INTRODUCTION — Insertion of a central venous catheter (CVC) in a human was first reported by Werner Forssman, a surgical intern, who described canulating his own right atrium via the cephalic vein in 1929. A technique that facilitates catheter placement into lumens and body cavities was subsequently introduced by Sven-Ivar Seldinger in 1953. Insertion of a CVC using the Seldinger technique has revolutionized medicine by allowing the central venous system to be accessed safely and easily.

CVCs are now common among critically ill patients. In the United States, over 15 million catheter days/year are recorded in the intensive care unit alone. Multi-lumen CVCs have become ubiquitous in the intensive care unit (ICU). New catheter designs, standardization of insertion techniques and subsequent central line management have reduced complication rates.

Mechanical complications associated with CVC placement and removal, and strategies to prevent these complications, are discussed here. The placement of central venous catheters and infectious and thrombotic complications are discussed separately. (See “Overview of central venous access”, section on ‘Indications’ and “Diagnosis of intravascular catheter-related infections” and “Catheter-related upper extremity venous thrombosis” and “Epidemiology, pathogenesis, and microbiology of intravascular catheter infections”.)

COMPLICATIONS — Numerous complications are associated with central venous catheter (CVC) placement. The most common are listed in the table.

Published rates of cannulation success and complications vary according to the anatomic site and operator experience. As an example, one review described an overall complication rate of 15 percent, while an observational cohort study of 385 consecutive CVC attempts over a six month period found that mechanical complications occurred in 33 percent of attempts. Complications included failure to place the catheter (22 percent), arterial puncture (5 percent), catheter malposition (4 percent), pneumothorax (1 percent), subcutaneous hematoma (1 percent), hemothorax (less than 1 percent), and asystolic cardiac arrest (less than 1 percent).

Most mechanical complications (e.g., pneumothorax) are detected at the time of catheter insertion. Mechanical complications at the time of catheter insertion are most common after attempted insertion in the subclavian (SC) vein. Despite this, SC insertion may be preferred in experienced hands since the rate of mechanical complications is largely operator dependent. Infectious and thrombotic complications usually occur later.

Catheter-related infection — Infection is a common complication of indwelling CVCs. The diagnosis, microbiology, and treatment of catheter-related infection is discussed in detail elsewhere. (See “Epidemiology, pathogenesis, and microbiology of intravascular catheter infections” and “Diagnosis of intravascular catheter-related infections” and “Treatment of intravascular catheter-related infections”.)

Catheter-induced thrombosis — Thrombosis is another common complication of indwelling central venous catheters. The diagnosis and treatment of upper extremity catheter-related thrombosis, and for patients with femoral catheters, lower extremity deep vein thrombosis is discussed elsewhere. (See “Catheter-related upper extremity venous thrombosis” and “Approach to the diagnosis and therapy of lower extremity deep vein thrombosis” and “Diagnosis of suspected deep vein thrombosis of the lower extremity” and “Overview of the treatment of lower extremity deep vein thrombosis (DVT)”.)

Arrhythmia — Ventricular dysrhythmias and bundle branch block are well recognized complications during central venous access procedures. Periprocedural arrhythmias are universally the result of guidewire or catheter placement into the right heart. Limiting the depth of guidewire insertion to less than 16 cm avoids this complication. Catheter migration up to 3 cm is common with patient movement and repositioning may cause delayed symptoms.

Vascular injury — Arterial puncture is noted in 3 to 15 percent of central venous access procedures. Immediate recognition and management of arterial puncture usually prevents subsequent complications. Once an arterial stick is suspected, the needle is immediately withdrawn and direct but nonocclusive pressure applied to the site continuously for...
15 minutes to prevent hematoma formation. Unrecognized arterial cannulation with subsequent dilation and catheter placement is associated with life-threatening hemorrhage and neurologic complications [9]. Late recognition of arterial cannulation increases the risk of hemorrhagic complications that may require surgical intervention. Measuring intraluminal pressure with a transducer prior to dilation aids in recognizing arterial puncture if location is unclear [4,10].

**Pulmonary complications** — Free aspiration of air into the syringe may occur with pleural puncture but is often the result of incomplete seal of the syringe and needle. Suspected pleural puncture should prompt close attention for signs or symptoms of cardiopulmonary distress due to pneumothorax. Pleural puncture can quickly evolve into tension pneumothorax with hemodynamic collapse, especially in patients receiving positive pressure ventilation. The need for emergency intravenous access may require continued attempts at the same or alternative locations. Avoid contralateral supradiaphragmatic access attempts in close succession due to the potential for bilateral pneumothoraces. Hemothorax, hydrothorax, and chylothorax occur in a small fraction of torso cannulations.

**Venous air embolism** — Central venous access procedures create a risk for venous air embolism [11]. Venous air embolism is a serious and poorly recognized complication that can occur at the time of CVC insertion, while the catheter is in place, or at the time of catheter removal [12-14]. Air is easily entrained into the vascular space when a needle or catheter is left open to the atmosphere. The effect of venous air embolization depends upon the rate and volume of air introduced into the venous circulation. Although the minimum volume of air that is lethal to humans has not been established, fatal doses of air measuring as little as 200 mL have been reported [15,16]. The lethal dose for humans has been theorized to be 3 to 5 mL/kg [17]. Upright positioning, hypovolemia, spontaneous inhalation during instrumentation, and inattention to catheter seals increase the risk for entraining air. Affected patients can suffer cardiovascular and pulmonary symptoms including tachyarrhythmias, chest pain, cardiovascular collapse, dyspnea, coughing, hypoxemia, and respiratory distress. Symptoms such as these in association with central line insertion or manipulation are highly suspicious for venous air embolism. Left lateral decubitus and Trendelenburg positioning to trap the air in the right ventricular apex is often recommended but has not been rigorously studied. Supportive measures including fluid resuscitation and adrenergic agents should be used, as needed. One hundred percent inspired oxygen may speed air resorption. (see "Air embolism")

**Bleeding** — Serious blood loss associated with CVC placement is uncommon. Hematomas that form in the neck after inadvertent cannulation of the carotid artery may obstruct the airway and be life-threatening [18]. It remains uncertain when and if coagulation defects should be corrected prior to nonemergent CVC placement. (See "Overview of central venous access", section on 'Coagulopathy and/or thrombocytopenia'.)

**PREVENTING COMPLICATIONS** — Central venous catheterization should be performed with the patient carefully positioned, using sterile conditions and topical analgesia. An experienced operator, ultrasound guidance, and nursing supervision are preferable, if available.

**Infection** — In a large, prospective cohort study, the following five steps (sometimes called the Pronovost checklist) reduced CVC-related bloodstream infections when instituted together [19]. (See "Prevention of intravascular catheter-related infections", section on 'Catheter teams and use of checklist'.)

