Health care–associated infections (HAIs) are an important cause of morbidity and mortality, and place a significant economic burden on the health care system. An estimated 1.7 million HAIs, or 4.5 infections per 100 hospital admissions, occurred in the United States in 2002, resulting in nearly 100,000 deaths.3

Prevention and Management of Health Care–Associated Infections

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Bloodstream infections, most of which are associated with central venous catheters (CVCs), and surgical site infections (SSIs) represent 11% and 20% of all HAIs, respectively.3-5 Agencies such as the National Healthcare Safety Network (NHSN; formerly the National Nosocomial Infections Surveillance System) of the Centers for Disease Control and Prevention (CDC), were formed in response to the growing awareness of HAIs as an urgent public health and patient safety issue.2 In 2007, Medicare declared it would no longer reimburse for HAIs, such as catheter-related bloodstream infections (CRBSIs) and SSIs, increasing the urgency for rational and effective prevention and treatment strategies to reduce the morbidity, mortality and costs associated with HAIs.6 The recent action plan proposed by the Department of Health and Human Services has identified CRBSIs and SSIs as priority areas for prevention.7

This review will address the pathogenesis, microbiology, and treatment of these 2 important HAIs and will highlight recent advances in the area of prevention.

CATHETER-RELATED BLOODSTREAM INFECTIONS

Intravascular catheters play a central role in the care of critically and chronically ill patients. Each year, more than 5 million US patients undergo insertion of CVCs.1 More than 250,000 intravascular CRBSIs occur annually, with an associated mortality rate of 12% to 25%.1 A recent meta-analysis found mortality to be significantly increased in intensive care unit (ICU) patients with CRBSIs versus those without CRBSIs (random-effects model: odds ratio [OR], 1.96; 95% confidence interval [CI], 1.25-3.09).9 Each episode significantly increases hospital length of stay (LOS) and the added health care costs range from $4,000 to $56,000 per episode.4,9,10 The NHSN has published surveillance criteria for defining CRBSIs.2 The criteria for patients older than 1 year of age
are as follows: isolation of a recognized pathogen from blood culture(s), the presence of clinical signs of sepsis and/or shock (i.e., fever, chills, or hypotension), a determination that the infection is not from other sources, and confirmation that the organism is not a contaminant.

Intravascular devices (IVDs) include peripheral vascular catheters (venous and arterial), pulmonary artery catheters, midline catheters, peripherally inserted central catheters (PICCs), and various CVCs, including tunneled (usually long-term devices) and nontunneled catheters (percutaneously placed CVCs commonly used in ICUs).

Microbiology

Antimicrobial resistance, now considered a global crisis, continues to loom large, and the organisms causing CRBSIs are no exception. In the past 2 decades, the proportion of CRBSIs resulting from antimicrobial-resistant organisms, such as methicillin-resistant Staphylococcus aureus (MRSA) and fluconazole-resistant Candida spp, has been inexorably increasing at an alarming rate. Overall, the organisms most frequently responsible for CRBSIs are coagulase-negative staphylococci (CoNS; 31%), S. aureus (20%), enterococci (9%), and Candida spp (9%). In one large, prospective surveillance study using data from SCOPE (Surveillance and Control of Pathogens of Epidemiological Importance) and comprising 24,179 cases of nosocomial BSI occurring over a 7-year period at 49 hospitals, Wisplinghoff et al found that rates of MRSA infection increased from 22% in 1995 to 75% in 2001 ($P<0.001$), and vancomycin resistance was seen in 60% of Enterococcus faecium isolates.

Pathogenesis

The pathogenesis of CRBSIs can be attributed to 2 major mechanisms: 1) colonization of the device and 2) contamination of the fluid being administered (Figure 1). Contaminated infusate is the cause of most epidemic IVD-related BSI and is rare. Colonization of the device may be either extraluminal (from surrounding skin or hematogenous seeding of the catheter tip) or intraluminal (caused by organism adherence to the device followed by the creation of a biofilm, a process responsible for persistent infection and hematogenous spread). In short-term devices, the extraluminal route is more frequent, whereas the intraluminal route is more common in long-term devices ($\geq 10$ days) or in short-term devices remaining in place for more than 4 to 7 days.

Diagnosis

The clinical diagnosis of CRBSI is difficult because the sensitivity of clinical signs of inflammation at the skin is low. The confirmatory test for CRBSI is positive blood culture.
catheter site is low, as is the specificity of signs of systemic infection.\textsuperscript{18,19} A number of techniques for the diagnosis of CRBSIs have been studied, including catheter-sparing and noncatheter-sparing methods. These are summarized in Table 1. A recent meta-analysis found paired quantitative blood cultures to be the most accurate diagnostic test, followed by quantitative culture of blood through the CVC and quantitative or semi-quantitative catheter segment culture.\textsuperscript{20}

Paired quantitative blood cultures are labor intensive and are almost twice the cost of standard blood cultures. The wide availability of radiometric blood culture systems (eg, BACTEC, Becton Dickinson), in which blood cultures are continuously monitored for microbial growth (approximately every 20 minutes), has led to their application for the detection of CRBSI.\textsuperscript{21} The differential time to positivity (the detection of positivity in a culture of blood drawn from an IVD at least 2 hours before the detection of positivity in a blood culture drawn simultaneously from a peripheral site) has been shown to be highly predictive of CRBSI in several studies for short- and long-term devices.\textsuperscript{11,21-23} Newer diagnostic techniques, including acridine orange leukocyte cytospin and endoluminal brush, are currently being investigated and show promise.\textsuperscript{11,24-28}

### Management

The management of CRBSIs relies on 2 major clinical decisions: 1) the appropriate and timely administration of systemic antimicrobial treatment and 2) catheter removal or catheter salvage treatment. Systemic antimicrobial treatment should be selected based on the suspected or proven presence of causative agents in accordance with published guidelines.

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**Table 1. Diagnosis of Catheter-Related Bloodstream Infections**

<table>
<thead>
<tr>
<th>Diagnostic Method</th>
<th>Description</th>
<th>Criteria for Positivity</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods not requiring CVC removal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qualitative blood culture through device</td>
<td>One or more blood cultures drawn through CVC</td>
<td>Any growth</td>
<td>87</td>
<td>83</td>
</tr>
<tr>
<td>Quantitative blood culture through device</td>
<td>Blood culture drawn through CVC, processed by pour-plate methods or a lysis-centrifugation technique</td>
<td>≥100 CFU/mL</td>
<td>77</td>
<td>90</td>
</tr>
<tr>
<td>Paired quantitative blood cultures</td>
<td>Simultaneous cultures drawn through CVC and percutaneously</td>
<td>Both cultures positive with CVC culture yielding 5-fold higher or more than peripherally drawn culture</td>
<td>87</td>
<td>98</td>
</tr>
<tr>
<td><strong>Methods requiring CVC removal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Differential time to positivity</td>
<td>Simultaneous blood cultures drawn, through CVC and percutaneously, and monitored continuously</td>
<td>Both cultures positive with CVC positive ≥2 h earlier than peripherally drawn culture</td>
<td>85</td>
<td>81</td>
</tr>
<tr>
<td>Qualitative catheter segment culture</td>
<td>Segment from removed CVC is immersed in broth media and incubated for 24-72 h</td>
<td>Any growth</td>
<td>90</td>
<td>72</td>
</tr>
<tr>
<td>Semi-quantitative catheter segment culture</td>
<td>A 5-cm segment from removed CVC is rolled 4 times across a blood agar plate and incubated</td>
<td>≥15 CFU</td>
<td>85</td>
<td>82</td>
</tr>
<tr>
<td>Quantitative catheter segment culture</td>
<td>Segment from removed CVC is flushed or sonicated with broth, serially diluted, plated on blood agar and incubated</td>
<td>≥1,000 CFU</td>
<td>83</td>
<td>87</td>
</tr>
</tbody>
</table>

CFU, colony-forming units; CVC, central venous catheter

Adapted from reference 20.
Table 2. Recommendations for Preventing Catheter-Related Bloodstream Infections

