Beyond Overdose: Identifying and Addressing Infections and Other Medical Complications of Fentanyl Use

Sarah E. Rowan, MD
Objectives

- Describe types of infections associated with injection drug use
- Discuss the treatment of acute bacterial or fungal infections and chronic viral illnesses
- Describe other medical complications that may arise from fentanyl use
- Review prevention measures
Jordan Nelson

SURVIVOR

I am an IV drug user. (Sepsis and IV Drug Use) I have been since eighth grade. I am 19 right now. When I first started showing signs of my infection, I just thought I was dope sick. I had extreme body pain. I could barely walk. I had no energy with extremely high fevers.

I went to the hospital several times but they didn’t know what was wrong with me. They just told me it was some kind of viral something. Then after the third visit to the ER and a blood culture, I was airlifted to the nearest hospital with resources to help me. At the time I was 100 pounds. I am 6 foot 2 and that doesn’t look good.

I was in the hospital for two months, but because I am an addict they were stingy on the pain meds, and I was in pain the whole time. After getting out of the hospital I was supposed to have a heart valve transplant, but that hospital refused to do it. Around a year and 2-3 treatments later, I applied for a surgery and was accepted at Abbott Heart Hospital, and the surgery was a success. That was in December of 2019. Now I am doing good, but I have to be extra careful with my dental stuff and not using so I won’t get re-infected.

Sepsis and IV Drug Use

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Pathophysiology of injection-related infections

- Organisms are introduced into the bloodstream when the skin is punctured.

- Organisms may come from the skin or oral microbiome, the environment, the drug, filters, water or other diluents, or residual blood in the needle or syringe from shared use of equipment.
Sites of bacterial/fungal infections

- **Injection site**
  - cellulitis, subcutaneous abscesses, and venous thrombophlebitis
- **Hematogenous spread**
  - bacteremia, endocarditis, osteomyelitis, septic joints, meningitis, etc
Most bacterial and fungal common pathogens

- *Staphylococcus aureus* (inc methicillin-resistant *S. aureus*)
- Group A *Streptococcus*
- *Viridans streptococcus species*
- *Candida* species
- Gram negative bacteria (less common)
- *Actinomyces* (less common)
Endocarditis

- Infection of the endocardial surface of the heart; usually one or more heart valves
- Septic emboli may cause infections in the lungs, brain, eye, spleen, kidney, eye, and spine or other bones
- Mortality 3-67% depending on size of vegetation, pathogen, surgery
- Approximately 90% of patients with right-sided IE are people who inject drugs (PWID)
- PWID comprise approximately 20% of cases of left-sided IE

Steps in the pathogenesis of endocarditis

- Valvular endothelial damage
- Platelet-fibrin thrombus formation
- Adherence of bacteria to platelet-thrombus plaque
- Local bacterial proliferation with hematogenous seeding

Septic Emboli and Empyema

Chest radiograph shows multiple ill-defined nodular opacities, some with cavitation. This is an example of multifocal patchy opacification.

CT of the chest showing a loculated pleural effusion (arrows), which is parapneumonic in origin. The pneumonia, which is not shown here, is evident in CT cuts above this level.

CT: computed tomography.

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DVT and septic pulmonary emboli

• Left IJ thrombus
Osteomyelitis, Epidural Abscess, Septic Joint

- **Osteomyelitis** = Bone Infection
- **Septic Joint** = Joint Infection
- **Spinal Epidural Abscess** = Infection in the epidural space between the dura mater and vertebral wall
Spinal epidural abscess in a 73-year-old patient. T1-weighted MRI shows epidural lesions (arrow) with surrounding contrast enhancement located at (A) C3/C4 and (B) T7–T9. Insets show corresponding axial sections. Staphylococcus aureus was identified in blood and cerebrospinal fluid.

MRI: magnetic resonance imaging.

L5/S1 vertebral osteomyelitis, discitis and paravertebral infection

Injection into bone and associated osteomyelitis

Septic tenosynovitis

Skin anatomy: Cellulitis, erysipelas, and skin abscess

Cellulitis and erysipelas manifest as areas of skin erythema, edema, and warmth; they develop as a result of bacterial entry via breaches in the skin barrier. Cellulitis involves the deeper dermis and subcutaneous fat; in contrast, erysipelas involves the upper dermis, and there is clear demarcation between involved and uninvolved tissue. A skin abscess is a collection of pus within the dermis or subcutaneous space.
Cellulitis and cutaneous abscess

- **Cellulitis** = Skin Infection

- **Skin abscess** — A skin abscess is a collection of pus within the dermis or subcutaneous space

