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## Complications of Injection Drug Abuse

### Introduction

Recreational drug use is a major problem in the United States and around the world. This is a separate problem from drugs of abuse during pregnancy, which may be associated with abruptio placenta, growth retardation, and birth defects. As of 2006, it was estimated that there were approximately 13.2 million intravenous drug users in the world. Most were living in developing nations.<sup>1</sup> In the United States, a 2005 survey showed that approximately 8% of adults had used an illicit drug within the previous month.<sup>2</sup> Injecting drugs rather than ingesting them by other means adds further health risks that are important

for emergency physicians to recognize to properly care for their patients.

Among those with abuse and dependency problems, people who inject substances place their health and lives at a greater risk, and frequently present a high financial burden to society due to chronic ill health.<sup>3</sup> Even a single incidence of injecting drugs of abuse can lead to long-term health disorders, while an ongoing injection habit potentially places every organ system at risk. Injection drug abuse results in heavy use of emergency department (ED) services.<sup>3,4</sup> These patients are frequently quite difficult to treat due to medical noncompliance, comorbid psychiatric issues, and, frequently, chaotic social situations.<sup>1,2,3</sup> This article will examine unique emergencies that occur as a result of recreational injection drug use.

### Figures 1 and 2. Skin Popping (top); Skin Ulcer and Cellulitis (bottom)



Images courtesy of Dr. David Efron.

## EXECUTIVE SUMMARY

- Injection drug users with a fever and no obvious source should be hospitalized for work-up for endovascular infection, including endocarditis.
- Injection drug use compromises one's immune system.
- Back pain in an injection drug user with fever should raise concern for epidural abscess or discitis.
- Injection drug users are at higher risk for suicide than the general population.
- Drug use has been a factor in a variety of negative social behaviors: traffic accidents, unemployment, homelessness, and violence.
- Intra-arterial injection may be associated with pseudoaneurysm, limb ischemia, and necrosis.
- *Clostridium* species are heat-resistant, making them a unique problem to users of black tar heroin.
- *S. aureus* is the most common organism causing endocarditis in injection drug users.
- Echocardiography and blood cultures remain the mainstays of endocarditis diagnosis.
- Mycotic pseudoaneurysms may require CT scan, ultrasound, or angiography for diagnosis.
- Approach any mass near an artery in an injection drug user with caution and exclude the diagnosis of pseudoaneurysm.

## The Nature of the Problem and of the Substances Injected

The most commonly injected drugs in the United States as of this writing include heroin and other opioids, powder or crack cocaine, a combination of heroin and cocaine (speedball), synthetic cathinones ("bath salts") under names such as Ivory Wave, Vanilla Sky, White Lightning, and others,<sup>5</sup> and other stimulants including methamphetamines. (See Table 1.) Phencyclidine, gamma-hydroxybutyric acid (GHB), and MDMA ("ecstasy") are abused less frequently. There are reports of injection abuse of ketamine,<sup>6</sup> methoxitamine (a ketamine analog),<sup>7</sup> anabolic androgenic steroids,<sup>8</sup> desomorphine (Krokodil)<sup>9</sup> and other home synthesized concoctions,<sup>10</sup> as well as various psychoactive crushed tablets.<sup>11</sup> Given the erratic character of production and supply, the precise nature of injected substance is at times unclear to the user,<sup>12</sup> and, in the case of synthetic cannabinoids, essentially undetectable by standard testing. Furthermore, many users inject more than one type of drug. The drugs are typically obtained from the dealer in the form of powder. The drugs are commonly "cut" (adulterated) many times before being consumed, with multiple different substances, some of which may have local irritant or systemic toxicity. Adulterants such as strychnine, clenbuterol (a long-acting beta-2 agonist), or methamphetamine may have their own toxicity. Additives

**Table 1. Some Complications of Various Injected Drugs**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Heroin</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <ul style="list-style-type: none"> <li>• CNS: Anoxic brain injury in overdose, ischemic stroke,<sup>81</sup> transverse myelopathy,<sup>72</sup> acute inflammatory polyradiculoneuropathy<sup>72</sup></li> <li>• Pulmonary: Pulmonary edema in overdose</li> <li>• GI: Constipation</li> <li>• Immunological: Immunosuppression</li> <li>• GU: Oligo and amenorrhea<sup>41</sup></li> <li>• Withdrawal produces severe dysphoria; cramping abdominal pain; nausea, vomiting, and diarrhea; piloerection, chills; increased risk of pregnancy complications; Takatsubo cardiomyopathy<sup>64,65</sup></li> </ul>                    |
| <b>Cocaine</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <ul style="list-style-type: none"> <li>• CNS: Vasculitis, ischemic and hemorrhagic stroke<sup>81</sup></li> <li>• Cardiovascular: Myocardial ischemia and infarction; end organ ischemia and infarction at various sites, including intestinal ischemia</li> <li>• Genitourinary: Acute kidney injury; pregnancy complications; teratogenic</li> <li>• Immunological: Immunosuppression<sup>41</sup></li> <li>• Psychiatric: Psychosis; high-risk behaviors resulting in trauma and sexually transmitted disease exposure; severe psychomotor agitation resulting in hyperthermia; post binge: severe depression, suicide</li> </ul> |
| <b>Amphetamines</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <ul style="list-style-type: none"> <li>• CNS: Ischemic and hemorrhagic stroke</li> <li>• Cardiovascular: Myocardial ischemia and infarction</li> <li>• Genitourinary: Pregnancy complications</li> <li>• Psychiatric: Psychosis, paranoia, propensity to high-risk behaviors<sup>41</sup></li> <li>• General: Anorexia, weight loss</li> </ul>                                                                                                                                                                                                                                                                                       |

may be contaminated with infectious agents. Other substances used to dilute drugs include, but are not limited to: quinine, lactose, starch, procaine, mannitol, inositol, caffeine, and magnesium silicate (talc).<sup>13</sup> It is not uncommon for

the drugs to be simply contaminated with dirt. At times, pharmacologically active components such as acetaminophen or caffeine appear as adulterants.<sup>14</sup> Levamisole, a common adulterant in U.S. samples of cocaine, is a known

cause of agranulocytosis and vasculitis.<sup>75</sup>

Before a drug can be injected, it has to be reconstituted. Depending on the substance (white powder or black tar heroin, cocaine) different diluents are used. The resulting suspension is usually heated and sometimes filtered through cotton prior to use.<sup>15</sup>