- **Hand hygiene** — An alcohol sanitizer or antimicrobial soap should be used immediately prior to donning sterile gloves.
- **Chlorhexidine** skin antisepsis — A chlorhexidine solution should be applied by back and forth rubbing for at least 30 seconds. The solution should be allowed to air dry for at least two minutes and should not be wiped or blotted. Chlorhexidine appears preferable to a povidone-iodine solution [20].
- **Maximal barrier precautions** — All operators should wear a mask, cap, sterile gown, and sterile gloves. In addition, a sterile full-body drape should be placed on the patient.
- **Avoid insertion into the femoral vein** — Insertion of a CVC into the subclavian vein is associated with the lowest risk of infection compared with insertion into the internal jugular or femoral vein (1.3 per 1000 catheter days compared with 2.7 per catheter days) [21].
- **Remove unnecessary CVCs** — A daily review of CVC necessity should be performed, with prompt removal of unnecessary CVCs.

Additional interventions that may reduce CVC-associated bloodstream infections include antibiotic impregnated CVCs, nursing supervision during insertion, and increased attention to ongoing catheter care after insertion:
Antibiotic impregnated CVCs – A meta-analysis of 11 randomized, controlled trials (2603 catheters) found that CVCs impregnated with chlorhexidine-silver sulfadiazine were less likely to cause bloodstream infection (odds ratio 0.56, 95% CI, 0.37-0.84) [22]. However, this finding has not been universal [23,24].

Nursing supervision – In a prospective cohort study, the patient's nurse used a check list defining best-practice to monitor the procedure, and was empowered to stop the procedure if best-practice was violated [25]. Over a six-month period, the CVC-related bloodstream infection rate decreased from 11 to zero infections per 1000 catheter days.

Vigilant catheter care – A prospective audit of post-insertion catheter care was conducted over a 28-day period (721 catheter-days) [26]. There were 323 breaches in catheter care and four catheter-related bloodstream infections (5.5 infections per 1000 catheter-days). The major breaches included dressings that were not intact (158 breaches per 1000 catheter-days) and incorrectly placed caps (156 breaches per 1000 catheter-days). This study suggests that there is substantial opportunity to better standardize and improve the maintenance of CVCs. Such care should also target earlier recognition of potentially infected catheter sites.

Mechanical problems — Factors associated with fewer mechanical complications (eg, bleeding, blood vessel injury, pneumothorax, failure to cannulate the vein) include increased operator experience, fewer insertion attempts, and ultrasound guidance.

Appropriate operator experience — It is unknown how many CVCs should be inserted by an operator each year to maintain his or her skills. However, experience is clearly important. In one prospective cohort study, operators who had previously inserted more than 50 CVCs were more likely to be successful at inserting subsequent CVCs, with fewer complications.

Limiting attempts — The number of attempts is also related to the likelihood of a mechanical complication. In a prospective cohort study, the incidence of mechanical complications was sixfold higher when insertion was attempted more than three times, compared with successful insertion on the first attempt. It is, therefore, reasonable for an operator to seek assistance if a CVC cannot be successfully inserted after three attempts [27].

Ultrasound guidance — Real-time two-dimensional ultrasound guidance is superior to blind, landmark-guided techniques, particularly when used during CVC insertion into the internal and subclavian veins in terms of reducing cannulation failure, arterial puncture, hematoma, and hemothorax. The use of real-time ultrasound to guide cannulation of the femoral vein is less well studied. However, the limited data suggest that real-time ultrasound may increase femoral vein cannulation success but does not decrease the risk of arterial puncture and hematoma [29]. (See "Overview of central venous access", section on 'Use of ultrasound' and "Principles of ultrasound-guided venous access".)

Confirm catheter positioning — A newly placed CVC is frequently used before it has been confirmed by a chest radiograph that it is correctly positioned. This is most common in the operating room and in emergent situations. Failure to confirm the position can be problematic since clinician judgment does not consistently predict catheter malposition or other mechanical complications, especially with less experienced operators [30].

A promising technique has been developed that uses a right atrial electrocardiogram (ECG) to confirm that a CVC has been accurately inserted. A randomized trial that compared CVC insertion using this technique with CVC insertion without it found that use of the technique improved the rate at which CVCs were correctly positioned (96 versus 76 percent) [31].

Preventing air embolism — Venous air embolism is a serious and poorly recognized complication of central venous catheterization. Venous air embolism can occur at the time of CVC insertion, while the catheter is in place, or at the time of catheter removal [12–14]. (see Venous air embolism above)

Trendelenburg positioning, Valsalva maneuver, prompt needle/catheter occlusion, and tight intravenous connections help to avoid this complication during CVC placement [11,32]. Prior to CVC removal, patients should be placed in the supine position. The CVC should be removed during exhalation, when intrathoracic pressure is greater than atmospheric pressure. Firm pressure should be applied for at least one minute following removal.

SUMMARY AND RECOMMENDATIONS
● We recommend that a protocol be used in all patients who require a CVC (Grade 1B). One protocol proven to reduce CVC-associated blood stream infections includes hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions, avoiding femoral vein insertion, and prompt removal of unnecessary catheters. (See ‘Infection’ above.)

● Increased operator experience, fewer insertion attempts, and ultrasound guidance are associated with fewer mechanical complications. (See ‘Mechanical problems’ above.)

● CVCs can be inserted into the internal jugular, external jugular, subclavian, femoral, or brachial vein (table 2). The optimal site is determined by operator preference, operator experience, patient anatomy, and clinical circumstances. (See “Overview of central venous access”, section on ‘Site selection’.)

● Numerous complications are associated with CVC placement (table 1). Mechanical complications (eg, pneumothorax) tend to be detected at the time of catheter insertion, whereas infectious and thrombotic complications usually occur later. Venous air embolism and bleeding are the complications most likely to occur when the CVC is removed. (See ‘Complications’ above and ‘Preventing air embolism’ above.)

