Right-sided native valve infective endocarditis

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INTRODUCTION

Right-sided native valve infective endocarditis (IE) refers to IE involving the tricuspid or pulmonic valve; isolated right-sided IE accounts for approximately 10 percent of all IE cases; concomitant left-sided and right-sided IE account for approximately 13 percent of all IE cases [1,2].

Risk factors for right-sided IE include injection drug use, presence of a cardiac implantable electronic device (CIED) or other intravascular device, and presence of an underlying right-sided cardiac anomaly. Issues related to right-sided IE among people who inject drugs and patients with an intravascular device will be reviewed here.

Issues related to right-sided IE among patients with CIEDs are discussed separately. (See "Infections involving cardiac implantable electronic devices: Epidemiology, microbiology, clinical manifestations, and diagnosis" and "Infections involving cardiac implantable electronic devices: Treatment and prevention".)

Issues related to right-sided IE in the setting of congenital heart disease are discussed separately. (See "Infective endocarditis in children", section on 'Congenital heart disease'.)

Other issues related to IE are discussed separately. (See "Overview of management of infective endocarditis in adults" and "Clinical manifestations and evaluation of adults with suspected left-

sided native valve endocarditis" and "Antimicrobial therapy of left-sided native valve endocarditis" and "Complications and outcome of infective endocarditis".)

EPIDEMIOLOGY

Risk factors for right-sided IE include [1,3-5]:

- Injection drug use (IDU).
- Presence of a cardiac implantable electronic device (CIED) – In such patients, development of right-sided IE usually reflects infection that has spread beyond the pocket, extending up to the insertion leads. (See "Infections involving cardiac implantable electronic devices: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'CIED systemic infection'.)
- Presence of an intravascular device such as central line, intra-aortic balloon pump, or ventricular assist device. (See "Intravascular catheter-related infection: Epidemiology, pathogenesis, and microbiology" and "Management of long-term mechanical circulatory support devices", section on 'Infection'.)
- Presence of an underlying right-sided cardiac anomaly. (See "Infective endocarditis in children", section on 'Congenital heart disease'.)

Approximately 90 percent of patients with right-sided IE are people who inject drugs (PWID); in contrast, PWID comprise approximately 20 percent of cases of left-sided IE [6]. Patients with a CIED or other intravascular device account for approximately 9 percent of patients with right-sided IE; patients with an underlying right-sided cardiac anomaly account for approximately 1 percent of patients with right-sided IE [7,8]. Patients may present with isolated right-sided IE (approximately 10 percent of all IE cases) or concomitant left-sided and right-sided IE (approximately 13 percent of all IE cases) [1].

Among PWID, the incidence of right-sided IE is 2 to 4 cases per 1000 years of IDU [1,9]. Historically, IE among PWID has been more common in males (ratio 3:1) [10]; however, the rate among females in the United States is rising [11,12]. Among more than 1600 patients with IE undergoing valve surgery in North Carolina between 2007 and 2017, IE associated with injection drug use was more common among patients who were younger (median age 33 versus 56 years), White (89 versus 63 percent), and female (47 versus 33 percent) [12].

As use of heroin in the United States nearly doubled between 2002 and 2013 [13], the rate of right-sided IE in PWID increased concomitantly, from 6 to 8 percent of hospitalizations (between

2000 and 2008) to 12 percent (in 2013) [11]. Over this interval, right-sided IE among PWID trended toward younger patients, White persons, and a more similar distribution of males versus females [11]. In a retrospective study of IE hospitalizations in the United States, IE in PWID increased from 15 to 29 percent of IE cases between 2010 and 2015 [14]. Similarly, in one report of hospitalizations for endocarditis in North Carolina between 2010 and 2015, the number of cases increased 12-fold, from 0.2 to 2.7 per 100,000 persons per year [15].

Steep rises in hospitalizations for IDU-associated IE have been seen in numerous states over the past decade [16,17]. Hospitalizations for IE among PWID increased approximately 12-fold between 2007 and 2017 in North Carolina, from 0.92 to 10.95 per 100,000 [12]. There were more than 2600 hospitalizations, with a steady increase in rates of surgery for IE among this group; in the final year of the study, 42 percent of valve surgeries for IE were performed in PWID. As of 2018, in some regions of the country, PWID comprised 58 percent of all surgeries for IE [18].

IE is more common in HIV-infected PWID than in HIV-uninfected PWID [19-21]. One case-control study among PWID in Baltimore noted a fourfold higher incidence of IE in HIV-infected PWID (13.8 versus 3.3 cases per 1000 person-years) [21]. Lower CD4 counts were associated with a higher risk of IE in PWID, even after controlling for frequency of drug injection.

PATHOGENESIS

Valve involvement — Right-sided IE accounts for approximately 10 percent of all IE cases [1]. Among patients with right-sided IE, the tricuspid valve is involved in approximately 90 percent of cases; the remainder are usually attributable to pulmonic valve involvement [1]. Rarely, involvement of the Eustachian valve, interventricular septum, and right ventricular free wall have been described [22,23]. Concomitant left-sided and right-sided IE account for approximately 13 percent of all IE cases [1].

Mechanism of disease — Among people who inject drugs (PWID), the pathogenesis of right-sided IE may include the following factors:

- Injection of particulate matter (such as talc) along with illicit drugs may cause endothelial damage to the tricuspid valve [10,24]. Particulate matter up to 8 to 10 microns in size may cross pulmonary capillaries and, in turn, abrade or damage the endothelium of the mitral or aortic valves [25]. It is unknown whether this valve damage confers increased IE risk in individuals who discontinue injection drug use (IDU).

- Repetitive IDU may produce cumulative subclinical damage to the tricuspid valve. In one study of asymptomatic patients with a history of heroin use but no history of IE, tricuspid

valve abnormalities were observed on transthoracic echocardiography [26]. However, others have not observed an increase in gross valvular abnormalities in PWID who died of causes other than IE [24].

- In the process of IDU, patients may also inject bacteria or fungi present on the surface of the skin, in the drug itself, or in diluents, fillers, or filters used to prepare drugs for injection [24]. Illicit drugs in contaminated syringes may contain up to 10^8 organisms/mL [24].

- PWID have higher rates of nasal and cutaneous colonization with *Staphylococcus aureus* than patients who use illicit drugs by the oral route exclusively [27].

- Cocaine injection may carry an extra risk of IE due to associated vasospasm, which can result in skin or other tissue damage [28]. In one study of 115 hospitalizations for PWID with history of cocaine use, IE was diagnosed in 20 percent of cases; a history of cocaine use was more common in those with IE than in those without [29].

- Use of saliva as a drug diluent and/or on injection equipment increases risk for infection from oropharyngeal flora, including *Haemophilus parainfluenzae*, *Eikenella corrodens*, and *Streptococcus milleri*.

Among patients with cardiac implantable electronic devices and other intravascular devices, the pathogenesis of right-sided IE begins with bacterial contamination at the time of implantation or subsequent handling.

The pathogenesis of vegetation formation is discussed separately. (See "Pathogenesis of vegetation formation in infective endocarditis".)

MICROBIOLOGY

S. aureus is the most common cause of right-sided IE, accounting for up to 70 percent of cases [25,30-34]. Streptococci and enterococci are the next most common pathogens, accounting for 5 to 30 percent and 2 to 5 percent of cases, respectively.