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rating&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>• Educate all relevant health care personnel regarding indications for IV catheter use, proper procedures for insertion and maintenance, and infection control measures</td>
<td>IA</td>
</tr>
<tr>
<td><strong>Surveillance</strong></td>
<td></td>
</tr>
<tr>
<td>• Conduct institutional surveillance for rates of CRBSI, monitor trends, identify lapses in infection control practices</td>
<td>IA</td>
</tr>
<tr>
<td>• Express ICU data as number of CRBSIs per 1,000 catheter-days</td>
<td>IB</td>
</tr>
<tr>
<td><strong>Antisepsis</strong></td>
<td></td>
</tr>
<tr>
<td>• Maximal sterile barrier precautions during catheter insertion: cap, mask, sterile gown, sterile gloves, and large sterile sheet</td>
<td>IA</td>
</tr>
<tr>
<td>• Hand hygiene: wash hands with antiseptic-containing soap and water or waterless alcohol-based product before insertion or any manipulation of any IV catheter</td>
<td>IA</td>
</tr>
<tr>
<td>• Gloves: required for any manipulation of any IV catheter</td>
<td>IA</td>
</tr>
<tr>
<td>• Sterile gloves required for arterial and central catheters</td>
<td>IA</td>
</tr>
<tr>
<td>• Clean gloves acceptable for peripheral IV catheters if site not touched after application of skin antiseptics</td>
<td>IA</td>
</tr>
<tr>
<td>• Cutaneous antisepsis: Use before insertion and during dressing changes; 2% chlorhexidine is preferred, an iodophor or 70% alcohol is acceptable</td>
<td>IA</td>
</tr>
<tr>
<td><strong>Insertion</strong></td>
<td></td>
</tr>
<tr>
<td>• When possible, use subclavian site when using a nontunneled CVC</td>
<td>IA</td>
</tr>
<tr>
<td>• Use designated personnel for insertion and maintenance of IV catheters</td>
<td>IA</td>
</tr>
<tr>
<td>• Use sterile gauze or sterile, transparent semipermeable dressing</td>
<td>IA</td>
</tr>
<tr>
<td>• Do not give prophylactic antibiotics to prevent catheter colonization or BSI</td>
<td>IA</td>
</tr>
<tr>
<td><strong>Maintenance</strong></td>
<td></td>
</tr>
<tr>
<td>• Change dressing at least weekly</td>
<td>IB</td>
</tr>
<tr>
<td>• Monitor site visually or by palpation through intact dressing on regular basis and remove dressing for full exam if tender, fever without obvious source, or other manifestations suggesting local or BSI</td>
<td>IB</td>
</tr>
<tr>
<td>• Do not routinely culture catheter tips</td>
<td>IB</td>
</tr>
<tr>
<td>• Do not use topical antibiotic ointments or creams (except with dialysis catheters)</td>
<td>IA</td>
</tr>
<tr>
<td>• Remove IV catheters as soon as no longer necessary</td>
<td>IA</td>
</tr>
<tr>
<td>• Do not routinely replace CVCs, PICCs, HD catheters, or pulmonary artery catheters to prevent CRBSIs</td>
<td>IB</td>
</tr>
<tr>
<td>• Replace PICCs at least every 72-96 h in adults</td>
<td>IB</td>
</tr>
<tr>
<td>• Replace administration sets no more frequently than 72 h unless infection or unless infusing blood product or lipid emulsions</td>
<td>IB</td>
</tr>
<tr>
<td>• If after implementing a comprehensive strategy to reduce rates of CRBSIs and rates remain high, use antimicrobial or antiseptic-impregnated CVC in adults if CVC is expected to remain &gt;5 d</td>
<td>IB</td>
</tr>
<tr>
<td><strong>Novel strategies not addressed in current guidelines</strong></td>
<td></td>
</tr>
<tr>
<td>• Consider antimicrobial lock solutions for use in all long-term devices</td>
<td>IB</td>
</tr>
<tr>
<td>• Chlorhexidine-impregnated dressings (Biopatch) should be used with all short-term catheters</td>
<td>IA</td>
</tr>
<tr>
<td>• A sutureless catheter securement device (StatLock) is preferred to sutures</td>
<td>IB</td>
</tr>
<tr>
<td>• Adhere to the IHI bundle for CVCs</td>
<td>IA</td>
</tr>
</tbody>
</table>

BSI, bloodstream infection; CRBSI, catheter-related bloodstream infection; CVC, central venous catheter; HD, hemodialysis; IHI, Institute for Healthcare Improvement; IV, intravenous; PICC, peripherally inserted central venous catheter

* CDC categories of evidence: IA, strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies; IB, strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale; IC, required by state or federal regulations, rules, or standards; II, suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

Adapted from reference 1.


<table>
<thead>
<tr>
<th>Strategy</th>
<th>Study</th>
<th>Design</th>
<th>Technology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial lock solution</td>
<td>Safdar et al, 2006&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Vancomycin-containing locks vs heparin</td>
<td>50% risk reduction (RR, 0.49; 95% CI, 0.26-0.95)</td>
</tr>
<tr>
<td></td>
<td>Yahav et al, 2008&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>Various antibiotics&lt;sup&gt;a&lt;/sup&gt; Antibiotic plus antiseptic&lt;sup&gt;b&lt;/sup&gt; Antiseptic&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Antibiotic solutions: RR, 0.44; 95% CI, 0.38-0.5 Nonantibiotic antiseptic solutions alone: RR, 0.9; 95% CI, 0.48-1.69 Nonantibiotic antiseptic solutions + other prevention methods:&lt;sup&gt;d&lt;/sup&gt; RR, 0.25; 95% CI, 0.13-0.5</td>
</tr>
<tr>
<td></td>
<td>Sanders et al, 2008&lt;sup&gt;78&lt;/sup&gt;</td>
<td>Double-blind randomized trial</td>
<td>Ethanol-containing locks vs heparin</td>
<td>OR, 0.18; 95% CI, 0.05-0.65</td>
</tr>
<tr>
<td>Antimicrobial catheters</td>
<td>Veenstra et al, 1999&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Antiseptic-impregnated CVCs&lt;sup&gt;e&lt;/sup&gt;</td>
<td>OR, 0.56; 95% CI, 0.37-0.84</td>
</tr>
<tr>
<td></td>
<td>Ramritu et al, 2008&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Systematic review</td>
<td>Antibiotic-impregnated CVCs&lt;sup&gt;f&lt;/sup&gt;</td>
<td>RR, 0.39; 95% CI, 0.17-0.92</td>
</tr>
<tr>
<td></td>
<td>Crnich et al, 2002&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Silver-impregnated CVCs</td>
<td>RR, 0.40; 95% CI, 0.24-0.68</td>
</tr>
<tr>
<td></td>
<td>Ramritu et al, 2008&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Systematic review</td>
<td>Antibiotic vs first-generation antiseptic-impregnated CVCs</td>
<td>RR, 0.12; 95% CI, 0.02-0.67&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Hockenhull et al, 2009&lt;sup&gt;76&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Anti-infective CVCs (all types)</td>
<td>OR, 0.49; 95% CI, 0.37-0.64&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chlorhexidine dressings</td>
<td>Ho et al, 2006&lt;sup&gt;45&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Chlorhexidine-impregnated dressing vs placebo or povidone-iodine dressing</td>
<td>Catheter or exit-site colonization: 14.3% vs 27.2%; OR, 0.4; 95% CI, 0.26-0.61 CRBSI: 2.2% vs 3.8%; OR, 0.58; 95% CI, 0.29-1.14; P=0.11</td>
</tr>
<tr>
<td></td>
<td>Timsit et al, 2009&lt;sup&gt;74&lt;/sup&gt;</td>
<td>Randomized controlled trial</td>
<td>Chlorhexidine-impregnated dressing vs standard dressing</td>
<td>CRBSI: 0.4 vs 1.3 per 1,000 catheter-days; HR, 0.024; 95% CI, 0.09-0.65; P=0.005</td>
</tr>
<tr>
<td>Cutaneous antiseptics</td>
<td>Chaiyakunapruk et al, 2002&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Chlorhexidine vs povidone-iodine</td>
<td>RR, 0.49; 95% CI, 0.28-0.88&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mupirocin prophylaxis</td>
<td>Tacconelli et al, 2003&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Meta-analysis</td>
<td>Mupirocin prophylaxis in dialysis patients&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Decrease in S. aureus bacteremia in hemodialysis patients by 78%; RR 0.22; 95% CI, 0.11-0.42</td>
</tr>
</tbody>
</table>

CI, confidence interval; CRBSI, catheter-related bloodstream infection; CVC, central venous catheter; EDTA, ethylenediaminetetraacetic acid; HR, hazard ratio; OR, odds ratio; RR, relative risk.

