Prevention of central line associated bloodstream infections in critical care units
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Purpose of review
Central line associated bloodstream infections (CLABSIs) are a common source of morbidity and mortality in neonatal and pediatric intensive care units. Successful preventive strategies have recently been reported which have resulted in significant reductions in CLABSIs and their associated adverse outcomes.

Recent findings
Current surveillance data indicate a recent decline in reported CLABSI rates, likely secondary to changes in diagnostic criteria and improvements in central line care. Recent pilot randomized trials in the neonatal intensive care unit population have assessed the safety and efficacy of chlorhexidine gluconate for cutaneous antisepsis and silver alginate-impregnated dressings. No significant reductions in CLABSIs have been noted with the use of either. The greatest success has come with implementation of evidence-based catheter care bundles, which have been shown in individual units and collaborative critical care networks to significantly reduce CLABSI rates.

Summary
CLABSIs remain a significant problem in neonatal and pediatric critical care units, but implementation of catheter care bundles can significantly reduce rates of these infections. The safety and efficacy of chlorhexidine gluconate, silver alginate, and antibiotic-coated catheters need to be assessed via large, multicenter trials. Creation of collaborative networks may facilitate this goal.

Keywords
central venous catheterization, evidence-based medicine, healthcare-associated infections, intensive care unit, neonatal, pediatrics

Introduction
Central line associated bloodstream infections (CLABSIs) are common in the neonatal and pediatric intensive care unit (NICU and PICU, respectively) populations. CLABSI can significantly increase medical costs, morbidity, and mortality [1–4]. These associated outcomes, combined with mandates in public reporting and proposals from insurance providers to withhold payment for healthcare-associated infections (HAIs) [5], have resulted in efforts among critical care units to curtail these infections as well as increase research efforts to improve central line care. In this review we focus on current issues surrounding the definition of CLABSI, recent data on improved methods for central line management, and successful approaches to preventing CLABSI among individual and collaborative NICUs and PICUs.

Defining a central line associated bloodstream infection
A CLABSI is defined as a laboratory-confirmed bloodstream infection (LCBI) without another identifiable source that occurs with a central line in place at the time of, or within 48 h before, the onset of infection [6]. Accurately defining an LCBI can be a challenge. To maintain consistency in public reporting and to assist in infection control, the National Healthcare Safety Network (NHSN) has devised and published definitions for common HAIs including CLABSIs [7,8]. In 2008, these definitions were modified with a major change involving more stringent criteria for the diagnosis of common skin contaminant-related LCBI [8]. The prior definition stated that, in addition to the presence of signs and symptoms of infection, a common skin contaminant had to be cultured from two or more blood cultures drawn on separate occasions or from one blood culture after which appropriate antimicrobial therapy is instituted [7]. The definition now only states that, in addition to signs and symptoms of infection, there must be two or more positive blood cultures to meet criteria [8].

The modification, in practice, has presented some pitfalls. Obtaining two blood cultures of adequate volume in critically ill neonates and children can be difficult and can thereby impact diagnosis [i.e. if only one culture is...
obtained and is positive for coagulase-negative staphylococci (CoNS), criteria are technically not met. Furthermore, many clinicians would likely institute antistaphylococcal therapy even if they were only able to obtain a single blood culture given the potential impact of delaying appropriate antimicrobial coverage. This would potentially make the results of subsequent blood cultures unreliable. Given that CoNS make up the majority of pathogens responsible for CLABSI [9], the potential for under-reporting must be considered. In 2007, using data from 2006 and the prior definition for an LCBI, the NHSN reported overall NICU and PICU-related CLABSI rates of 4.3 and 5.3 per 1000 central line days, respectively [10]. In 2009, using data from 2006 through 2008 and the new definition, they reported a benchmark CLABSI rate of 2.9 per 1000 for both NICU and PICU patients [11]. Whereas some of the decline in CLABSI surveillance rates may be due to improvements in central line care, the definition change is likely to have played a role. With so much pressure and emphasis now on ‘getting to zero’, accurate reporting of benchmark data has become critical and under-reporting potentially problematic. Furthermore, it remains to be determined whether this change has had any impact on practice. In particular, has the need for two positive blood cultures altered the clinician’s perception of what is or is not a true infection and thereby affected the continued problem of antimicrobial over-exposure in the ICU?