“hidden epidemic of suffering”
Necrotizing soft tissue infections

- Necrotizing soft tissue infections (NSTIs) include necrotizing forms of fasciitis, myositis, and cellulitis
- Fulminant tissue destruction
- Systemic toxicity
- If you are squeamish or get queasy, cover your eyes for the next slide.
Bilateral thigh necrotizing soft tissue infection

The pictures illustrate a case of necrotizing soft tissue infection that presented as increasing confusion over a few days in a 72-year-old with diabetes but no history of dementia. The patient presented late with tenderness and skin changes of the bilateral thighs (A, left thigh). During surgical exploration and debridement (B, C) the characteristic appearance of necrotic skin, underlying fascia, and dish-water fluid drainage can be seen.
OTHER SEVERE INJECTION-RELATED INFECTIONS (SIRIs)

- Blood stream infection (bacterial or fungal)
- Septic thrombophlebitis
- Bacterial or fungal pneumonia/Lung abscess/empyema
- Orthopedic hardware infection
- Muscle abscess/myositis
- Biliary tract infection
- Central nervous system infection (bacterial or fungal)
- Bacterial or fungal ophthalmologic infection
- Sinus infection
- Non-sexually transmitted genitourinary infection
- Other abscess
Factors that may increase the risk or severity of infection

- Localized tissue damage
  - Multiple injections, re-use of blunted syringes, acidic diluents
- Damaged veins
  - Repeated penetration leading to scarring, damaging substances
- Cardiac endothelial damage
  - Particulate matter, prior infection
- Cocaine
  - Constricts blood vessels → inadequate tissue perfusion and cardiac damage
  - May be dissolved in organic acids → tissue damage, favorable environment for bacteria

Socio-ecological model—multilevel risk factor associated with SBI

## Treatment for SIRIs

<table>
<thead>
<tr>
<th>Infection</th>
<th>Antibiotics</th>
<th>Duration of ABX (typically)</th>
<th>Possible Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocarditis</td>
<td>IV, possibly oral, possibly LA IV abx</td>
<td>4-6 weeks</td>
<td>Valve replacement, valve repair, AngioVac</td>
</tr>
<tr>
<td>Pleural Empyema</td>
<td>IV → oral</td>
<td>variable</td>
<td>Chest tube, thrombolytics, VATS</td>
</tr>
<tr>
<td>Osteomyelitis / Epidural abscess</td>
<td>IV, possibly oral, possibly LA IV abx</td>
<td>6-8 weeks</td>
<td>Debridement/drainage</td>
</tr>
<tr>
<td>Septic joint</td>
<td>IV, oral</td>
<td>4-6 weeks</td>
<td>Drainage, wash-outs</td>
</tr>
<tr>
<td>Cutaneous abscess</td>
<td>Oral or none</td>
<td>0-1 week</td>
<td>I+D (may be at the bedside)</td>
</tr>
<tr>
<td>Necrotizing soft tissue infection</td>
<td>IV → oral</td>
<td>variable</td>
<td>Aggressive debridement (OR)</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Oral, IV → oral</td>
<td>1 week</td>
<td></td>
</tr>
</tbody>
</table>
Acute injection-related infections requiring hospitalisation among people who inject drugs: Clinical features, microbiology and management, Single hospital in Melbourne, Jan 2017-April 2019

Drug and Alcohol Review, First published: 22 August 2022, DOI: (10.1111/dar.13525)

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Injection-related infections at Denver Health
July 1, 2021-June 30, 2022

>241 hospitalizations for injection-related infections in 1 year*

- Endocarditis: 24
- Osteomyelitis, Septic Arthritis, Bacteremia: 39
- Cellulitis, Soft tissue abscess: 178

*Preliminary data based on chart review, medical record reports, and estimates from prior studies
Injection-related infections at Denver Health  
July 1, 2021 - June 30, 2022

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estimated Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>had opioid use disorder?</td>
<td>60%</td>
</tr>
<tr>
<td>had stimulant use disorder?</td>
<td>54%</td>
</tr>
<tr>
<td>were Black or African American?</td>
<td>15%</td>
</tr>
<tr>
<td>were female?</td>
<td>35%</td>
</tr>
<tr>
<td>were Hispanic/Latinx?</td>
<td>50%</td>
</tr>
<tr>
<td>were monolingual Spanish-speakers (i.e., competent communicating in Spanish and not in English)?</td>
<td>16%</td>
</tr>
</tbody>
</table>
SIRIs are common and increasing

- PWID up to 50 times more likely to be admitted to hospital for treatment of a bacterial infection
- Skin and soft tissue infections \( \text{\textup{est}} \) 155,000 to 540,000 cases in US annually
- Estimated hospital admissions for IDU-associated endocarditis \( \text{\textup{\textup{>}}} \) 2900 in 2013 to \( \text{\textup{\textup{>}}} \) 20,000 in 2017