Historically, fungi and gram-negative bacilli were rare causes of right-sided IE [24,30,35-37], and polymicrobial IE had been reported in a small percentage of cases of right-sided IE [32,38]. However, the microbiology of right-sided IE is changing as PWID comprise a larger proportion of patients.

One large study of IE among PWID found that *S. aureus* was implicated in only 50 percent of cases [39]. Gram-negative rods were reported in up to 5 percent of cases (most commonly *Pseudomonas* spp and *Serratia* spp); *Candida* spp were reported in 5 percent.

Culture-negative right-sided IE among patients with cardiac devices has been described [1,40,41]. (See "Infections involving cardiac implantable electronic devices: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Microbiology'.)

CLINICAL MANIFESTATIONS

Signs and symptoms — Patients may present with isolated right-sided IE (approximately 10 percent of all IE cases), or concomitant left-sided and right-sided IE (approximately 13 percent of all IE cases) [1]. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

Fever is the most common symptom of right-sided IE (up to 90 percent of patients); it is often associated with chills, anorexia, and weight loss [42]. Fever patterns in IE vary widely; their temporal patterns or severity have no diagnostic utility. Other common symptoms include malaise, headache, myalgias, arthralgias, night sweats, abdominal pain, and dyspnea.

Septic pulmonary emboli are common among patients with right-sided IE, occurring in up to 53 percent of patients with tricuspid involvement; clinical manifestations of such emboli include cough, pleuritic chest pain, hemoptysis, and dyspnea [42]. Right-sided IE of the tricuspid valve may also present with pulmonary symptoms mimicking a respiratory tract infection. Other manifestations include anemia and microscopic hematuria (possibly due to immune complex deposition rather than systemic emboli) [1,2].

In the setting of delayed diagnosis, complications may include pulmonary infarcts, pulmonary abscesses, pleural effusion, empyema, and, rarely, pneumothorax [1,2,43]. These may be associated with right heart failure and right atrial dilatation with associated supraventricular arrhythmia [2]. In addition, mycotic aneurysm of the pulmonary artery can occur; rupture can lead to hemoptysis [44]. (See "Overview of pulmonary disease in people who inject drugs".)

Patients with isolated right-sided IE often do not have a detectable heart murmur (in contrast to patients with left-sided IE), and left-sided heart failure is unusual [24]. While manifestations of peripheral embolization are observed less frequently in patients with isolated right-sided IE, metastatic infection associated with *S. aureus* bacteremia in the setting of right-sided IE is possible. This is due to the propensity for bloodstream infections due to *S. aureus* to cause disseminated infection, which may occur with or without concurrent endocarditis. Rarely,

patients with right-sided IE can develop systemic emboli via an atrial septal abnormality, especially in the setting of concurrent pulmonary hypertension. (See "Atrial septal abnormalities (PFO, ASD, and ASA) and risk of cerebral emboli in adults", section on 'Paradoxical emboli'.)

Physical examination — In the setting of suspected IE, the physical examination should include assessment for evidence of right- and left-sided involvement. This includes cardiac examination (for signs of new regurgitant murmurs or heart failure), chest examination (for crackles, consolidation, or diminished breath sounds), and evaluation for evidence of septic emboli with special attention to the fundi, conjunctivae, skin, and digits. The physical examination should also include evaluation for bone or joint abnormalities (particularly focal back discomfort, suggesting vertebral osteomyelitis, discitis, and/or epidural abscess), abdominal pain (particularly left upper quadrant pain, which may reflect splenic infarction), and costovertebral angle tenderness (which may reflect renal infarction or psoas abscess). In addition, a neurologic examination should be undertaken to evaluate for evidence of focal neurologic impairment. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis" and "Clinical approach to Staphylococcus aureus bacteremia in adults", section on 'History and physical examination'.)

Serial bedside examinations are critical for detection of complications that may develop after initial evaluation and during the course of treatment.

Chest radiography — In patients with right-sided IE, chest radiography demonstrates septic pulmonary emboli (single or multiple pulmonary infiltrates with central cavitation) in more than half of cases (image 1) [45]. These lesions typically measure 5 to 35 mm and favor basilar and peripheral lung locations, and they may increase in number from one day to the next. The extent of septic pulmonary emboli may be better delineated on computed tomography than chest radiography.

Other findings on chest radiography may include pulmonary abscesses, pleural effusion, and pneumothorax.

Laboratory findings — Routine laboratory findings in the setting of IE are relatively nonspecific; they are discussed separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis", section on 'Laboratory and ECG findings'.)

DIAGNOSIS

Criteria for diagnosis — The diagnosis of right-sided IE should be suspected in patients with fever, with or without respiratory symptoms (such as cough, chest pain, hemoptysis), in the

setting of relevant risk factors (injection drug use [IDU], presence of an intravascular device).

The diagnosis of right-sided IE is established based on clinical manifestations, blood cultures (or other microbiologic data), and echocardiography; additional diagnostic evaluation for patients with suspected or known IE includes electrocardiography, chest radiography, and other radiographic imaging (tailored to clinical manifestations):

- A definitive diagnosis of right-sided IE may be established in the setting of positive blood cultures in combination with echocardiographic evidence of right-sided vegetation.
- A presumptive diagnosis of right-sided IE may be made in the setting of suggestive clinical history, physical examination findings, and laboratory data in the setting of relevant risk factor(s). As an example, a presumptive diagnosis of right-sided IE may be made for people who inject drugs (PWID) with pulmonary manifestations and positive blood cultures for *S. aureus*, even in the setting of negative echocardiography.

Patients with right-sided IE may fulfill the 2023 Duke-International Society for Cardiovascular Infectious Disease (ISCVID) criteria [46]. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis", section on '2023 Duke-ISCVID criteria'.)

However, these criteria were developed for evaluation of patients with left-sided IE, and their sensitivity is diminished in patients with suspected right-sided IE and cardiac device infection [47]. This is because patients with right-sided IE may not have an audible murmur, peripheral emboli, or immunologic and/or vascular phenomena. However, important clues for right-sided IE that are included in the modified Duke minor criteria include IDU and presence of septic pulmonary emboli.

Diagnostic evaluation — The initial evaluation for patients with suspected IE consists of blood cultures and echocardiography:

- At least three sets of blood cultures should be obtained from separate venipuncture sites (ideally spaced over 30 to 60 minutes) prior to initiation of antibiotic therapy. (See "Detection of bacteremia: Blood cultures and other diagnostic tests" and "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

  Following collection of blood cultures, the decision to start or withhold antibiotic therapy prior to a microbiologic diagnosis must be individualized. (See 'Empiric antibiotic therapy' below.)

- Echocardiography should be performed in all patients with suspected IE, particularly for patients with positive blood cultures and/or evidence of septic pulmonary emboli (algorithm 1). In general, transthoracic echocardiography (TTE) is the first diagnostic test for patients with suspected IE. Transesophageal echocardiography (TEE) has higher sensitivity than TTE (particularly in the setting of concomitant left-sided disease), and is better for detection of cardiac complications such as abscess, leaflet perforation, and pseudoaneurysm. In some circumstances, it is reasonable to forgo TTE and proceed to TEE. (See 'Echocardiography' below.)

Additional diagnostic evaluation for patients with suspected or known right-sided IE includes electrocardiography, chest radiography, and additional radiographic imaging tailored to clinical manifestations.