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REFERENCES

Complications of central venous catheterization

<table>
<thead>
<tr>
<th>Immediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Arterial puncture</td>
</tr>
<tr>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Air embolism</td>
</tr>
<tr>
<td>Thoracic duct injury (with left SC or left IJ approach)</td>
</tr>
<tr>
<td>Catheter malposition</td>
</tr>
<tr>
<td>Pneumothorax or hemothorax</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Venous thrombosis, pulmonary emboli</td>
</tr>
<tr>
<td>Catheter migration</td>
</tr>
<tr>
<td>Catheter embolization</td>
</tr>
<tr>
<td>Myocardial perforation</td>
</tr>
<tr>
<td>Nerve injury</td>
</tr>
</tbody>
</table>
## Advantages and disadvantages of central vein approaches

<table>
<thead>
<tr>
<th>Approach</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>External jugular</td>
<td>Superficial vessel that is often visible</td>
<td>Not ideal for prolonged venous access</td>
</tr>
<tr>
<td></td>
<td>Coagulopathy not prohibitive</td>
<td>Poor landmarks in obese patients</td>
</tr>
<tr>
<td></td>
<td>Minimal risk of pneumothorax (especially with US guidance)</td>
<td>High rate of malposition</td>
</tr>
<tr>
<td></td>
<td>Head-of-table access</td>
<td>Catheter may be difficult to thread</td>
</tr>
<tr>
<td></td>
<td>Prominent in elderly patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rapid venous access</td>
<td></td>
</tr>
<tr>
<td>Internal jugular</td>
<td>Minimal risk of pneumothorax (especially with US guidance)</td>
<td>Not ideal for prolonged access</td>
</tr>
<tr>
<td></td>
<td>Head-of-table access</td>
<td>Risk of carotid artery puncture</td>
</tr>
<tr>
<td></td>
<td>Procedure-related bleeding amenable to direct pressure</td>
<td>Uncomfortable</td>
</tr>
<tr>
<td></td>
<td>Lower failure rate with novice operator</td>
<td>Dressings and catheter difficult to maintain</td>
</tr>
<tr>
<td></td>
<td>Excellent target using US guidance</td>
<td>Thoracic duct injury possible on left</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor landmarks in obese/edematous patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potential access and maintenance issues with concomitant tracheostomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vein prone to collapse with hypovolemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficult access during emergencies when airway control being established</td>
</tr>
<tr>
<td>Subclavian</td>
<td>Easier to maintain dressings</td>
<td>Increased risk of pneumothorax</td>
</tr>
<tr>
<td></td>
<td>More comfortable for patient</td>
<td>Procedure-related bleeding less amenable to direct pressure</td>
</tr>
<tr>
<td></td>
<td>Better landmarks in obese patients</td>
<td>Decreased success rate with inexperience</td>
</tr>
<tr>
<td></td>
<td>Accessible when airway control is being established</td>
<td>Longer path from skin to vessel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Catheter malposition more common (especially right SCV)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interference with chest compressions</td>
</tr>
<tr>
<td>Femoral</td>
<td>Rapid access with high success rate</td>
<td>Delayed circulation of drugs during CPR</td>
</tr>
<tr>
<td></td>
<td>Does not interfere with CPR</td>
<td>Prevents patient mobilization</td>
</tr>
<tr>
<td></td>
<td>Does not interfere with intubation</td>
<td>Difficult to keep site sterile</td>
</tr>
<tr>
<td></td>
<td>No risk of pneumothorax</td>
<td>Difficult for PA catheter insertion</td>
</tr>
<tr>
<td></td>
<td>Trendelenburg position not necessary during insertion</td>
<td>Increased risk of iliofemoral thrombosis</td>
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</table>

US: ultrasound; SCV: subclavian vein; CPR: cardiopulmonary resuscitation; PA: pulmonary artery.
INTRODUCTION — Central venous catheter infections are common. In the United States, approximately 80,000 central venous catheter–related bloodstream infections occur in intensive care units each year [1,2]. In general, treatment of systemic intravenous catheter–related infection requires determination regarding catheter management (eg, salvage, exchange, or removal) and antibiotic therapy (eg, selection of empiric therapy with subsequent tailoring to culture and sensitivity data).

The treatment of intravascular catheter-related infections will be reviewed here. Issues related to hemodialysis catheters are discussed separately, as are issues related to prevention and diagnosis of catheter-related infections. (See "Tunneled, cuffed hemodialysis catheter-related bacteremia" and "Prevention of intravascular catheter-related infections" and "Diagnosis of intravascular catheter-related infections").

INDICATIONS FOR TREATMENT — The treatment guidelines discussed here apply to circumstances in which diagnostic criteria for catheter-related bloodstream infection (CRBSI) are met; these diagnostic criteria are discussed in detail separately (see "Diagnosis of intravascular catheter-related infections").

In general, systemic antibiotic therapy is NOT required in the following circumstances [1,3]:

- Positive catheter tip culture in the absence of clinical signs of infection
- Positive blood cultures obtained through a catheter with negative cultures through a peripheral vein
- Phlebitis in the absence of infection; the risk of CRBSI in this setting is very low [4-6]. (See "Superficial thrombophlebitis of the lower extremity").

CATHETER MANAGEMENT — In general, the first step for treatment of systemic intravenous catheter–related infection requires determination regarding catheter management (eg, salvage, exchange, or removal).

Removal — Following diagnosis of catheter-related infection, catheter removal is warranted in the following circumstances [1,7-11]:

- Severe sepsis
- Hemodynamic instability
- Endocarditis or evidence of metastatic infection
- Erythema or exudate due to suppurative thrombophlebitis
- Persistent bacteremia after 72 hours of antimicrobial therapy to which the organism is susceptible

The nature of the pathogen is also important for guiding decisions regarding catheter removal. Short-term catheters (indwelling <14 days) should be removed in the setting of catheter-related bloodstream infection (CRBSI) due to Staphylococcus aureus, enterococci, gram-negative bacilli, fungi, and mycobacteria. Long-term catheters (indwelling ≥14 days) should be removed in the setting of CRBSI due to S. aureus, Pseudomonas aeruginosa, fungi, or mycobacteria. Removal of long-term catheters can be a management challenge, particularly in the setting of surgically implantable intravascular devices. Therefore, it is important to establish true CRBSI. (See "Diagnosis of intravascular catheter-related infections").

In the setting of CRBSI due to organisms of relatively low virulence that are difficult to eradicate (eg, Bacillus spp, Micrococcus spp, or Propionibacteria), removal of both short- and long-term catheters is appropriate if blood culture contamination has been ruled out (eg, based on multiple positive culture results with at least one sample drawn from a peripheral vein) [12]. (See "Other organisms" below and "Diagnosis of intravascular catheter-related infections").

There is no evidence to support routine catheter exchange. In addition, catheter removal is not necessary for hemodynamically stable patients with unexplained fever in the absence of documented bloodstream infection and without endovascular prosthetic material (such as a prosthetic valve, pacemaker, or vascular graft) [3,13-15].
**Salvage** — Following diagnosis of catheter-related infection, catheter salvage may be attempted in the setting of uncomplicated CRBSI involving long-term catheters due to pathogens other than *S. aureus, P. aeruginosa*, fungi, or mycobacteria [1]. Salvage is also difficult in the setting of CRBSI due to organisms of relatively low virulence that are difficult to eradicate (eg, *Bacillus* spp, *Micrococcus* spp, or Propionibacteria). Catheter salvage in the setting of coagulase-negative staphylococcal infection does not influence resolution of bacteremia but may be a risk factor for recurrence (relative risk 6.6 in a retrospective series of 175 cases) [16].

