CME Reviewer(s)

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From MedscapeCME General Surgery

Preventing Central Line-Associated Bloodstream Infections: Do You Bundle? CME/CE

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The following test-and-teach case is an educational activity modeled on the interactive grand rounds approach. The questions within the activity are designed to test your current knowledge. After each question, you will be able to see whether you answered correctly and will then read evidence-based information that supports the most appropriate answer choice. Please note that these questions are designed to challenge you; you will not be penalized for answering the questions incorrectly. At the end of the case, there will be a short post-test assessment based on material covered in the activity.

Introduction of Patient Case

A 56-year-old, obese man weighing 127 kg is transferred to the intensive care unit (ICU) of your hospital with a diagnosis of acute pancreatitis. His symptoms began 5 days earlier when the patient was admitted to a 150-bed community hospital for abdominal pain. Ultrasound examination of the right upper quadrant reveal no gallstones, and the common bile duct and pancreatic duct appear normal. Serum lipase peaked at 1470 U/L.

The patient has a right femoral triple-lumen catheter that was placed on the day of admission at the outside hospital, which is now 5 days old. Total parenteral nutrition was begun 3 days earlier, and includes daily intralipids. Antibiotics have been administered for 4 days, including vancomycin 1 g every 12 hours and ciprofloxacin 400 mg every 8 hours. His vital signs are as follows: blood pressure, 86/55 mm Hg; heart rate, 124 beats per minute with a normal sinus rhythm; respiratory rate, 26 breaths per minute; and core temperature, 38.9°C.

A CT scan of the abdomen shows necrotizing pancreatitis; a minimal amount of ascites that are nonhemorrhagic; and normal kidneys, liver, bowel, and spleen (Figure 1). However, the patient's urine output has been < 20 mL in the past 4 hours. His bladder pressure is 14 mm Hg. In addition, he has not had a bowel movement in over 24 hours. You order a 1-L bolus of lactated Ringer's solution with no change in vital signs or urine output. Norepinephrine is begun and titrated to keep the mean arterial pressure at or above 60 mm Hg.

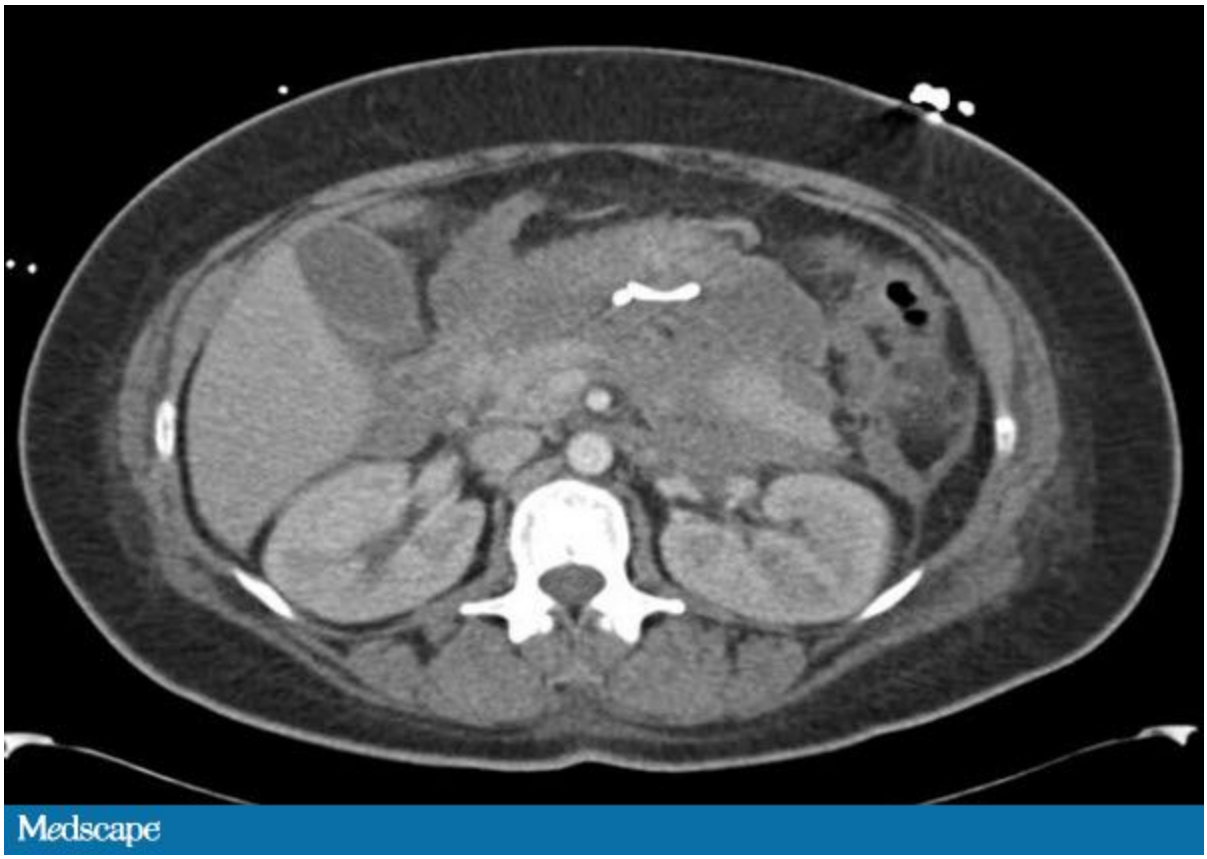


Figure 1. Necrotizing pancreatitis.

In your my mind, which of the following is the most likely cause of fever in this critically ill patient?

