Drugs and Bugs: Infections in Injection Drug Users

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Objectives

❖ Participants will be able to describe the common bacteria found in skin and soft tissue infections in injection drug users.

❖ Participants will employ appropriate screening tests for bloodborne pathogens in injection drug users.

❖ Participants will be able to describe serious infections in injection drug users including endocarditis, vertebral osteomyelitis, epidural abscess and necrotizing soft tissue infections.
A 24 year old woman presents with redness, swelling and pain due to an abscess on her arm at an injection site. On exam, she is afebrile, hemodynamically stable, and has an area of induration with fluctuance about 2 cm in diameter on the right arm. What is the best approach to treatment?
Infections in IDU’s

- The mortality rate in injection drug users younger than 30 is 10 times the rate in the general population.
- Overdose is a major contributor, but infection is another major cause of death.
- Infection is usually the reason for entry into the healthcare system, and is an opportunity for intervention.
Suboptimal Addiction Interventions for Patients Hospitalized with Injection Drug Use-Associated Infective Endocarditis

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ABSTRACT

BACKGROUND: Infective endocarditis is a serious infection, often resulting from injection drug use. Inpatient treatment regularly focuses on management of infection without attention to the underlying addiction. We aimed to determine the addiction interventions done in patients hospitalized with injection drug use-associated infective endocarditis.

METHODS: This is a retrospective review of patients hospitalized with injection drug use-associated infective endocarditis from January, 2004 through August, 2014 at a large academic tertiary care center in Boston, Massachusetts. For the initial and subsequent admissions, data were collected regarding addiction interventions, including consultation by social work, addiction clinical nurse and psychiatry, documentation of addiction in the discharge summary, plan for medication-assisted treatment and naloxone provision.

RESULTS: There were 102 patients admitted with injection drug use-associated infective endocarditis. 50 patients (49.0%) were readmitted and 28 (27.5%) patients had ongoing injection drug use at readmission. At initial admission, 86.4% of patients had social work consultation, 23.7% had addiction consultation, and 24.0% had psychiatry consultation. Addiction was mentioned in 55.9% of discharge summary plans. 7.8% of patients had a plan for medication-assisted treatment, and naloxone was never prescribed. Of 102 patients, 26 (25.5%) are deceased. The median age at death was 49.9 years (interquartile range 38.7–48.7).

CONCLUSIONS: We found that patients hospitalized with injection drug use-associated infective endocarditis had high rates of readmission, recurrent infective endocarditis and death. Despite this, addiction interventions were suboptimal. Improved addiction interventions are imperative in the treatment of injection drug use-associated infective endocarditis.

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Infections in IDU’s

- Skin and soft tissue infections
  - Necrotizing Fasciitis
  - Pyomyositis
- Endocarditis/Bacteremia
  - Endophthalmitis
  - Septic Arthritis/Osteomyelitis
  - Meningitis/Epidural Abscess
- Pneumonia/empyema
- TB
- Blood borne pathogens (HIV, HBV, HCV, Syphilis, Malaria, etc.)
Risk Factors for Infection

- Poor nutrition
- Injecting into heavily colonized areas
- Trading sex for drugs/increased high risk behavior due to drug use
- Living in shelters or other crowded living conditions
- Underlying HIV infection
- Tissue ischemia due to IV cocaine/heroin use
Other Risk Factors

- Not cleaning skin prior to injection
- Sharing paraphernalia
- Reusing needles
- Oral flora due to cheeking pills/crushing them
- Wound botulism related to black tar heroin
- Levamisole induced neutropenia/vasculitis
Opiate Effects on Immune System

- Heroin reduces chemotaxis, phagocytosis
- Opiates reduce cytokines and chemokines
- Heroin and morphine reduce natural killer cell activity and lymphocyte proliferation
- Some of these effects may lead to increased risk of viral infection
Microbiology of Skin and Soft Tissue Infections

- MRSA/MSSA
- GAS, GBS, other streptococci
- Eikenella and other oral flora (in IDU’s who lick needles)
- Gram negatives due to water
- Candida
- Unusual organisms: tetanus, botulism, etc.
Other Considerations

❖ Assess for readiness to quit/refer to drug treatment programs
❖ Screen for blood borne pathogens
❖ Vaccinate for vaccine-preventable diseases (HBV, HAV, HPV, Tdap, pneumococcus, flu)
❖ TB screening (PPD or IGRA)
❖ Screen for STI’s
❖ Harm Reduction
  ❖ Access to syringes by Rx or needle exchange program
  ❖ Instruction on how to clean syringes- back-up strategy, only when no new syringes/needles are available
Case #1 continued