If salvage is attempted, both systemic and antimicrobial lock therapy may be administered through the colonized catheter for the duration of therapy, depending upon the microorganism. The efficacy of antibiotic lock therapy remains uncertain and concerns have been raised about the emergence of antimicrobial resistance and fungal superinfection. The optimal antimicrobial dosing for lock therapy is also uncertain. Antibiotic lock therapy is not warranted for management of catheter infection for devices in place for <2 weeks; these are usually extraluminal infections [17].

Two sets of blood cultures should be obtained after 72 hours of appropriate antimicrobial therapy (for neonates, one set is acceptable); positive cultures should prompt catheter removal.

Catheter removal is not necessary for hemodynamically stable patients with unexplained fever in the absence of documented bloodstream infection and without endovascular prosthetic material (such as a prosthetic valve, pacemaker, or vascular graft) [3,13-15].

**Guidewire exchange** — For circumstances in which catheter removal is necessary for suspected catheter-related infection and the risk for mechanical complications or bleeding during catheter reinsertion is high, guidewire exchange of the catheter is acceptable (except in the setting of sepsis) [1,18]. However, most studies describing successful management of catheter infection via catheter exchange over a guidewire have been small, uncontrolled studies [19-23].

The benefit of antimicrobial impregnated catheters is uncertain. Many trials of antiseptic or antimicrobial-impregnated central venous catheters have reported a decreased incidence of catheter-related infections [24-26]. However, a randomized trial of 780 adult intensive care unit patients managed with chlorhexidine-coated or uncoated catheters failed to demonstrate a reduction in the rate of bloodstream infection [27]. Replacement of the catheter with an antimicrobial-impregnated catheter should be considered in settings where rates of CRBSIs exceed the National Healthcare Safety Network surveillance data threshold despite adherence to aseptic techniques (eg, >1.4 infections per 1000 catheter days) [28].

The tip of the removed catheter should be sent for culture; if the results are positive or if there is evidence of phlebitis, thrombosis, or purulence, the newly inserted catheter should be relocated to a new site [29].

**Children** — In general, indications for catheter removal and choice of empiric antimicrobial therapy for children with CRBSI are similar to those for adults [30-32]. In a prospective study of chronic venous access devices in over 1000 children with cancer, most episodes of CRBSI were caused by coagulase-negative staphylococci followed by *S. aureus* (34 and 25 percent of cases, respectively) [31].

Some pediatricians favor attempting treatment of bacterial CRBSI without catheter removal, given greater difficulty with vascular access among children than among adults. In such cases, both systemic and antimicrobial lock therapy may be warranted. (See 'Antibiotic lock therapy' below.)

The benefits of catheter removal must be weighed against the difficulty of obtaining alternative venous access. Several studies have reported successful CRBSI management among children without catheter removal; close monitoring is required, and the device should be removed in the event of clinical deterioration or recurrence of CRBSI [30,33,34].

Catheter removal is always necessary in the setting of fungemia. Treatment of catheter-associated fungemia without catheter removal has a low success rate and is associated with high mortality [35,36]. (See "Treatment of candidemia and invasive candidiasis in adults").

**ANTIBIOTIC THERAPY** — In general, empiric antibiotic therapy must be instituted before culture and susceptibility data are available. Subsequently therapy should be tailored to microbiology results as needed.

**Empiric therapy** — The initial choice of antibiotics for catheter-related blood stream infection (CRBSI) depends on the clinical circumstances, including the severity of illness, the risk factors for infection, and the likely pathogens associated with the specific intravascular device (table 1). In general, coagulase-negative staphylococci are the most common cause of catheter-related infection; most isolates are resistant to methicillin [37,38]. (See "Epidemiology, microbiology, and pathogenesis of coagulase-negative staphylococci").
Empiric therapy of CRBSI in healthcare settings should consist of vancomycin (table 1) [1]. In institutions with high rates of infection due to methicillin-resistant *S. aureus* (MRSA) isolates with vancomycin minimum inhibitory concentration (MIC) ≥2 mcg/mL, an alternative agent such as dalopamin should be used [39]. This is especially warranted in the setting of clinical failure on vancomycin in the absence of metastatic infection. Linezolid is not an appropriate agent for empiric therapy of CRBSI [40].

Additional agents with activity against coagulase-negative staphylococci and MRSA include dalopamin, linezolid, tedizolid, telavancin, dalbavancin, ortipavancin, ceftaroline, and quinupristin-dalfopristin. Clinical data regarding efficacy of these agents for treatment of CRBSI are limited. (See "Treatment of infections due to coagulase-negative staphylococci").

Addition of empiric coverage for gram-negative organisms depends on individual circumstances and the severity of disease. In the setting of suspected CRBSI among patients with neutropenia or sepsis, empiric antibiotic therapy for gram-negative bacilli (including *Pseudomonas*) is appropriate (table 1). Patients known to be colonized with drug-resistant organisms should receive empiric antibiotic therapy selected accordingly; therapy should be tailored depending on subsequent culture data.

Empiric therapy for suspected catheter-related candidemia should be administered for septic patients with the following risk factors (see "Treatment of candidemia and invasive candidiasis in adults" and "Candidemia in children: Treatment", section on 'Antifungal agents and dosing' and "Treatment of Candida infection in neonates"): 

- Total parenteral nutrition
- Prolonged use of broad-spectrum antibiotics
- Hematologic malignancy
- Bone marrow or solid organ transplant
- Femoral catheterization
- Colonization due to *Candida* species at multiple sites

Appropriate agents for empiric treatment include echinocandin or azole drugs. In children, many clinicians continue to use amphotericin B or lipid formulations of amphotericin, although the azoles and echinocandins appear to be safe in children. Fluconazol is appropriate for patients without azole exposure in the previous three months and in settings where the risk of *Candida krusei* or *Candida glabrata* is very low.

If catheter removal is not possible, antibiotics should be administered through the colonized catheter, although recurrent bacteremia is more likely if therapy is administered through a retained catheter than if the catheter is removed [41]. For multi-lumen catheters, administration of antibiotics may be rotated between lumens, although this practice has not been studied formally.

Intravenous administration of thrombolytic agents should not be used as an adjunctive treatment for catheter-related blood stream infection [42,43].

**Tailoring therapy** — Following initiation of empiric antibiotic therapy, therapy should be tailored to culture and susceptibility results as needed once data are available [1].