- (•) Necrotizing pancreatitis
- ( ) Ventilator-associated pneumonia
- ( ) Central line-associated bloodstream infection (CLABSI)
- ( ) *Clostridium difficile*-associated diarrhea

Save and Proceed

Causes of Fever in Critically Ill Patients

Any new onset of temperature ≥ 38.3°C is a reasonable trigger for a clinical assessment to determine the etiology of a patient's fever in the ICU setting.[1] Table 1 lists the most common causes of fever identified in critically ill patients. The initial assessment of fever should include a carefully performed physical examination, chest x-ray, and examination of pulmonary secretions. All intravascular devices should be inspected for evidence of erythema and expression of purulent exudate at the exit site. A minimum of 2 peripheral blood cultures, ie, one culture drawn percutaneously, and the other drawn through the vascular catheter, should be obtained to evaluate for CLABSI. Standard blood cultures drawn through intravascular devices have been shown to provide excellent sensitivity for the diagnosis of bloodstream infection when properly collected and processed.[2,3]

Table 1. Causes of Fever in Critically Ill Patients

Infection	Blood Product Reaction
Bacterial	Intracranial hemorrhage
Fungal	Pulmonary contusion or infarction
Viral	Thyroid storm
Mycobacterial	Adrenal insufficiency
Other (malarial, parasitic)	Immune reconstitution inflammatory syndrome
Drug fever	Fibroproliferative phase of acute respiratory distress syndrome
Pancreatitis	Fat emboli
Calculous or acalculous cholecystitis	Crush injury
Myocardial infarction	Bowel ischemia or infarction
Deep vein thrombosis	Septic thrombophlebitis
Solid organ rejection	Cerebral infarction

Fever in critically ill patients can be time-consuming and expensive to evaluate. A culture-based approach for the evaluation and management of fever in such patients is usually recommended.[4,5] Figures 2 and 3 provide the recommendations of the Infectious Diseases Society of America (ISDA) for the management of short-term central catheters or arterial catheters in the setting of fever.[5]

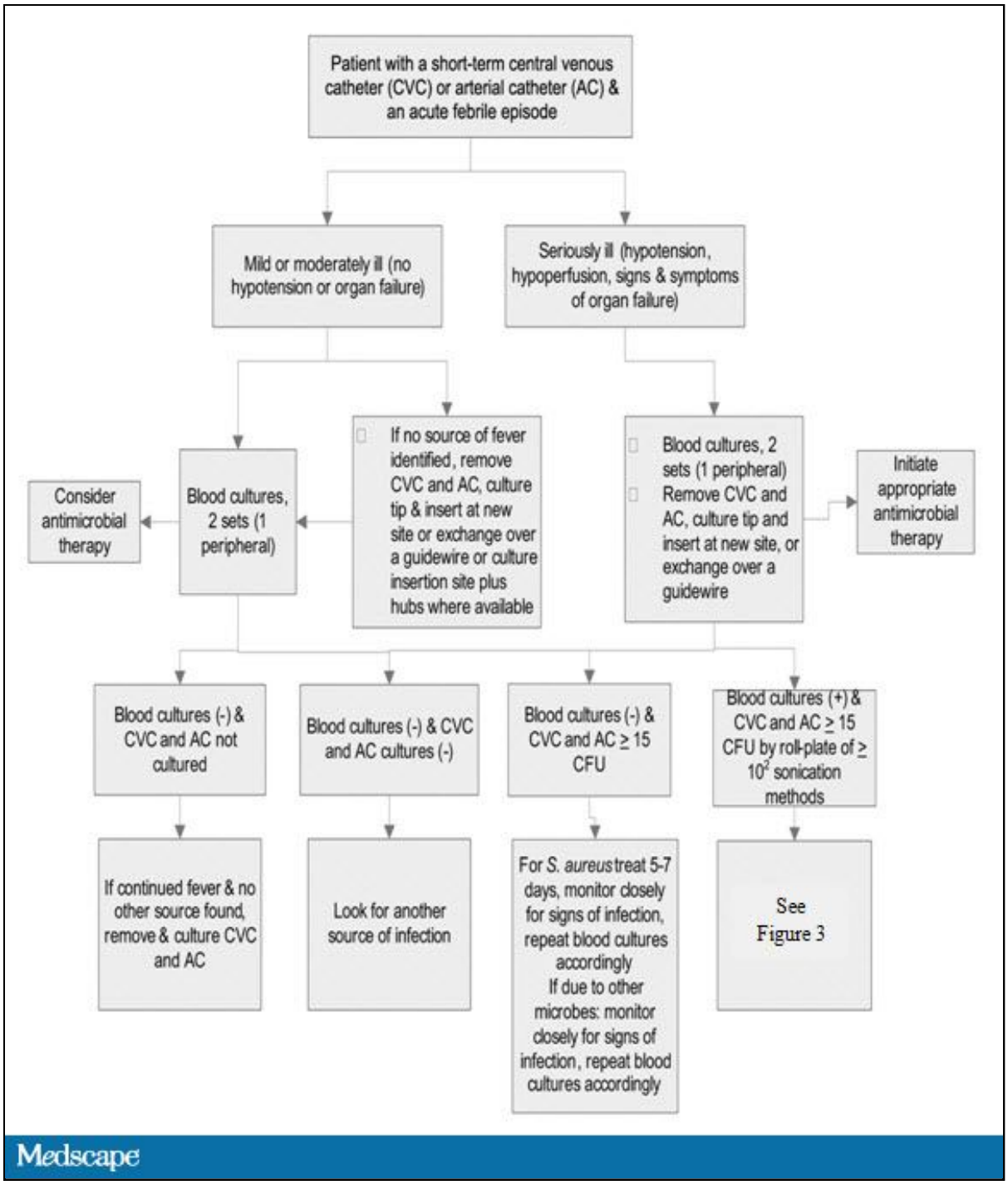


Figure 2. Algorithm for the evaluation of fever in a patient with a central catheter or arterial line.
CFU = colony-forming units