- 24 year old woman underwent incision and debridement, and was discharged from ED. She returns a few hours later with increasing pain and redness. She is febrile, pulse is 116, respirations 20 and BP 88/50. The arm is erythematous in the same area. What should you be concerned about?
Necrotizing Fasciitis

- Rare complication
- Need high index of suspicion
- Usual signs of NF may not be present (bullae, crepitus)
- The patient may be seen as drug-seeking, and diagnosis is often missed initially.
- Hallmark is pain out of proportion to exam, and hemodynamic instability
Diagnosis of Necrotizing Fasciitis

- If crepitus is present, it is helpful
- MRI or CT may demonstrate gas in soft tissues or fascial thickening and fat stranding; imaging can be both false positive and false negative
- Surgical debridement is mainstay of treatment, along with antibiotics
- Repeated debridement often needed (3.4 on average)
- Beta-hemolytic strep are predominant organisms
Case #2

- 36 year old woman presents to ED with complaint of cough productive of yellow sputum that has been going on for a while, but she attributes the cough to smoking. She was seen in the ED one week prior for a sore on her left leg. She said that the noticed the sore one day, and did not recall any prior trauma. She reports having used heroin years ago, but has been clean for a long time. She now has some chest pain with coughing, and reports feeling feverish for the past few days.
On exam, she has a temperature of 99.4, pulse 107, res 18 and BP 101/73. Pulse ox is 100% on RA. She is noted to have some rhonchi on lung exam and a few excoriations on her legs. No heart murmur is noted. What would you do next?
Next Step?

- A) This is likely a viral URI, discharge to f/u with PCP.
- B) Treat for CAP with a macrolide and discharge home.
- C) Obtain blood cultures and chest CT.
- D) Admit, treat with vancomycin and piperacillin/tazobactam and obtain echocardiogram
Case #2

- She was initially discharged on oral azithromycin, returned 1 week later with worsening pain/SOB
- After 2nd CXR, underwent thoracentesis; found to have exudative pleural effusion
- Now what would you do?
Pulmonary Infiltrates in IDU’s

- Not all infiltrates are pneumonia
- Have heightened suspicion for septic emboli
- Evaluate for underlying HIV infection
- Vaccinate against Pneumocococcus
Case #3

- 27 year old woman presents with fever, chills, cough and shortness of breath. She has been clean for 3 months, but used to inject crystal meth. On exam, temp is 100.9, P112, R18, BP 96/56. She has no heart murmur. lungs are clear and there are no skin abscesses on exam. WBC is 24,000, and creatinine is 1.8. What is your next step?
Blood cultures grow MSSA for 4 days

Echocardiogram demonstrates moderate tricuspid regurgitation and a 19x9 mm sessile vegetation

What is the best option for treatment?
Tricuspid valve endocarditis is most common in IDU, but left-sided endocarditis is increasing; multiple valves may be involved.

Staph aureus accounts for about 90% of cases; Groups A, B and G strep are second most common.

Gram negatives are less common.

Candida is most common type of fungus involved in endocarditis.
Endocarditis

- IDU’s with IE typically present with acute illness, and appear ill.
- Symptoms are present a few days to a week prior to presentation.
- Typical symptoms: fever, SOB, chest pain (often pleuritic due to septic emboli), cough often present.
- Severity of illness depends on whether there is metastatic infection or damage to heart valves.
Endocarditis: Clinical Findings

- Heart murmur may or may not be present
- Osler’s nodes/Janeway lesions are rare
- If heart failure is present, prognosis is poor
- Serratia and Candida cause large vegetations with a propensity for embolization
- If valve replacement is being considered, look for metastatic infection/drain abscesses prior to surgery
<table>
<thead>
<tr>
<th>Table 2. Definition of IE According to the Modified Duke Criteria*</th>
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<tbody>
<tr>
<td><strong>Definite IE</strong></td>
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<tr>
<td>Pathological criteria</td>
</tr>
<tr>
<td>Microorganisms demonstrated by culture or histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis</td>
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<tr>
<td>Clinical criteria</td>
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<tr>
<td>2 Major criteria, 1 major criterion and 3 minor criteria, or 5 minor criteria</td>
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<tr>
<td><strong>Possible IE</strong></td>
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<tr>
<td>1 Major criterion and 1 minor criterion, or 3 minor criteria</td>
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<tr>
<td><strong>Rejected</strong></td>
</tr>
<tr>
<td>Firm alternative diagnosis explaining evidence of IE; or resolution of IE syndrome with antibiotic therapy for ≤4 d; or no pathological evidence of IE at surgery or autopsy with antibiotic therapy for ≤4 d; or does not meet criteria for possible IE as above</td>
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</tbody>
</table>