## Lifetime risk of infection among PWID

<table>
<thead>
<tr>
<th>Condition</th>
<th>Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin/Soft Tissue Infections</td>
<td>6-67%</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0.5-12%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2-10%</td>
</tr>
<tr>
<td>Bone and Joint Infections</td>
<td>0.5-2%</td>
</tr>
<tr>
<td>Thrombosis and emboli</td>
<td>3-27%</td>
</tr>
</tbody>
</table>

Incidence and Costs of Drug-Associated Endocarditis in North Carolina
Among 44,851 hospitalizations for the specified infections, 2,830 (6.3%) were IDRIs. The proportion of infections attributable to drug use increased from 1.5% (2010) to 13.1% (2018), and the rate grew from 1.2 to 15.1 per 100,000. Compared with those who had non-drug-related infections, patients with IDRIs were younger (median age, 35 vs 46 years), more likely to be non-Hispanic white (81% vs 56%), and had longer hospitalizations (median, 8 vs 6 days). 43% of hospitalizations for IDRIs involved infective endocarditis.
Fig 1. Injection drug use-related SBI hospitalizations, overall and by SBI type, as a percentage of all hospitalizations, Hospital Discharge Data, Oregon, 2008–2018.

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0242165
Fig 2. Injection drug use-related SBI hospitalizations, by drug type, as a percentage of all hospitalizations, Hospital Discharge Data, Oregon, 2008–2018.

https://doi.org/10.1371/journal.pone.0242165
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0242165
Figure 1. Association of endocarditis with substance use, Dartmouth

IE incidence increased by 62% over the 6-year study, while DUA-IE incidence increased 440%
**Figure 1.** Hospitalization counts among Michigan residents between aged 18–64 years recorded in the Michigan Inpatient Hospitalization Database (MIDB) from 1 January 2016 to 31 December 2018.
Figure 3. Trends in hospitalization costs involving a substance use and infectious disease International Classification of Diseases diagnosis codes, Michigan, 2016–2018.
Fentanyl

• Increased injection frequency
  – LA and San Francisco 2017-2018

People reporting perceived illicit fentanyl use had a greater odds of high frequency* opioid use (adjusted odds ratio (aOR) = 2.36; 95% CI: 1.43–3.91; \(p = 0.001\)), high frequency injection (aOR = 1.84; 95% CI: 1.08–3.13; \(p = 0.03\)) and receptive syringe sharing (aOR = 2.16; 95% CI: 1.06–4.36; \(p = 0.03\)), as compared to people using heroin and other street drugs but not fentanyl

*High frequency = greater than 90 times in the past 30 days; high frequency injection defined as greater than 90 injections in the past 30 days

• High concentration of cutting agents

## Table 3

Percentage of major adulterants present versus drugs of abuse.

<table>
<thead>
<tr>
<th>Overall (%)</th>
<th>Levamisole</th>
<th>Phenacetin</th>
<th>Quinine/Quinidine</th>
<th>Caffeine</th>
<th>Acetaminophen</th>
<th>Procaaine</th>
<th>Lidoceaine</th>
<th>Diphenhydramine</th>
<th>Diltiazem</th>
<th>Atropine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin (n = 325)</td>
<td>4.3</td>
<td>5.2</td>
<td>42.5</td>
<td>51.1</td>
<td>6.5</td>
<td>22.2</td>
<td>17.2</td>
<td>6.8</td>
<td>7.4</td>
<td>–</td>
</tr>
<tr>
<td>Fentanyl (n = 109)</td>
<td>9.2</td>
<td>2.8</td>
<td>47.7</td>
<td>45.9</td>
<td>13.8</td>
<td>22.9</td>
<td>17.4</td>
<td>26.6</td>
<td>15.6</td>
<td>–</td>
</tr>
<tr>
<td>Furanylfentanyl (n = 16)</td>
<td>–</td>
<td>18.8</td>
<td>31.3</td>
<td>25.0</td>
<td>–</td>
<td>6.3</td>
<td>25.0</td>
<td>12.5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Acetylfentanyl (n = 16)</td>
<td>–</td>
<td>6.3</td>
<td>43.8</td>
<td>25.0</td>
<td>6.3</td>
<td>6.3</td>
<td>50.0</td>
<td>18.8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Butyrylfentanyl (n = 1)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>U-47700 (n = 4)</td>
<td>25.0</td>
<td>–</td>
<td>25.0</td>
<td>75.0</td>
<td>25.0</td>
<td>–</td>
<td>25.0</td>
<td>25.0</td>
<td>25.0</td>
<td>–</td>
</tr>
<tr>
<td>Tramadol (n = 31)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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</tr>
</tbody>
</table>

Transition from injecting opioids to smoking fentanyl in San Francisco, California
Transition from injecting opioids to smoking fentanyl in San Francisco, California

• The number of injections decreased precipitously among people who inject drugs in San Francisco from 2018 to 2020 while the number of days they smoke fentanyl increased.