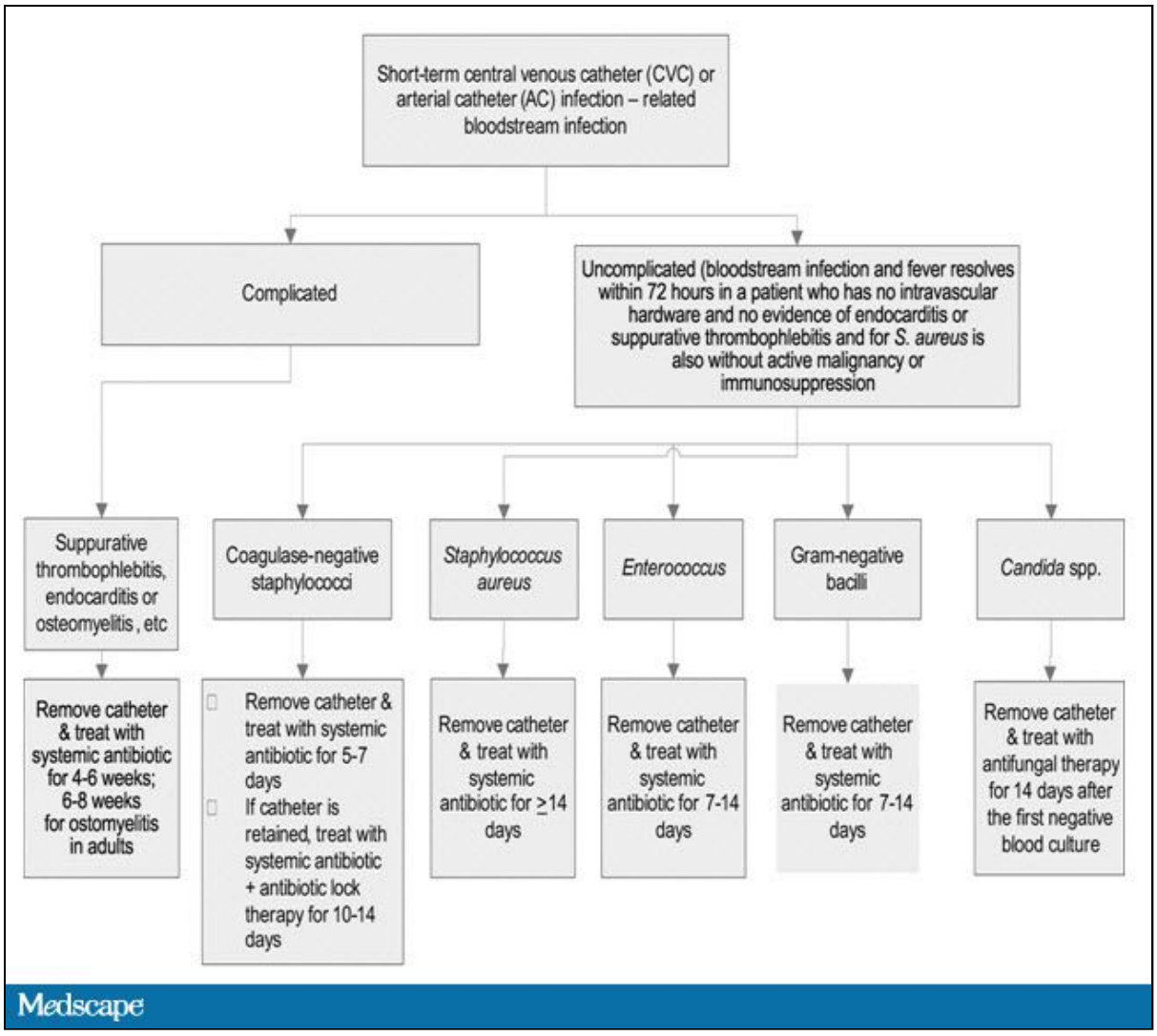


Figure 3. Further management of a febrile episode in a patient with a central catheter or arterial line.
CFU = colony-forming units; S aureus = Staphylococcus aureus

ICUs could reduce the cost of fever evaluations by eliminating automatic laboratory and radiologic tests for patients with a new temperature elevation. The Society of Critical Care Medicine (SCCM) and the IDSA recommend that tests to evaluate fever in the ICU setting be ordered on the basis of the patient's clinical assessment.[1] A clinical and laboratory evaluation for infection, conversely, may also be appropriate in euthermic or hypothermic patients, depending on clinical presentation. In patients who appear septic or have worsening organ function associated with fever, empirical antimicrobial therapy is warranted until culture results become available in order to avoid delays in therapy, which are associated with a greater risk for mortality.[6] Initial empirical antibiotic therapy should cover the most likely pathogens causing CLABSIs, and then switch to definitive therapy on the basis of the microbiological results (Table 2).[5]

Table 2. Intravenous Antimicrobial Treatment of Intravenous Catheter-Related Bloodstream Infection in Adults

Pathogen	Preferred Antimicrobial	Example Dosage[a]	Alternative Antimicrobial	Comment

	Agent		**Agent**	
Gram-positive cocci				
Staphylococcus aureus				
Methicillin susceptible	Penicillinase-resistant Pen[b]	Naf or Oxa, 2 g q4h	Cfaz, 2 g q8h; or Vm, 15 mg/kg q12h	Penicillinase-resistant Pen or Csps are preferred to Vm.[c] For patients receiving hemodialysis, administer Cfaz 20 mg/kg (actual weight), round to nearest 500-mg increment, after dialysis.
Methicillin resistant	Vm	Vm, 15 mg/kg q12h	Dapto, 6-8 mg/kg per day, or linezolid; or Vm plus (Rif or Gm); or TMP-SMZ alone (if susceptible)	Strains of *S aureus* with reduced susceptibility or resistance to Vm have been reported; strains resistant to Dapto have been reported.
Coagulase-negative staphylococci				
Methicillin susceptible	Penicillinase-resistant Pen	Naf or Oxa, 2 g q4h	First-generation Csp or Vm or TMP-SMZ (if susceptible)	Vm has dosing advantages over Naf and Oxa, but the latter are preferred.
Methicillin resistant	Vm	Vm, 15 mg/kg IV q12h	Dapto, 6 mg/kg/day, linezolid, or Quin/Dalf	For adults < 40 kg, linezolid dose should be 10 mg/kg; strains resistant to linezolid have been reported.
Enterococcus faecalis/Enterococcus faecium				
Amp susceptible	Amp or (Amp or Pen) ± aminoglycoside	Amp, 2 g q4h or q6h; or Amp ± Gm, 1 mg/kg q8h	Vm	VM may have dosing advantages over Amp, but there are concerns about Vm resistance; Quin/Dalf is not effective against *E faecalis.*
Amp resistant, Vm susceptible	Vm ± aminoglycoside	Vm, 15 mg/kg IV q12h ± Gm, 1 mg/kg q8h	Linezolid or Dapto, 6 mg/kg/day	
Gram-negative bacilli[d]				
Escherichia coli and *Klebsiella* species				