IE indicates infective endocarditis.
Modifications appear in boldface.
*These criteria have been universally accepted and are in current use.
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Definition of Terms

❖ Major Criteria

❖ Positive blood culture for typical organisms MSSA/MRSA, Viridans Strep, Strep bovis, HACEK group, or community-acquired enterococci; at least 2 positive cultures of blood samples drawn >12 h apart or all 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

❖ Single positive titer >1:800 or blood culture for Coxiella burnetti

❖ Evidence of intracardiac involvement

❖ Echocardiographic evidence of IE

❖ Minor Criteria

❖ Predisposing condition or IDU

❖ Fever

❖ Vascular Phenomena, arterial emboli, septic emboli

❖ Immunologic phenomena (Roth spots, GN, Osler's nodes, RF)

❖ Positive blood culture, but does not meet major criteria as above
A Retrospective Review: Significance of Vegetation Size in Injection Drug Users with Right-Sided Infective Endocarditis

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Background
Previously described prognostic markers in right-sided infective endocarditis (RSIE) include vegetation size ≥1cm, fever for more than three weeks, cardiac failure and severe sepsis. This study aimed to evaluate effectiveness of medical therapy for vegetations ≥1cm and explore determinants of outcome in a representative population of intravenous drug users (IDUs) at a metropolitan Australian health service.

Methods
Retrospective review of consecutive IDUs presenting to our institution with native-valve RSIE (by modified Duke criteria) over seven years (2005-2011). Data recorded included echocardiographic estimation of maximal vegetation diameter (classified as < or ≥1cm). Relationships between vegetation size and specified outcomes of death, septic shock, recurrence and relapse were examined by Chi-squared testing.

Results
Of 49 episodes five (10%) were managed surgically and a further four (8%) were lost to follow-up and excluded from the analysis. Of the remaining 40 evaluable medically treated patients (median age 28, range 20-55), 37 (93%) cultured methicillin-sensitive S. aureus and all had tricuspid valve involvement. Of 24 with vegetations ≥1cm, three died (mortality 13%) compared with one (6%) in 16 medically treated patients with vegetations <1cm (p=0.63). A Pittsburgh (PITT) bacteraemia score of ≥4 at presentation was associated with a mortality of 24% (four of 17 patients died) compared with 0 in 23 patients with PITT scores <4 (p=0.026).

Conclusion
Medical therapy alone can be effective for RSIE when large vegetations are present. However a high sepsis score at presentation may increase risk of death. Larger studies are required to determine optimal indications for early surgical intervention.
<table>
<thead>
<tr>
<th>Vegetation</th>
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<tr>
<td>Persistent vegetation after systemic embolization</td>
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<tr>
<td>Anterior mitral leaflet vegetation, particularly with size ≥10 mm*</td>
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<tr>
<td>≥1 Embolic events during first 2 wk of antimicrobial therapy*</td>
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<tr>
<td>Increase in vegetation size despite appropriate antimicrobial therapy*†</td>
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<tr>
<td>Valvular dysfunction</td>
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<tr>
<td>Acute aortic or mitral insufficiency with signs of ventricular failure†</td>
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<tr>
<td>Heart failure unresponsive to medical therapy†</td>
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<tr>
<td>Valve perforation or rupture†</td>
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<tr>
<td>Perivalvular extension</td>
</tr>
<tr>
<td>Valvular dehiscence, rupture, or fistula†</td>
</tr>
<tr>
<td>New heart block‡</td>
</tr>
<tr>
<td>Large abscess or extension of abscess despite appropriate antimicrobial therapy†</td>
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Injection Drug Use and Outcomes After Surgical Intervention for Infective Endocarditis

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Background. Infective endocarditis (IE) requiring surgical intervention in patients who actively inject drugs poses treatment challenges. Decisions regarding the need for operation are affected by concern for relapse of IE from ongoing injection drug use (IDU). The purpose of this study was to evaluate the effect of active IDU on outcomes after operation for IE.

Methods. All patients with IE surgically treated at Cleveland Clinic from July 1, 2007 to July 1, 2012 were identified from the Cleveland Clinic Infective Endocarditis Registry and the Cardiovascular Information Registry. Of 536 patients operated on for IE during the study period, 41 (8%) actively injected drugs. The primary outcome of the study was death or reoperation for IE.