• Main motivation for switching from injecting tar heroin to smoking fentanyl was related to their difficulties finding easily accessible veins.

• After switching to smoking fentanyl, people noticed many benefits including how the drug felt, improved health, fewer financial constraints, and reduced stigma.
Viral infections

Fig 1. HIV virus structure

Glycoprotein
Capsid
RNA
Reverse transcriptase

Hepatitis B Virus
Baltimore Group VII (dsDNA-RT)

Capsid
E antigen HBeAg
Lipid bilayer membrane
DNA polymerase
Large surface protein HBsAg
Medium surface protein HBsAg

VPG
RNA
Hepatitis A Virus
Global prevalence of injecting drug use and

Figure 2

Estimated prevalence of injecting drug use by country

The Lancet Global Health
Volume 5 Issue 12 Pages e1192-e1207 (December 2017)
DOI: 10.1016/S2214-109X(17)30375-3
Figure 3

Estimate

d HIV prevalence


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Figure 4

Estimated anti-hepatitis C virus prevalence among people who inject drugs by country.
Figure 5

Estimated hepatitis B virus surface antigen prevalence among people who inject drugs by country.
HIV

• Chronic viral infection, not curable but manageable with 1-2 pills/day for most people. Treatment is lifelong.
• Leads to severe immunodeficiency within 10 years for most people if not treated. Normal life expectancy if treated.
• Cannot be transmitted through sex when viral load is undetectable, transmission through needle sharing in setting of undetectable HIV is unknown.
HIV Outbreaks – Scott County 2015 and Seattle 2018

• Since 2016, IDU-associated outbreaks of HIV have been reported in Indiana, Massachusetts, Oregon, Pennsylvania, Washington State, West Virginia, and the Northern Kentucky/Cincinnati

• Outbreaks also reported in Athens, Greece, Tel-Aviv, Israel, Dublin, Ireland

• Scott County, Indiana 210+ HIV cases

• King County, Washington 14 related HIV diagnoses among heterosexuals who were living homeless, most of whom injected drugs, 286% increase from prior year


Human immunodeficiency virus diagnoses linked to Lawrence and Lowell, Massachusetts, January 2015–May 2018

Increasing HIV Diagnoses Among PWID

In an analysis of 529,349 Centers for Disease Control and Prevention (CDC)–funded HIV tests among PWID during 2012–2017, the percentage with newly diagnosed HIV increased by 4% per year, with particularly high increases among PWID who were <30 years old, male, and white.

Hepatitis C Virus

- RNA virus
- Replicates in liver & blood
- Survives outside body for days
- No environmental reservoir
- Transmitted blood-blood or maternal-child (5-10%)
- 3.2 million living with chronic HCV (1% of US)
- Curable with 1-3 pills/day for 8-12 weeks, covered by Medicaid
Clinical Course

- **Acute hepatitis**
  - HCV infection
  - Hepatic artery
  - IFNa expression
  - IFNg expression
  - Viral replication
  - HCV elimination in 30% of infected individuals
  - Viral persistence in 70% of infected individuals

  **0–24 weeks**

- **Chronic hepatitis C**
  - Infected hepatocyte
  - Necrotic hepatocyte
  - ISG expression in 50% of patients with CHC

  **24 weeks–50 years**

- **Liver cirrhosis**
  - 15–25% of patients with CHC
  - Cirrhotic liver nodules

  **10–40 years**

- **Hepatocellular carcinoma**
  - Hyperplastic or dysplastic liver nodule
  - Hepatocellular carcinoma
  - 3% of patients with cirrhosis per year

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**Figure 3.1. Number of reported acute hepatitis C virus infection cases and estimated infections* — United States, 2012–2019**

![Bar chart showing the number of reported acute hepatitis C virus infection cases and estimated infections from 2012 to 2019.](image)

<table>
<thead>
<tr>
<th>Year</th>
<th>Reported acute cases</th>
<th>Estimated acute infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>1,778</td>
<td>24,700</td>
</tr>
<tr>
<td>2013</td>
<td>2,138</td>
<td>29,700</td>
</tr>
<tr>
<td>2014</td>
<td>2,194</td>
<td>30,500</td>
</tr>
<tr>
<td>2015</td>
<td>2,436</td>
<td>33,900</td>
</tr>
<tr>
<td>2016</td>
<td>2,967</td>
<td>41,200</td>
</tr>
<tr>
<td>2017</td>
<td>3,216</td>
<td>44,700</td>
</tr>
<tr>
<td>2018</td>
<td>3,621</td>
<td>50,300</td>
</tr>
<tr>
<td>2019</td>
<td>4,136</td>
<td>57,500</td>
</tr>
</tbody>
</table>

Source: CDC, National Notifiable Diseases Surveillance System.