Heroin is worthy of special mention, as it accounts for such a large share of morbidity and mortality related to drug abuse, and is at the center of a current epidemic. It was first synthesized in 1874 and advertised as a cough suppressant in 1898.<sup>16</sup> It is notable that different global sources of heroin produce different products. Heroin historically came from three different regions: Mexico, Southeast Asia, and Southwest Asia, with Colombia emerging as a fourth source in the 1990s. Low solubility “black tar” heroin is associated with reduced HIV prevalence relative to the cold-water soluble heroin produced in Asia and Colombia, but has been associated with wound botulism, tetanus, and necrotizing fasciitis.<sup>15</sup>

Some users crush various psychoactive tablets<sup>17</sup> and inject them; others may inject oral liquid medication formulations. An individual is typically “initiated” into the practice of injecting drugs by an established user who commonly performs the first several initial injections.<sup>18</sup> Needle exchange programs, where they exist, supply both clean needles/syringes and, at times, sterile solution for drug reconstitution. Sharing the drug solution or cooker among several people (indirect syringe sharing) is a common practice. When a syringe is used to draw from a communal container, there is a risk of spreading blood-borne infections.<sup>19</sup>

The drugs are usually injected into hand and forearm veins, with the occasional inadvertent arterial or subcutaneous injection. As substance abusers’ veins are damaged and become unusable, skin popping is more common, as well as use of veins of the upper arms, neck, legs, and groin. There are reports of some users preferentially injecting in groin veins, believing it to be more discreet and easier to hide from family members.<sup>20,21</sup> Injecting cocaine appears to lead to especially rapid vein damage.<sup>22</sup> Some users develop chronic ulcers and

vascular granulation tissue and resort to injecting these alternative sites.

Medical emergencies stemming from drug abuse can be a function of the substance used, the adulterants present, and also the means of delivery. Injection drug users either attempt to inject intravenously, into soft tissue subcutaneously (skin pop) (see *Figure 1*), or intramuscularly. If the drug is delivered into a blood vessel, it acts quickly, resulting in a strong and quickly developing high, but also placing the user at a high risk of overdose and dependence.<sup>23</sup> The amount of drug needed to achieve the desired effect is typically less if it’s injected than if it is ingested, smoked, or snorted.

### Recognizing Injection Drug Abuse in Patients in the ED

Certain syndromes and complaints trigger a different work-up, treatment, and disposition once it is established that the patient injects drugs. Many times the patient volunteers the information. Talking to the patient in private and obtaining information from family members when appropriate can be very helpful. A soft-tissue abscess that only requires incision and drainage may require an X-ray to locate a broken needle in the IV drug user. Acute febrile illness in a drug user without an obvious source for fever usually mandates an admission and work-up for endocarditis. Injection drug use is a red flag for epidural abscess in a patient with back pain and fever. Certain past medical history features, such as frequent skin abscesses, infectious endocarditis, or epidural abscess, may prompt the physician to question the patient more carefully regarding injection drug use. On physical examination, the physician should note any recent injection marks, track marks, or scars from skin infections. Findings consistent with puffy hand syndrome<sup>16,24</sup> should also raise suspicion for active or prior injection drug abuse. Some drug abusers choose to place elaborate tattoos in an attempt to hide telltale skin changes.

Injection drugs users may have difficult vascular access; once access is established, they may use the new line to inject drugs of abuse and may be

### Figure 3. Endophthalmitis



Image courtesy of Dr. David Effron.

tempted to elope with an intravenous line in situ, an especially dangerous situation if a central line was placed for access. It is not unusual for these patients to continue to inject drugs while undergoing treatment in the hospital, resulting in seemingly puzzling fluctuations in their mental status.<sup>25,26</sup>

### Infectious Disease in Users

Infectious agents may be introduced by the drug itself, or from solvents used to reconstitute the drug, contaminants from the patient’s own skin, organisms contaminating drug paraphernalia, or other people in the case of needle-sharing.<sup>15</sup> (See *Tables 2 and 3*.) The resulting infectious complications vary from local bacterial infections (abscess and cellulitis, necrotizing fasciitis) to bacteremia. (See *Figure 2*.) This may cause sepsis or seeding of distant sites resulting in endocarditis, osteomyelitis, endophthalmitis (see *Figure 3*), and brain, splenic, or epidural abscess.

