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Infective endocarditis in persons who use drugs: Epidemiology, current management, and emerging treatments

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INTRODUCTION

Serious bacterial and fungal infections such as infective endocarditis (IE) are among the most common medical complications in persons who inject drugs (PWID).[1–3] IE once primarily impacted older adults and immunocompromised persons, but is increasingly common among younger persons as complications of injection drug use.[1,4–8] These infections can result in cardiac surgery,[9] sepsis, and death.[10,11] Herein, we review the epidemiology, current and emerging management strategies, clinical considerations and controversies, and propose an approach for the management of injection drug use-related infective endocarditis (IDU-IE).

Epidemiology

Trends in Incidence and Mortality—In recent years, hospitalizations for IE have increased, driven by a surge in IDU-IE. In a nationally representative sample of US hospitalizations from 2000 to 2013, IE hospitalizations rose 38% overall, but hospitalizations for IDU-IE increased 238%.[7] More recent analyses of US population-based data have demonstrated continued uptrends in IDU-IE hospitalizations, with estimates as high as a 12-fold increase between 2007 and 2017.[9,12–14] Canada has also seen an upsurge in IDU-IE cases. In Ontario, rates of admissions more than doubled since the end of 2011.[15] The increase in IDU-IE is likely not consistent across regions in North America. In a comparison of two urban counties in Pennsylvania, Alleghany county experienced a rise in IDU-IE hospitalizations that was nearly three-fold higher than Philadelphia, 443%, and 112%, respectively.[13] Of note, these large-scale, population-based analyses draw upon administrative data and use billing codes for the identification of IDU-IE.

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Numerous single- and multi-center studies have further characterized the rise in IDU-IE in greater clinical detail and confirmed that an increasing proportion of IE hospitalizations and surgeries are for IDU-IE. In a large hospital in North Carolina, IDU-IE increased to 56% of IE hospitalizations in 2014, from just 14% in 2009.[16] Furthermore, among patients who underwent heart valve surgery for IE across 8 academic centers in 2017, 28% were for IDU-IE, up from 19% in 2012,[8] echoing trends seen in other studies of IE surgeries.[9,17] Lastly, IDU-IE now accounts for increased mortality. In a study of US death certificates, there was a three-fold increase in IDU-IE as a cause of death from 1999 to 2016, compared with an only 1.5-fold increase in IE deaths overall.[8]

Demographics—Persons with IDU-IE have a demographic and clinical profile that is distinct from those with those with IE due to other causes (non-IDU-IE). Most notably, IDU-IE patients are consistently younger than patients with non-IDU-IE. In a nationally representative sample of IDU-IE patients in the US, the mean age was 38 years (versus 50 years for non-IDU-IE).[12] Persons with IDU-IE are also more commonly homeless (17–21%)[11,18] and/or experience significant poverty.[14,15] Hepatitis C virus (HCV) infection is frequent (36–82%). Many studies report 45–55% of IDU-IE patients to be female,[9,13,15,19] however, one study found that females accounted for only 13% of patients undergoing surgery.[20]

There remains substantial heterogeneity in the demographics of IDU-IE patients by region, which likely reflects variation in the epidemiology of PWID. For example, while the majority of patients with IDU-IE in the US are non-Hispanic and white, non-white patients comprised 40% of IDU-IE hospitalizations in the Northeast, but only 27% in the South.[14]

Clinical Characteristics—Although all four heart valves can be affected, IDU-IE most commonly involves the tricuspid valve (58–77% of cases).[11,21,22] Surgical intervention most commonly occurs on the aortic valve (40–64%), followed by mitral (36–45%) and tricuspid (28–39%), and many IDU-IE patients undergo surgery on multiple valves (20–54%).[9,13,23] The reasons for the predominance of left-sided valves in surgery is unclear, but may reflect infections with more embolic phenomena or poorer response to medical therapy than tricuspid disease.