<sup>a</sup>Gentamicin; gentamicin + citrate; gentamicin + vancomycin; gentamicin + cefazolin; cefotaxime. <sup>b</sup>Minocycline with EDTA.
<sup>c</sup>Citrate; citrate with tauridine. <sup>d</sup>Nasal mupirocin and exit-site iodine dressing. <sup>e</sup>Chlorhexidine-silver sulfadiazine. <sup>f</sup>Minocycline and rifampin. <sup>g</sup>Reduced risk with antibiotic catheters. <sup>h</sup>Reduced risk with anti-infective catheters: all types combined, see text for subgroup analysis. <sup>i</sup>Reduced with chlorhexidine. <sup>j</sup>Six studies used intranasal mupirocin 2 to 3 times daily for 5 to 14 days with various maintenance schedules; 4 studies used mupirocin applied to catheter exit site.
The decision of whether to remove the catheter is based on the type of catheter being used and the organism in question (Figure 2). This decision becomes more complex when specific patient characteristics are considered, such as the type of device required (tunneled or implanted) and the ease of venous access. Guidelines from the Infectious Diseases Society of America recommend the removal of nontunneled catheters in all complicated infections (e.g., thrombosis, endocarditis, osteomyelitis) and in all infections caused by *S. aureus*, gram-negative bacilli, *Enterococcus*, and *Candida* spp. The catheter may be retained with CoNS if systemic antibiotics are given in conjunction with antibiotic lock therapy. In CRBSIs associated with tunneled or implantable devices, the catheters also require removal for all complicated infections (e.g., thrombosis, endocarditis, osteomyelitis), tunnel or pocket infections and port abscesses, and for all infections caused by *S. aureus* and *Candida* spp. According to the recent guidelines, catheter salvage regimens, including the use of antibiotic lock therapy, may be attempted when necessary, for infections resulting from organisms other than *S. aureus*, fungi, *Pseudomonas aeruginosa*, *Bacillus* spp, *Micrococcus* spp, *Propionibacteria*, or *Mycobacteria*. Although device-sparing regimens using longer treatment durations and use of antibiotic lock solutions have been attempted for uncomplicated *S. aureus*, gram-negative bacilli, and even fungal pathogens, the data supporting the efficacy of this approach are scant; thus catheter salvage for *S. aureus* and other virulent organisms is not recommended.

The duration of therapy varies based on the organism and whether or not the device has been removed. Systemic therapy for CoNS infections ranges from 5 to 7 days when the catheter is removed, and from 10 to 14 days when the catheter is retained in conjunction with antibiotic lock therapy. With catheter removal and uncomplicated infection, the duration of systemic therapy for CRBSIs with *S. aureus* is a minimum of 14 days, 7 to 14 days for infections with gram-negative bacilli, and 14 days from the first negative blood culture for infections with *Candida* (Figure 2).

Transesophageal echocardiography (TEE) should be performed in all patients with a CRBSI caused by *S. aureus* because of the propensity of this organism to

**Figure 2. Management of catheter-related bloodstream infections.**

**AC**, arterial catheter; **ALT**, antimicrobial lock therapy; **CVC**, central venous catheter; **SAT**, systemic antimicrobial therapy

* Choose most appropriate systemic antimicrobial therapy based on current published guidelines.

* Remove retained catheter if there is clinical worsening, relapsing, or persisting infection.

* Current guidelines recommend considering catheter salvage therapy; however, outcomes may be poor.

Adapted from reference 18.
cause endocarditis. Rosen et al determined that TEE of all patients with a clinically uncomplicated CRBSI caused by S. aureus was a cost-effective way to determine duration of therapy—as short as 2 weeks if TEE results were negative.40

Catheter Salvage Strategies

When the need to retain an existing long-term catheter in a patient with a CRBSI is significant, salvage can be attempted by using antibiotic lock therapy as an adjunct to systemic therapy. Approximately 2 mL of solution is infused into the lumen of the catheter and allowed to remain there for a predetermined amount of time per day during the course of treatment. Solutions consist of the appropriately selected antibiotic, combined with heparin (if compatible). In the lock, antibiotic concentrations range from 100 to 1,000 times the usual systemic concentrations. This increased concentration has a greater likelihood of killing organisms embedded in biofilm. Current guidelines recommend that antibiotic lock solution be used for 10 to 14 days in conjunction with systemic treatment. Vancomycin, cefazolin, and ticarcillin-clavulanic acid (Timentin, GlaxoSmithKline)—all used in combination with heparin—have excellent stability when used in antibiotic lock treatment, retaining 90% of their activity after 10 days of dwell-time in the presence of susceptible organisms. CRBSI caused by Candida spp necessitates prompt removal of the catheter; however, this may not always be immediately possible. A solution of ethylenediaminetetraacetic acid (EDTA) with amphotericin B lipid complex showed promise in an in vitro model of a Candida biofilm formation, but further research is urgently needed.

Prevention

The CDC’s Healthcare Infection Control Practices Advisory Committee (HICPAC) has published extensive guidelines for the prevention of catheter-related infections. The guidelines, which are summarized in Table 2, focus on educating health care workers about catheter insertion and care; the surveillance of infection rates; practicing maximal antisepsis, including hand hygiene and barrier precautions; choosing the optimal insertion site and dedicated insertion personnel; and removing the device as soon as it is deemed unnecessary. Highlighted below are topics of importance in prevention, as well as novel strategies not addressed in the guidelines (Table 3). The recommendations are rated based on the strength of evidence supporting them. IA: strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies; IB: strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and a strong theoretical rationale; IC: required by state or federal regulations, rules, or standards; II: suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.1

Cutaneous Antisepsis

Iodophors, such as 10% povidone-iodine, historically have been the most widely used agent in the United States for skin antisepsis. However, recent studies, including a meta-analysis, have shown that 2% chlorhexidine (ChloraPrep, CareFusion) is the superior agent for preventing CRBSIs and is recommended by the HICPAC guidelines as the first-choice agent (rating IA).1,5,53

Topical Antimicrobials

The HICPAC guidelines specifically recommend against the use of topical antibiotic ointments or creams at the catheter insertion site, except in the case of hemodialysis catheters, to avoid promotion of fungal infections and antimicrobial resistance (rating IA).1 The guidelines also discourage the administration of intranasal antimicrobials before insertion or during the use of a catheter as a means to prevent colonization or CRBSI (rating IA).1 A meta-analysis of mupirocin prophylaxis to prevent S. aureus infections in patients undergoing dialysis showed a 63% reduction (95% CI, 50%-73%) in the rate of overall S. aureus infections.51 The study population included both hemodialysis and peritoneal dialysis patients. Of the 10 studies, 6 used intranasal mupirocin 2 to 3 times daily for 5 to 14 days with various maintenance schedules, and 4 used mupirocin applied to the catheter exit site. Among patients undergoing hemodialysis, S. aureus bacteremia was reduced by 78% (relative risk [RR], 0.22; 95% CI, 0.11-0.42). However, the differences in site, frequency, and duration of mupirocin treatment in the included studies and the resulting clinical heterogeneity make it difficult to draw robust conclusions.51 A randomized, double-blind, placebo-controlled trial evaluating mupirocin prophylaxis for nosocomial S. aureus infections in nonsurgical patients found that routine culture for S. aureus nasal carriage at admission and subsequent intranasal mupirocin use did not prevent nosocomial S. aureus infections.54 Additionally, reports of emerging mupirocin resistance are becoming commonplace.55-60 Routine use of topical or intranasal mupirocin for prophylaxis against CRBSIs is not recommended.

The limitations of mupirocin suggest that other topical approaches to preventing CRBSIs should be studied. One such agent is honey. Antibacterial properties of some types of honey have made this a promising agent to study. In a randomized controlled trial (RCT) examining the effect of thrice-weekly application of Medi-honey (commercially available; pooled antibacterial honeys including Leptospermum spp honey; Medihoney Pty Ltd.) to the exit site versus mupirocin on infection rates in 101 patients receiving hemodialysis via tunneled, cuffed, CVCs, the investigators found similar catheter-associated bacteremia rates in the 2 arms (0.97 vs 0.85 episodes per 1,000 catheter-days; P>0.05).61 Although these preliminary results are promising, a larger trial powered to show equivalence or superiority is needed.
to establish the use of Medihoney for the prevention of CRBSIs in patients receiving hemodialysis through tunneled, cuffed catheters.

Maximal Barrier Precautions

The use of maximal barrier precautions, including cap, sterile gown, mask, large sterile drape, and sterile gloves, significantly reduce the rate of CRBSIs when used during catheter insertion.162 In a study by Raad et al comparing maximal barrier precautions with control precautions (ie, sterile gloves and small drape), the BSI rate was 6.3 times higher in the control group (P=0.06).65 HICPAC guidelines recommend that maximal barrier precautions be used during all CVC insertions (rating IA).1

Insertion Site

According to the HICPAC guidelines, the preferred site for the insertion of nontunneled CVCs in adult patients is the subclavian vein (rating IA).1 The femoral site is associated with higher rates of catheter colonization as well as increased risk for deep vein thrombosis compared with other sites in adults.163-66 In an RCT comparing the femoral and subclavian sites, use of the femoral site was associated with a higher overall rate of infectious complications (19.8% vs 4.5%; P<0.001).66 The internal jugular site has been associated with higher rates of CRBSIs than the femoral and subclavian sites in several studies.166,67 However, a recent RCT comparing the jugular and femoral sites found no difference in the risk for infection between the sites (2.3 vs 1.5; P=0.42).67 A prospective, observational study comparing the subclavian, internal jugular, and femoral insertion sites found colonization lowest at the subclavian site but no difference in rates of infection between sites.68,69

Using real-time ultrasound guidance for catheter insertion decreases associated mechanical complications and infection.170,71 In a recent randomized study comparing real-time ultrasound guidance versus the landmark technique for catheter placement in the internal jugular vein resulted in significantly less complications, including fewer CRBSIs (P<0.001).71 A meta-analysis revealed that the use of ultrasound for insertion at the internal jugular and subclavian vein sites decreased failure (RR, 0.32; 95% CI, 0.18-0.55), complications during catheter placement (RR, 0.22; 95% CI, 0.10-0.45), and the need for multiple placement attempts (RR, 0.60; 95% CI, 0.45-0.79) in comparison with the landmark technique.70

Although no RCT to date has compared the 3 insertion sites, based on the available data, the subclavian site is the preferred site for CVC insertion with the use of real-time ultrasound to minimize mechanical complications.