Non-bacterial infections and otherwise uncommon bacterial infections may result from injection drug use. These include viral diseases such as human immunodeficiency virus (HIV), and bloodborne forms of hepatitis, notably hepatitis B and C, as well as fungal infections, most commonly systemic candidiasis. Hepatitis C and injection drug use go hand in hand. There is evidence that more than 60% of new hepatitis C patients injected drugs during the prior 6 months. Conversely, perhaps 70-90% of illicit drug users are infected with the hepatitis C virus.<sup>27,28</sup> Community-acquired pneumonia and pulmonary tuberculosis are common in

**Table 2. Infectious Complications of Injecting Drugs<sup>2</sup>**

- HIV infection: Acute, AIDS
- Bloodborne hepatitis: C and B
- Skin and subcutaneous tissue infections: Abscess, cellulitis
- Pneumonia: Typical community pathogens, aspiration, *Klebsiella pneumoniae*, tuberculosis, AIDS-associated opportunistic infections; pulmonary septic emboli, especially with multilobar involvement or lung abscess formation
- Cardiovascular: Endocarditis, infected pseudoaneurysm
- CNS: Epidural abscess of calvarium and spine, brain abscess
- Lymphatic system: Splenic abscess
- Endovascular: Mycotic pseudoaneurysm
- Musculoskeletal infections: Psoas abscess, septic arthritis, osteomyelitis
- Local extension of skin/subcutaneous tissue infection

drug users. This may be the result of a variety of factors, such as crowded living conditions, residence in homeless shelters, sharing smoke, and noncompliance with treatment. Notably, patients may not have contracted viral infections via drug use; one study from Baltimore indicated that 60% of injection drug users reported a history of a sexually transmitted disease, highlighting other high-risk behaviors present in habitual drug users.<sup>29</sup>

Drug users may fail to clean injection sites, predisposing them to infection from skin flora such as *Staphylococcus aureus* or *Streptococcus* species. In one report, abscesses were twice as likely to occur among those injection drug users who never cleaned the skin before shooting up.<sup>30</sup>

HIV infection may manifest itself as oral thrush or cervical adenopathy. Otherwise unusual bacterial infections that can be contracted as a result of injection drug use include tetanus,<sup>31</sup> wound botulism,<sup>32</sup> and syphilis. Approximately 40% of identified cases of tetanus, in one report from a 1997 California epidemic, occurred in injection heroin users.<sup>33</sup> Malaria transmission via injection drug use has been reported, although not in the United States.<sup>34</sup>

A new form of anthrax, injectional anthrax, was recently seen in Northern Europe in people who inject heroin. Notable features included frequent absence of eschar or pus when early incision and drainage were attempted. *Bacillus anthracis* is a common pathogen in southwest Asia, which is the source for most of Europe's heroin, and

represents a potential danger to someone examining skin lesions without protective gloves.<sup>35</sup> The disease is characterized by high mortality, and to date has not been reported in the United States.<sup>36</sup>

The combination of local irritant effect and vasoconstriction, especially from cocaine and inflammation, can result in the formation of chronic skin ulcers. Extensive venous and lymphatic damage can lead to venous insufficiency with dependent edema and ulcerations which may be or become infected. Endovascular infections apart from infective endocarditis include septic thrombophlebitis (see Figure 4), mycotic aneurysms, and sepsis. In a bacteremic injection-drug user, an endovascular source should be sought.<sup>2</sup>

Many drugs of abuse appear to weaken the immune system,<sup>37,38,39</sup> and as noted earlier, injection drug users have high rates of HIV infection. Furthermore, the lifestyle of drug abusers often is associated with marginalization in society, along with problems with personal hygiene, which may make drug users' predisposition to infections even greater. Fever in injection drug users, by history or as documented in the ED, usually mandates an admission and work-up for sepsis unless there is an obvious source for the fever. Injecting drugs increases the risk of osteomyelitis and septic arthritis both by contiguous and hematogenous spread,<sup>40</sup> as well as for infective endocarditis.

The incidence of suppurative infections in general is high in injection drug users.<sup>13</sup> While Gram-positive infections

**Table 3. Less Common Infectious Agents in the Injection Drug User**

- Wound tetanus
- Wound botulism
- Injectional anthrax
- Necrotizing fasciitis
- *Clostridium*-associated toxic shock syndrome
- Malaria
- Syphilis
- Osteomyelitis
- Brain abscess
- Systemic candidiasis

**Figure 4. Abscess with Septic Thrombophlebitis**



Image courtesy of Dr. David Efron.

are common, injection at heavily colonized sites such as the femoral vein predisposes to infection with Gram-negative flora. Licking needles prior to injection may increase the risk of anaerobic infections.<sup>2</sup>

Botulism, *Clostridium* necrotizing fasciitis in black tar heroin users, and malaria are some of the examples of unusual infectious complications in injection drug users. Black tar heroin may protect against certain infections during preparation, since it is heated in water before use, but clostridial spores survive boiling. Botulism may be difficult to diagnose, not simply because of its rarity, but also because it can masquerade as intoxication if the patient

## Figure 5. Retained Soft-tissue Needle



Image courtesy of Dr. David Effron.

presents with slurred speech, nausea and vomiting, and no evident bulbar palsy or dilated pupils.<sup>2</sup>

Apart from commonly encountered immune-compromising infections such as hepatitis C or HIV, there is evidence that injection drug use per se compromises one's immune system. There are receptors in the central nervous system as well as in the immune system for marijuana and opiates, which may play a role in immune modulation.<sup>41</sup> Amphetamines, cocaine, and opiates may perturb the homeostatic balance of pro-inflammatory and anti-inflammatory cytokines. Cocaine may alter immune function via sigma-1 receptors, as well as impair polymorphonuclear leukocyte chemotaxis. Marijuana and its more than 60 cannabinoids have been shown to alter functional activities of both B and T lymphocytes, and macrophages. Increased recurrence of genital viral lesions, as well as progression of fibrosis due to hepatitis C, has been associated with cannabis smoking.<sup>41</sup> A direct link between drug-induced immune dysfunction and greater susceptibility to infection with bacteria, protozoa, and viruses has been demonstrated.<sup>42</sup> It seems, therefore, that cocaine, marijuana, opioids, and amphetamines induce a decrease in host resistance to infection in a broad sense.

