 1:S20-4.
73. Phillips KT, Altman JK, Corsi KF, Stein MD. Development of a risk reduction intervention to reduce bacterial and viral infections for injection drug users. *Subst Use Misuse*. 2013;48(1-2):54-64.
74. Annie FH, Bates MC, Uejio CK, Bhagat A, Kochar T, Embrey S. The Impact of the Drug Epidemic on the Incidence of Sepsis in West Virginia. *Cureus*. 2018;10(10):e3521-e.
75. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths — United States, 2000–2014. *Morbidity and Mortality Weekly Report*. 2016;64(50 & 51):1378-82.
76. Bauman ZM, Morizio K, Singer M, Hood CR, Feliciano DV, Vercruysse GA. The Heroin Epidemic in America: A Surgeon's Perspective. *Surg Infect (Larchmt)*. 2019;20(5):351-8.
77. Des Jarlais DC, McKnight C, Arasteh K, Feelemyer J, Perlman DC, Hagan H, et al. Transitions from injecting to non-injecting drug use: potential protection against HCV infection. *J Subst Abuse Treat*. 2014;46(3):325-31.
78. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organization; 2014. xix + 159 pp. p.



Figure 1

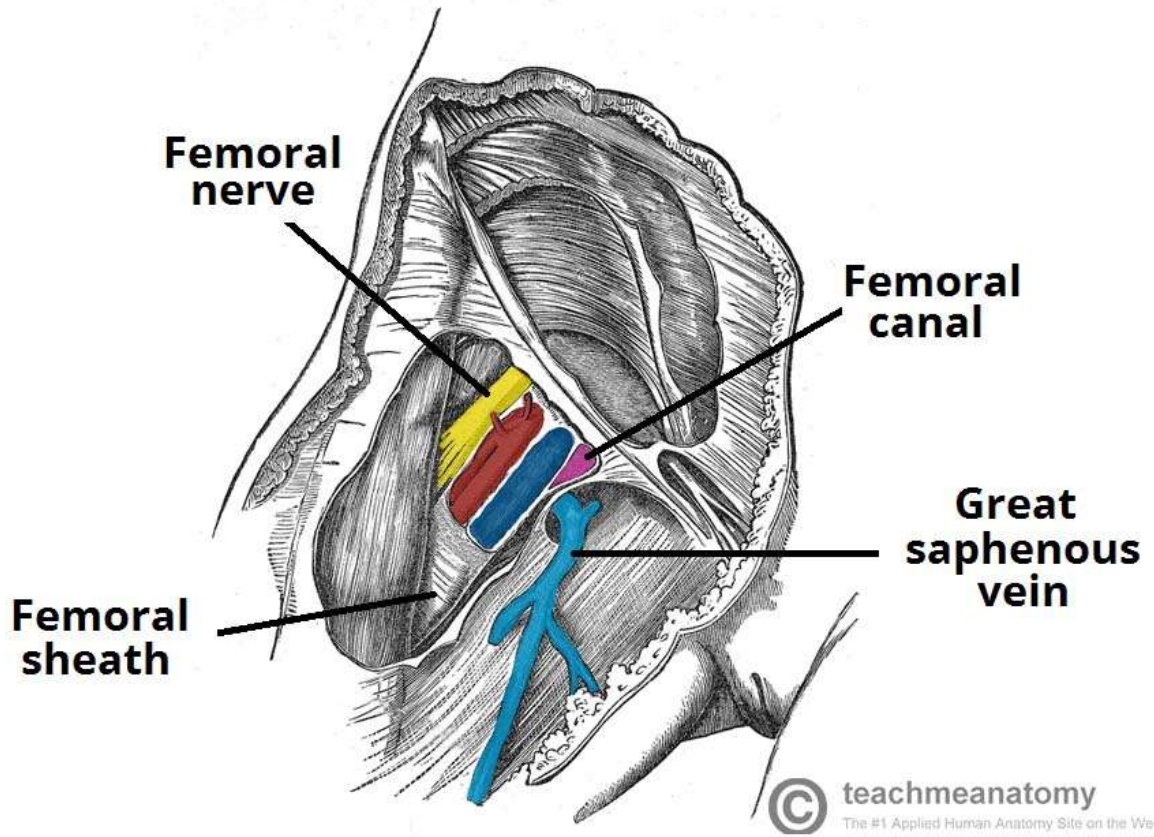


Figure 2

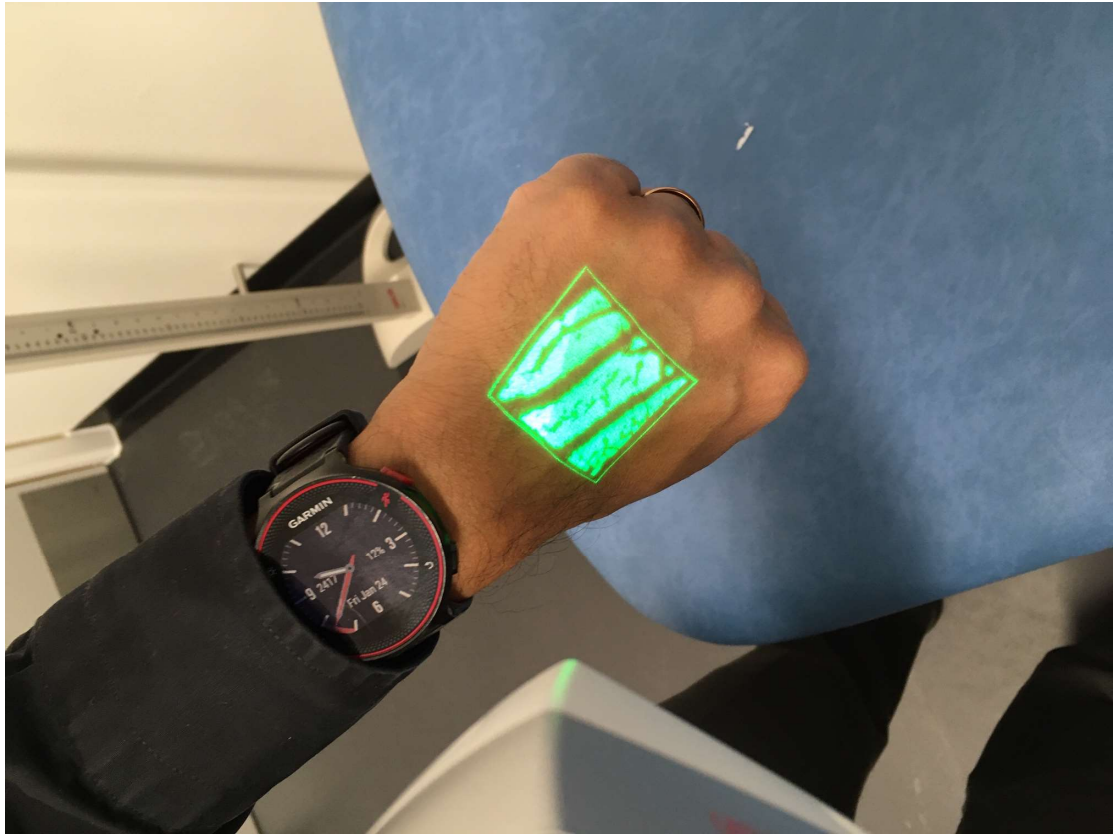


Figure 3



Figure 4

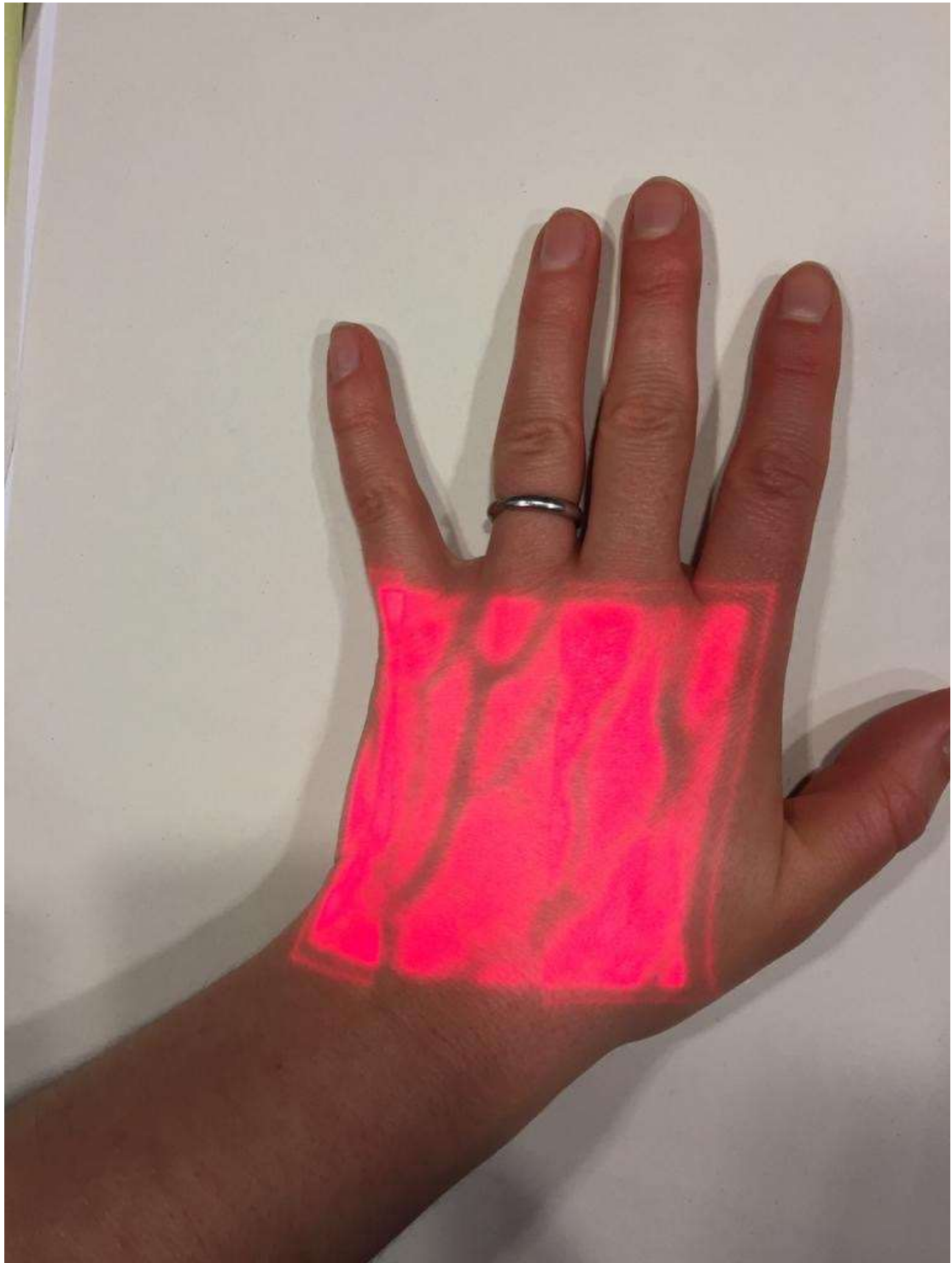


Figure 5



Figure 6

Appendix

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To whom it may concern, for the purpose of publication

24/8/20

I am happy to give permission, to Dr Roy Robertson, for the photograph taken today at Muirhouse Medical Group practice to be reproduced in the academic journal Addiction in the context of a publication on skin and vascular problems connected with injecting drug use.

A handwritten signature in black ink, appearing to read 'R. Robertson'.

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Dr Clare Briggs, Dr Hannah Beresford, Dr Steven McClure, Dr Hannah Cameron