Results. Patients who injected drugs had poorer survival free of reoperation, and the risk of events varied with time. In a multivariable Cox proportional hazards model, using time-dependent covariates, IDU was associated with a higher hazard of death or reoperation between 90 and 180 days (hazard ratio [HR], 9.8; 95% confidence interval [CI], 2.7–35.3) but not before 90 days (HR, 0.38; 95% CI, 0.05–3.1) or after 180 days (HR, 1.8; 95% CI, 0.8–3.8). Among patients who injected drugs, reoperation and death contributed equally to the outcome, whereas among patients who did not inject drugs, reoperation for IE was far less common.

Conclusions. Between 3 and 6 months after operation for IE, patients who inject drugs have a hazard of death or reoperation that is about 10 times that of patients who do not inject drugs. Before and after the HRs are much smaller and not statistically significant.

Antimicrobial Therapy

- Treatment is going to be based on bacteriology
- Treatment course usually begins from the date of first negative blood culture
- Parenteral therapy is recommended, but if it is not possible to give parenteral therapy, there is experience with oral therapy (short course ciprofloxacin plus rifampin or oral linezolid)
A 56 year old man with chronic back pain presents with complaint of worsening back pain. He has been in the emergency department twice, and was sent home. He now presents to your outpatient clinic and is complaining of worsening pain and is requesting pain medication. What do you need to consider in your differential diagnosis, and what should you do next?
Epidural Abscess/Vertebral Osteomyelitis

- Usually occurs as a result of hematogenous seeding
- Both infections may be present
Vertebral Osteomyelitis

- Can occur from hematogenous seeding, especially with prior staph aureus bacteremia
- The segmental arteries supplying vertebrae usually supply two adjacent vertebral endplates and the intervertebral disc; bone destruction of 2 adjacent vertebral bodies is not unusual
- Presents as worsening back pain over a period of weeks
Vertebral Osteomyelitis

- The usual time to presentation is about 6 weeks, but is often less in individuals with history of IDU
- Fever is present in about half
- Back pain is worse with percussion and with movement
- MRSA/MSSA are most common organisms, but may also see enteric gram negatives, GBS, TB, fungi
Epidural Abscess

- Less common than vertebral osteomyelitis; often occurs with vertebral osteomyelitis
- If not recognized, can cause severe neurological impairment including paralysis
- Diagnosis is often missed initially, and if neurological symptoms are present, they may not be reversible
Epidural Abscess

- Initially presents with back pain that is severe and gets worse over time
- Patients may describe shooting or electrical pain
- Urine retention and incontinence may develop
- Paralysis is a late manifestation, and may not be reversible
Vertebral Osteomyelitis/Epidural Abscess

- Must maintain a high index of suspicion
- Realize that bacteremia alone can cause back pain, but neuroimaging should be performed to rule out above in appropriate setting
- Diagnosis often delayed, but should be suspected when there is worsening back pain, with or without fever
- Inflammatory markers may be normal
Treatment of Epidural Abscess

- Realize that non-contiguous epidural abscesses may be present
- Urgent surgical intervention often needed to prevent neurological deterioration
- Once neurological deficits are present, they may not be reversible
- Small epidural abscesses can be treated with antibiotics, but should be evaluated by a surgeon
Vertebral Osteomyelitis

- MRI is recommended; CT, gallium scan or PET scan be performed if MR is contraindicated
- Complete neurological exam
- 2 sets of blood cultures and baseline ESR/CRP
- Also consider screening for TB
Vertebral Osteomyelitis

- Image-guided biopsy or aspiration should be done when microbiological diagnosis is not known.
- Aspiration or biopsy is not necessary in the presence of staph aureus or staph lugdunensis bacteremia or serology positive for brucellosis within the last 3 months and compatible imaging.
- If initial biopsy/aspirate does not yield an organism, a second aspirate is recommended if blood cultures are negative.
For patients who are hemodynamically stable with normal neurological exams, empiric antibiotic treatment is not recommended. It is recommended to hold antibiotics until a microbiological diagnosis can be established.

6 weeks of intravenous antibiotics are recommended for most patients with vertebral osteomyelitis.
When should surgery be considered?

- Surgical intervention is recommended when there are neurological deficits, persistent sepsis without other source; progressive deformity or pain despite adequate treatment
- Follow-up MRI is not routinely recommended
- Be aware that vertebral osteomyelitis causes pain that persists for an extended period of time
A 26 year old man with a history of injection drug use presents with fever, headache, sore throat, and diarrhea. You order an HIV test, and it is positive. He has a girlfriend with whom he shares needles. She has also recently been tested for HIV and is negative. She wants to know if she is at risk for HIV infection. What do you tell them?
What advice do you give the patient about HIV transmission risk to his girlfriend?
PrEP 101

Are you HIV-negative but at very high risk for HIV? Taken every day, PrEP can help keep you free from HIV.