**Coagulase-negative Staphylococcus** — Coagulase-negative staphylococci are the most common cause of catheter-related infection. Interpreting blood cultures positive for coagulase-negative *Staphylococcus* can be challenging, since this organism is both the most common blood culture contaminant as well the most common cause of CRBSI. A high proportion of positive blood cultures performed on samples drawn from multiple sites (both peripherally and through the suspected catheter) is the best indicator for true CRBSI due to this organism [44,45]. (See "Diagnosis of intravascular catheter-related infections").

No randomized trials have established the optimal approach to management of CRBSI due to coagulase-negative *Staphylococcus*. Some experts favor treatment with antibiotics following catheter removal (five to seven days). However, such infections may resolve with removal of the catheter in the absence of antibiotic therapy. Therefore, in the absence of endovascular hardware, some experts favor forgoing antibiotic therapy unless fever and/or bacteremia persist after catheter withdrawal. Patients with endovascular hardware should have the catheter removed and more prolonged therapy is warranted. If infective endocarditis is excluded, three weeks of therapy is appropriate. If catheter salvage is necessary, antibiotic therapy is warranted (systemically as well as via antibiotic lock therapy [ALT] in some cases) for 10 to 14 days (table 1). (See Antibiotic lock therapy below.)
Most patients have a benign clinical course; rarely, severe infection with poor outcome occurs. This is especially true for infection due to *Staphylococcus lugdunensis*, an uncommon cause of catheter-related infection; however, it can cause endocarditis and metastatic infections similar to those caused by *S. aureus* [46]. (See “*Staphylococcus lugdunensis*”.)

**S. aureus** — In general, management of CRBSI due to *S. aureus* consists of catheter removal and systemic antibiotic therapy [1]. Following catheter removal, a new catheter may be placed if additional blood cultures demonstrate no growth at 72 hours.

Treatment with vancomycin should be initiated pending susceptibility data (table 1). Patients who received empiric vancomycin and are found to have CRBSI due to methicillin-susceptible *S. aureus* should be switched to nafcillin or oxacillin. No randomized trials have established the optimal duration of therapy for CRBSI due to *S. aureus*; the duration depends on the nature of the infection, as discussed below [8,47-52]. (See “Clinical approach to *Staphylococcus aureus* bacteremia in adults”.)

The frequency of infective endocarditis (IE) among patients with *S. aureus* bacteremia is 25 to 32 percent, and many cases are not suspected clinically [53-55]. Therefore, in general, transesophageal echocardiogram (TEE) should be pursued in the setting of *S. aureus* bacteremia to rule out IE; transthoracic echocardiography (TTE) is not sufficient for ruling out IE due to *S. aureus*. Possible exceptions are patients whose fever and bacteremia resolve within 72 hours following catheter removal who have no underlying cardiac predisposing conditions or clinical signs of endocarditis. Valvular vegetations and/or regurgitation may progress within the first week after onset of bacteremia; therefore, most favor performing TEE five to seven days after the onset of bacteremia [47,56]. Echocardiographic examination is not used routinely for infants and children with CRBSI who do not have other indicators of endocarditis [1] (see ‘Children’ above).

Hematogenous complications of *S. aureus* bacteremia (eg, endocarditis, with or without metastatic sites of infection) occur in 25 to 30 percent of cases [53-55]. Risk factors include community-acquired infection (suggesting longer duration of bacteremia), prosthetic intravascular device (eg, pacemaker or recently placed vascular graft), comorbid immunocompromising conditions (including AIDS, diabetes, renal failure, or immunosuppressive medication), valvular abnormality predisposing to endocarditis, dialysis dependence, suppurative thrombophlebitis, and delay in catheter removal [9,57].

Patients with hematogenous complications of *S. aureus* bacteremia should receive four to six weeks of antimicrobial therapy. Positive blood cultures 72 hours following initiation of appropriate antibiotic therapy and catheter removal are a useful predictor for hematogenous complications [9,53,57-59]. In the absence of hematogenous complications or risk factors, a shorter duration of therapy (≥14 days) is appropriate [1].

Patients with catheter tip culture positive for *S. aureus* in the setting of negative peripheral blood culture should be observed closely. However, some favor antibiotic therapy for seven days [1]. Additional blood cultures should be obtained to evaluate for clearance of bacteremia, together with close monitoring for signs of persistent infection.

Patients with catheter-drawn blood culture positive for *S. aureus* in the setting of negative peripheral blood culture should also be observed closely. Additional blood cultures should be obtained both peripherally and through the catheter. If both repeat cultures are positive, treatment for CRBSI is warranted. If only the catheter culture is positive, the optimal approach is uncertain. The device should best be removed if feasible; otherwise, some favor 14 days of systemic antibiotic therapy with repeat blood cultures, while others favor close clinical observation with repeat blood cultures. Clinical signs of infection should prompt catheter removal.

Salvage of CRBSI due to *S. aureus* using four weeks of antibiotic lock therapy combined with systemic therapy has a low success rate; most patients eventually relapse and require removal of the catheter [60-62]. This approach is appropriate only in the setting of major contraindications to catheter removal (eg, no alternative venous access, significant bleeding diathesis, quality of life issues). If possible, guidewire exchange should be performed. Some experts favor replacement using an antimicrobial impregnated catheter with an anti-infective intraluminal surface, though this approach is controversial [1]. (See ‘Guidewire exchange’ above.)

Studies have documented the benefit of infectious diseases consultation for patients with *S. aureus* bacteremia with a reduction in morbidity, relapses, and mortality [63,64].

Treatment for CRBSI due to *S. aureus* bacteremia is discussed further separately. (See “Clinical approach to *Staphylococcus aureus* bacteremia in adults” and “*Staphylococcus aureus* bacteremia in children: Management and outcome”.)
Enterococcus — In general, management of enterococcal CRBSI consists of catheter removal (if feasible) and systemic antibiotic therapy [1]. Catheter salvage should not be attempted in the setting of insertion site or pocket infection, suppurrative thrombophlebitis, sepsis, endocarditis, persistent bacteremia, or metastatic infection.

The antibiotic of choice for susceptible enterococci is ampicillin; vancomycin should be used if the pathogen is resistant to ampicillin (table 1). In cases of CRBSI due to ampicillin- and vancomycin-resistant enterococci, linezolid or daptomycin may be used, based on antibiotic susceptibility results. (See "Treatment of enterococcal infections", section on 'Bacteremia'.)

No randomized trials have established the role of combination antimicrobial therapy or the optimal duration of therapy for enterococcal CRBSI. Among patients with uncomplicated enterococcal CRBSI treated with combination therapy versus monotherapy, no significant differences in outcomes have been observed in several retrospective cohort studies [65,66]. In the setting of catheter salvage, one large series found that combination therapy with gentamicin and ampicillin was more effective than monotherapy [67].