IDU-IE results from bacteria entering the bloodstream from the skin or injection equipment including syringes, needles, cookers, cottons, and water. As such, a variety of organisms are implicated in IDU-IE including bacteria and fungi. Among bacteria, *Staphylococcus aureus* is the most common organism in IE, whether due to drug use or not.[24] It is involved in 43–95% of first-episode IDU-IE and accounts for 20–63% of recurrent infections.[21–23] Unfortunately, a growing proportion of IDU-IE cases occur as the result of antimicrobial resistant organisms. To date, many of these infections have included MRSA, which have more than doubled in recent years in this population.[25] Furthermore, although it affects only a small proportion of patients, fungal endovascular infections, specifically *Candida spp.,* merit special attention given their growing prevalence PWID and the challenges they pose to clinical management. In a large US surveillance study from 2017, 11% of patients with candidal bloodstream infections (candidemia) had a history of IDU, and the proportion of patients with candidemia who had injected drugs more than doubled from 2014 to 2017.[20]

Fungal endocarditis is uncommon in first-time infections, but is more common in recurrent infections (7–14%).[21,22]

Opioids are involved in a majority of reported IDU-IE cases, although there is variation by region. For example, in a cohort from Maine, heroin was the most common drug used by persons with IDU-IE and was associated with 60% of the infections.[18] In contrast, in a hospital in central North Carolina, prescription opioids were involved in 68–96% of IDU-IE.[21] Stimulants, such as cocaine and methamphetamine, comprise substantial proportions in those studies (19–31%). Current public health reports indicate increasing overdoses due to both stimulants and combined stimulant/opioid use.[26,27] A series of IDU-associated infections in Western New York from 2017 found that a majority of patients use both cocaine and opioids (69%), although these patients primarily had skin and soft tissue infections and only 14% had IE.[28] As the epidemiology of the drug epidemic in North America continues to change, we expect fentanyl and other illicitly-produced synthetic opioids, as well as stimulants, to be implicated in more IDU-IE cases. Future studies are needed to delineate the prevalence of these substances and polysubstance use in IDU-IE in order to inform the addiction care needs of this population.

DISCUSSION

Current Management Strategies

Management of IDU-IE is generally consistent with management of non-IDU-IE, which may include medical or combined medical-surgical therapy. The care of persons with IDU-IE should also include components to address the underlying substance use disorder (SUD).

Medical Management—Antimicrobial treatment for IE generally consists of 2–6 weeks of parenteral antibiotics. Antibiotic choice and duration are tailored based on the organism species and its antimicrobial susceptibility profile, the presence of a prosthetic valve or other material, the patient's ability to tolerate specific antimicrobials, and tissue penetration to areas of metastatic or distant infection.

Full details of antimicrobial regimens are delineated in the guidelines published by the American Heart Association (AHA) and endorsed by the Infectious Diseases Society of America (IDSA), and are generally not unique for IDU-IE.[29] While most antimicrobial courses are 4–6 weeks, one notable exception is short-course therapy for uncomplicated tricuspid endocarditis in IDU-IE due to methicillin-susceptible *S. aureus*, where an anti-Staphylococcal penicillin can be given intravenously for two weeks.[30,31]

Home intravenous antibiotics can be a safe option for select PWID that also reduce costs and hospital duration.[32–34] Observational cohort studies have shown that PWID (housed and homeless) can achieve good cure rates.[35] Fanucchi et al (2019) demonstrated the feasibility and effectiveness of OPAT for PWID in a pilot randomized trial.[33] In their model, they found that OPAT provided in an integrated outpatient model that includes MOUD treatment for severe injection-related infection has clinical outcomes that are similar to those of prolonged hospitalization while shortening hospital length of stay.

Surgical Management—For patients with IE—drug related or otherwise—decisions about valve surgery must be individualized. Surgery prior to the completion of antibiotics (i.e. “early” surgery) is most commonly considered on the basis of anatomic and structural concerns, such as new valvular regurgitation, symptomatic right or left heart failure or heart block, which may be a presenting sign of an intracardiac abscess.[29] Other reasons to consider early surgery include persistent bacteremia, ongoing embolic phenomena or large vegetations (>10mm on the anterior leaflet of the mitral valve or ≥20mm on the tricuspid valve). Finally, certain organisms, which are more common in IDU-IE, such as *Pseudomonas aeruginosa* and fungi, indicate early surgical consideration due to their association with high mortality (> 40% and >60%, respectively).[36–38]

Several studies support the role of surgery during the initial hospitalization for left-sided native valve IE.[39–41] Observational data on prosthetic valve IE have shown that patients with strong surgical indications also benefit from early surgery.[42] However, these studies have not specified IDU-IE within the population, except one, which included only 9 such cases.[40] Despite the association between surgery and improved outcomes, aortic valve surgeries for IE have decreased since 2013 for both IDU-IE and IE overall.[43]