Simulation-Based Training

A recent observational study, completed in an urban teaching hospital, evaluated the impact of a simulation-based educational intervention on the rates of CRBSI in a medical ICU.72 Ninety-two second- and third-year internal medicine and emergency medicine residents completed the program, which included a pretest, an informational video demonstrating proper CVC insertion techniques, training with ultrasound, hands-on practice using the simulator device, and a post-test with a required minimum score.72 There were 3.2 infections per 1,000 catheter-days in the 16 months prior to the intervention in this medical ICU. During this same time period, the surgical ICU at the same hospital reported 4.86 infections per 1,000 catheter-days. The rate of CRBSIs in the medical ICU during the 16-month intervention period, following completion of the training by all second- and third-year residents, decreased to 0.5 per 1,000 catheter-days. During the same 16-month period, the rate in the surgical ICU, where no rotating residents completed the simulation training, remained stable at 5.26 per 1,000 catheter-days.72 This study highlights the use of cutting-edge methods for the successful education of health care personnel regarding proper CVC insertion, fulfilling an important recommendation in the CDC guidelines for the prevention of CRBSIs.1

Chlorhexidine-Impregnated Dressings

The placement of a chlorhexidine-impregnated sponge dressing (Biopatch, Johnson & Johnson Gateway) over the CVC insertion site has been shown to decrease CRBSIs in several randomized trials.5,73-75 A large, open RCT compared the number of CRBSIs in an intervention group using these dressings (n=300) with a control group using standard sterile dressings (n=301) in chemotherapy patients, with 9,731 catheterization days. The results demonstrated a significant reduction in CRBSIs in the intervention group (6.35%, 19) compared with the control group (11.3%, 34; RR, 0.54; 95% CI, 0.31-.094; P=0.016).75 In ICU patients, the use of chlorhexidine-impregnated dressings led to significantly fewer CRBSIs compared with standard sterile dressings, in a large RCT (hazard ratio, 0.024; 95% CI, 0.09-0.65; P=0.005).74

The latest CDC guidelines make no recommendations regarding the use of chlorhexidine-impregnated dressings. However, the current data suggest that these dressings are effective in reducing CRBSIs, thus their use is recommended (rating IA).5,73-75

Antimicrobial-Impregnated Catheters

The HICPAC guidelines recommend the use of antimicrobial-coated catheters if the device is expected to remain in place longer than 5 days and while used in combination with a comprehensive CRBSI reduction strategy (rating IB).1 However, the majority of the studies have focused on the use of antimicrobial-coated CVCs used as short-term devices; few data have been published on their use as long-term devices.7,46 Several types of catheters are available: catheters coated either externally (first-generation) or externally and internally (second-generation) with chlorhexidine and silver-sulfadiazine (CHSS), catheters coated with minocycline
or rifampin, and silver-impregnated catheters. Silver-coated catheters include silver, platinum, and carbon-coated catheters and silver ion/alloy catheters.

A meta-analysis of externally CHSS-coated catheters found a decrease in the incidence of both catheter colonization (OR, 0.44; 95% CI, 0.36-0.54) and CRBSI (OR, 0.56; 95% CI, 0.37-0.84) compared with uncoated catheters. A more recent meta-analysis found a reduced risk for CRBSI when first-generation CHSS-coated catheters (RR, 0.66; 95% CI, 0.47-0.93) were compared with uncoated catheters but no significant risk reduction among patients in the ICU (RR, 0.77; 95% CI, 0.53-1.13). The second-generation CHSS-coated catheters significantly reduced CRBSIs in ICU patients (RR, 0.70; 95% CI, 0.30-1.62). Minocycline- and rifampicin-coated catheters were significantly more effective relative to CHSS catheters (RR, 0.12; 95% CI, 0.02-0.67).

The most recent meta-analysis of 27 trials evaluating use of all types of anti-infective catheters found a significant reduction in CRBSIs (OR, 0.49; 95% CI, 0.37-0.64). Subgroup analysis based on catheter type revealed reductions in CRBSI for nearly all types compared with standard catheters: CHSS-impregnated (5 trials; OR, 0.51; 95% CI, 0.26-1.0), silver-impregnated (6 trials; OR, 0.55; 95% CI, 0.33-0.92), minocycline-rifampin (5 trials; OR, 0.26; 95% CI, 0.15-0.47), miconazole-rifampin (1 trial; OR, 0.12; 95% CI, 0-6.07), benzalkonium chloride-impregnated (1 trial; OR, 0; 95% CI, 0.06-16.45), and CHSS-coated (9 trials; OR, 0.62; 95% CI, 0.4-0.98).

The choice of which catheter to use is governed by many factors including efficacy, cost, cost-effectiveness, and risk for promoting drug resistance. A 2008 analysis found an estimated cost savings of approximately $227 for every anti-infective catheter inserted. Antibiotic resistance is a particular concern with antibiotic-impregnated catheters, although trials assessing the efficacy of minocycline-rifampin-coated catheters found no evidence of the emergence of drug resistance.

### Antimicrobial Lock Solutions

The major mechanism for CRBSIs in patients with long-term devices is intraluminal colonization. For this reason, antimicrobial lock solutions have been tried as a logical step to prevent colonization of the intraluminal surfaces of long-term devices and thereby reduce the rate of CRBSIs. A small amount of the antimicrobial solution is instilled into the lumen of the catheter and allowed to remain for a specific amount of time, after which it is either flushed or removed. A meta-analysis of 7 randomized trials, involving mostly cancer patients in whom vancomycin-containing lock solutions were used demonstrated a significantly reduced risk for CRBSIs (RR, 0.49; 95% CI, 0.26-0.95). A recent systematic review and meta-analysis of patients undergoing hemodialysis included studies of several lock solutions: various antibiotic combinations, minocycline with EDTA, and nonantibiotic antiseptic solutions including citrate and citrate with taurolidine. All lock solutions tested showed benefit regarding prevention of CRBSIs. Ethanol has proved safe and effective as an antimicrobial lock solution. A recently published, prospective, double-blind, RCT comparing ethanol with heparinized saline in immunosuppressed hematology patients showed a 4-fold decrease in the number of CRBSIs in the ethanol group compared with the controls (OR, 0.18; 95% CI, 0.05-0.65). Although in vitro studies show a number of new antibiotics have promise as lock solutions, further research of their efficacy in a clinical trial is necessary. Antimicrobial lock solutions are recommended for prevention of CRBSIs in long-term devices in patients at high risk for CRBSIs, such as those on hemodialysis. In general, antiseptic lock solutions are preferable to antibiotic lock solutions because of their greater spectrum of activity and smaller risk for promoting antibiotic resistance.

### Needle-Free Connectors

In addition to the previously described protective measures, the role of needle-free connectors in the prevention of CRBSIs should be mentioned. Needle-free connectors were developed in response to demands for enhanced safety for health care workers (to prevent needlestick injuries) and are integral components of infusion systems in use across North America. Although needle-free connectors, when properly used, clearly reduce the risk for needlestick injuries during access of an IVD or injection port, some reports published over the past decade have raised concerns about a potential increased risk for iatrogenic BSI associated with their use. Most of these studies have been retrospective and uncontrolled, and suboptimal manipulation of the device, rather than the device itself, may have been responsible for the increased incidence of BSIs in some settings. Typically, health care personnel disinfect the connector with 70% (v/v) isopropyl alcohol before IV administration. Although needle-free connectors appeared to reduce contamination in comparison with standard caps, a recent study by Menyah et al found that conventional methods of disinfection may not prevent microbial entry if the luer-activated device (LAD) is heavily contaminated, which may account for the increased risk for BSIs seen in some reports. This issue has been addressed with the development of new technology. The V-Link with VitalShield (Baxter Healthcare) is an LAD protected with an interior and exterior antimicrobial coating and was recently approved by the FDA. The V-Link with VitalShield is effective against 99.9% of pathogens known to cause CRBSIs in vitro testing.

Saralex-CL (Menyah Healthcare Systems), another promising device, is an antimicrobial-barrier cap that threads onto the end of a needle-free LAD system. A recent prospective in vitro study compared standard disinfection of common LADs using 70% isopropyl alcohol with the new antiseptic-barrier cap, Saralex-CL. This new cap system, which uses a solution of 0.25 mL of 2% CHG in 70% isopropyl alcohol to bathe the connector septum, was effective in preventing transmission of pathogens across the membranes of precontaminated
LADs compared with standard techniques (positive control, 100% transmission; standard, 20 of 30; 67% transmission; Saralex-CL, 1 of 60; 1.6% transmission; \( P<0.001 \)).