What Is PrEP?

- PrEP, or pre-exposure prophylaxis, is daily medicine that can reduce your chance of getting HIV.
- PrEP can stop HIV from taking hold and spreading throughout your body.
- Daily PrEP reduces the risk of getting HIV from sex by more than 90%. Among people who inject drugs, it reduces the risk by more than 70%.
- Your risk of getting HIV from sex can be even lower if you combine PrEP with condoms and other prevention methods.

Is PrEP Right For You?

PrEP may benefit you if you are HIV-negative and ANY of the following apply to you.

You are a gay/bisexual man and
- have an HIV-positive partner.
- have multiple partners, a partner with multiple partners, or a partner whose HIV status is unknown—and you also
  - have sex without a condom, or
  - recently had a sexually transmitted disease (STD).

You are a heterosexual and
- have an HIV-positive partner.
- have multiple partners, a partner with multiple partners, or a partner whose HIV status is unknown—and you also
  - don’t always use a condom for sex with people who inject drugs, or
  - don’t always use a condom for sex with bisexual men.

You inject drugs and
- share needles or equipment to inject drugs.
- recently went to a drug treatment program.
- are at risk for getting HIV from sex.

Visit Your Doctor

- To find out if PrEP is right for you.
- Every 3 months, if you take PrEP, for repeat HIV tests, prescription refills, and follow-up.
- If you have any symptoms while taking PrEP that become severe or don’t go away.

How Can You Get Help To Pay For PrEP?

- Most private and state Medicaid plans cover PrEP. If you are on Medicaid, check with your benefits counselor.
- If you have health insurance, you may receive copay assistance from drug manufacturers or patient advocacy foundations.
- If you are without medical insurance, consider enrolling in an insurance marketplace, manufacturer patient assistance program,
PrEP Recommendations

❖ Anyone in an ongoing relationship with an HIV+ partner

❖ A gay or bisexual man who has had sex without a condom, or has been diagnosed with an STI and is not in a mutually monogamous relationship with a partner who has tested HIV negative

❖ A heterosexual man or woman who does not always use condoms with a partner who is at risk for HIV infection

❖ Anyone who has injected drugs within the last 6 months, or has been in a treatment program for IDU
Before PrEP

- Document that individual is HIV negative
- Anyone with signs/symptoms of acute HIV infection should not start PrEP
- Normal renal function at baseline
- Document hepatitis B infection/vaccination status
- Truvada is the only medication currently approved for PrEP; prescribe no more than 90 days at a time
# HBV Serology

<table>
<thead>
<tr>
<th>HBsAG</th>
<th>Total Anti-HBc</th>
<th>IgM Anti-HBc</th>
<th>Anti-HBs</th>
<th>Interpretation</th>
<th>Action</th>
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<tbody>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>-</td>
<td>Negative</td>
<td>Susceptible</td>
<td>Vaccinate</td>
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<td>-</td>
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<td>Chronic HBV</td>
<td>Treat</td>
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<td>Negative</td>
<td>Acute HBV</td>
<td>Follow and Evaluate</td>
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<tr>
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<td>Positive</td>
<td>-</td>
<td>Negative</td>
<td>Further testing</td>
<td></td>
</tr>
</tbody>
</table>
While on PrEP:

- Follow-up every 3 months for HIV testing and medication adherence counseling
- Screen for STI symptoms every visit/testing every 6 months
- Assess for pregnancy every 3 months
- Assess access to clean needles/syringes and drug treatment services
- Check renal function 3 months after starting Truvada and every 6 months after that
Prevalence of HCV is high in injection drug users

HCV is transmitted by needles, syringes, cotton, cookers and other paraphernalia

HCV is curable, but risk of reinfection is high with ongoing drug use

It is recommended to screen IDU’s at least annually if negative; confirm infection if positive
More Advice

❖ One needle, one person, one time
❖ Use all sterile supplies every time for every injection
❖ Do not inject another person
❖ Drug treatment (methadone/suboxone) lowers risk of infections
❖ Use condoms correctly for sexual activity
Conclusions

- IDU’s are at high risk for a large variety of infections, many of which are preventable.
- We can vaccinate, refer to drug treatment, provide education on access to clean needles, and decrease risk of bloodborne pathogens.
- Infection often provides an entry into healthcare, and gives us an opportunity to reduce harm.
- Every interaction in the healthcare system has the opportunity to help an individual get to recovery.