There appears to be little rationale for systematically withholding surgery in PWID. In fact, surgical intervention for first-episode IDU-IE has been associated with improved all-cause mortality in one cohort of Canadian patients.[11] Surgery typically includes open valve replacement or repair, that latter of which is performed less commonly than replacement.[23] Valvectomy is an option for source control for tricuspid valve IE nonresponsive to medical therapy, although it is rarely performed. While most surgeries address only one valve, 22–25% involve two valves and 3–4% target three. There is also accumulating evidence for the use of a vacuum-assisted percutaneous debridement of tricuspid vegetations in IDU-IE.[44,45] This device has been used in patients with hemodynamic compromise or other acute comorbidities felt to render them poor surgical candidates and has also been employed as a strategy for source control. While patient outcomes have generally been favorable in these case series, further data is needed to determine indications for using this approach.

Addiction Management—IE among PWID is the result of an unaddressed SUD. If the underlying SUD remains untreated, patients are likely to experience poor outcomes. As such, medications for opioid use disorder (MOUD)—naltrexone, buprenorphine, and methadone—and addiction treatment should be considered essential components of treatment for IDU-IE. The National Academies of Medicine, Science and Engineering have specifically highlighted the need for inpatient OUD care as a key action step in addressing the intersection of the opioid epidemic and infectious diseases.[46]

Studies integrating IE and OUD treatment in both the inpatient and outpatient settings have shown promising results.[33,47–49] In a cohort of IDU-IE patients from Ontario, Canada, addiction treatment referral was the only factor aside from surgery that improved mortality.[11] In one study from Missouri, inpatient addiction consultation for patients with infections was strongly associated with antibiotic completion, less discharges against medical advice (AMA) and increased MOUD receipt.[50] MOUD receipt remains rare; less than 12% of patients with IDU-IE are discharged with a plan to start an MOUD.[51,52] Multidisciplinary IE

treatment teams that provide a comprehensive inpatient treatment package are sensible interventions to coordinate care and improve patient outcomes. These may include cardiologists, cardiac surgeons, hospitalists, addiction medicine and infectious diseases specialists, as well as case managers to help address underlying social and structural issues that are often barriers to retention in care and recovery.

Additionally, patients can benefit from harm reduction services. Harm reduction is an approach to care that aims to nonjudgmentally determine where a person is with respect to motivation for behavior change and to offer them care to improve their health, starting at that point.[53] Often applied in settings of substance use, harm reduction services can include those that focus on ensuring that patients have access to sterile injection equipment, that they are educated on safer injection practices (e.g., cleaning skin, using sterile water, heating cookers), and that they receive naloxone and overdose education. Implementation of harm reduction education in the hospital or helping patients to link to syringe service programs (SSPs) at discharge may help reduce the risk of repeat infections and fatal overdoses.

Clinical Outcomes

Short- and long-term—In the early period following IDU-IE, patients have relatively good outcomes. In-hospital mortality has been reported at 5–10% and is consistently lower than those hospitalized for IE due to reasons other than injecting drugs.[9,12–14,18] For patients undergoing valve surgery for IDU-IE, in-hospital and thirty-day mortality is no different between IDU-IE and IE due to other causes.[54]

Long-term outcomes following IDU-IE are not as good and likely reflect the inadequate state of addiction care delivered to patients with IDU-IE. For those undergoing surgery, mortality appears to worsen, compared with those with non-IDU-IE, in the mid-term postoperative period (e.g. at 3- or 6-month timepoints).[55,56] One-year mortality in North America has been reported to be 16–20%.[11,19] A cohort from Boston had 26% mortality at a median 306 days of follow-up, with a median age of death of 41 years, underscoring the devastating consequences of IDU-IE to young persons.[51] While data on very long-term outcomes (>5 years) is limited, one meta-analysis reported 5- and 10-year postoperative mortality at a dismal 62% and 57%, respectively, with a higher hazard ratio for IDU-IE, compared to others with IE (HR 1.47, 95% CI 1.05–2.05).[57]

One factor contributing to post-hospitalization outcomes is the relatively high proportion of AMA discharges in IDU-IE. Of hospitalizations for IDU-IE, 5–22% result in AMA discharges, compared with 1–2% among other IE patients.[9,12,13,58] These discharges almost certainly indicate a truncation in care for a serious infection and implore providers to address the root causes of this outcome. AMA discharges are driven by numerous factors, including negative experiences with staff and inadequate pain management.[59] Given that SUDs are largely inadequately addressed and treated during a hospitalization,[51,60] patients may experience drug withdrawal syndromes contributing to their decision to leave the hospital.[59,61]