*The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases that met the classification criteria for a confirmed case by a factor that adjusted for underascertainment and underreporting. The 95% bootstrap confidence intervals for the estimated number of infections are displayed in the Appendix.*
Hepatitis C (HCV)

- Acute cases of infection more than tripling between 2010 and 2017
- Perinatal HCV increasing
- Perinatal cases in CO: 2 in 2018, 1 in 2019, 3 in 2020

Prevalence of HCV in women delivering at Magee-Womens Hospital of UPMC (cases per 100 000 and total numbers per year from 2006 to 2014).


CDPHE 2020 Viral Hepatitis Report
Figure 4.1: Reported Acute HCV Cases and Rate per 100,000, 2011-2020

- **Number of New Diagnoses**
- **Rate per 100,000**

Diagram showing the trend of reported acute HCV cases and rate per 100,000 from 2011 to 2020.
Mortality of HCV, other reportable infectious diseases - United States (2003-2013)

HCV causes more deaths in the U.S. than all other reportable infectious diseases combined

HCV Treatment for PWUD

• AASLD-IDSA
  – Should be no restriction based on substance use
  – Scaling up treatment of PWID is necessary to positively impact the epidemic

• Adherence has been shown to be high (82%) among PWID

• Reinfection rates are low: 2.4/100 person-years though may increase with ongoing use over time

• NY Clinic: Cure rates 90-95% among PWUD

• NY Syringe Service Program: 53 PWID treated for HCV; 91% cured

Aspinall, CID 2013; Eckhardt OFID 2018; Norton, Int J Drug Policy 2017
It is estimated that 40 – 74% of people who inject drugs are infected with HCV. Treatment reduces the risk of ongoing disease transmission. It is impossible to eliminate HCV without addressing the epidemic in this population.
Figure 2.1. Number of reported acute hepatitis B virus infection cases and estimated infections* — United States, 2012–2019

Source: CDC, National Notifiable Diseases Surveillance System.

* The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases that met the classification criteria for a confirmed case by a factor that adjusted for underascertainment and underreporting. The 95% bootstrap confidence intervals for the estimated number of infections are displayed in the Appendix.
Table 2.3. Reported risk behaviors or exposures*† among reported cases of acute hepatitis B virus infection — United States, 2019

<table>
<thead>
<tr>
<th>Risk behaviors/exposures</th>
<th>Risk identified</th>
<th>No risk identified</th>
<th>Risk data missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection drug use</td>
<td>631</td>
<td>1,149</td>
<td>1,412</td>
</tr>
<tr>
<td>Multiple sexual partners</td>
<td>241</td>
<td>801</td>
<td>2,150</td>
</tr>
<tr>
<td>Surgery</td>
<td>120</td>
<td>1,139</td>
<td>1,933</td>
</tr>
<tr>
<td>Sexual contact §</td>
<td>92</td>
<td>807</td>
<td>2,293</td>
</tr>
<tr>
<td>Needlestick</td>
<td>73</td>
<td>1,121</td>
<td>1,998</td>
</tr>
<tr>
<td>Men who have sex with men ¶</td>
<td>79</td>
<td>374</td>
<td>1,568</td>
</tr>
<tr>
<td>Household contact (non-sexual) §</td>
<td>17</td>
<td>882</td>
<td>2,293</td>
</tr>
<tr>
<td>Dialysis patient</td>
<td>34</td>
<td>1,258</td>
<td>1,900</td>
</tr>
<tr>
<td>Occupational</td>
<td>2</td>
<td>1,536</td>
<td>1,654</td>
</tr>
<tr>
<td>Transfusion</td>
<td>4</td>
<td>1,269</td>
<td>1,919</td>
</tr>
</tbody>
</table>

Source: CDC, Nationally Notifiable Diseases Surveillance System.

* Case reports with at least one of the following risk behaviors/exposures reported 6 weeks to 6 months prior to symptom onset or documented seroconversion if asymptomatic: 1) injection drug use; 2) multiple sexual partners; 3) underwent surgery; 4) men who have sex with men; 5) sexual contact with suspected/confirmed hepatitis B case; 6) sustained a percutaneous injury; 7) household contact with suspected/confirmed hepatitis B case; 8) occupational exposure to blood; 9) dialysis; and 10) transfusion. Reported cases may include more than one risk behavior/exposure.

† Risk behaviors/exposures data from one state was classified as ‘missing’ because of errors in reporting.

§ Cases with more than one type of contact reported were categorized according to a hierarchy: (1) sexual contact; (2) household contact (nonsexual).