ESBL negative	Third-generation Csp	Ctri, 1-2 g/day	Cipro or Atm	Susceptibility of strains varies
ESBL positive	Carbapenem	Erta, 1 g/day; Imi, 500 mg q6h; Mero, 1 g q8h; or Dori, 500 mg q8h	Cipro or Atm	
Enterobacter species and *Serratia marescens*	Carbapenem		Cefepime or Cipro	
Acinetobacter species	Amp/Sulb or carbapenem	Amp/Sulb, 3 g q6h; or Imi, 500 mg q6h; Mero, 1 g q8h		Susceptibility of strains varies
Stenotrophomonas maltophilia	TMP-SMZ	TMP-SMZ, 3-5 mg/kg q8h	Tic and Civ	
Pseudomonas aeruginosa	Fourth-generation Csp or carbapenem or Pip and Tazo with or without aminoglycoside	Cefepime, 2 g q8h; or Imi, 500 mg q6h; or Pip and Tazo, 4.5 g q6h, Amik, 15 mg/kg q24h or Tobra 5-7 mg/kg q24h		Susceptibility of strains varies
Burkholderia cepacia	TMP-SMZ or carbapenem	TMP-SMZ, 3-5 mg/kg q8h; or Imi, 500 mg q6h; or Mero, 1 g q8h		Other species, such, as *B acidovorans* and *B pickieii*, may be susceptible to same antimicrobial agents.
Fungi				
Candida albicans or other *Candida* species	Echinocandin or fluconazole (if organism is susceptible)	Caspo, 70-mg loading dose, then 50 mg/day; micafungin, 100 mg/day; anidulafungin, 200-mg loading dose followed by 100 mg/day; or fluconazole, 400-600 mg/day	Lipid AmB preparations	Echinocandin should be used to treat critically ill patients until fungal isolate is identified.
Uncommon pathogens				
Corynebacterium jeikeium (group JK)	Vm	Vm, 15 mg/kg q12h	Linezolid (based on in vitro activity)	Check susceptibilities for other corynebacteria
Chryseobacterium (*Flavobacterium*) species	Fluoroquinolone, such as Lvfx	Lvfx, 750 mg q24h	TMP-SMZ or Imi or Mero	Based on in vitro activity

Ochrobactrum anthropi	TMP-SMZ or fluoroquinolone	TMP-SMZ, 3-5 mg/kg q8h; or Cipro, 400 mg q12h	Imi, Mero, Erta, or Dori plus aminoglycoside	
Malassezia furfur	AmB		Voriconazole	Intravenous lipids should be discontinued; some experts recommend removal of catheter. Different species have wide spectra of susceptibility to antimicrobials.
Mycobacterium species	Susceptibility varies by species			

AmB = amphotericin B; Amik = ; Amp = ampicillin; Atm = aztreonam; Caspo = ; Cfaz = cefazolin; Clv = clavulanate; Cipro = ciprofloxacin; Csp = cephalosporin; Ctri = ceftriaxone; Czid = ceftazidime; Dapto = daptomycin; Dori = doripenum; Erta = ertapenem; ESGL = extended-spectrum beta-lactamases; Gm = gentamicin; Imi = imipenem; iv = intravenous; Ket = ketoconazole; Lvfx = levofloxacin; Mero = meropenem; Meth = methicillin; Mez = mezlocillin; Naf = nafcillin; Oxa = oxacillin; Pen = penicillin; PenG = penicillin G; Pip = piperacillin; po = by mouth; q4h = every 4 hours; q6h = every 6 hours; q12h = every 12 hours; Quin/Dalf = quinupristin/dalfopristin; Rif = rifampin; Sulb = sulbactam; Tic = ticarcillin; TMP-SMZ = trimethoprim-sulfamethoxazole; Tobra = tobramycin; Vm = vancomycin

[a]Initial antibiotic dosages for adult patients with normal renal and hepatic function and no known drug interactions; fluoroquinolones should not be used for patients younger than 18 years of age.

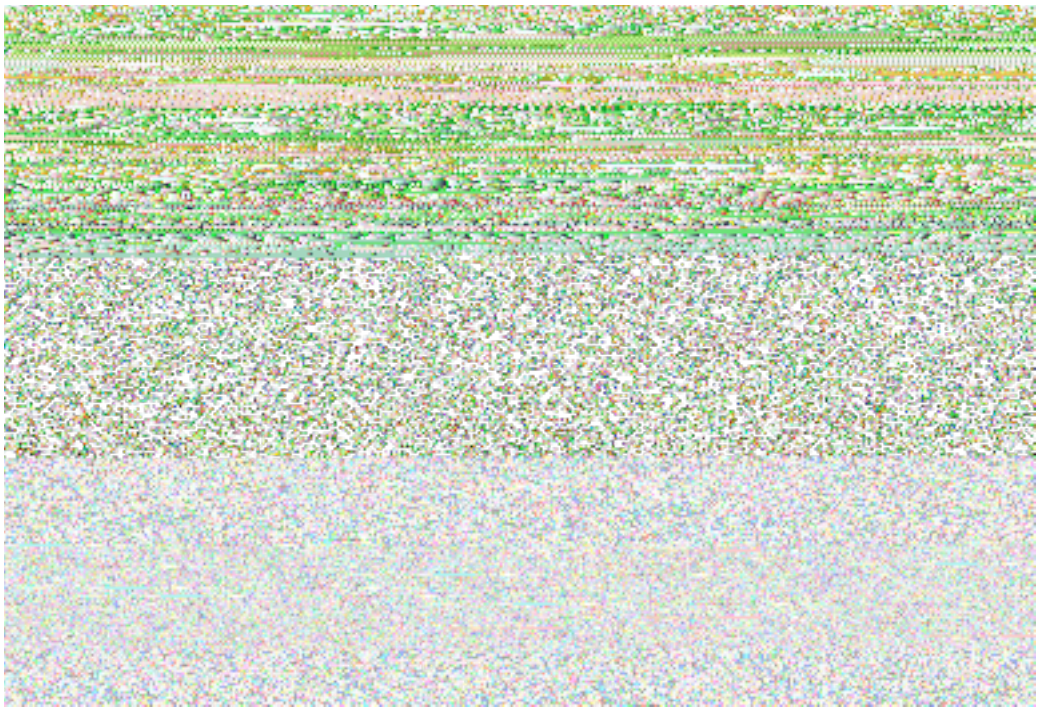
[b]Pen, if the strain is susceptible

[c]Some clinicians will add an aminoglycoside for the first 5 days of therapy.

[d]Pending susceptibility results for the isolate

From Mermel LA, et al. *Clin Infect Dis*. 2009;49:1-45.[5]

The Patient and the Rash



A culture-based evaluation of the patient's fever complicated by septic shock is undertaken. A quantitative culture and Gram stain of an endotracheal aspirate, urine culture, and culture of the purulent material expressed from the femoral exit site are sent to the laboratory. Blood cultures are also obtained from a peripheral site and from the distal port of the femoral catheter. After discussion with the clinical pharmacist in your unit, it is decided to change the patient's antimicrobial treatment due to the presence of septic shock, which occurred while on the current antibiotic regimen.

Which of the following antibiotic combinations should be prescribed for the patient at this time?