Clinical Considerations

Infectious diseases involvement in addiction care—Infectious diseases providers can play a unique role in the care of SUD in the context of IDU-IE and comparable invasive injection-related infections, such as spinal, bone, joint and severe soft tissue infections, as well as typically chronic infections, such as HIV and viral hepatitis. Encountered with such patients regularly, it is sensible for ID providers to undertake prescribing of MOUD and naloxone, provide education on safer injection practices and refer patients to SSPs, where available.[62,63] Guidelines for the care of HCV already specifically recommend that providers include MOUD, referral to SSPs and overdose education alongside direct acting antivirals.[64] Persons with invasive injection-related infections would also greatly benefit from these resources.

Recurrent valve surgery—Recurrent IE is common among PWID and is associated with significant mortality. In a cohort of 87 PWID with IDU-IE, 25% experienced recurrent IE, the majority of which occurred within a year of the first episode.[21] Of those with recurrent IE, nearly one-quarter required surgical intervention and over a third died within a year. Within the medical and surgical communities, uncertainty remains regarding initial and, more commonly, repeat valve surgery in IDU-IE. One qualitative study of healthcare providers showed a wide range of opinions on how to approach repeat valve surgeries, from those who recommended strict single surgery policies to those who felt patients should be offered as many surgeries as needed.[65] A bioethical analysis has highlighted that some of the opinions surrounding offering recurrent valve surgery may be informed by feelings of underpreparedness in treating IDU-IE, implicit and explicit bias, and a lack of transparency in criteria for surgical decision-making. Clearly, a patient-centered approach and thoughtful guidance from a multi-disciplinary group is necessary for optimal patient care.

Emerging Treatment Approaches

There are a number of emerging treatment approaches that hold the potential to redefine our approach to IDU-IE. First, few studies have assessed the efficacy of oral antibiotic regimens for IE. Two small trials have examined oral therapy for native valve IE and found satisfactory cure rates for oral therapy in right-sided IE in PWID, and in partial oral therapy for left-sided disease.[66] More recently, Iversen et al (2018) conducted a large randomized noninferiority, multicenter trial to determine if partial oral antibiotic treatment resulted in similar efficacy and safety as a full course of intravenous treatment. The Partial Oral Treatment of Endocarditis (POET) Trial randomized 400 patients with stable left-sided disease to either a full intravenous antibiotic course or switch to oral regimen after initial intravenous antibiotics. The composite outcome of the trial was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from the time of randomization until 6 months after antibiotic treatment was completed. The composite outcome occurred in 12.1% in the intravenously treated group and in 9.0% in the orally treated group, resulting in a between-group difference of 3.1 percentage points, which met noninferiority criteria. While these results are promising for the population at large, there are reasons that these findings should be interpreted with caution in the setting of PWID. First, though the study did include patients with *Staphylococcus aureus* endocarditis (n=35), none were identified as methicillin-resistant.

Conversely, invasive MRSA is among the commonest pathogens in endocarditis among PWID in North America,[21,25] therefore, findings from this trial may not be generalizable to patients with MRSA endocarditis. Second, there were only five PWID out of the 400 total enrollees in this trial (1.25%). There is, however, no reason to believe that oral antibiotics are less biologically effective in PWID than in non-PWID. Overall, the POET trial adds to an emerging evidence-base for oral antibiotics in the treatment of endocarditis and provides a launching pad for further research in IDU-IE.

Long-acting glycopeptides are also emerging as a potential treatment for endocarditis, though experience is limited. Dalbavancin and oritavancin have been approved by the US Food and Drug Administration (FDA) for the treatment of acute skin and skin structure infections caused by gram-positive bacteria. They are administered intravenously, but their long half-lives allow for weekly dosing, making them appealing choices for persons requiring parenteral therapy for prolonged durations. Phase II studies for complicated bacteremia and endocarditis have ended, but data remains forthcoming. Retrospective observational cohorts and case series are emerging regarding their efficacy and safety. Tobudic et al performed a two-year retrospective analysis of adults with endocarditis who were treated with dalbavancin.[67] In this series of 27 patients with a mix of prosthetic and native valves, organisms, and therapies prior to dalbavancin, the authors noted that 93% of patients achieved microbiological and clinical success. Another retrospective series among people who use drugs with serious gram-positive infections demonstrated similar results. Bryson-Cahn and colleagues noted that none of the 9 patients with endocarditis were known to have failed dalbavancin step-down treatment, but 4 (44%) were lost to follow up.[68] A number of other observational studies have corroborated these findings and suggest that dalbavancin may be effective as consolidation therapy in patients with endocarditis following initial treatment with approved intravenous antibiotics.[69–71] Evidence for the treatment of endocarditis with oritavancin is more scarce.[72]