* A total of 2,471 acute hepatitis C cases were reported among males in 2019.
Hepatitis A

Overview

Since March 2017, CDC’s Division of Viral Hepatitis (DVH) has been assisting several state and local health departments with hepatitis A outbreaks, spread through person-to-person contact, that have occurred primarily among persons who use injection and non-injection drugs, and/or persons who are homeless, and their close direct contacts.

See related Health Advisory June 11, 2018.
30.6% of persons diagnosed with HAV in 2020 reported IDU.

Figure 1.1: Reported HAV Cases and Rate per 100,000, 2011-2020

Data used in this graph can be found in Table 1.1 in the appendix.
Viral Hepatitis in Colorado, 2020

Table 0.1: Diagnoses and Rate per 100,000 of Hepatitis in Colorado, 2020

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>95</td>
<td>1.6</td>
</tr>
<tr>
<td>Hepatitis B, Acute</td>
<td>12</td>
<td>0.2</td>
</tr>
<tr>
<td>Hepatitis B, Chronic</td>
<td>176</td>
<td>3.0</td>
</tr>
<tr>
<td>Hepatitis C, Acute</td>
<td>10</td>
<td>0.2</td>
</tr>
<tr>
<td>Hepatitis C, Chronic</td>
<td>1,852</td>
<td>32.0</td>
</tr>
</tbody>
</table>
Miscellaneous Conditions – soil and spores

- **Clostridium botulinum** (botulism – descending paralysis)
- Bacillus cereus
- Bacillus anthracis
- Clostridium tetani (lockjaw, problems swallowing, stiffness in the neck, and rigid abdomen muscles)
- Clostridium perfringens (gas gangrene)

### Constellation of findings that should prompt consideration of botulism

<table>
<thead>
<tr>
<th>At least one of the following symptoms of cranial neuropathy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blurred vision</td>
</tr>
<tr>
<td>Double vision</td>
</tr>
<tr>
<td>Difficulty speaking, including slurred speech</td>
</tr>
<tr>
<td>Any change in sound of voice, including hoarseness</td>
</tr>
<tr>
<td>Dysphagia/pooling of secretions/drooling</td>
</tr>
<tr>
<td>Thick tongue sensation</td>
</tr>
</tbody>
</table>

PLUS at least one of the following signs of neuropathy:

- **Ptosis**
- Signs suggestive of extraocular neuropathy
  - Extraocular palsy
  - Decreased tracking of objects
  - Fatigability manifested by avoiding light shining in the eye
- Signs suggestive of facial neuropathy
  - Facial paresis
  - Loss of facial expression
  - Poor feeding or poor suck using pacifier
  - Fatigability while eating
  - Fixed pupils (not including abnormally or sluggishly reactive pupils)

Descending paralysis, beginning with cranial nerves

PLUS lack of fever (temperature ≤37.8°C or ≤100.4°F)

These clinical criteria have been proposed as a tool to improve identification of patients with botulism. When all three are present, the sensitivity for botulism is approximately 78 to 89%. The specificity is unknown.

Miscellaneous – Vascular and Tissue Injuries

- Venous sclerosis from acidifiers, esp citric acid
- Phlebitis
- Superficial clots
- Deep venous thrombosis (DVT)
- Emboli

- Levamisole (toxic in humans)
- Mycotic aneurysm
- AV fistulas
- Sinus tracts


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Arterial Pseudoaneurysm

Duplex ultrasound image demonstrating a left groin pseudoaneurysm due to injected drug use. Yin-yang sign indicating turbulent pulsatile blood flow is seen within the pseudoaneurysm. The likely site of the neck communicating with the adjacent artery is also demonstrated (red arrow).
Pulmonary Diseases

- Cocaine-associated lung injuries (all routes of injection)
- Aspiration
- Granulomas
- Interstitial lung disease
- Pulmonary edema
- Lower lobe bronchiectasis
- 10X higher risk for community acquired pneumonia
Severe Rhabdomyolysis and Hemodialysis in a 27-Year-Old Male

- M30 pills / Speedballs
- Smoked and snorted
- Contained methamphetamines and fentanyl

Prevention

• Optimize hospitalization
• Optimize success at time of discharge
• Referral to harm reduction services
• Education and Training – prevention, signs of infection, when to seek medical care
• Basic needs: food, clean water, a place to rest, clean clothing, and showers

SSPs are associated with a 46%–54% reduction in odds of sharing injection equipment and a 50% reduction in odds of acquiring new HIV infections

• Substance treatment services
### Core Quality Measures to be Discussed and Offered to All Patients With IDU-Associated Infections During Infectious Diseases Consultations (or any admission)

| Substance Use Disorder Care | |  |
|-------------------------------|------------------------------------------------|
| Harm reduction education | Location of needle exchange facilities, education on safer injection techniques, discussion of source of current infection tailored to pathogen-specific risk factors |
| Addiction medicine consultation | For patients at rural facilities, this includes telemedicine consultation with X-waivered providers experienced with initiating MOUDs |
| Linkage to postdischarge OUD care | Appointment at methadone clinic, community substance use disorder clinic, or with X-waivered provider scheduled for patients on MOUDs |