Data on the clinical efficacy of antimicrobial-coated LADs and antimicrobial-barrier caps is awaited.

**Catheter Securement**

Choices for device securement include sutures, tape, and catheter-securement devices such as StatLock (Venetec International, a subsidiary of CR Bard). Sutures may be uncomfortable for the patient, pose a risk for needlestick injury to the provider, and foster inflammation at the catheter insertion site, increasing the risk for infection. StatLock, a sutureless catheter-securement device, reduces catheter-related complications including CRBSIs.95-97 An RCT comparing sutures to StatLock for PICC securement revealed a significant decrease in the number of CRBSIs in the StatLock group versus the suture group (2 vs 10, respectively; \( P=0.032 \)).96 We recommend the use of a securement device for peripheral IV and extended-dwell catheters, such as PICCs.

**Intensive Insulin Therapy**

The appropriate level of glycemic control in critically ill patients is controversial. A large RCT of 1,548 critically ill patients in an ICU, the majority of whom were surgical patients, compared intensive insulin therapy (maintenance of blood glucose level between 80 and 110 mg/dL) with conventional insulin therapy (insulin given only if blood glucose level was above 215 mg/dL and maintenance of levels between 180 and 200 mg/dL).98 The study found reduced overall mortality with intensive treatment (8% with conventional treatment vs 4.6% with intensive treatment; \( P<0.04 \)); the greatest reduction in mortality was seen in patients with multiorgan failure resulting from a septic focus.98

A similar study in medical ICU patients found no reduction in mortality nor difference in bacteremia rates with intensive therapy.99

A meta-analysis that included 29 RCTs with 8,432 patients found no difference in hospital mortality with tight glucose control (21.6% vs 23.3%; RR, 0.93; 95% CI, 0.85-1.03), and the results did not change when patients were stratified by type of ICU: surgical, medical, or medical-surgical. However, tight glucose control was associated with a reduced risk for septicemia (10.9% vs 13.4%; RR, 0.76; 95% CI, 0.59-0.97).100

In the NICE-SUGAR (Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation) study, a large RCT of 6,104 adult ICU patients, intensive glycemic control (goal 81-108 mg/dL) was associated with increased mortality compared with conventional control (goal ≤180 mg/dL; OR, 1.14; 95% CI, 1.02-1.28; \( P=0.02 \)).101 The study population included more medical than surgical ICU patients (intensive group: 36.9% surgical, 63.1% medical; conventional group: 37.2% surgical, 62.8% medical). Severe hypoglycemia (≤40 mg/dL) was significantly more common in the intensive control group (6.8% vs 0.5%; \( P<0.001 \)).101

A recent meta-analysis of 26 trials involving 13,567 patients, including the data from the NICE-SUGAR trial, found no mortality benefit from intensive insulin therapy in critically ill patients (pooled RR of death with intensive therapy vs conventional therapy, 0.93; 95% CI, 0.83-1.04).102 However, when analyzed separately, surgical ICU patients had decreased mortality with intensive insulin therapy (RR, 0.63; 95% CI, 0.44-0.91).

Pending the results of ongoing and future research, the use of intensive glycemic control in surgical ICU patients should be considered to reduce the risk for HAI s, particularly BSIs. However, avoidance of severe hypoglycemia is critical and a glycemic target that can be achieved safely should be chosen.

**Multifaceted Approach**

A multifaceted approach must be used to effectively reduce the risk for CRBSIs. The Institute for Healthcare Improvement (IHI) has developed the concept of “bundles” to aid in risk reduction. A bundle, according to the IHI, is a structured way of improving the processes of care and patient outcomes using a set of practices, generally 3 to 5, that when performed collectively and reliably have been shown to improve patient outcomes.103 The IHI-recommended evidence-based bundle for CVC care includes the following: 1) proper hand hygiene; 2) maximal barrier precautions during insertion of catheter; 3) chlorhexidine skin antisepsis; 4) optimal catheter site selection, with subclavian vein as preferred site for nontunneled catheters; and 5) daily review of line necessity with prompt removal of unnecessary lines.103

In a large multicenter study by Pronovost et al, in which evidence-based interventions nearly identical to those of the IHI CVC bundle were used for 18 months, a significant reduction in CRBSIs from baseline was observed, with incidence rate ratios at 0 to 3 months of 0.62 (95% CI, 0.47-0.81) and at 16 to 18 months of 0.34 (95% CI, 0.23-0.5).104 These numbers represented up to a 66% reduction in rates of CRBSIs.

Bhutta et al undertook a prospective quasi-experimental study in a children’s hospital. The study included the stepwise introduction of interventions over a 5-year period.105 The interventions included maximal barrier precautions, a transition to antibiotic-impregnated CVCs, annual hand-washing campaigns, and the use of chlorhexidine in lieu of povidone-iodine. Significant decreases in rates of infection occurred over the intervention period. These were sustained over the 3-year follow-up. Annual rates decreased from 9.7 per 1,000 catheter-days in 1997 to 3.0 per 1,000 catheter-days in 2005 (RR, 0.75; 95% CI, 0.55-1.26). The investigators agreed that multifaceted interventions of this nature reduce CRBSIs, but require a multidisciplinary team effort and institutional support.

The recent implementation of a multifaceted approach in a pediatric cardiac ICU, which included CVC insertion and maintenance bundles, chlorhexidine-impregnated dressings, nurse and physician education, and the addition of a unit-based infection control nurse, resulted in a...
reduction in CRBSIs from 7.8 to 2.3 infections per 1,000 catheter-days over a period of less than 2 years.106

SURGICAL SITE INFECTIONS

BACKGROUND
An estimated 30 million surgical procedures requiring general anesthesia are performed each year in the United States, with about 1% to 3% resulting in surgical site infections (SSIs).107,108 SSIs are responsible for approximately 20% of all HAIs.108 These serious infections cost more than $20,000 per hospital admission and increase hospital LOS by more than 9 days.3,108-111 Patients who develop SSIs have at least twice the mortality rate as those who do not develop SSIs, are 60% more likely to be admitted to the ICU, and are 5 times more likely to be readmitted to the hospital.109 The overall burden on the US health care system is estimated at $10 billion per year.111 Rates of SSIs range from less than 1% to nearly 17%, depending on type of procedure and individual patient risk factors, according to the latest data from the NHSN.112

Definitions
The CDC has assigned specific categories and definitions for SSIs.115 These definitions are important in both diagnosis and surveillance of SSIs. The major categories for SSIs are superficial incisional (eg, cellulitis); deep incisional (eg, an abscess of deep soft tissue at the incision site); and organ/space (eg, a remote abscess in an organ or organ space accessed intraoperatively).113 Although organ/space infections represent only 33% of all SSIs, they are responsible for more than 90% of SSI-related deaths.114

Microbiology and Pathogenesis
Any specific organism responsible for an SSI is related to the type (ie, clean, clean-contaminated, contaminated, or dirty) and location of the surgery.114 Clean surgeries—including most cardiac and orthopedic procedures—are susceptible to mainly the endogenous flora of the skin (ie, staphylococcal species). Clean-contaminated surgeries may involve opening a viscous organ, and infecting organisms often are polymicrobial, representing the endogenous flora of that organ or proximal mucosa.115 The organisms responsible for SSIs have remained relatively stable over the past few decades. S. aureus is the most common organism, followed by CoNS, Enterococcus spp, and gram-negative bacilli. However, as is occurring in other HAIs such as CRBSIs, antimicrobial-resistant strains are increasing in prevalence.111 A recent study reporting on data from 26 community hospitals in the southern United States revealed that MRSA was the most common cause of SSIs (17%), followed by methicillin-susceptible S. aureus (MSSA; 15%), gram-negative bacilli (14%), CoNS (11%), Enterococcus spp (8%), Streptococcus spp (3%), fungi (3%), and anaerobes (3%).111 Table 4 summarizes the microbiology of SSIs.114,116-118

The pathogenesis of SSIs typically stems from inoculation of the surgical site intraoperatively (either externally from the patient’s skin or internally from mucous membranes); and contamination from health care professionals, the outside environment, internally from opened organs, and less frequently from a distant focus of infection.107 Endogenous organisms originating from the patient are responsible for the vast majority of SSIs.119

Several risk factors for SSIs (eg, organism virulence, patient factors, operative or treatment-related factors) have been identified.114,120 Major patient factors associated with SSIs include obesity, diabetes, older age, malnutrition, hypoxemia, poor tissue perfusion, remote infection, perioperative transfusions, and colonization with staphylococci.114,121,122 Type and risk level of the surgery, as defined by the National Nosocomial Infections Surveillance System risk categories (Table 5), operating room characteristics (ie, ventilation, equipment), use of foreign materials, inadequate antisepsis of skin, surgical technique, inadequate antibiotic prophylaxis, hypothermia, oxygenation, and length of procedure all are operative or treatment-related factors associated with increased risk for SSIs.114,120,122-127

Diagnosis and Treatment
The diagnosis of an SSI is dependent on the CDC definitions and criteria for the specific type of SSI as previously mentioned.113 The infection must occur within 30 days of the procedure, or within 1 year of the procedure if foreign material has been left in place.113 Treatment of an SSI is based on the type of infection (incisional vs organ/space), the infecting organism, and the location of the infection. However, general principles can be applied to all SSIs. The most important measure in the treatment of an SSI is source control.115 For example, all abscesses must be drained, necrotic tissues must be debrided or resected, and infected hardware may need to be removed. Systemic antibiotics, selected based on cultured or suspected organisms, are used as adjunct therapy.