- **Electrocardiography (ECG)** – Baseline ECG should be performed as part of the initial evaluation for all patients with suspected IE, with subsequent telemetry monitoring or serial electrocardiograms. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis" and "ECG tutorial: Basic principles of ECG analysis".)

  The presence of heart block or conduction delay (which may manifest initially as a prolonged PR interval) may provide an important clue to paravalvular extension of infection to the valve annulus and adjacent septum. In addition, the presence of findings consistent with ischemia or infarction may suggest the presence of emboli to the coronary circulation. These complications may be observed in patients with left-sided or bilateral IE, but generally do not occur in the setting of isolated right-sided IE.

- **Chest radiography** – Chest radiography is warranted to evaluate for presence of septic pulmonary emboli, infiltrate (with or without cavitation), congestive heart failure, lung abscess, and potential alternative causes of fever and systemic symptoms. (See 'Chest radiography' above.)

- **Computed tomography (CT)** – In patients with persistent fever and/or physical findings suggestive of focal infection, CT of the torso (chest, abdomen, and pelvis) is useful to evaluate for subclinical sites of metastatic infection (such as splenic infarct, renal infarcts, psoas abscess, or other sites of infection) that may warrant localized drainage [48,49]. Routine brain or spine imaging with CT or magnetic resonance imaging (MRI) is not necessary in the absence of focal neurologic signs or symptoms.

- **Additional radiographic imaging** to evaluate for complications of IE should be tailored to findings on history and physical examination [48]. As examples, patients with back pain

should be evaluated for vertebral osteomyelitis or epidural abscess with MRI, and patients with headache, neurologic deficits, or meningeal signs should be evaluated with head MRI for neurologic complications (including intracranial mycotic aneurysm or central nervous system bleeding). (See "Overview of infected (mycotic) arterial aneurysm".)

For patients who undergo valve replacement, the valve should be sent for culture and histopathology. (See 'Microbiology cultures' below.)

General issues related to diagnosis of left-sided native valve endocarditis are discussed separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

Diagnostic tools

Microbiology cultures — Microbiologic tools for diagnosis of IE include blood cultures and valve culture. The results of a valve tissue gram stain may be useful in guiding antimicrobial therapy if it yields an unexpected finding (eg, a gram-negative rod on valve tissue in a patient whose blood cultures had thus far grown only *S. aureus*). The sensitivity and specificity of these tools for diagnosis of IE are discussed separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

Some centers perform routine molecular analysis of explanted valve tissue, sequencing ribosomal ribonucleic acid (rRNA) to identify microorganisms, which may provide additional diagnostic information [50]. Clinicians should be careful to distinguish these results from cultures, the latter of which assess for viable organisms. Unexpected results from molecular analysis should be interpreted on a case-by-case basis.

Cardiac imaging

Echocardiography — Among PWID, the sensitivity of TTE may be comparable with TEE for diagnosis of right-sided IE [51-53]. Given that PWID are at risk for left-sided as well as right-sided IE, the approach to echocardiography for diagnosis of right-sided IE is the same as the approach for diagnosis of left-sided IE (algorithm 1); this is discussed further separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis" and "Clinical approach to Staphylococcus aureus bacteremia in adults".)

Issues related to echocardiography for diagnosis of IE associated with cardiac devices are discussed separately. (See "Infections involving cardiac implantable electronic devices: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

Other imaging tools — Additional cardiac imaging tools for diagnosis of IE include cardiac MRI, cardiac CT, cardiac CT angiography (CTA), and fluorodeoxyglucose positron emission tomography with CT or CTA.

Issues related to these tools for diagnosis of IE are discussed separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of bacteremia in the absence of evidence for valvular vegetation includes alternative causes of bacteremia (which may coexist with IE); these are summarized separately. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis", section on 'Differential diagnosis'.)

The differential diagnosis for febrile illness accompanied by pulmonary symptoms includes:

- **Pneumonia** – Pneumonia refers to infection of the lower respiratory tract; the diagnosis requires demonstration of an infiltrate on chest imaging in a patient with a clinically compatible syndrome (eg, fever, dyspnea, cough, and leukocytosis). (See "Overview of pulmonary disease in people who inject drugs", section on 'Pneumonia' and "Overview of community-acquired pneumonia in adults".)

- **Pulmonary embolism/infarction** – Pulmonary embolism refers to obstruction of a pulmonary artery or one of its branches by thrombus or other material that originated elsewhere in the body. Symptoms may include dyspnea, chest pain, and cough. The diagnosis is usually established via computed tomographic pulmonary angiography. (See "Epidemiology and pathogenesis of acute pulmonary embolism in adults".)

- **Hypersensitivity pneumonitis** – Hypersensitivity pneumonitis refers to lung inflammation due to inhaled dust, fungi, or chemicals. Clinical manifestations include fever, chills, malaise, cough, chest tightness, and dyspnea. The diagnostic approach may include radiographic imaging, laboratory testing, bronchoscopy, and lung biopsy. (See "Overview of pulmonary disease in people who inject drugs" and "Hypersensitivity pneumonitis (extrinsic allergic alveolitis): Clinical manifestations and diagnosis".)

MANAGEMENT

In general, successful management of right-sided IE requires parenteral antimicrobial therapy and removal of any indwelling intravascular devices, if present; the approach to antibiotic selection is discussed below. In addition, surgical consultation is warranted in all patients with IE; indications for surgery are discussed below.

Empiric antibiotic therapy — Following collection of blood cultures, the decision to start or withhold antibiotic therapy prior to a microbiologic diagnosis must be individualized. For patients with hemodynamic instability and clinical presentation suggestive of IE, we suggest administration of empiric antibiotic therapy once blood cultures have been obtained. For patients who are clinically stable, antimicrobial therapy may be deferred while awaiting the results of blood cultures and other diagnostic tests.

Issues related to selection of empiric therapy for patients with suspected or known right-sided IE are as discussed separately for left-sided IE. (See "Antimicrobial therapy of left-sided native valve endocarditis", section on 'Empiric therapy'.)

Surgical assessment — Surgical consultation is warranted in patients with IE; indications for surgical intervention may develop or progress rapidly.

- **Indications** - Indications for surgery in right-sided IE include [48,54]:

  - Very large vegetation (≥20 mm)
  - Recurrent septic pulmonary emboli
  - Presence of a highly resistant organism
  - Persistent bacteremia despite appropriate antimicrobial therapy

  Less common indications for surgery in right-sided IE include [48,55]:

  - Right heart failure due to severe tricuspid regurgitation (poorly responsive to medical management) - In general, tricuspid regurgitation is better tolerated (from a hemodynamic standpoint) than mitral regurgitation; therefore, heart failure is a less common indication for surgery in patients isolated tricuspid valve endocarditis.

  - Heart block

  - Paravalvular abscess

- **Surgical approach** – Surgical approaches for tricuspid valve surgery include repair or replacement. In general, valve repair is preferred over valve replacement; the approach depends on the extent of valvular damage and local expertise [48]. In a systematic review and meta-analysis including 12 retrospective studies including more than 1000 patients

who underwent valve repair or valve replacement for management of tricuspid valve endocarditis, no difference in mortality was observed [56]. Valve repair was associated with lower risk for recurrent IE (relative risk 0.17, 95% CI 0.05 to 0.57), need for reoperation (relative risk 0.26, 95% CI 0.07 to 0.92), and need for permanent pacemaker placement (relative risk 0.20, 95% CI 0.11 to 0.35)

Monitoring response to initial therapy — Patients with *S. aureus* endocarditis may remain febrile for five to seven days after initiation of therapy. Patients with right-sided IE and septic pulmonary emboli may remain febrile for an even longer duration of time.