<table>
<thead>
<tr>
<th>Communicable diseases testing</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>□ HIV p24 Ag, 1/2 Ab □ HIV RNA</td>
</tr>
<tr>
<td>Hepatitis A immunity</td>
<td>□ Hepatitis A IgG</td>
</tr>
<tr>
<td>Hepatitis B screening</td>
<td>□ HepB surface Ag □ HepB core Ab □ HepB surface Ab</td>
</tr>
<tr>
<td>Hepatitis C testing</td>
<td>□ HepC antibody □ HepC RNA □ HepC genotype</td>
</tr>
<tr>
<td>Syphilis</td>
<td>□ RPR</td>
</tr>
<tr>
<td>Gonorrhea/chlamydia</td>
<td>□ G/C urine nucleic acid amplification test</td>
</tr>
<tr>
<td>Latent TB testing</td>
<td>□ Interferon gamma release assay</td>
</tr>
<tr>
<td>Pregnancy testing</td>
<td>□ Urine beta HCG</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunizations</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>Immunize all nonimmune PWID</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Immunize all nonimmune PWID</td>
</tr>
<tr>
<td>Tetanus booster</td>
<td>Every 10 years; booster recommended every 5 years for patients with necrotizing skin and soft tissue–associated infections</td>
</tr>
</tbody>
</table>

Reducing Harms from Patient-Directed Discharges

- Prospective multicenter bundled quality improvement project of PWID with SIRI
- 3 hospitals in Missouri
- Multidisciplinary care while inpatient
- Oral antibiotics in the event of a PDD
- Health coaches, a therapist, a case manager, free clinic follow-up, and medications in an outpatient bridge program

Sophia Lewis et al. Patients With Serious Injection Drug Use–Related Infections who Experience Patient-Directed Discharges on Oral Antibiotics Have High Rates of Antibiotic Adherence but Require Multidisciplinary Outpatient Support for Retention in Care, *Open Forum Infectious Diseases*, Volume 9, Issue 2, February 2022,
Reducing Harms from Patient-Directed Discharges

- 166 PWID with SIRI
- 61 completed IV antibiotics inpatient (37%)
- 105 had a PDD on oral antibiotics (63%)
- No significant difference in 90-day readmission rates ($P = .819$)
- Factors protective against readmission included antibiotic and MOUD adherence, engagement with support team, and clinic follow-up.

Sophia Lewis et al. Patients With Serious Injection Drug Use–Related Infections who Experience Patient-Directed Discharges on Oral Antibiotics Have High Rates of Antibiotic Adherence but Require Multidisciplinary Outpatient Support for Retention in Care, *Open Forum Infectious Diseases*, Volume 9, Issue 2, February 2022,
Harm Reduction Tools

- Wash hands first
- Sterile one-use needles (smallest gauge) and equipment
  - Re-using blunts the needle tip which can cause trauma to tissues and veins, increasing infection risk
  - If reuse is unavoidable, clean with water, bleach, hydrogen peroxide if possible
  - Keep needle capped as long as possible
- Use sterile water if possible, if not, use clean water
- Do not use cigarette butts for filters (they contain glass)
- Clean site with alcohol prep pad in one direction
- Vary injection sites to give veins time to heal, inject 1 inch up from prior, toward the heart
- Avoid licking needles, avoid vein fishing and injecting in areas of vein damage or inflammation
- Be especially careful muscle or skin popping
Figure 1. Six Moments of Infection Prevention in Injection Drug Use Model.

1. **CONTAMINATED NEEDLE BEFORE STARTING INJECTION**
   - **RISKS** | HIV, HBV, HCV, delta agent
   - ! ALWAYS use a clean, fresh needle.
   - NEVER share needles. Do not reuse needles.
   - ! GET VACCINATED to prevent HAV & HBV.

2. **CONTAMINATED ACIDIFICATION AGENT/WATER**
   - **RISKS** | *Candida* and others

3. **DIRTY/SHARED SPOON**
   - **RISKS** | HIV, HBV, HCV, delta agent
   - ! ALWAYS use a clean spoon and
   - NEVER share spoons

4. **DIRTY FILTER**
   - ! ALWAYS use fresh, clean cotton.
   - ! NEVER use cigarette filters – they can contain glass particles.

5. **UNCLEANED SKIN**
   - **RISKS** | Skin organisms can lead to MRSA endocarditis, skin abscesses.
   - ! ALWAYS clean your skin beforehand.
   - ! Twist alcohol swab in a circular, outward motion for 30 seconds – about the length of “Twinkle, Twinkle, Little Star” – on dry skin.