In addition to uncertain efficacy, other barriers to treatment uptake with long-acting glycopeptides exist. First, some argue that the cost of these medications does not justify their use. Given that dalbavancin is not FDA-approved for endocarditis, insurers may decline to cover its cost, thereby shifting the cost to hospitals and patients. However, multiple analyses have suggested that costs to the system may be offset by decreased hospital length of stay.[71,73] Further research is needed to examine the economic impact and cost-effectiveness of these antibiotics. Another barrier to dalbavancin use is the lack of a defined optimal dosing and monitoring schedules. Several dosing strategies have been proposed that include once and twice weekly dosing with variable loading and maintenance dosages.[67,68] Despite anecdotal success, more rigorous evaluation is clearly needed.

Barriers to Treating Endocarditis

A number of barriers have been discussed in previous sections, however, we have identified two important system-level barriers to treating endocarditis in PWID: lack of infrastructure and work force and the rapidly evolving North American drug epidemic.

First, in a recent survey of infectious diseases physicians only 22% reported that their primary hospital provided a dedicated multidisciplinary addiction service.[62] These

respondents were significantly more likely to “agree/strongly agree” that physicians should actively manage SUDs than were physicians whose facilities did not provide a dedicated service. Furthermore, though nearly half of the respondents felt that infectious diseases providers should actively manage SUDs, only 3% reported having a waiver from the Drug Enforcement Agency (DEA) to prescribe buprenorphine in the outpatient setting. To overcome this barrier, more providers are needed who are willing and able to prescribe buprenorphine. Reevaluating restrictive federal policies, such as eliminating the requirement for a waiver to prescribe outpatient buprenorphine,[74] would likely expand treatment access.[75] Additionally, a large proportion (34–57%) of those hospitalized with injection-related infections in studies from Medicaid non-expansion states were uninsured,[9,34] limiting the availability of outpatient services and MOUD. Medicaid expansion has been linked to improved OUD-related outcomes such as overdose[76] and would conceivably also have a positive effect on IDU-IE outcomes.

Second, drug overdose data suggests that persons using drugs are shifting from using opioids only to polysubstance use that includes stimulants (i.e., cocaine and methamphetamine). This evolution poses significant challenges to addressing IDU-IE given that stimulant use disorder lacks effective pharmacotherapies, unlike OUD. With no approved treatments for stimulant use disorder, few addiction providers to engage with patients, and areas with insufficient harm reduction infrastructure,[77] it is possible that increasing stimulant use will herald increases in IE and other invasive bacterial and fungal infections.

Proposed Treatment Recommendations

In the absence of comprehensive, multidisciplinary clinical guidelines, we propose the following treatment paradigm for IE among PWID in Tables 1 and 2. We strongly encourage a standardized management approach to decrease variability due to provider or institutional beliefs. In clinical settings where electronic health records exist, this can be facilitated by a standardized “endocarditis order set.”

SUMMARY

Endocarditis among PWID is an increasingly common problem associated with significant morbidity and mortality. Much like increasing HCV infections and mounting outbreaks of HIV, endocarditis has increased alongside the US drug epidemic. Addressing SUD is a key element of comprehensive care, and more work is need to integrate efforts to address endocarditis treatment, the underlying SUD and structural factors that might limit retention in care, long-term recovery, and prevention of infections. There remains an urgent need for multidisciplinary guidelines and best practices that are tailored to the unique needs of people who use drugs with endocarditis.

CLINICS CARE POINTS:

- Patients with infective endocarditis and opioid use disorder should be offered medications for opioid use disorder (MOUD) during the hospitalization or peri-hospitalization period.

- Outpatient parenteral antibiotic treatment can be considered in the treatment of IDU-IE for certain patients. Future management strategies may include oral antibiotics and long-acting glycopeptides.
- Discussions regarding co-occurring substance use disorders, injection practices, and overdose risk should take place with all patients with injection-related endocarditis.
- All patients should be counseled regarding the principles of harm reduction, including safer injection practices, and be provided with overdose education and naloxone upon hospital discharge.