The initial microbiologic response to therapy should be assessed by obtaining repeat blood cultures 48 hours after antibiotics are begun; it is reasonable to obtain at least two sets of blood cultures every 24 to 48 hours until bloodstream infection has cleared. (See "Antimicrobial therapy of left-sided native valve endocarditis", section on 'Clinical response to initial therapy' and "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

Thereafter, careful serial physical examinations should be performed to evaluate for complications. Patients who develop new complications while on appropriate antimicrobial therapy (such as metastatic infection) should have a repeat echocardiogram to assess for worsening valve dysfunction, cardiac abscess, or fistula.

Targeted antibiotic therapy

Uncomplicated right-sided NVE due to MSSA — For patients with uncomplicated right-sided NVE due to methicillin-susceptible *S. aureus* (MSSA), we favor a two-week regimen of nafcillin or oxacillin (12 g per 24 hours IV in four or six divided doses) or flucloxacillin (2 g IV every four to six hours) [48,57]. For patients with hypersensitivity to the preceding agents, a two-week regimen of cefazolin (2 g IV every eight hours) may be given, although this agent is not as well studied for treatment of right-sided IE as the semisynthetic penicillins.

Exclusion criteria for the above approach include:

- Presence of concomitant left-sided endocarditis
- Presence of cardiac complications (such as paravalvular abscess, heart block)
- Extrapulmonary metastatic infection
- Failure to defervesce and clear blood cultures within 48 to 72 hours of appropriate antibiotic therapy
- Renal failure

The above approach is supported by a randomized trial including 90 PWID with uncomplicated right-sided MSSA IE treated with cloxacillin (with or without gentamicin); treatment was curative in 89 and 86 percent of patients, respectively [58]. The approach to choice of antibiotic agent for treatment of right-sided IE due to MSSA is also based on data for treatment of MSSA bacteremia and MSSA left-sided IE; this is discussed further separately. (See "Clinical approach to Staphylococcus aureus bacteremia in adults", section on 'Methicillin-sensitive S. aureus' and "Antimicrobial therapy of left-sided native valve endocarditis", section on 'Methicillin susceptible'.)

We are in agreement with the American Heart Association guidelines, which recommend against use of adjunctive aminoglycoside therapy in the two-week beta-lactam regimen for treatment of uncomplicated right-sided IE due to MSSA [48]. While such combination therapy has been shown to be effective in randomized trials [57,59], a growing body of literature suggests use of adjunctive aminoglycoside therapy does not confer additional benefit over beta-lactam monotherapy and may cause harm [57,58,60,61]. Issues related to nephrotoxicity associated with adjunctive aminoglycoside therapy are discussed further separately. (See "Clinical approach to Staphylococcus aureus bacteremia in adults" and "Antimicrobial therapy of left-sided native valve endocarditis", section on 'Methicillin susceptible'.)

For patients with beta-lactam hypersensitivity, alternative agents include treatment with vancomycin (or teicoplanin) for four weeks; administration of glycopeptides for two weeks has been associated with high rates of treatment failure [57,59,60,62]. As an example, in a randomized trial including 31 patients with right-sided IE due to *S. aureus* treated with cloxacillin-gentamicin, vancomycin-gentamicin, or teicoplanin-gentamicin, cure rates were 100, 60, and 70 percent, respectively [59].

For patients unable to tolerate vancomycin, daptomycin (6 mg/kg intravenously every 24 hours for 4 weeks) is an acceptable alternative agent [48]. Data on use of daptomycin for treatment of right-sided IE are limited. In one randomized trial including 124 patients with *S. aureus* bacteremia (of whom 10 patients had a final diagnosis of uncomplicated right-sided IE) treated with daptomycin monotherapy or gentamicin plus either an antistaphylococcal penicillin or vancomycin for 14 to 28 days, treatment success rates for patients with right-sided IE were 50 versus 25 percent, respectively (absolute difference 25, 95% CI -33 to 83) [63].

Completion of treatment with oral therapy has been evaluated in small case series; further study is needed to guide this approach [64-66].

Targeted therapy for other patients — For patients with complicated right-sided IE due to MSSA (eg, patients with one or more of the above exclusion criteria for treatment of

uncomplicated infection), treatment is as for left-sided IE due to MSSA. (See "Antimicrobial therapy of left-sided native valve endocarditis", section on 'Methicillin susceptible'.)

For patients with right-sided IE due to methicillin-resistant *S. aureus* or other pathogens, treatment is as for left-sided IE. (See "Antimicrobial therapy of left-sided native valve endocarditis".)

Completing antibiotic therapy

- **Clinical approach** – Once hemodynamically stable, the bacteremia has cleared (as evidenced by negative blood cultures), and a decision on early surgery has been addressed, intravenous therapy may be completed on an outpatient basis. Patients must be capable of managing the technical aspects of intravenous therapy.

  A history of recent injection drug use should not automatically exclude candidacy for outpatient parenteral antimicrobial therapy (OPAT). Emerging literature has demonstrated that selected PWID have good outcomes participating in OPAT for IE and comparable invasive infections [67]. Some centers have developed specific criteria to identify PWID who may be eligible for OPAT [68]. Many criteria used in consideration of OPAT among PWID resemble those among the general population of patients evaluated for OPAT (eg, stable housing, social support, transportation to appointments). Decisions about OPAT for all patients should be made on a case-by-case basis and, in the case of PWID, should include input from addiction-treating providers, if available. (See "Outpatient parenteral antimicrobial therapy", section on 'Patient selection'.)

  Patients on OPAT require careful monitoring and must have ready access to full medical care should complications occur [48,69]. Patients should be counseled regarding the need for immediate evaluation in the setting of new fever, chills, or other signs of systemic toxicity, including a thorough clinical evaluation and repeat blood cultures [48]. (See "Outpatient parenteral antimicrobial therapy".)

  While on antimicrobial therapy, patients should be monitored for antimicrobial toxicity. Weekly laboratory monitoring (eg, complete blood count, chemistries, liver function tests) should be performed. The specific tests are indicated by the specific antimicrobial regimen (table 1).

- **Patients who are unable to complete parenteral antimicrobial therapy** – For patients who are unable to complete parenteral antimicrobial therapy (either inpatient or outpatient), completion of treatment with oral therapy is an alternative consideration; however, data to support this approach are very limited [70]. In a retrospective study

including more than 100 PWID with complicated *S. aureus* bacteremia who received a partial course of inpatient parenteral therapy, those who were discharged with oral antibiotic therapy had a lower rate of microbiological failure or death than those who did not receive oral antibiotics on discharge (13 versus 44 percent), although there were significant differences in baseline characteristics between the two groups [71].

The optimal oral antibiotic regimen is uncertain, and data are limited. Some regimens proposed by the AHA 2022 statement on management of endocarditis in PWID are summarized in the table (table 2) [70]. Patients discharged on oral therapy should be followed closely and be evaluated in the outpatient setting within one week after discharge.