Endocarditis, osteomyelitis, and epidural abscess are discussed below.

## Cutaneous and Musculoskeletal Manifestations of Drug Abuse

The appearance of skin-popping, cutaneous abscess, and cellulitis can be self-evident, as is scarring, making IV access for therapeutic purposes extremely difficult.

In one study, the two most common reasons for admission in intravenous drug users were cellulitis and abscess, respectively. Soft-tissue necrosis, osteomyelitis, and compartment syndrome from inadver-

tent arterial injection were unusual.<sup>10</sup> Infection in unusual places, such as the sternoclavicular or sacroiliac joints, should raise suspicion for injection drug abuse with hematogenous seeding. Organisms involved commonly are staphylococci and streptococci. The presence of anaerobic species and *Eikenella corrodens* is postulated to be from the practice of licking needles prior to injection.<sup>10</sup>

The substance desomorphine, the presumed active drug in "krokodil," has received attention in the media. Drug injection in Russia became widespread after the social and economic disintegration that followed the collapse of the Soviet Union in 1991.<sup>9</sup> Injecting liquid poppy straw adulterated with pseudoephedrine or other ephedrine-based stimulants from shared drug-mixing solutions, apart from being an obvious source of HIV spread, was associated with phlebitis and gangrene. Codeine, available in Russia inexpensively and over-the-counter, was boiled with a diluting agent such as paint thinner, but also with gasoline, hydrochloric acid, and red phosphorus from the striking surfaces of matches, and injected intravenously without using any filter. This resulted in abscesses, large-scale necrosis, and crocodile bite-like skin lesions, earning the name "the drug that

eats junkies."<sup>12</sup> The presence of krokodil outside of the former Soviet Union has not been substantiated.<sup>43</sup>

Narcotic drug users are at risk for rhabdomyolysis, metabolic derangements, and acute kidney injury. There may be complications from lying in the same position for hours, but there may also be a myotoxic effect of heroin.<sup>44</sup> Compartment syndrome with hyperkalemia has been described.<sup>5</sup> Rhabdomyolysis, cardiac and hepatic injury with renal failure, agitation, hyperthermia, and tachycardia have been reported with injection of 3,4-methylenedioxypyrovalerone (MDPV).<sup>45</sup>

Deep venous thrombosis is a recognized complication of injection drug use, especially when groin area veins are injected.<sup>46</sup> As noted earlier, a state of unconsciousness combined with direct muscle toxicity places users at risk for muscle and nerve compression injuries with risk of rhabdomyolysis and renal failure.<sup>5,10,44</sup> A broken needle imbedded in soft tissue can cause pain, may serve as a nidus for infection, or can migrate locally or intravascularly. (See Figure 5.) Musculoskeletal infections such as osteomyelitis or discitis may be indolent, causing pain without fever.<sup>2</sup>

## Vascular Complications of Drug Injection

Injecting at sites where an artery lies in close proximity to the skin places patients at risk of inadvertent intra-arterial injection. Potential complications include pseudoaneurysm formation, mycotic pseudoaneurysm, arteritis with subsequent vasospasm and thrombosis, compartment syndrome, and tissue necrosis including amputation of a forearm or fingertips<sup>17</sup> and distal particle embolization.<sup>47</sup> Among common drugs of abuse, cocaine is especially damaging to arteries.<sup>1</sup> Pseudoaneurysm is a rare<sup>48</sup> but potentially fatal complication. A pseudoaneurysm is a collection of blood in soft tissue that communicates with the arterial lumen. It presents as a painful pulsatile or non-pulsatile mass, at times mimicking an abscess. The mass is prone to spontaneous free rupture.<sup>48</sup> Most pseudoaneurysms develop in the femoral artery due to its close

proximity to the femoral vein. Incision and drainage can result in disastrous consequences. Liberal use of duplex ultrasound or arteriography is advisable in cases of “red abscess” in the vicinity of a major artery.<sup>1,46</sup> Arteriography has the theoretical risk of rupture of an aneurysm during injection. In addition to bleeding, local nerve compression by the pseudoaneurysm can produce characteristic distal praxis.<sup>1</sup> There are reports of upper and lower extremity arterial involvement.<sup>21,49</sup> Prompt vascular surgery consultation is necessary. Temporizing measures in case of bleeding include direct pressure and proximal arterial tourniquet application.

Arteritis induced by endothelial damage or particle injection can produce extensive distal soft-tissue damage in cases of acute arterial insufficiency caused by either thrombosis or distal embolization.<sup>1</sup> If this complication is suspected, systemic anticoagulation with heparin and vascular surgery consultation are suggested. CT angiogram is the imaging modality of choice.<sup>1</sup> Nervous plexus block for pain control has been described. Peripheral pulses may be present initially, leading to false reassurance and premature discharge.<sup>50</sup>

Alternative imaging may include duplex ultrasonography, which may demonstrate femoral artery occlusion, arteriovenous fistula, or deep venous thrombosis. Even if the duplex scan is negative, it may be necessary to re-image using duplex or magnetic resonance angiography (MRA), depending upon one’s clinical suspicion for pseudoaneurysm. Management of pseudoaneurysms may include excision or ligation, saphenous vein interposition, or primary axial reanastomosis with arterial reconstruction. There is significant risk for graft infection and eventual amputation.<sup>1</sup>

## Pulmonary Complications of Injecting Drugs

The lungs serve as a filter for impurities in drugs administered intravenously, and for venous emboli. Pyrogens injected may cause fever, tachycardia, and tachypnea within 10–20 minutes of injection, the so-called “cotton fever.” This tends to be a self-limited

**Table 4. Complications of Infective Endocarditis<sup>63</sup>**

- Cardiac: Acute valvular insufficiency, congestive heart failure, intracardiac abscess and fistula formation, cardiogenic shock, acute coronary syndrome, heart block, myocarditis, pericarditis
- Embolic right-sided: Pulmonary emboli, lung abscess, empyema, pulmonary hypertension
- Embolic left-sided: Renal, splenic, hepatic, brain, ocular, vertebral abscesses (septic-pyemic complications)
- CNS: Stroke (ischemic and hemorrhagic), epidural abscess
- Acute renal failure
- Vascular: Mycotic aneurysms at various sites (intracranial most common)
- Rheumatologic: Arthritis, spondylodiscitis
- Systemic: Septic shock

phenomenon.