- Vancomycin, cefepime, and metronidazole
- Linezolid, imipenem, and clindamycin
- Fluconazole and vancomycin
- Vancomycin, meropenem, and micafungin

Save and Proceed

An antimicrobial regimen that included vancomycin, meropenem, and micafungin is prescribed due to the patient's severity of illness. The rationale for this antimicrobial regimen was that its use provided broad-spectrum activity against both gram-positive and gram-negative bacteria as well as *Candida*, which is important in light of the probable CLABSI. Micafungin was chosen over fluconazole due to its activity against fluconazole-resistant strains, which is important in this septic patient.[5]

Pathogens Associated With CLABSIs

A European point prevalence study analyzed 89 episodes of CLABSIs occurring during 1 week in 107 hospitals from

21 countries (1.02 episodes/1000 admissions).[7] Most (67%) catheters were nontunneled central catheters, in the jugular vein (44%); had been implanted for over 7 days (70%); were made of polyurethane (61%); and were multilumen (67%).[7] Of the 105 different microorganisms isolated from CLABSIs, the 7 most frequent were coagulase-negative staphylococci, *Staphylococcus aureus, Enterobacter* species, *Candida* species, *Klebsiella* species, *Pseudomonas* species, and *Enterococcus* species. Similarly, a prospective, multicenter, observational study carried out in the ICUs of 9 Spanish hospitals found that during 20,981 patient-days, 626 catheters had been placed in the jugular vein, 585 in the subclavian vein, and 387 in the femoral vein; and 503 were peripherally inserted central catheters.[8] During the study period, 66 episodes of CLABSI were diagnosed or about 3% of all inserted catheters.[8] The microorganisms involved included coagulase-negative staphylococci, *Acinetobacter baumannii*, *S aureus*, *Candida* species, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, and *Enterobacter* species.[8] Similar distributions of pathogens associated with CLABSIs have been reported in other countries, including the United States.[9]

Given the critical nature of the patient's medical condition and the strong clinical suspicion for the presence of a CLABSI complicated with acute pancreatitis, what is the optimal management of the patient's femoral catheter?

- Leave the femoral catheter in place until blood culture results are known
- Change the femoral catheter over a wire, and send the tip of the catheter to the laboratory for culture
- Place a new central catheter in either the jugular or subclavian vein, and remove the femoral catheter
- Leave the femoral catheter in place, but place an antibiotic lock with vancomycin flushed through the catheter to prevent subsequent infection

Save and Proceed

Management of the Existing Venous Catheter

After obtaining blood cultures and starting a new antimicrobial regimen, you discuss the need to remove the femoral catheter and the necessity for new vascular access with the patient's care team (ie, the nurse, the clinical nurse specialist in charge of the peripherally inserted central venous catheter team, and the nephrology consultant). It is believed that a peripherally inserted central venous catheter is not an option for this patient because of the increased risk for venous thrombosis. This would limit further use of the subclavian and internal jugular veins for hemodialysis on the side of the peripherally inserted central venous catheter, if thrombosis were to develop.

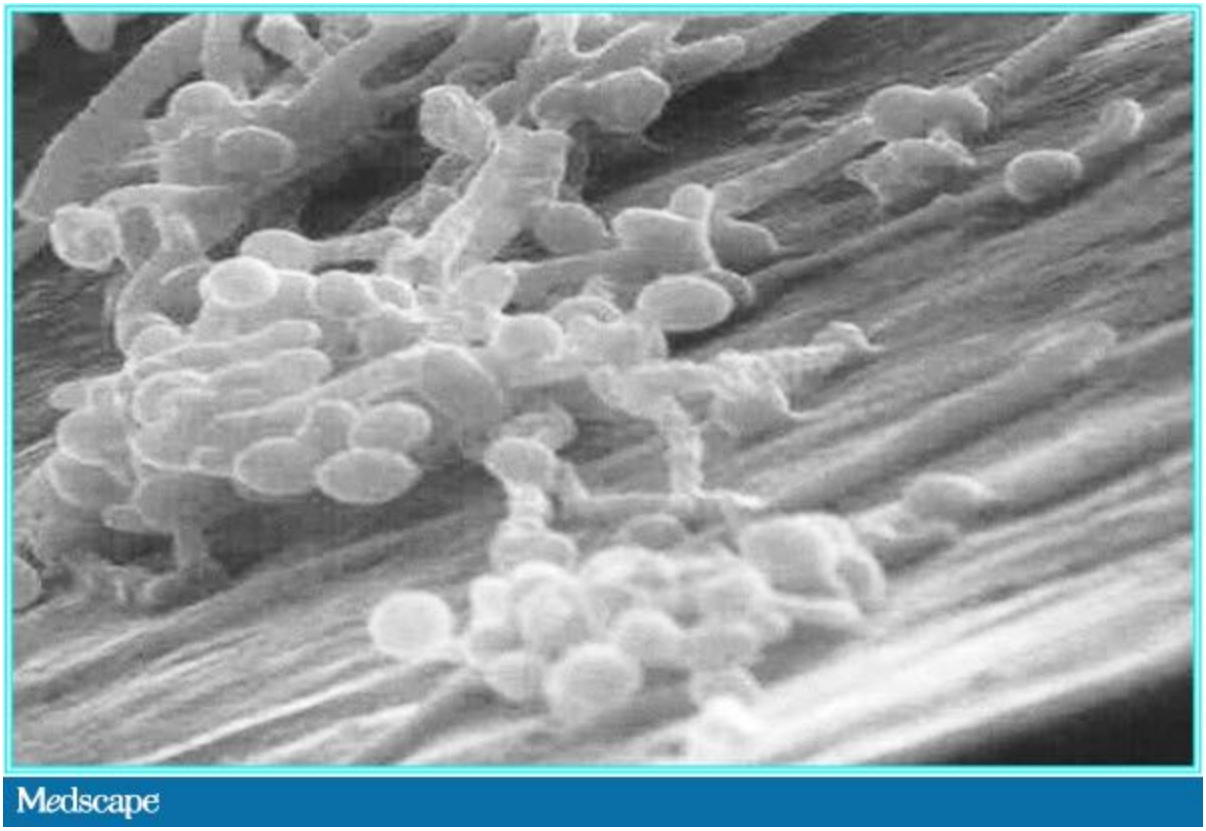


Figure 4. *Candida albicans* biofilm.