Issues related to echocardiographic monitoring during therapy are discussed separately. (See "Overview of management of infective endocarditis in adults", section on 'Echo monitoring during therapy'.)

Patients should be monitored for development of complications related to IE (see "Complications and outcome of infective endocarditis"). Development of complications should prompt evaluation for cardiac surgery.

Follow up — Issues related to follow up after completion of antibiotic therapy for IE are discussed separately. (See "Overview of management of infective endocarditis in adults", section on 'Follow-up'.)

Additional issues for PWID — People who inject drugs (PWID) may have coinfection with HIV, hepatitis C, or hepatitis B. Accordingly, laboratory testing for these conditions should be pursued, and patients should be immunized against hepatitis A and hepatitis B if needed (see related topics). In addition, PWID with opioid use disorder warrant evaluation, management, and harm reduction interventions; these include provision of naloxone, education on safe injection strategies, and referral to syringe programs and overdose prevention centers, where legal and available (see related topics).

REPEAT EPISODES

Repeat episodes of right-sided IE may occur [72,73]. In general, ongoing injection drug use increases risk of recurrent IE [72].

It can be difficult to distinguish whether a repeat episode represents a relapse of the original infection or a new infection. Relapsed infection should be suspected if the repeat episode

occurs within six months of the original infection.

Bacterial isolates should be retested carefully for complete antibiotic susceptibility profiles. Molecular studies (such as pulsed-field gel electrophoresis) on serial isolates can be used to for definitive distinction, although in general such testing is not routinely available [72,74].

Patients with relapse of IE following completion of appropriate antimicrobial therapy should receive a repeat course of antibiotics (tailored to susceptibility results) as described above. In addition, attention should be given to management of relevant risk factors such as injection drug use.

OUTCOMES

- **Overall prognosis** − In general, the prognosis for right-sided IE among people who inject drugs (PWID) who do not require surgery is relatively favorable [25,32,54,58,60,75]. In one retrospective study including 220 PWID with right-sided IE, the overall mortality was 6 percent [54]. Factors associated with increased mortality on multivariate analysis included vegetation size >2 cm (odds ratio [OR] 10.2, 95% CI 1.6-78) and fungal etiology (OR 46.2, 95% CI 2.4-1100): mortality 67 versus 3.6 percent with non-fungal etiology.

- **Vegetation size** − Vegetation size has prognostic importance among PWID with right-sided IE. In one series including 51 patients with tricuspid valve IE (most of whom were cured with medical therapy), patients with vegetation >1 cm were more likely to develop congestive heart failure [76]. In another study including 122 patients of tricuspid valve IE, mortality rates in patients with vegetations <1 cm, 1.1 to 2 cm, and >2 cm were 0, 3, and 33 percent, respectively [31].

- **HIV infection** − HIV infection does not appear to be a clear risk factor for poor outcome in IE associated with injection drug use (IDU). In one study including 283 PWID with IE, mortality was not influenced by HIV infection [77]. However, among the 216 HIV-infected patients, survival was lower among the patients with CD4 counts <200/microL.

- **Surgical outcomes and PWID**

  - **Initial valve surgery**

    - **Short-term outcomes** − In some studies, worse short-term outcomes have been observed among PWID, including higher rates of postoperative complications such as pneumonia, renal insufficiency, sepsis, and embolism [78].

In one study including more than 11,000 valve operations for IE, the risk-adjusted short-term mortality was higher among those with IDU (OR 1.51, 95% CI 1.19-1.91) [18].

In contrast, other data suggest better short-term outcomes among PWID with IE (including lower mortality rate during the index admission [14]); this may be attributable to younger age, fewer comorbidities, and more frequent incidence of right-sided IE among PWID and IE [14].

- **Long-term outcomes** − Long-term outcomes after surgery for right-sided IE have been observed to be less favorable among PWID than other patients in several studies; frequently, surgery is successful but such patients are often readmitted because of reinfection and complications of ongoing drug use [79-82]. One series of PWID with IE noted a 45 percent mortality (median follow-up period 22 months) [83]; another noted a mortality rate of 33 percent (median follow-up period 3.5 years) [34]. In another study including PWID and IE and patients with IE in the absence of IDU, readmission rates were similar between the groups, but reasons for readmission differed; PWID with IE were more likely to be readmitted for IE, septicemia, and drug abuse than patients with IE in the absence of IDU [14].

- **Repeat valve surgery** − Repeat valve surgery for IE among PWID is associated with increased risk for mortality. In one cohort study including 925 patients, the 30-day mortality among PWID who underwent repeat valve surgery compared with first-time surgery was 8.2 versus 4.8 percent [84]. On multivariable analysis, repeat valve surgery was associated with an increased risk of 30-day mortality (OR 2.22, 95% CI 1.22-4.06). However, there was no direct comparison with outcomes among the general population undergoing valve surgery for IE.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Treatment and prevention of infective endocarditis".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading

level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Endocarditis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Valve involvement** – Right-sided native valve infective endocarditis (IE) refers to IE involving the tricuspid or pulmonic valve; isolated right-sided IE accounts for approximately 10 percent of all IE cases; concomitant left-sided and right-sided IE account for approximately 13 percent of all IE cases. Among patients with right-sided IE, the tricuspid valve is involved more frequently than the pulmonic valve. (See 'Valve involvement' above.)

- **Risk factors** – Risk factors for right-sided IE include injection drug use, presence of a cardiac implantable electronic device or other intravascular device, and presence of an underlying right-sided cardiac anomaly. (See 'Epidemiology' above.)

- **Microbiology** – Right-sided IE is attributable to *Staphylococcus aureus* in a majority of cases. Streptococci and enterococci are the next most common pathogens. (See 'Microbiology' above.)

- **Signs and symptoms** – Right-sided IE commonly presents with fever (up to 90 percent of patients); it is often associated with chills, anorexia, and weight loss. Other common symptoms include malaise, headache, myalgias, arthralgias, night sweats, abdominal pain, and dyspnea. Septic pulmonary emboli occur in up to 75 percent of patients with tricuspid involvement; clinical manifestations include cough, pleuritic chest pain, hemoptysis, and dyspnea. Patients with isolated right-sided IE often do not have a detectable heart murmur (in contrast to patients with left-sided IE), and left-sided heart failure is unusual. (See 'Signs and symptoms' above.)

- **Diagnosis**

  - **Criteria for diagnosis** – The diagnosis of right-sided IE should be suspected in patients with fever, with or without respiratory symptoms (such as cough, chest pain, hemoptysis), in the setting of relevant risk factors. A definitive diagnosis of right-sided IE may be established in the setting of positive blood cultures in combination with echocardiographic evidence of right-sided vegetation. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis", section on '2023 Duke-ISCVID criteria'.)

    A presumptive diagnosis of right-sided IE may be made in the setting of suggestive clinical history, physical examination findings, and laboratory data in the setting of relevant risk factors. (See 'Criteria for diagnosis' above.)

  - **Diagnostic evaluation** – The diagnostic evaluation for patients with suspected IE includes blood cultures (at least three sets obtained from separate venipuncture sites prior to initiation of antibiotic therapy) and echocardiography (algorithm 1), as well as electrocardiography, chest radiography, and additional radiographic imaging tailored to clinical manifestations. (See 'Diagnostic evaluation' above.)