The so called “pocket shot” attempt to access the internal jugular vein can result in a pneumothorax. Pneumomediastinum and air embolism have been described in injection drug users.<sup>51</sup> Injected foreign particulate material can lead to perivascular pulmonary granuloma formation<sup>26</sup> in drug users and eventually may result in pulmonary hypertension<sup>52</sup> and cor pulmonale.<sup>11,53</sup> Crushing and injecting tablets gives intravascular entry not just to the intended drug, but possibly to talc (magnesium trisilicate), potato starch, crospovidone, cornstarch, sugars, local anesthetics, or cellulose, some of which are insoluble. Embolization of foreign bodies may cause not only pulmonary embolization, pulmonary hypertension, and granulomatosis, but arterial embolization as well due to systemic shunts.<sup>52</sup>

Pulmonary edema is a well-known complication of heroin overdose associated with potential for requiring intubation and mechanical ventilation. This presents similarly to non-cardiogenic pulmonary edema from other causes.

The above considerations assume increased need for clinical awareness when evaluating the drug user. Dyspnea, cough, or sputum production may be attributed by the patient and caregiver to nicotine abuse, as most patients who abuse intravenous drugs are smokers.<sup>54</sup>

Drug users have a 10-fold higher risk of contracting community-acquired pneumonia than the general population.<sup>2</sup> How much of this is attributable to concomitant cigarette smoking and

poor nutrition is unclear.<sup>2</sup> Eosinophilic pneumonia, pneumonitis, and pulmonary fibrosis may result from chronic substance use. Injecting particulate matter can result in venous and arterial thromboembolism.

## Acute Infective Endocarditis in the Injection Drug User

Acute endocarditis, especially affecting the right side of the heart, commonly afflicts injection drug users and should be one of the primary concerns in an injection drug user with a fever without another obvious source. Infective endocarditis has an incidence of 1.5–3.3 cases per 1000 injection drug users annually, and up to 20% of injection drug users hospitalized with fever will turn out to have endocarditis.<sup>2,55</sup> In injection drug users, the tricuspid valve is the most commonly involved, followed by the mitral, then the aortic valve, with pulmonic and eustachian valve involvement relatively uncommon.<sup>56,57</sup> Tricuspid endocarditis is most commonly caused by *S. aureus*. Patients with endocarditis may present with fever, cough, pleuritic chest pain, and dyspnea.<sup>2</sup> (See Table 4.)

Multivalve disease also occurs, and the incidence of left-sided involvement appears to be rising; these two conditions are associated with a more severe clinical course.<sup>58</sup> The most common causative agent in infective endocarditis in the injection drug user is *Staphylococcus aureus*, with a

**Table 5. Modified Duke Criteria for the Diagnosis of Infective Endocarditis<sup>61,63</sup>**

| MAJOR CRITERIA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                             |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| Blood cultures positive for infective endocarditis (IE):<br>• Typical microorganisms consistent with IE from two separate blood cultures: <i>Viridans streptococci</i> , <i>Streptococcus bovis</i> , HACEK group, <i>Staphylococcus aureus</i> ; or Community-acquired enterococci, in the absence of a primary focus;<br>or<br>• Microorganisms consistent with IE from persistently positive blood cultures:<br>At least two positive blood cultures of blood samples drawn > 12 h apart; or<br>All of three or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)<br>or<br>• Single positive blood culture for <i>Coxiella burnetii</i> or phase 1 IgG antibody titer > 1:800 |                                                                                                             |
| Evidence of endocardial involvement<br>• Echocardiography positive for IE<br>• Vegetation – abscess – new partial dehiscence of prosthetic valve<br>• New valvular regurgitation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                             |
| MINOR CRITERIA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                             |
| • Predisposition: Predisposing heart condition, injection drug use<br>• Fever: Temperature > 38°C<br>• Vascular phenomena: Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhages, conjunctival hemorrhages, Janeway lesions<br>• Immunologic phenomena: Glomerulonephritis, Osler’s nodes, Roth’s spots, rheumatoid factor<br>• Microbiological evidence: Positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE                                                                                                                                                                                          |                                                                                                             |
| Diagnosis of IE is definite in the presence of:<br>• 2 major criteria; or<br>• 1 major and 3 minor criteria; or<br>• 5 minor criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Diagnosis of IE is possible in the presence of:<br>• 1 major and 1 minor criteria; or<br>• 3 minor criteria |

high proportion of isolates being community-acquired methicillin resistant *S. aureus* (MRSA), followed by *Streptococcus* species. A multitude of other bacteria, including human oropharyngeal flora, *Pseudomonas* species, *Acinetobacter*, and *Candida*, have been isolated. Polymicrobial infections have also been described.<sup>59,60</sup> Prior endocarditis, AIDS, and cocaine abuse place the injection drug user at even greater risk for infection. Mortality is higher in HIV-infected individuals whose CD4 cell count is below 200 per mm<sup>3</sup>.<sup>61</sup>

The diagnosis of infective endocarditis commonly relies on the Duke Criteria<sup>62</sup> (see Table 5) and can be easy when a classic combination of sepsis, valvular damage, and peripheral immunological changes and embolic phenomena are apparent. However, early in the course, especially if a history of injection drug use is not apparent, the diagnosis can be difficult.