**Cutaneous antisepsis and chlorhexidine gluconate**

The majority of CLABSIs are believed to be preventable. Considerable efforts have focused on improving and developing novel techniques for central line placement and management (Table 1). Selection of an appropriate cutaneous antiseptic is one crucial aspect of CLABSI prevention [6]. Guidelines for adult and pediatric populations recommend the use of chlorhexidine gluconate (CHG) over povidone iodine, and most PICUs have adopted this practice. However, controversy still exists as to its safety and efficacy in neonates [6]. Although CHG may reduce bacterial colonization as compared with povidone iodine, its use in the NICU has not been shown to reduce the risk of CLABSI [12]. Some data suggest that 2% CHG exposure may result in local skin reactions [13,14]. As a result of this and the concern for systemic absorption, the Federal Drug Administration (FDA) has not approved CHG for cutaneous use in infants below 2 months of age.

In an effort to further explore this issue, a pilot-randomized trial was conducted in five NICUs to assess systemic absorption of CHG and to compare rates of contact dermatitis with the use of an alcohol-based 2% CHG vs. 10% povidone iodine for cutaneous antisepsis in infants requiring a peripherally inserted central catheter (PICC) [15]. Enrollment was limited to infants more than 1500 g and above 7 days and below 2 months of age. Twenty-four infants were enrolled in each group. No cases of severe dermatitis were observed. Ten neonates had serum CHG levels evaluated, with measurable amounts detected in seven. Serum concentrations of CHG were noted to increase with the number of cutaneous applications. No significant differences were noted between groups with respect to rates of bloodstream infection (BSI) [15]. Despite evidence of systemic absorption and the fact that the FDA does not approve its cutaneous use in infants below 2 months of age, CHG is still utilized in this population, with some reporting safety and efficacy with its intermittent application [14]. In order to definitively assess CHG use in the neonates in both the NICU and PICU populations, a large, randomized controlled trial of infants below 2 months of age, with analysis of subgroups including the extremely low birth weight population, is needed. In the meantime, lack of data to support its efficacy and concerns regarding risks of systemic absorption and what effect it may have on the neonate remain a deterrent to its use.

**Catheter site care**

Proper catheter site care is vital to CLABSI prevention, as contamination of the catheter hub is believed the most common source of these infections [16,17]. The NICU at Westchester Medical Center conducted a recent investigation aimed at evaluating the impact of a new approach to catheter hub care [18]. An educational program was developed which included reinforcement of hand hygiene, the use of a hub care checklist, and 2% CHG in 70% isopropyl alcohol to scrub the catheter hub. Adherence to protocols resulted in a decrease in PICC-related BSI from 23 infections per 1000 catheter-days to 12 [odds ratio (OR) 0.33, 95% confidence interval (CI)]

### Key points

- CLABSI impacts on morbidity, mortality, and healthcare cost in ICUs.
- The establishment of a uniform definition of CLABSI is very helpful for research but may not be as useful for the clinical setting.
- The most effective current strategy for decreasing CLABSI rates is the use of evidence-based central line bundles.
- Further research is needed to fully evaluate antimicrobial coated catheters and antimicrobial dressings in children.
- Chlorhexidine gluconate application in neonates for the prevention of CLABSI should be further evaluated to fully understand its risks and benefits.
Table 1 Studies evaluating potential improvements in catheter insertion and maintenance