Bacterial and fungal biofilms are known to form on vascular catheters, making treatment of the infection problematic (Figure 4).[10,11] The ability of a pathogen to form a biofilm is a potential virulence factor shielding it from the host's immune response and the activity of the antimicrobial agents.[12] For CLABSIs attributed to certain high-risk pathogens, including *Candida* species, failure to remove vascular catheters has been associated with excess risk for recurrent infections, greater rates of mortality, and higher hospital costs.[13-16] For instance, a recent study by Tumbarello and colleagues found that *Candida* isolates associated with a bloodstream infection that were capable of biofilm formation correlated with a greater risk for hospital mortality compared with nonbiofilm producers.[17]

Thus, most expert opinion and guidelines recommend the removal of central venous catheters in patients with local signs of infection (eg, exit-site inflammation, purulent discharge) or positive blood cultures.[1,5,10,13]

Delayed treatment of subsequently identified invasive *Candida* is the most important determinant of outcome identified in patients with this type of infection.[14,15,18] Typically, delays in treatment of patients with a *Candida* infection occur because clinicians fail to recognize the risk factors associated with an invasive fungal infection (Table 3), and await the results of positive blood cultures before initiating appropriate therapy. In addition, inadequate dosing of fluconazole has been associated with excess mortality.[14] Most guidelines recommend initiating therapy for invasive fungal infection empirically in high-risk patients, with an agent that is likely to cover potentially azole-resistant *Candida* species, until the results of microbiological testing are available.[19]

Table 3. Does My Patient Have an Invasive *Candida* Infection?

Risk Factors for Invasive Fungal Infections

LOS in ICU	Blood transfusion
Broad-spectrum antibiotics	CVCs
Hemodialysis	Diabetes
Candida colonization	TPN
Severity of Illness	Pancreatitis
Mechanical ventilation	Steroids
GI surgery	

CVCs = central venous catheters; GI = gastrointestinal; ICU = intensive care unit; LOS = length of stay; TPN = total parenteral nutrition

The current recommendation of the IDSA is to remove intravascular catheters in the presence of a CLABSI whenever clinically possible.[5,19] However, a recent meta-analysis by Nucci and colleagues of 2 clinical trials of specific antifungal therapy found that failure to remove vascular catheters in patients with a fungal bloodstream infection was only associated with worse outcomes in their univariate analysis, but not in the multivariate analysis.[20] The study authors concluded that other risk factors associated with failure to remove central venous catheters accounted for the mortality risk in patients with *Candida* bloodstream infections.[20] Therefore, the recommendations of the IDSA to remove central catheters in patients with fungal bloodstream infections should be changed allowing clinicians the option to maintain central catheters in place depending on patient-specific factors. An accompanying editorial suggested that the existing expert guideline recommendations to remove central catheters should be followed at the present time. However, clinicians at the bedside must balance the risk of not removing central venous catheters in patients with CLABSIs vs the risks associated with placement of a new central catheter.[21]

After discussion with the unit charge nurse, who oversees implementation of the infection control protocols for the ICU, a new central catheter and dialysis catheter will be inserted prior to removal of the femoral catheter.

Which of the following practices should *not* be followed when placing a new central catheter in order to minimize the occurrence of any subsequent CLABSIs?

- Full sterile technique with body length sterile drapes
- Skin disinfection with 2% chlorhexidine gluconate/70% isopropyl alcohol skin antiseptic
- Use the femoral vein because it is an easy site for placement of a central catheter
- Place a transparent dressing and perform site care with a chlorhexidine-based antiseptic every 5 days

Save and Proceed

Selection of Location for Central Catheters

The decision was made to insert a right subclavian triple-lumen catheter for vascular access and a left internal jugular dialysis catheter. The left femoral vein was ruled out due to the increased risk for infection at that site.

Several studies have shown that the risk for CLABSIs is greatest for the femoral site. Merrer and colleagues in a multicenter, randomized study found a statistically significant increase in rates of colonization at the femoral site compared with the subclavian site (19.8% vs 4.5%; $P < .001$). However, they were unable to demonstrate a difference in catheter-related bloodstream infections between the 2 sites.[22] The most common pathogens colonizing the femoral site included coagulase-negative staphylococci, enterococci, and gram-negative bacilli. In addition, Warren and colleagues performed a quality improvement project in the ICU of a university-affiliated medical center aimed at reducing CLABSIs that included avoidance of the femoral site.[23] They were able to demonstrate a significant reduction in CLABSIs. However, how much of this reduction was attributed to avoidance of the femoral site could not be ascertained from the investigation.

Two prospective, nonrandomized studies comparing femoral, internal jugular, and subclavian sites showed higher rates of CLABSIs and catheter colonization at the femoral site.[24,25] The study by Lorente and colleagues also demonstrated that the internal jugular site had a greater risk for colonization and CLABSIs than the subclavian site.[25] Potential explanations for this observation include the jugular vein's proximity to the oropharynx; higher local skin temperature; and difficulty maintaining an occlusive dressing, which may contribute to increased skin flora density. In addition, the presence of a tracheostomy increases the occurrence of CLABSIs, particularly when the internal jugular site is accessed.[26] This may be due to the expression of airway secretions from the tracheostomy in close proximity to the jugular insertion site. Similarly, a recent randomized trial by Parienti and colleagues in France found that there was no significant difference in rates of colonization or CLABSIs in critically ill patients who had femoral and internal jugular catheters for renal replacement therapy.[27] However, subgroup analysis suggested that patients with lower body mass indices had higher infection rates when using the jugular site, whereas those with higher body mass indices had increased infection rates with femoral vein access.[27] The patient's obesity was another factor placing him at increased risk for a CLABSI due to use of the femoral site. On the basis of data by Parienti and colleagues, it is more than justified to avoid the femoral site for all subsequent central catheters in this patient to reduce the future likelihood of a CLABSI.

An observational study by Deshpande and colleagues demonstrated no significant differences in CLABSI or colonization rates between the femoral, internal jugular, and subclavian sites in a prospective study of 657 ICU patients.[28] This unique study employed "experienced operators," either critical care attendings or fellows, to insert the vascular catheters. The study authors suggested that operator experience improved the rates of sterile technique, which lowers the risk for infection. Taken together, these studies support the argument that site-specific differences in CLABSIs occur. The subclavian site appears to have the lowest risk for CLABSIs, followed by the internal jugular and femoral sites, respectively. In patients with a tracheostomy, especially if there are excessive secretions or inability to provide an occlusive dressing to the catheter site, an alternative site for line insertion should be sought. Similarly, the femoral site should be avoided if possible, especially in obese patients. Finally, experience appears to matter when central catheters are placed. The most experienced operator should place, or at least oversee the placement of central catheters, in critically ill patients in order to minimize the occurrence of CLABSIs.

The nephrology attending inserts a new triple-lumen catheter in the right subclavian position and a dialysis catheter in the left internal jugular vein. The femoral catheter is subsequently removed. All procedures are performed without complication. The next morning, you receive a call from microbiology that yeast has been identified in the blood culture specimen obtained from the original femoral catheter. The yeast is identified as *Candida glabrata*. The infection control nurse finds out that the transferring hospital did not employ a bundle for the prevention of CLABSIs.