The emergency physician should use caution in the evaluation of any drug user, and should be especially careful about discharging home a febrile patient who is found to have telltale skin infection, petechiae or vasculitis, a pulmonary infiltrate, an unexplained internal abscess, white blood cells in urine without dysuria, or when a young patient presents with new-onset heart failure or multilobar pneumonia consistent with tricuspid endocarditis.

Extreme caution should be exercised before giving antithrombotic medications to patients known to inject drugs and who present with symptoms of acute stroke or acute myocardial infarction, as these medications are generally contraindicated in infectious endocarditis. These patients should be admitted and have multiple blood cultures obtained.<sup>60,62</sup> Echocardiography should be performed as soon as possible, usually with a transthoracic

echocardiogram first followed by transesophageal echocardiogram as necessary.<sup>63</sup>

As with other forms of severe sepsis, broad-spectrum antibiotics and appropriate supportive measures should be instituted. Emergent cardiac surgery is indicated for patients with intractable heart failure or cardiogenic shock.<sup>63</sup> Many of the complications of endocarditis will require collaboration among many specialists in managing these sick patients. The emergency physician should consider transferring these patients early if the institution lacks the ability to perform the necessary testing and consultations.

## Other Cardiovascular Complications of Drug Use

A transient drug-linked cardiomyopathy may be precipitated by the intense stress of sympathetic overstimulation, which is a form of Takotsubo cardiomyopathy. The condition is characterized by a transient decrease in ejection fraction, classically with apical ballooning noted on echocardiogram, without significant coronary artery disease. Patients may present with chest pain, dyspnea, pulmonary edema, and, more unusually, cardiogenic shock. Reported drugs associated with this syndrome include opioids and drugs with adrenergic properties.<sup>64</sup> This is not a rare disease, occurring in perhaps 1% of cases of presentation as acute coronary syndrome or ST-elevation myocardial infarction (STEMI) mimic, and has been attributed to drug withdrawal as well, notably withdrawal from oxycodone or from beta blockers such as metoprolol.<sup>65</sup>

Cocaine use has been associated with thoracic aortic dissection, renal artery dissection, and intestinal ischemia.<sup>1</sup> Maternal cocaine use has been associated with aortic arch thrombosis in a neonate.<sup>1</sup>

Buerger’s disease, otherwise known as thromboangiitis obliterans, an inflammatory occlusive vascular disorder usually associated with tobacco smoking, has been reported with cannabis use.<sup>66</sup> This may cause Raynaud’s phenomenon, painful ulcerations, gangrene, or amputation.

## Figure 6. Cervical Epidural Abscess



Image courtesy of Dr. David Effron.

## Psychosocial Aspects of Injection Drug Use in the ED

Injection drug users have high prevalence of comorbid major psychiatric disorders and a much higher risk of attempted and completed suicide than the general population.<sup>67-69</sup> The incidence of personality disorders is also high, as well as precarious living situations, impulsiveness, and risk-taking behaviors.<sup>70</sup> Most of these patients abuse multiple substances and may misuse or seek various psychoactive substances. They may not know what substances or contaminants they have smoked, ingested, or injected. In fact, a high percentage of street samples may lack the alleged drug entirely. Multiple factors make these patients poor historians and highly non-compliant patients. Often the emergency department is their only source of care.<sup>3,71</sup>

Patients may have problems at school or at work, interpersonal problems with partners or children, violence, and trauma. High-risk sexual behavior, legal problems for intoxication, driving under the influence, and altercations are common. Bizarre behavior, anxiety, agitation, and psychosis may result from a variety of substances, including some substances which are not injected, as with synthetic cannabinoids such as K2 and spice. Negative social and health consequences of drug abuse include, but are not

limited to: unemployment, homelessness, violence, and mental health disorders. Whether these social issues stem from underlying psychosocial issues or from the substances themselves may be difficult to discern in the emergency setting.

## Central Nervous System (CNS) Complications of IV Drug Use

Injecting drugs is considered to be a risk factor for stroke.<sup>72</sup> Heroin-related stroke has been associated with large vessel arteritis,<sup>73</sup> and amphetamine use has been linked to cerebral vasculitis as a cause for ischemic stroke.<sup>74</sup> Strokes associated with cannabis use classically have been ischemic in nature,<sup>75</sup> although vasospasm has been proposed as a mechanism for cannabis-associated stroke.<sup>76</sup> Amphetamine, cocaine, and the related ecstasy have become important causes of thoracic aortic dissection and of intracranial hemorrhage among young adults.<sup>77</sup> More recently, the synthetic cannabinoid spice has been linked to subarachnoid hemorrhage and hemorrhagic stroke.<sup>78</sup>

Persistent unexplained headache in an injection drug user should raise concern for intracerebral abscess<sup>80</sup> in addition to other life-threatening processes.

Of special concern are infectious CNS complications such as spine spondylitis, discitis, and epidural abscess of the cranium and spine.<sup>79,80</sup> Localized back pain in a patient with a history of injecting drugs and without another obvious explanation should prompt appropriate imaging. Standard diagnosis entails magnetic resonance imaging (MRI) with pre- and post-gadolinium contrast imaging to exclude these complications.<sup>79</sup> There is no predictable level at which the spine may be involved in the injection drug user; one survey found the lumbar level to be the most common level; another found the most common level to be cervical.<sup>71,79</sup> (See *Figure 6*.)