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Comparison</th>
<th>Population</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Garland et al. [15**]</td>
<td>Randomized</td>
<td>CHG vs. PI</td>
<td>N = 48; neonates &gt;1500 g, &gt;7 days, &lt;60 days old</td>
<td>No dermatitis; measurable serum CHG levels in seven of 10; no significant difference in colonization or BSI</td>
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<tr>
<td>Levy et al. [19]</td>
<td>Randomized, controlled</td>
<td>CHG sponge vs. clear occlusive</td>
<td>N = 145; children 0–18 years; admitted postop. to a pediatric cardiac ICU</td>
<td>Significant reduction in colonization with CHG; no significant difference in BSI</td>
</tr>
<tr>
<td>Khattak et al. [20]</td>
<td>Randomized, controlled</td>
<td>Silver alginate vs. clear occlusive</td>
<td>N = 50; neonates 500–1500 g, &gt;3 days old</td>
<td>Measurable serum silver levels (below toxic); no skin reactions; no significant difference in CLABSI but lower rates in study group (6.7 vs. 12.3 per 1000 central line days)</td>
</tr>
<tr>
<td>Hill et al. [21]</td>
<td>Randomized, controlled</td>
<td>Silver alginate vs. clear occlusive</td>
<td>N = 118; NICU patients &gt;3 days old</td>
<td>Study group of significantly lower birth weight (1330 vs. 2450 g); no skin reactions noted; no significant difference in CLABSI; delay in onset of infection in treatment group (18 vs. 5 days)</td>
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<tr>
<td>Chelliah et al. [22]</td>
<td>Prospective, observational</td>
<td>Minocycline–rifampin coated vs. noncoated</td>
<td>N = 225; all PICU patients</td>
<td>No significant difference in CLABSI; delay in onset of infection in treatment group (18 vs. 5 days)</td>
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BSI, bloodstream infection; CHG, chlorhexidine gluconate; CLABSI, central line associated bloodstream infection; NICU, newborn intensive care unit; PI, povidone iodine; PICU, pediatric intensive care unit.

In addition to catheter hub care, some recent investigations have evaluated antimicrobial impregnated dressings. As of the most recent Center for Healthcare Safety and Prevention guidelines from 2002, no recommendations were made regarding the use of CHG or silver impregnated dressings. In the PICU population, there has only been one randomized controlled trial conducted, in a pediatric cardiac intensive care unit in Israel, which evaluated the impact of CHG-impregnated dressings on CLABSI [17]. The investigators determined that there was less central line colonization with the use of these dressings, but the BSI rate did not differ significantly between study and control populations [19]. Of note, there were only seven BSI identifications in the 145 postoperative patients over the course of the study (three in the control group, four in the CHG, making it difficult to draw any definitive conclusions.

In conclusion, the use of CHG-impregnated dressings in the NICU is well tolerated in the premature neonatal population but as the use of silver-impregnated dressings may be well tolerated in the premature neonatal population, but as these were not measured. These data seem to suggest that the use of topically applied silver alginate central line dressings in very low birth weight infants, with a PICC in PICU [21]. No statistically significant difference was observed between groups with respect to CLABSI (12.4% in the study group and 17.2% in controls) and no adverse reactions were observed [21]. Systemic absorption of silver and those using standard dressings. Twenty-five patients were enrolled in each group and, although serum silver concentrations were collected and infection rates compared between the groups using silver alginate dressings and those using standard dressings, the difference was considered to be toxic. No adverse skin reactions or impairment of hepatic or renal function were noted, and a concentration of 0.17–0.91. Cost savings from this initiative were determined to be between $88,759 and $241,800 [18].
with the use of CHG, larger trials are needed to better assess their safety and efficacy before routine use can be advocated.