Prevention
The most recent CDC guidelines for the prevention of SSIs are summarized in Table 6.114 The general principles encompass the following measures: preoperative (eg, patient preparation, surgical team member preparation, appropriate antimicrobial prophylaxis); intraoperative (eg, operating room and environmental factors, surgical attire and technique); and postoperative measures (eg, appropriate wound management, infection surveillance).114 Highlighted below are important topics in the prevention of SSIs, as well as newer strategies not addressed in the guidelines.

Preoperative Antimicrobial Prophylaxis
The importance of appropriate preoperative antimicrobials for SSI prophylaxis cannot be overstated. Several studies performed since the 1960s have shown that
Table 4. Common Surgical Site Pathogens According to Procedure and Recommended Antibiotic Prophylaxis

<table>
<thead>
<tr>
<th>Operation</th>
<th>Likely Pathogens</th>
<th>Recommended Prophylaxis and Adult Preoperative Dosage&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head and neck</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involving oral or pharyngeal mucosa</td>
<td>Oropharyngeal anaerobes, EGN, upper respiratory flora</td>
<td>Clindamycin 600-900 mg IV AND gentamicin 1.5 mg/kg IV OR cefazolin 1-2 g IV + metronidazole 500 mg IV</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td></td>
<td>Staphylococcus aureus, CoNS                                                                                                 Cefazolin 1-2 g IV OR vancomycin 1 g IV</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td></td>
<td>S. aureus, CoNS, gram-negative bacilli, Pseudomonas spp, streptococci spp                                                                                                  Ophthalmic drops: aminoglycoside, quinolone, or neomycin-gramicidin-polymyxin B; multiple drops topically over 2-24 h Cefazolin 100 mg subconjunctivally</td>
</tr>
<tr>
<td>Thoracic</td>
<td></td>
<td>S. aureus, CoNS, Streptococcus pneumoniae, EGN                                                                                      Cefazolin 1-2 g IV OR vancomycin&lt;sup&gt;b&lt;/sup&gt; 1 g IV</td>
</tr>
<tr>
<td>(Noncardiac)</td>
<td></td>
<td>Cefazolin 1-2 g IV                                                                                                           Cefazolin 1-2 g IV OR vancomycin&lt;sup&gt;b&lt;/sup&gt; 1 g IV</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td>S. aureus, CoNS                                                                                                            Cefazolin 1-2 g IV OR vancomycin 1 g</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esoph/gastro/duodenal</td>
<td>EGN, streptococci, staphylococci                                               High risk only&lt;sup&gt;c&lt;/sup&gt;: cefazolin 1-2 g IV</td>
<td></td>
</tr>
<tr>
<td>Biliary tract</td>
<td>EGN, streptococci, staphylococci, enterococci, clostridia                          High risk only&lt;sup&gt;c&lt;/sup&gt;: cefazolin 1-2 g IV</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>EGN, anaerobes, enterococci                                                      Cefoxitin 1-2 g IV + ampicillin/sulbactam 3 g IV AND PO&lt;sup&gt;e&lt;/sup&gt; on day prior: neomycin 1 g + erythromycin 1 g at 1 PM, 2 PM, and 11 PM Cefazolin 100 mg subconjunctivally</td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>EGN, anaerobes, enterococci                                                      Uncomplicated: cefoxitin 1-2 g IV</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td>Complexed: ampicillin/sulbactam 3 g IV</td>
</tr>
<tr>
<td>Hysterectomy (all types)</td>
<td>EGN, enterococci, GBS, anaerobes                                                Cefoxitin or cefazolin 1-2 g IV OR ampicillin/sulbactam 3 g IV</td>
<td></td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>EGN, enterococci, GBS, anaerobes                                                Cefazolin 1-2 g IV given after cord is clamped</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gynecologic/OB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td>EGN, enterococci                                                                                                           High risk&lt;sup&gt;f&lt;/sup&gt;: ciprofloxacin 500 mg PO or 400 mg IV</td>
</tr>
<tr>
<td>Orthopedic</td>
<td></td>
<td>S. aureus, CoNS                                                                                                            Cefazolin 1-2 g IV OR vancomycin 1 g IV</td>
</tr>
<tr>
<td>Vascular</td>
<td></td>
<td>S. aureus, CoNS, EGN, clostridia, enterococci                                                                                Cefazolin 1-2 g IV OR vancomycin 1 g IV</td>
</tr>
</tbody>
</table>

<sup>a</sup> If more than a 4-hour procedure, redose every 1 to 2 half-lives of drug (in patients with normal renal function).  
<sup>b</sup> Vancomycin should be used if institutional rates of methicillin-resistant Staphylococcus aureus (MRSA) or methicillin-resistant CoNS surgical site infections are high (>10%), or in patients with known MRSA colonization.  
<sup>c</sup> Decreased stomach acidity, gastric obstruction, gastrointestinal hemorrhage, decreased gastric motility, obesity.  
<sup>d</sup> If over age 70 years, acute cholecystitis, nonfunctioning gallbladder, obstructive jaundice, common duct stones.  
<sup>e</sup> Give after bowel preparation.  
<sup>f</sup> Positive or unknown urine culture, preoperative catheter, transrectal prostate biopsy, use of prosthetic.

Adapted from references 114, 116-118, and 132.
appropriate antibiotics, given just prior to surgery and discontinued within 24 hours postoperatively, significantly reduce the rates of SSI.\textsuperscript{123-133} Current recommendations by the National Surgical Infection Prevention Project include selection of antibiotic based on published guidelines for the individual procedure; IV administration of the antibiotic within 60 minutes prior to incision (120 minutes if using a fluoroquinolone or vancomycin); and discontinuation of antibiotics within 24 hours post-surgery (48 hours post-cardiac surgery).\textsuperscript{132}

Administering the dose just prior to surgery ensures adequate tissue perfusion levels at the time of incision, and discontinuing therapy within 24 hours decreases rates of antimicrobial resistance.\textsuperscript{129,130,132} Moreover, a single preoperative dose may be as effective in preventing SSIs as continuing therapy for 24 hours postoperatively, as shown in a 1998 meta-analysis.\textsuperscript{144} Although benefits are clear, compliance with these guidelines is not yet 100%. In 2002, the percentages of patients who received the appropriate preoperative antibiotic, had the antibiotic administered within 60 minutes of incision, and discontinued therapy within 24 hours were 91.4%, 47.6%, and 40.75%, respectively; the corresponding percentages in 2004 were 92.2%, 69.7%, and 52.9%.\textsuperscript{117} Translating the principles of appropriate antibiotic prophylaxis into practice and taking into account regional and local patterns of antimicrobial resistance, should be important goals of every health care institution.

**Novel Measures for Prevention of SSIs**

**Supplemental Perioperative Oxygenation**

Oxygen-dependent killing by neutrophils is an essential innate mechanism in the prevention and control of infection.\textsuperscript{135-137} In 2 RCTs, patients with normal arterial oxygen saturations given 80% oxygen perioperatively had significantly decreased rates of SSIs compared with patients given 30% oxygen.\textsuperscript{124,138} After reviewing 4 RCTs in a 2009 meta-analysis of the use of supplemental perioperative oxygen for reducing SSIs among patients undergoing colorectal surgery, the authors found that the overall rate for SSIs was reduced with supplemental perioperative oxygen.\textsuperscript{139} Two of these trials found significant reduction in SSI rates using perioperative hyperoxygenation (80% supplemental oxygen compared with 30% oxygen).\textsuperscript{139} One study, using 80% oxygen mixed with 20% nitrogen versus 30% oxygen, found no significant difference between the 2 groups, and a final study using 80% oxygen versus 30% oxygen found an increased SSI rate in patients receiving 80% FiO\(_2\) (fractional inspired concentration of oxygen).\textsuperscript{139} The meta-analysis revealed a significant reduction in SSI incidence when using a fixed-effects model (relative risk [RR], 0.70; 95% CI, 0.52-0.94; \(P=0.01\)) but no statistical significance was found when the authors used the random-effects model (RR, 0.74; 95% CI, 0.39-1.43; \(P=0.37\)) and an ID test revealed moderate heterogeneity.\textsuperscript{139} A second meta-analysis, also published in 2009, had similar results (fixed-effects model: RR, 0.742; 95% CI, 0.599-0.919; \(P=0.002\)).\textsuperscript{140} The authors included an additional RCT, by Myles et al, which differed from other studies in that the control group received a nitrous oxide mixture and the intraoperative oxygen was continued for a variable period postoperatively in the intervention group.\textsuperscript{133} Although the data appear to favor its use, further research is necessary to clarify the role of supplemental perioperative oxygenation for the prevention of SSIs.