Both white blood cell count and inflammatory markers are normal in some patients with a spinal abscess,<sup>71</sup> although one report cited a mean erythrocyte sedimentation rate (ESR) and mean C-reactive protein (CRP) of 61 mg/dL and 88 mg/dL, respectively,

in IV drug users with pyogenic infections of the spine.<sup>79</sup> Distal neurological deficits, while usually absent on presentation, signify cord compression and are associated with severe permanent neurologic sequelae and death.<sup>70</sup> Systemic signs of inflammation and sepsis eventually develop, but early on are commonly lacking, and their absence cannot be relied upon to rule out this complication. Timely diagnosis followed by emergent neurosurgical or spine consultation and aggressive treatment offers the best chance of recovery.<sup>71</sup> While *Staphylococcus* species are most commonly the culprit, a variety of other organisms have been isolated, necessitating broad antibiotic coverage until culture results become available. Viral as well as bacterial infections may exist concomitantly. One study of pyogenic infections of the spine in intravenous drug users noted that more than 40% had hepatitis C, 12-13% had hepatitis B, and 22-23% were positive for HIV, and that nearly one-third had an identifiable organism on blood cultures.<sup>40,79</sup>

Transverse myelitis is an unusual but well-described complication of heroin overdose. Symptoms may include extremity paresis, sensory loss, incontinence, or urinary retention. MRI of the spine shows characteristic findings, including effacement of ventral and dorsal subarachnoid spaces with patchy increased intramedullary signal.<sup>72</sup>

## Conclusions

Injection drug users are subject to a wide variety of behavioral, cutaneous, immunologic, infectious, cardiac, neurologic, vascular, renal, musculoskeletal, and psychiatric disorders. It is prudent to treat these patients as any other immunocompromised patients. A history of substance use may be inaccurate, as these substances are illicit, and the people who consume them may not be fully aware of what they were taking, necessitating supportive care regardless of the agent. Behavioral disorders can make this group of patients particularly challenging to manage.

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## Questions

- A list of the most commonly injected drugs in the United States does not include:
  - heroin
  - methamphetamines and other stimulants
  - ketamine and methoxitamine
  - cocaine
- Adulterants with their own toxicity include:
  - strychnine
  - lactose
  - starch
  - mannitol
  - both B and D
- Which is true regarding specific forms of heroin?
  - "Black tar" heroin is associated with reduced HIV prevalence.
  - "Cold-water" heroin is associated with reduced HIV prevalence.
  - "Black tar" heroin is associated with higher risk of tetanus, botulism, and necrotizing fasciitis than cold water heroin.
  - Both A and C are true.
  - Skin-popping causes a more rapid high than does intravenous use.

4. Which of these statements is true?
- Injection drug users who test positive for HIV uniformly contracted the virus from their drug habit.
  - Most new cases of hepatitis C in one report had used injection drugs.
  - The most common fungal infection in injection drug users is *Cryptococcus*.
  - Community-acquired pneumonia and tuberculosis are rarely encountered in drug users.
5. Complications of intra-arterial injection include:
- mycotic pseudoaneurysm.
  - compartment syndrome.
  - tissue necrosis.
  - amputation of digits.
  - all of the above.
6. A patient presents with swelling in his groin. He reluctantly admits using the site for the past 6 months to inject heroin. The area is soft and fluctuant. He is afebrile. You should:
- Aspirate first to demonstrate that this is an abscess before draining.
  - Incise and drain, since injection drug users are prone to infection.
  - Assure the patient that this is an enlarged lymph node, and discharge home.
  - Obtain duplex ultrasound or CT angiography to investigate.
  - Consult infectious disease to discuss antibiotic therapy.
7. Which is true concerning behavior among substance abusers?
- They usually live in luxurious housing as befits their lifestyle.
  - There is a high degree of violence and problems with interpersonal behavior.
  - They reliably know and volunteer what they have injected.
  - Suicide attempts are rare.
8. A 27-year-old male presents with a cough, fever, and shortness of breath. His vital signs indicate a temperature of 39.7 degrees C and a resting pulse of 123/minute. He has multiple scars on his forearms. A chest X-ray shows multiple round infiltrates in both lungs. Which tests will be most definitely diagnostic in diagnosing endocarditis?
- sedimentation rate and CRP as acute phase reactants
  - CBC
  - three blood cultures taken in the ED over one hour and transthoracic echocardiogram
  - ECG and serial troponins
  - contrast CT of the chest
9. The most common organism causing epidural abscess is:
- Staph. aureus*
  - Pseudomonas aeruginosa*
  - Strep. viridans*
  - Eikenella corrodens*
  - Mycobacterium tuberculosis*
10. Which of the following central nervous system disorders are more common in IV drug users?
- hemorrhagic stroke
  - subarachnoid hemorrhage
  - ischemic stroke
  - brain abscess
  - all of the above

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Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in patients presenting to the emergency department;
- apply state-of-the-art diagnostic and therapeutic techniques to patients with the particular medical problems discussed in the publication;
- discuss the differential diagnosis of the particular medical problems discussed in the publication;
- explain both the likely and rare complications that may be associated with the particular medical problems discussed in the publication.