**Antimicrobial-coated catheters**

Data from adults seem to suggest that central lines impregnated with antimicrobials like minocycline and rifampin may reduce central line colonization and CLABSI [24,25]. These data led to recommendations for their use in adults with expected central line needs for more than 5 days [6]. In children below 3 kg, no antimicrobial-coated catheters are available, and there is little evidence to support their use in larger children. Data for use in the PICU population are limited to one prospective, observational study of 225 central lines [22]. Although no statistically significant difference was noted in the rate of CLABSI with the use of minocycline- and rifampin-coated catheters as compared with uncoated catheters (7.5 vs. 8.6 per 1000 central line days), the investigators did note that the median time to infection was nearly three-fold longer in children who had an antibiotic-coated catheter. It is therefore possible that the use of antibiotic-coated catheters may delay onset of infection. This, coupled with prompt removal of catheters when no longer necessary, may result in reductions in CLABSI rates. However, further evidence is needed to understand the risks and benefits of antimicrobial-coated catheters in children.

**Catheter bundles**

Although approaches to individual aspects of central line management may be efficacious in reducing CLABSI, the greatest success has been reported with the use of catheter care bundles (Table 2). A bundle is a group of evidence-based interventions that, when implemented together, results in a better outcome than when executed individually [26*].

In the NICU at Yale-New Haven Children’s Hospital, we implemented a central line bundle based predominantly on the Healthcare Infection Control Practices Advisory Committee (HICPAC) guidelines [6] and aimed at reducing CLABSI and HAI among our hospitalized neonates [27]. A unit-wide educational effort was initiated which included a formalized, evidence-based training program for catheter placement and maintenance, implementation of daily discussions on patient care rounds regarding the continued need for a central line, and regular CLABSI surveillance and feedback to the staff [27]. Preinitiative and postinitiative data were compared and determined that CLABSI rates decreased significantly from 8.4 per 1000 central line days to 1.7 (rate difference: −6.7, 95% CI −9.0 to −4.5) and the overall rate of healthcare-associated BSI from 5.8 to 1.4 per 1000 patient days (rate difference −4.4, 95% CI −5.6 to −3.3) [27].

State-wide and national collaboratives aimed at reducing CLABSI have also been established. In 2006, 13 NICUs in California participated in an effort to reduce rate of CLABSI [28**]. Interventions included organization of a leadership team in each NICU with physician, nursing, and infection control representatives and implementation of evidence-based best practices for hand hygiene and line placement and management. Conference calls were conducted and a team visited each NICU to assist in implementation of bundles. A 25% reduction in CLABSI

**Table 2 Best practices for central line insertion and maintenance**

<table>
<thead>
<tr>
<th>Education, training, leadership</th>
<th>Assemble team with representatives from all aspects of central line care</th>
<th>Designate team leaders (both physician and nursing)</th>
<th>Conduct formalized education, training, and assessment of all personnel involved in central line insertion and care</th>
<th>Create an insertion checklist</th>
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<tbody>
<tr>
<td>Catheter insertion</td>
<td>Perform proper hand hygiene prior to all aspects of catheter insertion and care</td>
<td>Utilize maximal sterile barrier precautions during insertion including cap, mask, sterile gown and sterile gloves, and large sterile drape to cover entirety of work area</td>
<td>Use an assistant</td>
<td>For children &lt;2 months, utilize 2% chlorhexidine gluconate for cutaneous antisepsis. Scrub for 30 s for nonfemoral lines and 2 min for femoral lines and allow to air dry</td>
</tr>
<tr>
<td>Catheter maintenance</td>
<td>Minimize catheter entry</td>
<td>Use a sterile, transparent dressing</td>
<td>Change dressings when visibly damp, loosened, or soiled</td>
<td>Use prepackaged dressing change kit and checklist</td>
</tr>
<tr>
<td>Catheter removal</td>
<td>Replace administration sets, including add-on devices, no more frequently than every 96 h unless they are soiled or suspected to be infected</td>
<td>Assess daily and remove when catheter is no longer needed</td>
<td>Disinfect hub with alcohol or chlorhexidine gluconate</td>
<td>Replace tubing that is used to administer blood, blood products, or lipids within 24 h of initiating infusion</td>
</tr>
<tr>
<td>Surveillance</td>
<td>Conduct regular surveillance of unit-based data utilizing standard definitions and provide periodic feedback to staff</td>
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Data from [6,17**].
in all birth weight groups was observed as the overall rate of CLABSI declined from 4.3 to 3.2 infections per 1000 central line days [28].