6. **CONTAMINATED NEEDLE AFTER FILLING SYRINGE (USUALLY FROM SYRINGE)**
   - **RISKS** | Oral organisms can lead to strep endocarditis.
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommended Harm Reduction Practice</th>
</tr>
</thead>
</table>
| *Eikenella corrodens, Haemophilus parainfluenzae, Neisseria spp. Prevotella spp, Streptococcus spp.* | • Avoid introducing saliva into the injection process  
• Avoid reuse of needles                                                         |
| *Staphylococcus spp, Streptococcus pyogenes,*                          | • Clean injection sites with alcohol swabs before injection  
• Discard any used injection paraphernalia, particularly if materials were injected into a site with active infection |
| *Pseudomonas aeruginosa, Serratia marcescens,*                          | • Inquire about the use of tripelennamine and pentazocine.  
• Encourage the use of sterile water                                              |
| *Clostridia spp.*                                                       | • Provide tetanus vaccine/booster  
• Avoid injecting into the muscle                                                   |
| *Candida spp.*                                                          | • Encourage the use of sterile acidification agents such as ascorbic acid *(available at many needle exchange facilities)* |
| *Human Immunodeficiency Virus (HIV)*                                    | • Avoid sharing needles  
• Link patients to nearest needle exchange facility  
• Immunize against HBV if nonimmune  
• Offer pre-exposure prophylaxis for HIV                                          |
Annual number of syringes exchanged and HIV incidence among people who inject drugs (PWID), New York City, 1990–2002
Number of HIV cases per year of diagnosis among PWID - France, 1990–2009
Source: National Health Surveillance Institute (InVS), 2011
GETTING OFF RIGHT: A SAFETY MANUAL FOR INJECTION DRUG USERS

Potential Health Complications of Injection Drug Use

Many, if not all, of the things that can go wrong during the process of preparing and injecting drugs fall into one of three categories: drug-related, technique-related, and hygiene-related mishaps. Because we’re forced to use blackmarket, unregulated drugs, we don’t have control over the quality or purity of the substances we use. While we may not be able to do much about the actual drugs we use, we can work to improve our injection technique and hygiene which can have far-ranging effects on our health.

There are numerous and potentially very serious health complications associated with injecting illicit drugs, from injection-related injuries like tracking and bruising, to bacterial and fungal infections, from communicable diseases, to drug overdoses and other medical emergencies. This section of the manual describes some of the medical and health problems that can result from injecting drugs and offers suggestions for how to prevent them. Overdose prevention and survival are addressed in chapter four.

BACTERIAL, VIRAL, AND OTHER INFECTIONS
Vein Care
When it comes to sepsis, remember IT'S ABOUT TIME™. Watch for:

- **T**emperature: higher or lower than normal
- **I**nfection: may have signs and symptoms of an infection
- **M**ental Decline: confused, sleepy, difficult to rouse
- **E**xtremely Ill: severe pain, discomfort, shortness of breath

If you experience a combination of these symptoms: seek urgent medical care, call 911, or go to the hospital with an advocate. Ask: “Could it be sepsis?”

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sepsis.org
Optimizing Partnerships

MAT

HCV Treatment

HIV, HCV, HBV Testing

HAV, HBV, Tetanus Vaccines

Overdose Prevention

Vein Care

Syringe Access

Linkage to HIV Care and PrEP

Prevention of Bacterial Infections

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Thank You! Questions?

<table>
<thead>
<tr>
<th>Clinical Syndrome</th>
<th>Pathogen</th>
<th>Exposure / Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Botulism, Tetanus</td>
<td>Spore forming bacteria i.e. Clostridia spp.</td>
<td>Environmental contamination of drugs</td>
</tr>
<tr>
<td>Soft Tissue, Osteoarticular and Endovascular Infections</td>
<td>Gram negative bacteria i.e. Pseudomonas aeruginosa, Serratia marcescens</td>
<td>Water is required to dissolve drugs prior to injection</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>Eikenella spp., Neisseria sicca, Streptococcus spp.</td>
<td>Lemon juice may be used as an acidification agent to dissolve brown heroin or crack cocaine</td>
</tr>
<tr>
<td>Injection Site Abscess</td>
<td>Candida albicans</td>
<td>Saliva is introduced through licking needles</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>Gram positive bacteria i.e. Staphylococcus spp., Streptococcus pyogenes</td>
<td>Non-sterile injection equipment and technique</td>
</tr>
<tr>
<td>Septic Arthritis</td>
<td>HIV, HBV, HCV</td>
<td>Needle sharing transmits blood-borne pathogens</td>
</tr>
</tbody>
</table>