- **Management**

  - **Empiric antibiotic therapy** – While awaiting blood culture results, the decision to start or withhold antibiotic therapy must be individualized. For patients with hemodynamic instability and clinical presentation suggestive of IE, we suggest administration of empiric antibiotic therapy (**Grade 2C**). For patients who are clinically stable, antimicrobial therapy may be deferred while awaiting the results of blood cultures and other diagnostic tests. (See 'Empiric antibiotic therapy' above.)

  - **Surgical assessment** – Surgical consultation is warranted for all patients with IE. Indications for surgery in right-sided IE include very large vegetations, recurrent septic pulmonary emboli, presence of a highly resistant organism, and/or persistent bacteremia. (See 'Surgical assessment' above.)

  - **Targeted antibiotic therapy**

    - **Uncomplicated right-sided NVE due to MSSA** – For patients with uncomplicated native valve right-sided IE due to methicillin-susceptible *S. aureus* (MSSA), we recommend treatment with a beta-lactam antibiotic (in preference to vancomycin or daptomycin) (**Grade 1B**). Regimens include nafcillin, oxacillin, or flucloxacillin;

the duration of therapy is two weeks. For patients with hypersensitivity to the preceding agents, a two-week regimen of cefazolin may be given; however, this agent is not as well studied for treatment of right-sided IE as the semisynthetic penicillins. We recommend NOT administering adjunctive aminoglycosides for treatment of right-sided IE due to MSSA (**Grade 1B**). (See 'Uncomplicated right-sided NVE due to MSSA' above.)

- **Targeted therapy for other patients** – For patients with complicated right-sided IE due to MSSA or right-sided IE due to methicillin-resistant *S. aureus* or other pathogens, treatment is as for left-sided IE. Such patients include those with concomitant left-sided IE, presence of cardiac complications (such as paravalvular abscess, heart block), metastatic infection, failure to defervesce within 48 to 72 hours of appropriate antibiotic therapy, and renal failure. (See 'Targeted therapy for other patients' above.)

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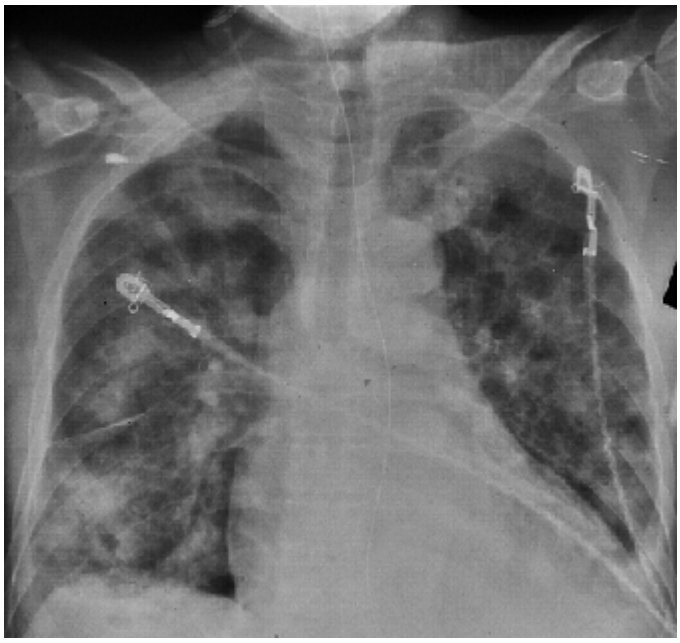
Topic 2149 Version 41.0

GRAPHICS

Septic embolization in an intravenous drug user with tricuspid valve endocarditis

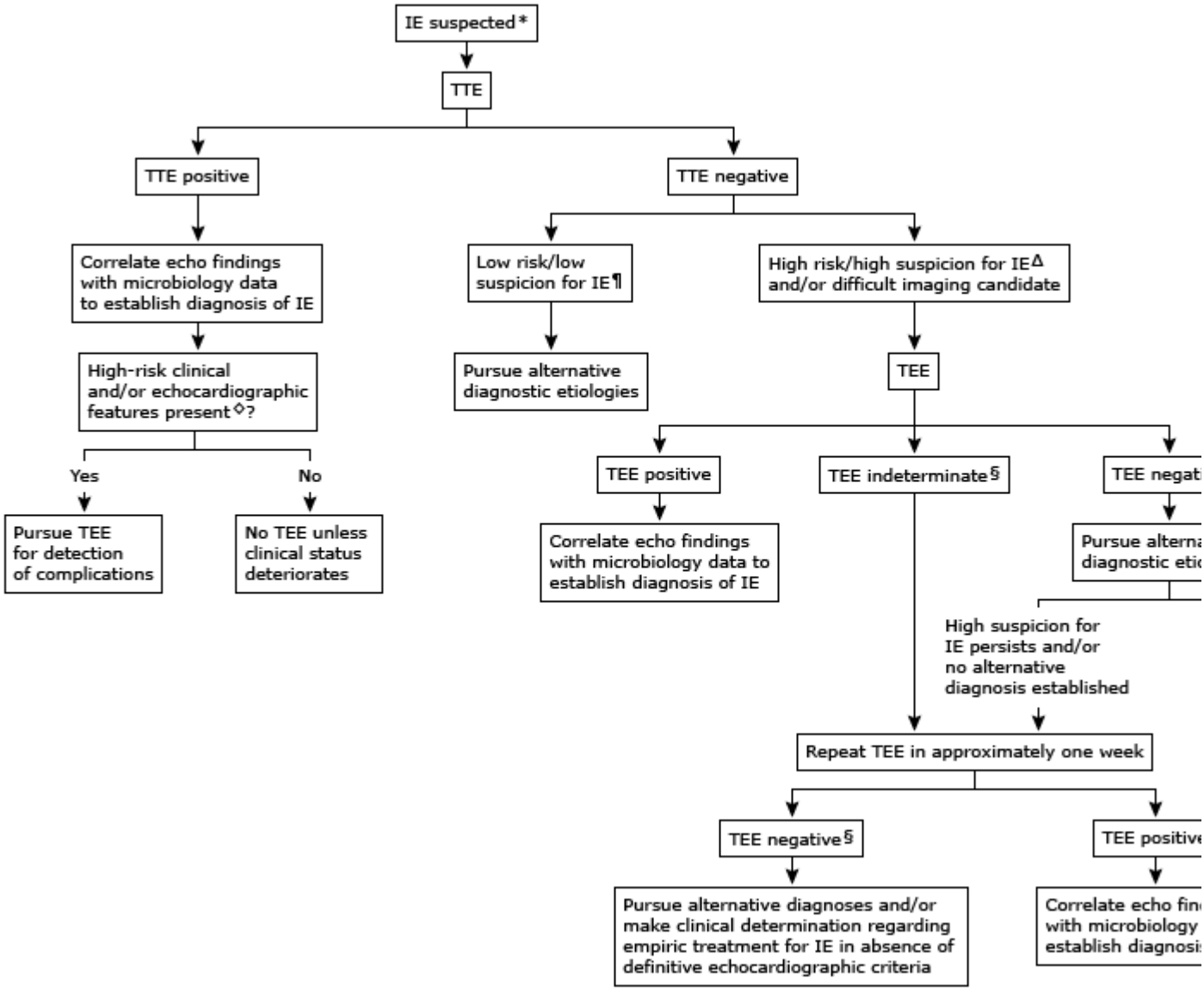


Chest radiograph shows multiple ill-defined nodular opacities, some with cavitation. This is an example of multifocal patchy opacification.