How strong is the evidence in support of routinely applied bundles and protocols for the prevention of CLABSIs?

- There is little-to-no evidence supporting bundles and protocols for the prevention of CLABSIs
- The evidence in support of bundles and protocols for the prevention of CLABSIs is based on small studies and case reports
- Few, if any, guidelines recommend the use of bundles and protocols for the prevention of CLABSIs
- There is strong evidence supporting the use bundles and protocols for the prevention of CLABSIs on the basis of multiple clinical studies, including multicenter trials

Save and Proceed

Bundles and Protocols for the Prevention of CLABSIs

Faced with the complex care required for patients receiving mechanical ventilation in the ICU setting, computerized clinical decision support (CCDS) systems have been increasingly advocated as a means of maintaining the quality of medical care and easing the burden on clinical staff.[29] Examples of therapies in which CCDS systems have been used to enhance the implementation of protocols in the ICU setting include antibiotic therapy, managing ventilator settings, blood transfusions, glucose control, traumatic shock resuscitation, and septic shock.[30-39] Unfortunately, most hospitals do not have the information systems in place to employ CCDS on a routine basis. The main advantage of CCDS systems in the ICU setting is that they allow the application of consistent patient care. Consistent or protocolized medical care has the advantage of allowing precise changes in the treatment protocol to occur that can subsequently be assessed for their impact on clinical outcomes. Although CCDS has not directly been applied to the prevention of CLABSIs, the same principles have been utilized to develop protocols and bundles for the prevention of this important nosocomial infection.

A bundle is typically a group of evidence-based interventions that, when implemented together, may result in improved clinical outcomes than when implemented individually. This occurs despite not knowing which of the elements has the greatest impact on the clinical outcome of interest. One of the most widely applied bundles for the prevention of CLABSIs is the Institute for Healthcare Improvement's central catheter bundle, which includes the following components: (1) hand hygiene; (2) maximal barrier precautions upon catheter insertion; (3) chlorhexidine skin antisepsis; (4) optimal catheter site selection, with avoidance of the femoral vein for central venous access in adult patients; and (5) daily review of catheter necessity.[40] This relatively simple collection of interventions has been used by many hospitals worldwide to reduce catheter-related bloodstream infection rates close to zero, or in some circumstances to zero for prolonged periods of time. Table 4 provides a summary of several of the largest and most successful clinical experiences using central catheter bundles for the prevention of CLABSIs.[41-47]

Table 4. Published Results of Use of Institute for Healthcare Improvement Central Catheter Bundle

Study	Site	IHI Bundle?	Mean CRBSI per 1000 Catheter-Days	
			Pre-	Post-
Berriel-Cass D, et al.[41]	Single center	Yes + a,b,c	9.6	3.0
Pronovost P, et al.[42]	Multicentered	Yes + a,b	7.7	2.3
Jain M, et al.[43]	Single ICU	No + c	5.9	3.1
Bonello RS, et al.[44]	Multicentered	Yes + a	5.2	2.7

Costello JM, et al.[45]	Single CICU	No + a,b,c,d	7.8	2.3
Galpern D, et al.[46]	Single center	Yes + a,b	5.0	0.9
Venkatram S, et al.[47]	Single MICU	Yes + a,b,c,d	10.8	1.7

CICU = cardiac intensive care unit; CRBSI = catheter-related bloodstream infection; ICU = intensive care unit; IHI = Institute for Healthcare Improvement; MICU = medical intensive care unit; a = catheter checklist; b = central venous line insertion card; c = sterile dressing; d = access maintenance bundles

In the largest study of bundles for the prevention of CLABSIs, Pronovost and colleagues conducted a collaborative cohort study predominantly in adult ICUs in Michigan.[42] Among the 103 participating ICUs, 375,757 catheter-days were analyzed. Three months after implementing the bundle, the rate of catheter-related bloodstream infections per 1000 catheter-days decreased from 2.7 infections to 0 infections ($P < .002$). In addition, this decrease was observed in the subsequent 18 months of follow-up. Thus, other hospitals can assume that implementation of a similar prevention bundle will produce comparable results without actually monitoring for a treatment effect.

Although the strength of a bundle comes from the simplicity, consistency, and evidence behind each of its components, attempting to add additional components, although well intentioned, may be associated with lower rates of adherence and worse outcomes. Alternatively, expansion of a bundle may result in better outcomes. Therefore, it is important to assess the impact of any protocol bundle over time to determine whether it requires revision. Miller and colleagues recently carried out a multicenter study at 29 pediatric ICUs across the United States to evaluate the use of prevention bundles for CLABSIs in children.[448] The investigators performed a multi-institutional, time-seriesdesign study with historical control data. The intervention consisted of 2 central venous catheter-care practice bundles, which were derived from adult efforts, pediatrician consensus, and US Centers for DiseaseControl and Prevention (CDC) recommendations (Table 5). Use of the 2 bundles resulted in a 43% reduction in CLABSI rates across the 29 pediatric units (5.4 vs 3.1 CLABSIs per 1000 central line-days; $P < .0001$) (Figure 5).[48] By the end of the study, compliance rates for the insertion bundle and maintenance bundle were 84% and 82%, respectively.[48] In addition, Miller and colleagues found that compliance with the maintenance bundle was independently associated with CLABSI reduction (relative risk, 0.41 [95% confidence interval, 0.20-0.85]; $P = .017$).

Intervention 1: Insertion Bundle

- Wash hands before the procedure.
- For all children younger than 2 months of age, use chlorhexidine gluconate to scrub the insertion site for 30 seconds for all areas except the groin, which should be scrubbed for 2 minutes. Scrubbing should be followed by 30-60 seconds of air-drying.
- No iodine skin preparation or ointment is used at the insertion site.
- Prepackage or fill the insertion cart, tray, or box, including full sterile barriers.
- Create an insertion checklist, which empowers staff to stop a nonemergent procedure if it does not follow sterile insertion practices.
- Use only polyurethane or polytetrafluoroethylene catheters.*
- Conduct insertion training for all care providers, including slides and video.