**Maintenance of Normothermia**

Mild hypothermia, which often occurs during surgery, causes vasoconstriction and decreases oxygenation of tissues.\textsuperscript{126,142} An RCT of patients undergoing colorectal surgery compared routine operative thermal care with additional operative warming.\textsuperscript{126} In the normothermia group, patients’ core temperatures were maintained near 36.5°C; in the hypothermia group, the core temperature was allowed to decrease to approximately 34.5°C. The group that received additional warming had a 6% SSI rate compared with 19% (\(P=0.009\)) in the routine care group, and had shorter hospital LOS by 2.6 days (\(P=0.01\)).\textsuperscript{126} Maintenance of normothermia in patients undergoing colorectal surgery is a performance measure of the Surgical Care Improvement Project and is recommended to decrease the risk for SSIs.\textsuperscript{117}

**Antibiotic Sutures**

Two-thirds of all SSIs are confined to the incision.\textsuperscript{144} To address this issue, specialized antimicrobial sutures have been developed. Plus Sutures (Ethicon, Johnson & Johnson) are a family of sutures—monocryl, coated vicryl, PDS—enhanced with triclosan, a broad-spectrum antibiotic. In vitro and animal studies have demonstrated the safety and effectiveness of these products\textsuperscript{143-145} and recent clinical studies have shown promising results.\textsuperscript{146-148} Justinger et al compared the use of coated VICRYL Plus Sutures (Ethicon, Johnson & Johnson) with polydioxanone sutures (PDS II, Ethicon, Johnson & Johnson) in midline laparotomy procedures.\textsuperscript{147} Of patients in the PDS group, 10.8% had wound infection (113 of 1,045), whereas 4.9% (51 of 1,043) in the antibiotic-coated suture group developed infections (\(P<0.001\)). Alternative antimicrobial suture technologies, including sutures coated with the antiseptics chlorhexidine or octenidine in combination with fatty acids, are currently being studied and show promise as well.\textsuperscript{149} Further clinical studies, including RCTs and/or comparative effectiveness studies, are needed to explore the role of antimicrobial-impregnated sutures for the prevention of SSIs.

**Nasal Decolonization**

Over the past several decades *S. aureus* consistently has been the leading organism causing SSIs.\textsuperscript{111,114,150,151} Because nasal colonization with *S. aureus* precedes infection, agents that can eradicate *S. aureus* nasal carriage may be important in reducing invasive infection.\textsuperscript{152} This is particularly relevant for MRSA, because nasal colonization with MRSA poses a greater risk for invasive infection than nasal colonization with MSSA.\textsuperscript{153} Several different methods for the eradication of MRSA carriage have been studied and are highlighted in a recent review.\textsuperscript{154} Mupirocin, a topical antibiotic, is a commonly...
A randomized, double-blind, placebo-controlled trial involving 891 surgery patients (cardiothoracic, general, oncologic, gynecologic, and neurologic) evaluating preoperative treatment with intranasal mupirocin, applied with a cotton swab twice daily for 5 days, showed no significant reduction in the overall rate of *S. aureus* SSIs (2.3% vs 2.4%), but did exhibit a significant decrease in the rate of all nosocomial *S. aureus* infections among those who were *S. aureus* carriers (OR, 0.49; 95% CI, 0.25-0.92; *P* = 0.02). In orthopedic patients, a double-blind, randomized, placebo-controlled study with 614 patients found a decrease in the colonization rate in the mupirocin group compared with the placebo group, 86.8% and 34.6%, respectively, but no significant decrease in SSIs. A 2003 evidence-based review found that although mupirocin significantly decreased nasal colonization, the incidence of SSIs was not reduced and mupirocin could not be recommended for routine use. A 2005 systematic review and meta-analysis concluded that intranasal treatment with mupirocin significantly decreased SSIs in patients undergoing nongeneral surgery, but was not efficacious in patients undergoing general surgery. A 2008 evidence-based review found that treatment with mupirocin reduced the rate of postoperative *S. aureus* infections in those patients who were *S. aureus* carriers.

A recent Cochrane Review evaluated the use of mupirocin for the prevention of *S. aureus* infections in patients with known *S. aureus* nasal carriage. In the subgroup analysis of surgical patients, there was a significant reduction in the rate of overall nosocomial *S. aureus* infections (RR, 0.55; 95% CI, 0.34-0.88; *I*² = 0%, fixed-effects model); however, no significant reduction in the rate of SSIs caused by *S. aureus* were found (RR, 0.63; 95% CI, 0.38-1.04). These findings were consistent with the previous review by van Rijen described above. The absence of significant findings in this analysis of SSIs was likely the result of a lack of power, as described by the authors; however, the mixed surgical populations (such as general surgery patients) of the included studies likely contributed to heterogeneity as well.

Mupirocin is known to be safe and 94% effective for the decolonization of *S. aureus* nasal carriage, which has led to its widespread use. New agents are needed as resistance to mupirocin has been well described. Retapamulin (*Altabax*, GlaxoSmithKline), a new topical antibiotic ointment, shows promise for use in the future, as in vitro studies demonstrate good activity against *Streptococcus pyogenes* and *S. aureus*, including strains resistant to methicillin and mupirocin.

Although further studies are needed in this area, mupirocin may be considered for use in patients who are undergoing nongeneral surgery and who are colonized preoperatively with MRSA. Surveillance to detect mupirocin resistance should be undertaken if a decolonization program is implemented.

### Glycemic Control

Elevated blood glucose levels in the operative and perioperative periods have been associated with greater risk for SSIs. However, the appropriate treatment of hyperglycemia is not clear. The current CDC guidelines for the prevention of SSIs recommend maintaining serum glucose levels below 200 mg/dL in surgical patients with diabetes. Several issues remain unresolved in this area: 1) whether lower blood glucose targets, using intensive insulin therapy regimens, are beneficial for reducing infectious complications.
Table 6. Guidelines for Prevention of Surgical Site Infections