The risk of infective endocarditis in the setting of enterococcal CRBSI is relatively low if infection is due to Enterococcus faecium. In a multicenter study involving over 200 cases of CRBSI due to vancomycin-resistant enterococci, definite endocarditis was demonstrated in 1.5 percent of cases [68]. The risk was considerably higher if infection was due to Enterococcus faecalis. Echocardiographic evaluation is warranted for patients with signs and symptoms of IE (eg, new murmur or embolic phenomena), persistent bacteremia, or the presence of a prosthetic valve or other endovascular foreign bodies [69,70]. (See "Treatment of enterococcal infections", section on 'Bacteremia' and "Antimicrobial therapy of native valve endocarditis", section on 'Enterococci'.)

Antibiotic therapy should be administered for 7 to 14 days if no evidence of endocarditis or metastatic infection is present [1]. This duration is appropriate in the setting of catheter removal as well as in the setting of catheter salvage together with both systemic and antibiotic lock therapy.

Gram-negative rods — In general, management of CRBSI due to gram-negative bacilli consists of catheter removal (if feasible) and systemic antibiotic therapy [1]. Catheter salvage should not be attempted in the setting of insertion site or pocket infection, suppurrative thrombophlebitis, sepsis, endocarditis, persistent bacteremia, or metastatic infection.

Empiric antibiotic therapy with activity against gram-negative organisms should be initiated (table 1). Critically ill patients with risk factors for multidrug-resistant (MDR) gram-negative infections (such as previous MDR gram-negative infection, critical illness, neutropenia, prior antibiotic therapy, or presence of a femoral catheter) should receive empiric therapy with a carbapenem; alternatively, some favor empiric therapy with two antimicrobial agents of different classes with gram-negative activity [71-74]. When culture and susceptibility data are available, the initial antibiotic regimen can be adjusted to a single agent for the remainder of the therapeutic course (usually 7 to 14 days) [75].

In patients with gram-negative bacillary CRBSI involving a long-term catheter and persistent bacteremia or severe sepsis despite systemic and antibiotic lock therapy, the device should be removed and an evaluation for metastatic infection should be pursued. Routine evaluation for IE is generally not necessary in patients with CRBSI due to gram-negative rods.

Candida — In general, management of CRBSI due to Candida species consists of catheter removal and systemic antibiotic therapy. This is discussed in further detail separately. (See "Treatment of candidemia and invasive candidiasis in adults" and "Treatment of Candida infection in neonates" and "Candidemia in children: Treatment".)

Other organisms — In general, confirmation of true bloodstream infection due to Corynebacterium, Bacillus, and Micrococcus requires at least two positive blood cultures obtained from different sites; isolation of these organisms from a single blood culture is not sufficient [1].

CRBSI due to Micrococcus and Bacillus species are difficult to eradicate unless the infected catheter is removed [76,77]. The antibiotic of choice for these organisms is vancomycin (table 1); duration of therapy must be tailored to clinical circumstances. (See 'Duration of therapy' below.)

Catheter colonization — In the setting of positive catheter-drawn blood cultures for coagulase-negative staphylococci or gram-negative bacilli and negative concurrent percutaneous blood cultures, an intraluminally colonized catheter may be present. As such, there may be an increased risk for subsequent CRBSI, especially if the device is left in place. In such circumstances, we favor following the patient closely and obtaining additional percutaneous blood cultures if the patient continues to exhibit clinical manifestations of CRBSI. However, some clinicians may favor removing the device or
exchanging it over a guide wire. Alternatively, antibiotic lock therapy (without systemic therapy) may be administered if removal is not feasible. (See 'Antibiotic lock therapy' below.)

**Duration of therapy** — The duration of antimicrobial therapy for CRBSI depends on the clinical circumstances. In general, for uncomplicated CRBSI with negative blood cultures following catheter removal or guidewire exchange and institution of appropriate antibiotic therapy, the duration of therapy is usually 10 to 14 days (day 1 is the first day on which negative blood cultures are obtained) \(^{[1]}\). The duration of therapy may be extended to four to six weeks in patients with recent prosthetic valve placement placed prosthetic valves, even if investigation fails to demonstrate evidence of IE.

Patients with persistent bacteremia >72 hours following catheter removal should generally receive treatment for at least four to six weeks. For patients with complications related to bacteremia (such as suppurative thrombophlebitis, endocarditis, osteomyelitis, metastatic infection), the duration of therapy should be tailored accordingly, depending on the nature of infection. (See related topics.)

Antibiotics can be discontinued in patients with suspected CRBSI if blood cultures are negative and no other source of infection can be identified.

**Antibiotic lock therapy** — The premise of ALT is to achieve sufficient therapeutic concentrations to kill microbes growing in a biofilm \(^{[78-83]}\). ALT may be a useful adjunctive therapy together with systemic antibiotic therapy for intraluminal infections due to coagulase-negative staphylococci or gram-negative organisms in the setting of CRBSI when the catheter cannot be removed \(^{[1,84-90]}\). ALT should not be used for extraluminal infections nor for management of infections due to *S. aureus*, *P. aeruginosa*, drug-resistant gram-negative bacilli, or *Candida*

ALT for the treatment of CRBSI is discussed in detail elsewhere. (See "Antibiotic lock therapy for treatment of catheter-related bloodstream infections");

**Therapy for children** — In general, the approach to treatment of CRBSI in children is as described for adults (table 1). If catheter removal is not feasible, antibiotic lock therapy should be used for catheter salvage; if antibiotic lock therapy is not feasible, systemic antibiotics should be administered through the colonized catheter. (See 'Children' above and 'Antibiotic lock therapy' above.)

Antifungal therapy should be initiated when yeast is isolated from a blood culture or when the suspicion of fungemia is high \(^{[34,91-93]}\). (See 'Empiric therapy' above and "Candidemia in children: Treatment", section on 'Antifungal agents and dosing'.)

Echocardiographic examination is not used routinely for infants and children with CRBSI who do not have other indicators of endocarditis \(^{[1]}\).

**FOLLOW-UP** — Patients with catheter-related bloodstream infection (CRBSI) must be monitored closely during and following therapy to detect relapses or signs of metastatic infection. Blood cultures should be drawn after treatment has been initiated to demonstrate clearance of bacteremia.

**Persistent bacteremia** — Repeatedly positive blood cultures and/or persistent symptoms 72 hours after catheter removal with appropriate antibiotic therapy should prompt evaluation for sequelae of CRBSI, including suppurative thrombophlebitis, endocarditis, and metastatic foci of infection. (See related topics.)