**These procedures are according to the CDC recommendations.*

Intervention 2: Maintenance Bundle

- Assess daily whether catheter is needed;
- Catheter-site care;
- No iodine ointment;
- Use a chlorhexidine gluconate scrub to sites for dressing changes (30-second scrub, 30-second air-dry);

- Change gauze dressings every 2 days unless they are soiled, dampened, or loosened*;
- Change clear dressings every 7 days unless they are soiled, dampened, or loosened*;
- Use a prepackaged dressing-change kit or supply area;
- Catheter hub, cap, and tubing care;
- Replace administration sets, including add-on devices, no more frequently than every 72 hours unless they are soiled or suspected to be infected;
- Replace tubing that is used to administer blood, blood products, or lipids within 24 hours of initiating infusion*;
- Change caps no more often than 72 hours (or according to manufacturer recommendations); however, caps should be replaced when the administration set is changed*; and
- The prepackaged cap-change kit, or supply area elements, are to be designated by the local institution.

**These procedures are according to the CDC recommendations.*

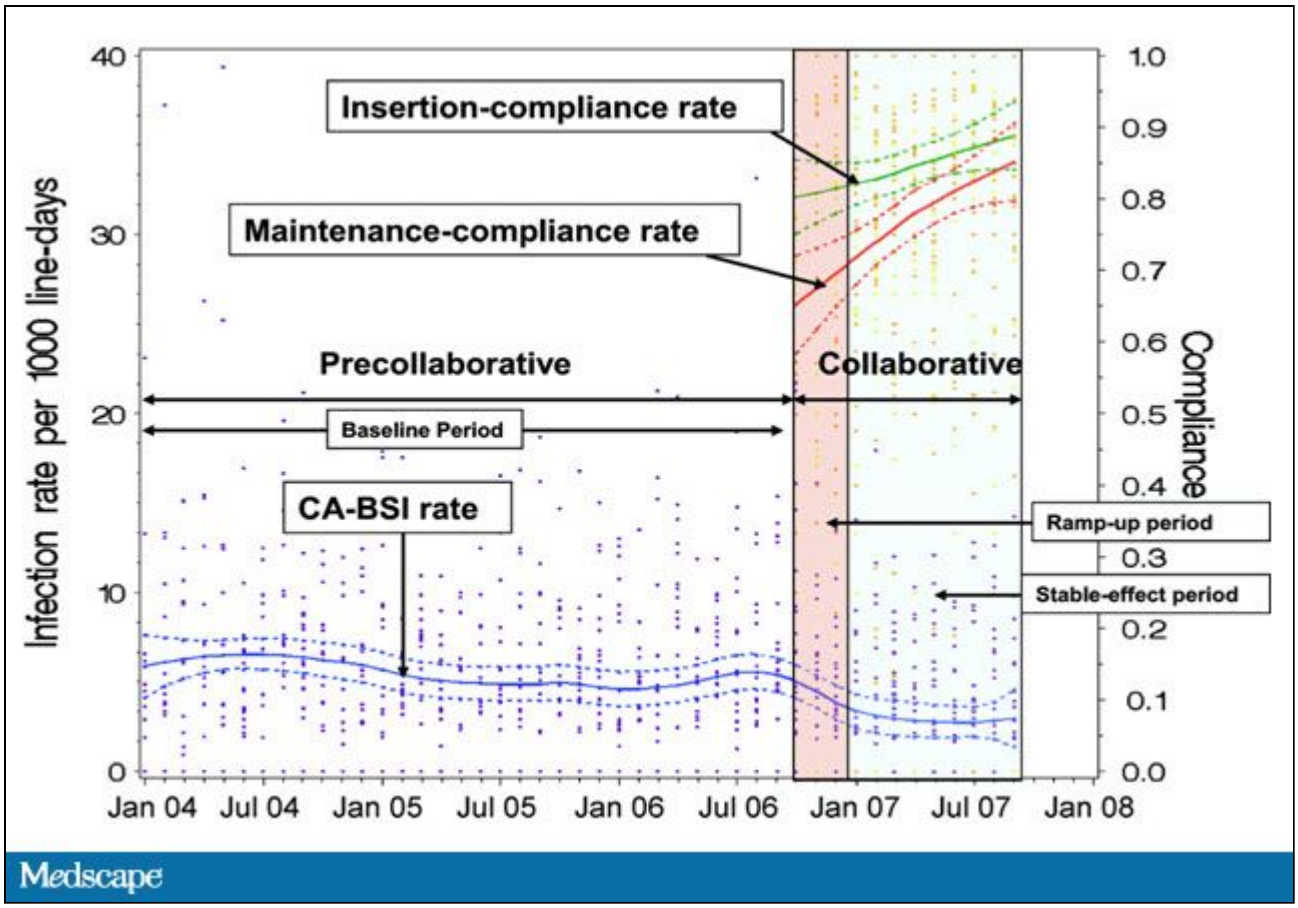


Figure 5. Use of bundles reduces the rates of catheter-associated bloodstream infections in children.

The study by Miller and colleagues demonstrates the importance of having the correct bundle in place for optimal prevention of CLABSIs. Both insertion and site maintenance are important aspects of patient care for the prevention of CLABSIs. However, clinicians need to be mindful that other factors may play a role in the development of CLABSIs in the ICU.

Glucose Control in Critically Ill Patients

The nurse informs you that the patient's last 2 blood glucose levels were 280 mg/dL and 300 mg/dL, and that he is tolerating enteral nutrition administered through a nasojejunal feeding tube.

Which of the following additional interventions will have the greatest impact on the prevention of future CLABSIs?

- Administration of a high-protein enteral feeding solution
- Routine red blood cell transfusions to maintain the patient's hemoglobin level above 12 g/dL
- Use of intravenous insulin to keep the patient's blood glucose level in the range of 150-180 mg/dL
- Use of heparin flushes administered directly into the ports of the central catheter

Save and Proceed

The current recommendations for the maintenance of blood glucose levels in critically ill patients are based on data accumulated over the past 10 years. Studies in both the ICU and critical care setting have demonstrated a direct correlation between patients' blood glucose levels upon admittance as well as during their hospital stays and survival. Specifically, reduced patient mortality and improved outcomes were noted in individuals who achieved a blood glucose level < 200 mg/dL during their hospital stays.[49,50] Moreover, the greatest benefit was seen in patients who attained a blood glucose level < 110 mg/dL. For these reasons, the American Diabetes Association and the American College of Endocrinology recommend a blood glucose level < 100 mg/dL for all patients in the ICU.[49,50] In addition, the authors of the Surviving Sepsis Campaign advocate blood sugar goals < 150 mg/dL in critically ill patients in order to limit hypoglycemia and simplify management.[51] Overall, studies support intensive glucose control in patients who are expected to stay in the ICU longer than 3-5 days. However, it is not always possible to predict the length of ICU stays, and clinician discretion is needed.

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