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# EMERGENCY MEDICINE **REPORTS**

## Complications of Injection Drug Abuse

### Some Complications of Various Injected Drugs

#### Heroin

- CNS: Anoxic brain injury in overdose, ischemic stroke, transverse myelopathy, acute inflammatory polyradiculoneuropathy
- Pulmonary: Pulmonary edema in overdose
- GI: Constipation
- Immunological: Immunosuppression
- GU: Oligo and amenorrhea
- Withdrawal produces severe dysphoria; cramping abdominal pain; nausea, vomiting, and diarrhea; piloerection, chills; increased risk of pregnancy complications; Takatsubo cardiomyopathy

#### Cocaine

- CNS: Vasculitis, ischemic and hemorrhagic stroke
- Cardiovascular: Myocardial ischemia and infarction; end organ ischemia and infarction at various sites, including intestinal ischemia
- Genitourinary: Acute kidney injury; pregnancy complications; teratogenic
- Immunological: Immunosuppression
- Psychiatric: Psychosis; high-risk behaviors resulting in trauma and sexually transmitted disease exposure; severe psychomotor agitation resulting in hyperthermia; post binge: severe depression, suicide

#### Amphetamines

- CNS: Ischemic and hemorrhagic stroke
- Cardiovascular: Myocardial ischemia and infarction
- Genitourinary: Pregnancy complications
- Psychiatric: Psychosis, paranoia, propensity to high-risk behaviors
- General: Anorexia, weight loss

### Infectious Complications of Injecting Drugs

- HIV infection: Acute, AIDS
- Bloodborne hepatitis: C and B
- Skin and subcutaneous tissue infections: Abscess, cellulitis
- Pneumonia: Typical community pathogens, aspiration, *Klebsiella pneumoniae*, tuberculosis, AIDS-associated opportunistic infections; pulmonary septic emboli, especially with multilobar involvement or lung abscess formation
- Cardiovascular: Endocarditis, infected pseudoaneurysm
- CNS: Epidural abscess of calvarium and spine, brain abscess
- Lymphatic system: Splenic abscess
- Endovascular: Mycotic pseudoaneurysm
- Musculoskeletal infections: Psoas abscess, septic arthritis, osteomyelitis
- Local extension of skin/subcutaneous tissue infection

### Skin Popping (top); Skin Ulcer and Cellulitis (bottom)



Images courtesy of Dr. David Efron.

### Less Common Infectious Agents in the Injection Drug User

- Wound tetanus
- Wound botulism
- Injectional anthrax
- Necrotizing fasciitis
- *Clostridium*-associated toxic shock syndrome
- Malaria
- Syphilis
- Osteomyelitis
- Brain abscess
- Systemic candidiasis

### Endophthalmitis



Image courtesy of Dr. David Efron.

## Complications of Infective Endocarditis

- Cardiac: Acute valvular insufficiency, congestive heart failure, intracardiac abscess and fistula formation, cardiogenic shock, acute coronary syndrome, heart block, myocarditis, pericarditis
- Embolic right-sided: Pulmonary emboli, lung abscess, empyema, pulmonary hypertension
- Embolic left-sided: Renal, splenic, hepatic, brain, ocular, vertebral abscesses (septic-pyemic complications)
- CNS: Stroke (ischemic and hemorrhagic), epidural abscess
- Acute renal failure
- Vascular: Mycotic aneurysms at various sites (intracranial most common)
- Rheumatologic: Arthritis, spondylodiscitis
- Systemic: Septic shock

## Modified Duke Criteria for the Diagnosis of Infective Endocarditis

| MAJOR CRITERIA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Blood cultures positive for infective endocarditis (IE): <ul style="list-style-type: none"> <li>• Typical microorganisms consistent with IE from two separate blood cultures: <i>Viridans streptococci</i>, <i>Streptococcus bovis</i>, HACEK group, <i>Staphylococcus aureus</i>; or Community-acquired enterococci, in the absence of a primary focus;</li> </ul> or <ul style="list-style-type: none"> <li>• Microorganisms consistent with IE from persistently positive blood cultures: At least two positive blood cultures of blood samples drawn &gt; 12 h apart; or All of three or a majority of <math>\geq 4</math> separate cultures of blood (with first and last sample drawn at least 1 h apart)</li> </ul> or <ul style="list-style-type: none"> <li>• Single positive blood culture for <i>Coxiella burnetii</i> or phase 1 IgG antibody titer &gt; 1:800</li> </ul> |                                                                                                                                                                  |
| Evidence of endocardial involvement <ul style="list-style-type: none"> <li>• Echocardiography positive for IE</li> <li>• Vegetation – abscess – new partial dehiscence of prosthetic valve</li> <li>• New valvular regurgitation</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                  |
| MINOR CRITERIA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                  |
| <ul style="list-style-type: none"> <li>• Predisposition: Predisposing heart condition, injection drug use</li> <li>• Fever: Temperature &gt; 38°C</li> <li>• Vascular phenomena: Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhages, conjunctival hemorrhages, Janeway lesions</li> <li>• Immunologic phenomena: Glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor</li> <li>• Microbiological evidence: Positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE</li> </ul>                                                                                                                                                                                                                                                                 |                                                                                                                                                                  |
| Diagnosis of IE is definite in the presence of: <ul style="list-style-type: none"> <li>• 2 major criteria; or</li> <li>• 1 major and 3 minor criteria; or</li> <li>• 5 minor criteria</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Diagnosis of IE is possible in the presence of: <ul style="list-style-type: none"> <li>• 1 major and 1 minor criteria; or</li> <li>• 3 minor criteria</li> </ul> |

## Abscess with Septic Thrombophlebitis



Image courtesy of Dr. David Effron.

## Cervical Epidural Abscess

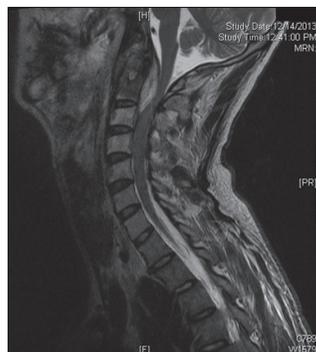


Image courtesy of Dr. David Effron.

## Retained Soft-tissue Needle



Image courtesy of Dr. David Effron.

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