**LOCAL SITE INFECTIONS** — Surgically implanted tunneled catheters have different insertion and exit sites; the original insertion site is closed after creation of a tunnel and a separate exit site. In contrast, percutaneously inserted catheters have one site that serves as both the insertion and exit site. Up until six weeks following tunneled catheter placement, the insertion site and exit site may be considered contiguous; after healing has completed, they may be considered distinct.

**Insertion site infection** — Insertion site infection of tunneled catheters should prompt catheter removal; guidewire catheter exchange is not appropriate as it can lead to bacteremia and septic emboli. Cultures should be obtained, including culture of the exudate, blood cultures from a peripheral vein, and culture of the catheter tip.

Antimicrobial therapy for ≤7 days is sufficient if bloodstream infection is excluded on the basis of the clinical picture and negative blood cultures (table 1). (See 'Empiric therapy' above and 'Tailoring therapy' above.)

**Exit site infection** — In the setting of suspected exit site infection, site drainage cultures and blood cultures should be obtained. Uncomplicated exit site infections (eg, those without systemic signs of infection, positive blood cultures, or purulence) may be managed with topical antibiotic agents based on culture results (eg, mupirocinointment for *S. aureus* infection and *ketoconazole* or lotrimin ointment for *Candida* infection).
Exit site infections that do not resolve with these interventions and/or exit site infections accompanied by purulent drainage should prompt administration of systemic antibiotics for ≤7 days. Failure of systemic antibiotics should prompt immediate catheter removal (table 1). (See ‘Empiric therapy’ above and ‘Tailoring therapy’ above.)

Tunnel infection — A tunnel (or pocket) infection involves the region where a surgically implanted catheter runs beneath the skin. Clinical findings include erythema, tenderness, and induration overlying the subcutaneous tunnel tract (which extends for ≥2 cm from the exit site). However, signs of exit site infection may or may not be present, particularly in neutropenic patients (in such circumstances, patients may complain of pain in the absence of erythema or swelling). The above findings should prompt catheter removal; in some circumstances, incision and drainage may also be appropriate. Antibiotics should be administered for ≤7 days (table 1). (See ‘Empiric therapy’ above and ‘Tailoring therapy’ above.)

Thrombophlebitis — Thrombophlebitis in the absence of other signs of infection (purulence, temperature above 38°C) need not be treated with antimicrobial therapy; warm soaks and elevation of the extremity should be sufficient. Determination regarding catheter removal depends on clinical circumstances, including the catheter indication, duration, and feasibility of replacement. Superficial phlebitis and septic thrombophlebitis are discussed in detail separately. (See “Catheter-related upper extremity venous thrombosis” and “Superficial thrombophlebitis of the lower extremity” and “Suppurative (septic) thrombophlebitis”.)

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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 topics (see "Patient information: Central line infections (The Basics)"

SUMMARY AND RECOMMENDATIONS

● In general, for circumstances in which systemic intravenous catheter-related infection diagnostic criteria are met, treatment requires determination regarding catheter management (eg, removal, salvage, or exchange) and antibiotic therapy (eg, selection of empiric therapy with subsequent tailoring to culture and sensitivity data). (See ‘Indications for treatment’ above.)

● In general, systemic antibiotic therapy is NOT required in the following circumstances (see ‘Indications for treatment’ above):
  • Positive catheter tip culture in the absence of clinical signs of infection
  • Positive blood cultures obtained through a catheter with negative cultures through a peripheral vein
  • Phlebitis in the absence of infection

● Following diagnosis of catheter-related infection, catheter removal is appropriate in the setting of severe sepsis, hemodynamic instability, suppurative thrombophlebitis, endocarditis, or persistent bacteremia after 72 hours of antimicrobial therapy to which the organism is susceptible. (See ‘Removal’ above.)

● The type of pathogen is important for guiding decisions regarding catheter management. Long-term catheters (indwelling ≥14 days) should be removed in the setting of catheter-related bloodstream infection (CRBSI) due to Staphylococcus aureus, Pseudomonas aeruginosa, fungi, or mycobacteria. Organisms of relatively low virulence that are difficult to eradicate (eg, Bacillus spp, Micrococcus spp, or Propionibacteria) should also prompt catheter removal if blood culture contamination has been ruled out. (See ‘Removal’ above.)

● Catheter salvage may be attempted in the setting of uncomplicated CRBSI of long-term catheters due to pathogens other than those outlined above. For circumstances in which catheter removal is necessary and risk for complications during catheter reinsertion is high, guidewire exchange of the catheter may be appropriate. (See ‘Salvage’ above and ‘Guidewire exchange’ above.)

● Adjunctive antibiotic lock therapy in combination with systemic therapy for intraluminal infections due to coagulase-negative staphylococci can be a useful strategy for the treatment of CRBSI when the catheter cannot be removed. Antibiotic lock therapy should not be used for extraluminal infections nor for management of infections due to S.
aureus, P. aeruginosa, resistant gram-negative bacilli, or Candida. (See 'Antibiotic lock therapy' above and "Antibiotic lock therapy for treatment of catheter-related bloodstream infections".)

- Empiric antibiotic therapy for CRBSI in healthcare settings should include activity against methicillin-resistant S. aureus; vancomycin is a reasonable agent (table 1). Patients with neutropenia or sepsis should also receive empiric antibiotic therapy for gram-negative organisms (including Pseudomonas) (table 1). Patients known to be colonized with drug-resistant organisms should receive empiric antibiotic therapy selected accordingly; therapy should be tailored based on subsequent culture data. (See 'Empiric therapy' above.)

- Following initiation of empiric treatment, antibiotic therapy should be tailored to culture and susceptibility results as needed once data are available. (See 'Tailoring therapy' above.)

- In general, transesophageal echocardiogram (TEE) should be pursued in the setting of S. aureus bacteremia to rule out infective endocarditis (IE). Possible exceptions include patients whose fever and bacteremia resolve within 72 hours following catheter removal and have no underlying cardiac predisposing conditions or clinical signs of endocarditis. (See 'S. aureus' above.)

- In general, for uncomplicated CRBSI with negative blood cultures following catheter removal or guidewire exchange and institution of appropriate antibiotic therapy, the duration of therapy is 10 to 14 days (day 1 is the first day on which negative blood cultures are obtained). Patients with persistent bacteremia >72 hours following catheter removal should receive treatment for at least four to six weeks. For patients with complications related to bacteremia (such as suppurative thrombophlebitis, endocarditis, osteomyelitis, metastatic infection), the duration of therapy should be tailored accordingly, depending on the nature of infection. (See 'Duration of therapy' above.)