Courtesy of Paul Stark, MD.

Graphic 59037 Version 4.0

An approach to use of echocardiography for diagnosis of native valve infective endocarditis



Issues related to clinical manifestations, diagnosis, and treatment of IE are discussed further in the text (refer to the UpToDate topics on clinical manifestations, diagnosis, and treatment of infective endocarditis). Issues related to diagnosis of prosthetic valve endocarditis and cardiac device infections are discussed in the text (refer to the UpToDate topics on prosthetic valve endocarditis and cardiac device infections).

IE: infective endocarditis; TTE: transthoracic echocardiogram; TEE: transesophageal echocardiogram.

* The diagnosis of IE should be suspected in patients with fever (with or without bacteremia) and/or relevant cardiac risk factors (prior IE, presence of a prosthetic valve or cardiac device, history of valvular or congenital heart disease) or noncardiac risk factors (intravenous drug use, indwelling intravenous lines, immunosuppression, or a recent dental or surgical procedure).

¶ Low risk/low suspicion for IE: for example, patient with fever and previously known cardiac murmur and no other stigmata of IE.

Δ High risk/high suspicion for IE: for example, *S. aureus* bacteremia, new murmur, prior IE, congenital heart disease. Patients with prosthetic heart valve or intracardiac device are also high risk; the approach to diagnosis of IE in these circumstances is discussed further separately (refer to the UpToDate topics on prosthetic valve endocarditis and cardiac device infections).

◇ High-risk clinical features include new atrioventricular block (prolonged PR interval), persistent fever despite appropriate antimicrobial therapy, and *Staphylococcus aureus* bacteremia; high-risk echocardiographic features include large or mobile vegetations, valvular insufficiency, suggestion of paravalvular extension, or ventricular dysfunction.

§ Patients with high suspicion for paravalvular complications (such as prolonged PR interval) and indeterminate or negative TEE may warrant additional imaging such as cardiac computed tomography; refer to text for further discussion.

Modified from: Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A scientific statement for healthcare professionals from the American Heart Association. Circulation 2015; 132:1435.

Graphic 106519 Version 2.0

Features of selected antimicrobials used for outpatient parenteral antibiotic therapy

Anti-infective	Oral bioavailability (percent)*	Doses per day¶	Infusion time	Delivery device[Δ]	Monitor	
					CBC-diff	i
Amikacin	NA	1 to 3	30 to 60 minutes depending on dose	Grav, Elas	Once weekly	T w
Ampicillin	50	4 to 6	3 to 5 minutes push or 10 to 15 minutes infusion	Grav, EID, IVP	Once weekly	C w
Ampicillin-sulbactam	NA	3 to 4	10 to 15 minutes push or 15 to 30 minutes infusion	Grav, EID, Elas, IVP	Once weekly	C w
Azithromycin	28 to 52	1	60 minutes	Grav	Once weekly	N r r
Aztreonam	NA	2 to 4	3 to 5 minutes push or 20 to 60 minutes infusion	Grav, EID, Elas, IVP	Once weekly	C w
Cefazolin	NA	3 to 4	3 to 5 minutes push or 30 to 60 minutes infusion	Grav, Elas, IVP	Once weekly	C w

Cefepime	NA	2 to 3	5 minutes push or 30 minutes infusion	Grav, Elas, IVP	Once weekly	C w
Cefoxitin	NA	3 to 4	3 to 5 minutes push or 20 to 30 minutes infusion	Grav, Elas, IVP	Once weekly	C w
Ceftaroline	NA	2 to 3	5 minutes push or 5 to 60 minutes	Grav, IVP	Once weekly	C w
Ceftazidime	NA	3	3 to 5 minutes push or 15 to 30 minutes infusion	Grav, Elas, IVP	Once weekly	C w
Ceftazidime-avibactam	NA	3	120 minutes	Grav, EID	Once weekly	C w
Ceftolozane-tazobactam	NA	3	60 minutes	Grav, EID	Once weekly	C w
Ceftriaxone	NA	1 to 2	1 to 4 minutes push or 30 minutes infusion	Grav, Elas, IVP	Once weekly	C w
Ciprofloxacin	50 to 85	2 to 3	60 minutes	Grav, Elas	Not required routinely	N r r
Clindamycin	90	3 to 4	10 to 60 minutes (not to exceed 30 mg/minute)	Grav, Elas	Once weekly	C w

Colistin	NA	2 to 4	3 to 5 minutes IVP; 30 minutes for infusion	Grav, IVP	Once weekly	T w
Daptomycin	NA	1	2 minutes push or 30 minutes infusion	Grav, Elas, IVP	Once weekly	C w
Dalbavancin	NA	Once per week	30 minutes	Grav	Not required routinely	N r r
Ertapenem	NA	1	30 minutes	Grav, Elas	Once weekly	C w
Gentamicin	NA	1 to 3	30 to 120 minutes depending on dose	Grav, EID, Elas	Once weekly	T w
Imipenem	NA	3 to 4	20 to 60 minutes depending on dose	Grav	Once weekly	C w
Levofloxacin	90	1	60 to 90 minutes	Grav	Not required	N r

			depending on dose		routinely	r
Linezolid	100	2	30 to 120 minutes	Grav, EID	Once weekly	N r r
Meropenem	NA	3 to 4	30 minutes	Grav, Elas	Once weekly	O w
Metronidazole	100	2 to 4	30 to 60 minutes	Grav, EID, Elas	Once weekly	N r r
Nafcillin	NA	4 to 6	30 to 60 minutes	Grav, EID	Once weekly	O w
Oritavancin	NA	Once	180 minutes	Grav	Not required routinely	N r r

Oxacillin	NA	4 to 6	10 to 30 minutes	Grav, Elas	Once weekly	C w
Penicillin G	25 to 73	4 to 6	15 to 30 minutes	Grav, EID	Once weekly	C w
Piperacillin-tazobactam	NA	3 to 4	30 to 240 minutes (extended infusion)	Grav, EID	Once weekly	C w
Polymyxin B	NA	1	60 to 90 minutes	Grav	Once weekly	T w
Rifampin	70 to 90	1 to 3	30 minutes	Grav	Once weekly	C w
Tedizolid	91	1	60 minutes	Grav	Once weekly	N r r
Telavancin	NA	1	60 minutes	Grav	Once weekly	T w

Tigecycline	NA	2	30 to 60 minutes	Grav	Once weekly	C w
Tobramycin	NA	1 to 3	30 to 120 minutes depending on dose	Grav, EID, Elas	Once weekly	T w
Trimethoprim/sulfamethoxazole	85	2 to 4	60 to 90 minutes	Grav	Once weekly	C w
Vancomycin	NA	1 to 2	60 to 120 minutes depending on dose	Grav, EID, Elas	Once weekly	C w

Use of the information presented in this table should be tailored to individual patient circumstances.

CBC: complete blood cell count; BMP: basic metabolic profile; K: potassium; Cr: creatinine; BUN: blood urea nitrogen; ALT: alanine transaminase; AST: aspartate transaminase; ALK: alkaline phosphatase; Tbil: total bilirubin; ADR: adverse drug reaction; NA: not applicable/no oral formulation; Grav: gravity; Elas: elastomeric; EID: electronic infusion device; IVP: intravenous push; po: by mouth; CK: creatine kinase; ULN: upper limit of normal; IV: intravenous; QTc: corrected QT-interval; LFT: liver function tests.