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative</strong></td>
<td></td>
</tr>
<tr>
<td>Patient Preparation</td>
<td></td>
</tr>
<tr>
<td>• Identify and treat all infections remote to surgical site before elective operations</td>
<td>IA</td>
</tr>
<tr>
<td>• Do not remove hair preoperatively, unless it will interfere with operation</td>
<td>IA</td>
</tr>
<tr>
<td>• Control serum blood glucose in diabetics, avoid hyperglycemia perioperatively</td>
<td>IB</td>
</tr>
<tr>
<td>• Encourage tobacco cessation</td>
<td>IB</td>
</tr>
<tr>
<td>• Do not withhold necessary blood products as a means to prevent SSI</td>
<td>IB</td>
</tr>
<tr>
<td>• Wash area to remove gross contamination before antiseptic skin preparation</td>
<td>IB</td>
</tr>
<tr>
<td>• Use appropriate antiseptic agent for skin preparation</td>
<td>IB</td>
</tr>
<tr>
<td>Surgical Team</td>
<td></td>
</tr>
<tr>
<td>• Keep nails short, no artificial nails</td>
<td>IA</td>
</tr>
<tr>
<td>• Preoperative surgical scrub for at least 2-5 min with appropriate antiseptic</td>
<td>IB</td>
</tr>
<tr>
<td>• Educate staff on need to report any possible transmissible infectious illness</td>
<td>IB</td>
</tr>
<tr>
<td>• Develop policies concerning patient care duties when staff have possible</td>
<td>IB</td>
</tr>
<tr>
<td>transmissible infectious conditions</td>
<td></td>
</tr>
<tr>
<td>• Staff with draining skin lesions must be excluded from duty until infection</td>
<td>IB</td>
</tr>
<tr>
<td>resolved</td>
<td></td>
</tr>
<tr>
<td>• Staff who are colonized with organisms (S. aureus or group A streptococci)</td>
<td>IB</td>
</tr>
<tr>
<td>should not be excluded unless linked to dissemination of the organism</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial Prophylaxis</td>
<td></td>
</tr>
<tr>
<td>• Select based on efficacy for common pathogens of specific operation and</td>
<td>IA</td>
</tr>
<tr>
<td>guidelines</td>
<td></td>
</tr>
<tr>
<td>• Give IV, timed for maximal bactericidal concentrations in serum and tissues</td>
<td>IB</td>
</tr>
<tr>
<td>when incision is made, during operation, and until, at most, a few hours</td>
<td></td>
</tr>
<tr>
<td>after incision is closed</td>
<td></td>
</tr>
<tr>
<td>• Do not routinely use vancomycin for antimicrobial prophylaxis</td>
<td>IB</td>
</tr>
<tr>
<td><strong>Intraoperative</strong></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td></td>
</tr>
<tr>
<td>• Maintain positive pressure ventilation in operating room</td>
<td>IB</td>
</tr>
<tr>
<td>• Minimum of 15 air changes per hour, filter all air through appropriate filters,</td>
<td>IB</td>
</tr>
<tr>
<td>introduce all air at ceiling and exhaust near floor</td>
<td></td>
</tr>
<tr>
<td>• Do not use UV radiation to prevent SSI</td>
<td>IB</td>
</tr>
<tr>
<td>• Use EPA-approved disinfectant to clean areas with visible soiling or body fluid</td>
<td>IB</td>
</tr>
<tr>
<td>contamination between operations</td>
<td></td>
</tr>
<tr>
<td>• Do not perform routine environmental sampling, only as part of epidemiologic</td>
<td>IB</td>
</tr>
<tr>
<td>investigation</td>
<td></td>
</tr>
<tr>
<td>• Sterilize all surgical instruments according to published guidelines</td>
<td>IB</td>
</tr>
<tr>
<td>• Wear surgical mask covering mouth and nose if sterile instruments are exposed,</td>
<td>IB</td>
</tr>
<tr>
<td>when entering operating room, and throughout operation</td>
<td></td>
</tr>
<tr>
<td>• Wear cap or hood to cover all hair, and sterile gloves after donning sterile</td>
<td>IB</td>
</tr>
<tr>
<td>gown</td>
<td></td>
</tr>
<tr>
<td>Surgical Technique</td>
<td></td>
</tr>
<tr>
<td>• Maintain aseptic principles when placing intravascular devices</td>
<td>IA</td>
</tr>
<tr>
<td>• Handle tissue gently, maintain hemostasis, minimize devitalized tissue and</td>
<td>IB</td>
</tr>
<tr>
<td>foreign bodies, eradicat dead space</td>
<td></td>
</tr>
<tr>
<td>• Use delayed primary skin closure if site considered heavily contaminated</td>
<td>IB</td>
</tr>
<tr>
<td>• Use closed suction drain if drainage is necessary and remove as soon as possible</td>
<td>IB</td>
</tr>
<tr>
<td><strong>Post-operative</strong></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td></td>
</tr>
<tr>
<td>• Sterile dressing for 24-48 h for primary closures</td>
<td>IB</td>
</tr>
<tr>
<td>• Wash hands before and after dressing changes or any contact with site</td>
<td>IB</td>
</tr>
</tbody>
</table>

CDC Definitions of SSI To Identify SSI Among Inpatients and Outpatients

• Assign surgical wound classification upon completion of operation
• Periodically calculate operation-specific SSI rates stratified by variables associated with increased SSI risk and report these rates to surgical team members

Novel Strategies Not Addressed in Guidelines

• Actively maintain normothermia of patient intraoperatively
• Consider use of hyperoxygenation intra- and perioperatively
• Consider preoperative decolonization of MRSA in known carriers undergoing nongeneral surgery

CDC, Centers for Disease Control and Prevention; EPA, Environmental Protection Agency; MRSA, methicillin-resistant Staphylococcus aureus; SSI, surgical site infection; UV, ultraviolet

* CDC categories of evidence: IA, strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies; IB, strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and a strong theoretical rationale; IC, required by state or federal regulations, rules, or standards; II, suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

Adapted from reference 114.
specifically SSIs; 2) the appropriate timing of these measures (ie, preoperative, intraoperative, postoperative); and 3) the treatment of hyperglycemia in diabetic versus nondiabetic patients and in those with impaired fasting glucose or undiagnosed diabetes at the time of surgery.

Van den Berghe et al found decreased mortality with intensive insulin therapy (goal 80-110 mg/dL) compared with conventional therapy (insulin given when blood glucose >215 mg/dL, goal 180-200 mg/dL) in an RCT of 1,548 mostly cardiac surgery ICU patients (8% with conventional treatment vs 4.6% with intensive treatment; P<0.04) with the greatest reduction in mortality seen in patients with multiorgan failure resulting from sepsis. However, SSI was not an outcome in this study. Other studies have demonstrated a benefit with intensive insulin therapy regimens for the reduction of infectious complications in surgical patients, with the most work done in cardiac surgery patients.

A meta-analysis of 26 trials involving 13,567 patients (medical and surgical), found no overall mortality benefit of intensive insulin therapy in critically ill patients (95% CI, 0.83-1.04). However, when analyzed separately, patients in the surgical ICU did have a mortality benefit, whereas those in nonsurgical ICUs did not (RR, 0.63; 95% CI, 0.44-0.91).

Gandhi et al undertook an RCT of 400 patients undergoing cardiac surgery to determine the effect of intraoperative intensive insulin treatment versus conventional treatment. Intraoperatively, patients in the intensive treatment group received continuous infusions of insulin once their blood glucose level was above 100 mg/dL and

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**Table 7. Meta-Analyses Examining the Efficacy of Decolonization With Mupirocin for the Prevention of SSIs**

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Study Design</th>
<th>Studies Included</th>
<th>Patient Populations</th>
<th>Outcomes Randomized Trials</th>
<th>Outcomes Nonrandomized Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kallen AJ et al (2005)</td>
<td>Systematic review and meta-analysis</td>
<td>Randomized and non-randomized trials155-157,172-175</td>
<td>Mixed surgical: Orthopedic (2) Gastrointestinal (2) Cardiac (2)</td>
<td>Nongeneral surgery: (cardiothoracic, orthopedic, neurosurgery) 6% vs 7.6% (RR, 0.80; 95% CI, 0.58-1.1) General surgery: 8.4% vs 8.1% (RR, 1.04; 95% CI, 0.81-1.33)</td>
<td>Nongeneral surgery: (cardiothoracic, orthopedic, neurosurgery) 1.7% vs 4.1% (RR, 0.4; 95% CI, 0.29-0.56) General surgery: 11.3% vs 18% (RR, 0.63; 95% CI, 0.35-1.14)</td>
</tr>
<tr>
<td>Trautmann M et al (2008)</td>
<td>Systematic review</td>
<td>Randomized and non-randomized trials155-157,172-175</td>
<td>Mixed surgical: Orthopedic (3) Gastrointestinal (2) Cardiac (5)</td>
<td>Cardiac surgery: 1 trial with no difference in rate180 Gastrointestinal surgery: 1 trial with no difference in rate172</td>
<td>Cardiac surgery: 3 trials with significant reductions in SSIs155,174,177 Orthopedic surgery: 1 trial with significant reduction in SSI rates173 1 with insignificant trend toward reduction157 1 with no reduction in overall SSIs reported178 Gastrointestinal surgery: 1 trial with no difference in rate172,175 MRSA SSI rates found decreased MRSA SSI rates based on 2 trials175-177</td>
</tr>
<tr>
<td>Van Rijen M et al (2008)</td>
<td>Cochrane Systematic Review and meta-analysis</td>
<td>Randomized controlled trials156,157,180-186</td>
<td>4 of 9 trials surgical: Cardiac (2) Orthopedic Mixed surgical</td>
<td>Decrease in rate of S. aureus infections in known carriers (RR, 0.55; 95% CI, 0.34-0.88)</td>
<td>NA</td>
</tr>
</tbody>
</table>

CI, confidence interval; MRSA, methicillin-resistant Staphylococcus aureus; NA, not applicable; RR, relative risk; SSI, surgical site infection
maintained between 80 and 100 mg/dL. Patients in the conventional treatment group did not receive insulin during surgery unless the blood glucose level exceeded 200 mg/dL. Postoperatively, both groups were treated identically with an insulin infusion to maintain blood glucose levels between 80 and 100 mg/dL. Rates of death (4% vs 0%, respectively; \( P=0.061 \)) and stroke (8% vs 1%, respectively; \( P=0.02 \)) were significantly higher in the intensive treatment group than in the conventional treatment group.\(^{169}\)

A recent Cochrane Review, including 5 RCTs, evaluating perioperative glycemic control found insufficient evidence for the strict use of intensive insulin therapy over conventional therapy for the prevention of SSIs.\(^{165}\)

Although there may be benefits of intensive insulin therapy in surgical patients, they must be weighed against the increased risk for hypoglycemic events and mortality as observed in some studies.\(^{169-171}\) Given the conflicting results of studies, no recommendation regarding intensive insulin therapy in surgical patients for the prevention of SSIs could be made.

References


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**Note:** This text is a transcription of the document contained in the image, and is not intended to be a comprehensive or authoritative representation of all content therein. It is provided for reference and does not indicate the full context or quality of the original material.


Drs. Bearden and Safdar have no relevant disclosures to report.