- Patients with CRBSI must be monitored closely during and following therapy to detect relapses or signs of metastatic infection. Blood cultures should be drawn after treatment has been initiated to demonstrate clearance of bacteremia. Repeatedly positive blood cultures and/or persistent symptoms 72 hours after catheter removal with appropriate antibiotic therapy should prompt evaluation for sequelae of CRBSI, including suppurative thrombophlebitis, endocarditis, and metastatic foci of infection. (See 'Follow-up' above.)

- Management of local site infections depends on the nature of the infection. (See 'Local site infections' above.)

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REFERENCES


Intravenous antimicrobial treatment of intravenous catheter-related bloodstream infection according to the specific pathogen isolated

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Preferred antimicrobial agent</th>
<th>Alternative antimicrobial agent</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-positive cocci</strong></td>
<td></td>
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<tr>
<td><em>Staphylococcus aureus</em></td>
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</tr>
<tr>
<td>Methicillin susceptible</td>
<td>Nafcillin or oxacillin*</td>
<td>Cefazolin or vancomycin</td>
<td>Strains of <em>S. aureus</em> with reduced susceptibility or resistance to vancomycin have been reported; strains resistant to linezolid and strains resistant to daptomycin have been reported</td>
</tr>
<tr>
<td>Methicillin resistant</td>
<td>Vancomycin</td>
<td>Daptomycin(^\alpha)</td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin susceptible</td>
<td>Nafcillin or oxacillin</td>
<td>First-generation cephalosporin or vancomycin(^\beta)</td>
<td>Vancomycin has dosing advantages over nafcillin and oxacillin, but the latter are preferred because of concerns about increasing vancomycin resistance</td>
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<tr>
<td>Methicillin resistant</td>
<td>Vancomycin</td>
<td>Daptomycin or linezolid(^\beta)</td>
<td>Strains resistant to linezolid have been reported</td>
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<tr>
<td><em>Enterococcus faecalis</em></td>
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<td></td>
</tr>
<tr>
<td>Ampicillin susceptible</td>
<td>Ampicillin (or penicillin) ± gentamicin</td>
<td>Vancomycin</td>
<td>Preliminary studies demonstrate efficacy of ampicillin and ceftriaxone is comparable to ampicillin and gentamicin for <em>E. faecalis</em> endocarditis(^{11})</td>
</tr>
<tr>
<td>Ampicillin resistant, vancomycin susceptible</td>
<td>Vancomycin ± gentamicin</td>
<td>Linezolid or daptomycin(^\dagger)</td>
<td>Telavancin is active against vancomycin-susceptible <em>E. faecalis</em> while quinupristin/dalfopristin is not effective against <em>E. faecalis</em></td>
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<tr>
<td>Ampicillin resistant</td>
<td>Linezolid or daptomycin(^\dagger)</td>
<td>Quinupristin/dalfopristin(^\dagger)</td>
<td>Susceptibility of vancomycin-</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
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<tr>
<td>vancomycin resistant</td>
<td></td>
<td></td>
<td>resistant enterococci isolates varies; quinupristin/dalfopristin is not effective against <em>E. faecalis</em></td>
</tr>
<tr>
<td><strong>Escherichia coli and Klebsiella species</strong></td>
<td></td>
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<tr>
<td><strong>ESBL negative</strong></td>
<td>Third-generation cephalosporin (eg, ceftriaxone)</td>
<td>Ciprofloxacin or aztreonam</td>
<td>Susceptibility of strains varies</td>
</tr>
<tr>
<td><strong>ESBL positive</strong></td>
<td>Carbapenem (eg, ertapenem, imipenem, meropenem, or doripenem)</td>
<td>Ciprofloxacin or newer beta-lactamase inhibitor combinations (ceftolozane-tazobactam(^2) or ceftazidime-avibactam(^3))</td>
<td>Susceptibility of strains varies</td>
</tr>
<tr>
<td><strong>Enterobacter species and Serratia marcescens</strong></td>
<td>Carbapenem (eg, ertapenem, imipenem, or meropenem)</td>
<td>Cefepime or ciprofloxacin</td>
<td>Susceptibility of strains varies</td>
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<tr>
<td><strong>Acinetobacter species</strong></td>
<td>Ampicillin/sulbactam or carbapenem (eg, imipenem or meropenem)</td>
<td>Polymyxins (polymyxin B/colistin) or tigecycline (often combination of agents needed for resistant isolates)</td>
<td>Susceptibility of strains varies</td>
</tr>
<tr>
<td><strong>Stenotrophomonas maltophilia</strong></td>
<td>TMP-SMZ</td>
<td>Ticarcillin-clavulanate</td>
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<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td>Fourth-generation cephalosporin (ceftazidime) or piperacillin-tazobactam, with or without aminoglycoside (tobramycin)</td>
<td>Carbapenem (imipenem or meropenem), ciprofloxacin, or aztreonam</td>
<td>Susceptibility of strains varies</td>
</tr>
<tr>
<td><strong>Burkholderia cepacia</strong></td>
<td>TMP-SMZ</td>
<td>Carbapenem (imipenem or meropenem)</td>
<td>Other species, such as <em>B. acidovorans and B. pickiei</em>, may be susceptible to same antimicrobial agents</td>
</tr>
<tr>
<td><strong>Uncommon pathogens</strong></td>
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<tr>
<td><strong>Corynebacterium jeikeium</strong> (group JK)</td>
<td>Vancomycin</td>
<td>Linezolid (based on in vitro activity)</td>
<td>Check susceptibilities for other corynebacteria</td>
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<tr>
<td><strong>Chryseobacterium (Flavobacterium) species</strong></td>
<td>Levofoxacin</td>
<td>TMP-SMZ, carbapenem (imipenem or meropenem)</td>
<td>Based on in vitro activity</td>
</tr>
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<td><strong>Ochrobacterium anthropi</strong></td>
<td>TMP-SMZ or ciprofloxacin</td>
<td>Imipenem, meropenem, ertapenem, or doripenem plus</td>
<td>--</td>
</tr>
<tr>
<td>Malassezia furfur</td>
<td>Amphotericin B</td>
<td>Voriconazole</td>
<td>aminoglycoside</td>
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</table>

Intravenous lipids should be discontinued; some experts recommend removal of catheter.

See *S. aureus* section of the text regarding important antibiotic management issues concerning linezolid.

TMP-SMX: trimethoprim-sulfamethoxazole; ESBL: extended-spectrum beta-lactamase. * Penicillin, if the strain is susceptible. ¶ Pediatric experience is limited. Δ Additional alternative agents include linezolid, tedizolid, ceftaroline, telavancin, dalbavancin, and oritavancin. ◊ Pending susceptibility results for the isolate.