Similarly, in 2007 the New York State Department of Health funded a collaborative between its regional perinatal centers aimed at devising an evidence-based initiative to reduce CLABSI [29]. Their objectives were to create a network to identify key performance criteria and to plan and implement quality improvement initiatives, to select a meaningful performance indicator, to identify sites with low CLABSI and to organize site visits, and to develop an evidence-based care bundle to reduce CLABSI [29]. Representatives from each regional perinatal centers participated in workshops aimed at addressing these aims [29]. When 6 months of postintervention data were analyzed, it was determined that, although NICU site was a major determinant of outcome, the use of central line maintenance checklists (part of their catheter care bundle) was associated with a reduction in CLABSI rates [30].

Individual PICUs and dedicated pediatric cardiac intensive care units have demonstrated similar success with the utilization of catheter care bundles [31,32]. Two large multicenter PICU collaborative efforts have been conducted to date [17**,33]. Miller et al. [17**] reported data from a long-term collaborative initiated in 2006 by the National Association of Children’s Hospitals and Related Institutions (NACHRI). The collaborative incorporated 29 PICUs in a multicenter prospective study using historical data for comparison [17**]. Their approach included selection of multidisciplinary team members at each site to lead the initiative, multiple centralized workshops, resource-intensive education and monitoring at the unit level, and funding to support the collaborative. Their major goal was a 50% reduction in CLABSI rates within 1 year through 90% adherence to insertion bundles and 70% adherence to maintenance bundles. What resulted was a significant reduction in CLABSI from 5.4 to 3.1 per 1000 central line days as well as 84% insertion and 82% maintenance adherence. Of note, the only significant predictor of CLABSI reduction was adherence to the maintenance, not the insertion, bundle [17**].

As membership of NICU and PICU collaboratives like NACHRI continues to grow, data from these networks will hopefully assist in further assessing the efficacy and sustainability of current ‘best practices’. In addition, these large collaboratives present an opportunity to conduct large, multicenter randomized controlled trials which could definitely assess the safety and effectiveness of further approaches to pediatric catheter care, such as antibiotic-coated catheters and the use of CHG in neonates.

**Conclusion**

Central line associated bloodstream infections remain a major problem in neonatal and pediatric critical care units. Recent efforts have focused on improvements in materials as well as in techniques for cutaneous antisepsis and catheter site care. Growing interest and attention to preventing HAI has also initiated much needed funding for collaborative research aimed at better defining the problem and at further improving technology and strategies for central line care. To date, the most effective strategy remains the use of evidence-based central line bundles which have been shown to have substantial impacts on CLABSI rates and their associated morbidity and mortality, as well as costs to the healthcare system.

**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- **of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 136–137).

The only randomized trial comparing the safety (including systemic absorption) and efficacy of cutaneous antiseptic with chlorhexidine gluconate with povidone-iodine antiseptic for central venous catheter placement in neonates. J Perinatol 2009; 29:808–813.

The first published study from this multicenter national collaborative’s efforts to decrease NICU central line-associated bloodstream infections. J Perinatol 2009; 29:591–599.


The first published study from this multicenter national collaborative’s efforts to eradicate CLABSIs.


A detailed description of the methodology and results from a state-wide collaborative to reduce neonatal CLABSI.


This is a great starting point for parties interested in establishing methods to prevent central line infections.

Aq u a l i t yi m p r o v e m e n t i n i t i a t i v et o prevent central line infections. JAMA 2009; 301:591–599.

An excellent ‘how to’ description of the processes involved in identifying a clinical problem and creating a collaborative plan to solve it.


Reluctant to conclude that the hospital catheter-related infection rate is too high, the panel of experts convened to assess the evidence and to provide guidance. BMJ 2007; 334:362–365.


The largest multicenter adult 2 × 2 factorial study on the use of CHG dressing and less frequent dressing changes to reduce CLABSIs.