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Synopsis

Infective endocarditis associated with injection drug use (IDU-IE) is markedly increasing in the United States and Canada, concurrent with other infections associated with injecting drugs. Long-term outcomes following IDU-IE are dismal, and likely in part stem from insufficient substance use disorder treatment. In this review, we summarize the principles of antimicrobial and surgical management for IDU-IE. We discuss approaches to opioid use disorder care and harm reduction in the inpatient setting and review opportunities to address preventable infections among persons injecting drugs. Lastly, we highlight barriers to implementing optimal treatment and consider novel approaches that may reshape IDU-IE treatment in coming years.

Key Points

- Infective endocarditis associated with injection drug use (IDU-IE) has increased substantially in North America.
- IDU-IE predominantly affects young persons and is primarily driven by *Staphylococcus aureus*.
- IDU-IE management involves antimicrobial therapy, heart valve surgery (if indicated), and evaluation for and treatment of co-existing substance use disorders.
- While rates of in-hospital death are low in IDU-IE, long-term outcomes are poor.

Table 1.

Recommended components of inpatient care for persons with injection drug use-associated infective endocarditis

Infective Endocarditis Care
Antimicrobial Therapy ● Empiric therapy ● Narrowed, organism-directed therapy based on culture data *
Cardiac surgery consultation
Screening for viral infections impacting persons who inject drugs ● See Table 2
Immunization for certain infections of concern in persons who inject drugs ● See Table 2
Dental prophylaxis[78] ● Prescription for amoxicillin 2g once to be taken 30–60 prior to procedure ○ Alternative options for penicillin-allergic patients and parenteral options are available ● Patient education.
Referral for outpatient follow-up care with infectious diseases and, if indicated, cardiology and cardiac surgery
Substance Use Disorder Care
● Addiction medicine consultation (where available) ● For support where no specialized addiction consultation is available, providers requesting clinical assistance should utilize peer mentoring through: ○ "Warm line" clinician-to-clinician phone consultation (e.g. https://nccc.ucsf.edu/clinical-resources/substance-use-resources/) ○ Project ECHO (Extension for Community Healthcare Outcomes) sessions for opioid use disorder care (e.g. https://echo.unc.edu/; https://www.bmcobat.org/project-echo/massachusetts-obat-echo/) ○ Direct mentoring from experienced clinicians (e.g. https://pcssnow.org/mentoring/)
● Offer of inpatient medications for opioid use disorder, notably buprenorphine and methadone ○ Attention should be paid to medication interactions and pain management needs
● Referral to outpatient addiction treatment provider
● Naloxone prescription and overdose education
● Information for accessible syringe services program, where legal and available

* Full details of antimicrobial regimens are available in guidelines published by the American Heart Association.[29]

Table 2.

Screening, immunization and prophylaxis recommendations for infectious diseases in hospitalized persons who inject drugs.*

Hepatitis A ● Screening for preexisting immunity: Hepatitis A IgG ● Immunization: Two-dose vaccine. Interval between doses depends on vaccine preparation.
Hepatitis B ● Screening: surface antigen, core IgG and surface antibody ● Immunization: If all of the above are negative, immunize with two- or three-dose vaccine series.**
Hepatitis C ● Screening: Hepatitis C antibody with reflex to RNA. For persons with known antibody positivity, screen with Hepatitis C RNA.
Tetanus ● Immunization: ○ Adults without documented prior receipt of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine should receive one dose of Tdap. ○ Adults with prior documented Tdap should receive a tetanus and diphtheria toxoids (Td) booster vaccine if ten years have elapsed since their last documented tetanus and diphtheria vaccine.
Pneumococcus ● Immunization: One-time dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) for patients with chronic heart, lung or liver disease, alcohol use disorder, or cigarette smoking, as well as certain other chronic medical conditions, asplenia or immunocompromising conditions.
HIV ● Pre-exposure prophylaxis (PrEP) can be offered to patients at risk of HIV acquisition from injecting drugs or sex. ● Post-exposure prophylaxis (PEP) can be offered to persons with high-risk exposure and as a bridge to PrEP[79]

* Special situations exist for the immunization of pregnant women or those with incomplete or unknown vaccination or other special populations. Consult recommendations from the American Committee on Immunization Practices for full details.

** The two-dose, novel adjuvant Hepatitis B vaccine is given across a four-week interval and, thus, a full vaccination series may be possible during a hospitalization for patients who remain hospitalized for the full duration of infective endocarditis therapy.