* Bioavailability: changing to oral medications when possible is part of good antimicrobial stewardship. Clinicians should consider the full clinical situation, including the appropriateness of oral antimicrobials for the condition being treated. Potential for interaction with foods and other medications as well as concomitant illnesses and the potential for impaired gut absorption must also be considered.

¶ Doses per day: assumes normal renal and hepatic function. More than 2 to 3 doses per day may be impractical for pediatric outpatient parenteral antimicrobial therapy (OPAT) that requires adult infusion assistance for every dose. Dosing more frequently than once daily is typically not practical for patients who receive care in infusion centers.

Δ Devices: very limited published information on the use of these devices in OPAT. Individual infusion pharmacies have variable policies and device availability. Not all drugs are compatible with all delivery options. EIDs can be programmed to automatically deliver multiple doses per day but they require that the patient be connected to a small device virtually continuously and are not covered by all insurance carriers. Elas are very simple to use but also are not covered by all insurance carriers. Gravity delivery (infusion without a pump, using a roller clamp) is less expensive but also less convenient due to longer infusion times and complexity for patients to learn. Depending upon care setting, use of a traditional infusion pump may be selected in lieu of gravity for rate control. IVP is very convenient because of rapid infusion time.

◇ These are recommendations based on frequency and seriousness of reported adverse events. The monitoring plan for an individual patient may be different based on the comorbid conditions and anticipated duration of OPAT. For instance, for shorter courses of linezolid, ceftriaxone, or clindamycin, it may not be necessary to monitor LFTs and/or renal function. Alternatively, for longer courses of fluoroquinolones, weekly lab monitoring may be appropriate. For patients with normal baseline labs, less intense monitoring may be appropriate.

§ Risk of Torsades de Pointes (TdP): known, known to prolong QTc interval and cause TdP even when taken as recommended; possible, can cause QTc prolongation but not known to cause TdP when taken as recommended; conditional, associated with TdP but only under certain conditions (ie, excessive dose, with hypokalemia, with other interacting drugs) or by creating conditions that induce TdP (inhibiting metabolism of QTc prolonging drugs); special, high risk of TdP in patients with congenital long QT syndromes due to other actions. Source for TdP risk[1].

¥ Aminoglycoside monitoring: monitor concentrations minimum weekly. Goal aminoglycoside trough values differ according to the drug, infection, and dosing strategy.

‡ For medications with limited stability, home delivery more frequently than once weekly will be required. Some drugs may be reconstituted in the home using a use-activated container, if available.

Reference:

1. Woosley RL, Heise CW, Gallo T, et al. QTdrugs List. Oro Valley, AZ: AZCERT, Inc. Available at: https://www.crediblemeds.org.

Graphic 121957 Version 10.0

Proposed alternative antibiotic regimens for completing treatment of right-sided endocarditis due to *Staphylococcus aureus* among patients who are unabl to complete standard parenteral therapy

Regimen	Comments
Dicloxacillin 1 g orally every 6 hours **plus** Rifampin 600 mg orally every 12 hours	▪ For treatment of MSSA infection only. ▪ Rifampin reduces methadone levels and concurrent use may require methadone dose adjustments.[1] In patients on methadone, consider alternative regimens; do not prioritize rifampin over methadone. ▪ Regimen studied in POET trial.[2]
Linezolid 600 mg orally every 12 hours **plus** Rifampin* 600 mg orally every 12 hours	▪ Rifampin reduces methadone levels and concurrent use may require methadone dose adjustments.[1] In patients on methadone, consider alternative regimens, including linezolid monotherapy; do not prioritize rifampin over methadone. ▪ For linezolid administration longer than one to two weeks, laboratory monitoring is warranted.¶ ▪ Risk of serotonin syndrome in patients receiving linezolid with other serotonergic medications (eg, tramadol, SSRI, MAOI). Consider alternative regimens when possible.¶ ▪ Regimen studied in POET trial.[2]
Ciprofloxacin 750 mg orally every 12 hours **plus** Rifampin 300 mg orally every 8 hours	▪ For use only if ciprofloxacin susceptibility is confirmed; if susceptibility data are not available, the regimen should not be used for treatment of MRSA infection. ▪ Rifampin reduces methadone levels and concurrent use may require methadone dose adjustments.[1] In patients on methadone, consider alternative regimens; do not prioritize rifampin over methadone. ▪ Fluoroquinolones may cause significant QT interval prolongation and torsades de pointes; risk is increased with concurrent methadone and other QT-prolonging medications; obtain baseline ECG and monitor. ▪ Combination studied in a small prospective cohort.[3]
Trimethoprim-sulfamethoxazole 2 double-strength tablets (160 mg/800 mg per tablet) orally every 12 hours	▪ Kidney function monitoring may be warranted. ▪ No randomized trial data for treatment of IE are available.
Doxycycline 100 mg orally every 12 hours	▪ May be considered for patients who are intolerant of other antibiotic regimens. ▪ Risk for photosensitivity. ▪ No randomized trial data for treatment of IE are available.

Dalbavancin 1000 mg IV loading dose, then 500 mg IV once weekly **or** 1500 mg IV loading dose, then 1000 mg IV once every other week	▪ May be considered for patients in whom oral absorption of medications is limited or there are other contraindications to oral antibiotics. ▪ No randomized trial data for treatment of IE are available.
Oritavancin 1200 mg IV weekly	▪ May be considered for patients in whom oral absorption of medications is limited or there are other contraindications to oral antibiotics. ▪ No randomized trial data for treatment of IE are available.

Dosing in this table is intended for adult patients with normal organ (ie, kidney, liver) function. For dose adjustments, refer to the Lexicomp drug monographs included with UpToDate. Refer to UpToDate topic on right-sided endocarditis for guidance regarding duration of treatment.

MSSA: methicillin-susceptible *S. aureus*; POET: Partial Oral Versus Intravenous Antibiotic Treatment trial; SSRI: selective serotonin reuptake inhibitor; MAOI: monoamine oxidase inhibitor; ECG: electrocardiogram; MRSA: methicillin-resistant *S. aureus*; IE: infectious endocarditis; IV: intravenously.

* In areas where fusidic acid is available, fusidic acid (750 mg orally every 12 hours) may be used instead of rifampin.

¶ Refer to the UpToDate topic on linezolid for further discussion.

References:

1. *Badhan RKS, Gittins R, Al Zabit D. The optimization of methadone dosing whilst treating with rifampicin: A pharmacokinetic modeling study. Drug Alcohol Depend 2019; 200:168.*
2. *Iversen K, Ihlemann N, Gill SU, et al. Partial oral versus intravenous antibiotic treatment of endocarditis. N Engl J Med 2019; 380:415.*
3. *Heldman AW, Hartert TV, Ray SC, et al. Oral antibiotic treatment of right-sided staphylococcal endocarditis in injection drug users: prospective randomized comparison with parenteral therapy. Am J Med 1996; 101:68.*

Adapted from: Baddour LM, Weimer MB, Wurcel AG, et al. Management of infective endocarditis in people who inject drugs: A scientific statement from the American Heart Association. Circulation 2022; 146:e187.

Graphic 140428 Version 2.0