Decreasing Central Line Associated Bloodstream Infection in Neonatal Intensive Care

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Health care associated infection (HAI) and central line associated bloodstream infection (CLABSI) are major foci of efforts in the realm of safety and error reduction because they represent such an obvious example of a breakdown in the systems of hospital care. Despite the attention that is placed on this topic and the resources expended in research and technology to reduce these infections, the problem persists.

This discussion attempts to shed light on why the problem of CLABSI has not been eliminated as have certain infectious diseases or simple public safety problems. The article discusses the specific evidence-based strategies that have been shown to be effective in reducing CLABSI, the barriers to their adoption in the complex hospital environment, and how they can be successfully overcome.

The authors’ goal is to convince readers that the journey toward decreasing CLABSI to zero begins and ends with the reader’s appreciation that it is more about how we do the right care processes rather than choosing the right processes. The mantra of quality improvement—ensuring that the right process is being used at the right time—is all too often given short shrift as users search for the newest products, policies and best practices. This truism is perhaps best exemplified by model newborn intensive care units (NICUs) throughout the country that have maintained low levels of infection even as patients, products, policies, and practices have so

KEYWORDS
- Central line associated bloodstream infection
- Nosocomial infection
- Bloodstream infection
- Quality improvement
dramatically changed over 3 decades\textsuperscript{1,2} (S. Butler, personal communication, October 2009). Their achievement demonstrates that it is how we sustain best practices within the NICU that is critical to continually decreasing CLABSI toward a zero infection rate.\textsuperscript{3}

**WHY DOES CONTEXT MATTER?**

Context refers to the complicated milieu that makes up the unique culture of each NICU. These units are complex workplaces in which hundreds of providers interact either directly or indirectly with large numbers of patients and their families, often for many days or even months. It is not surprising that this merging of various individuals’ knowledge, experiences, attitudes, and languages produces many unique and even unstable combinations of these personal factors. The evolution of these combinations is nonlinear and unit-specific. Introducing new processes inevitably stresses these relationships and challenges their evaluation. Studies of organizational learning highlight specific leadership characteristics that are associated with receptivity to change, such as encouraging openness to excellence, learning mechanisms that encourage information flow and aid systems-thinking, and commitment of resources.\textsuperscript{4} Each of these factors is uniquely different from center to center. Successful introduction of new processes is thus dependent on understanding the unique human dynamics of each organization. Berwick\textsuperscript{5} describes this process as using the construct of “context” as set forth by Pawon and Tilley.\textsuperscript{6}

**Why Does This Matter to the NICU Patient?**

**Mortality**

Attributable mortality is the proportion of deaths in hospitalized patients who acquire a bloodstream infection that is due to the infection and not the underlying disease. The attributable mortality for bloodstream infection, calculated from case control studies, typically ranges from 15\% to 35\% for adult patients.\textsuperscript{7} Several studies have reported attributable mortality due to HAI in neonates. The rates in these studies vary from 24\% in the pre-surfactant era to 11\% in the post-surfactant era.\textsuperscript{8–10}

**Morbidity**

The toll of CLABSI in neonates extends beyond the short-term mortality statistics. Newborn sepsis has been shown to be associated with adverse outcomes in multiple systems, the most important of which is the central nervous system (CNS). In short-term and longitudinal follow up studies, the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network and others have shown an association between sepsis, poor growth, and adverse neurodevelopmental outcome at 2 years.\textsuperscript{10–12} Abnormalities of the white matter in magnetic resonance imaging studies are reported to be the predominant CNS lesion associated with sepsis.\textsuperscript{12,13} This association is supported by emerging evidence that links white matter injury to pre-oligodendroglial cell damage from reactive oxygen species and inflammatory cytokines.\textsuperscript{14}

Other systems are also affected by sepsis, most likely through similar mechanisms mediated by inflammatory cytokines. Neonatal sepsis has been associated with longer duration of mechanical ventilation, higher incidence of chronic lung disease, and hepatic fibrosis.\textsuperscript{10,15,16} Finally, the cumulative toll of the multisystem injury resulting from sepsis along with the actual short-term morbidity of the sepsis event itself contribute substantially to the duration of hospitalization of affected infants.\textsuperscript{10,17,18}
**What are the Technical Issues?**

**Hand colonization**

Hand colonization of hospital personnel with pathogenic organisms is associated with transmission of these organisms and HAI.\(^2,19–21\) The role of hand colonization in the transmission of pathogenic organisms has been the subject of numerous cohort and prospective studies, beginning in the nineteenth century with observations by Labarraque and Semmelweis.\(^22–24\) Efforts at reducing hand colonization have led to decreased HAI in hospital-wide studies\(^25–28\) and in the NICU.\(^29–32\) More important are studies that have demonstrated the direct transmission of pathogens from health care workers to catheter material.\(^24,33,34\) This pathway is the key to understanding and appreciating the crucial role of hand colonization in the acquisition of CLABSIs. When hands with high bacterial colony counts come into contact with connections, access ports, or catheter hubs, the organisms become resident in those areas. The potential transformation of individual bacterial colonies to a living planktonic layer or biofilm increases with each exposure.\(^35,36\) Contact with surfaces inside the isolette in the general area of the patient but not part of the central line setup is still problematic, as the accumulation of high pathogenic bacterial counts on these surfaces indirectly contributes to central line contamination when they are touched after hand antisepsis and the central line is subsequently manipulated.\(^37,38\)

**Central line colonization**

CLABSI prevention is dependent on our ever-changing understanding of the mechanisms of line colonization and subsequent infection. Adult CLABSI studies point to either extraluminal or intraluminal line contamination.\(^39–42\) Accordingly, access techniques and equipment have evolved to obviate open disconnection of lines or, wherever necessary, to ensure decontamination of the hub entry point prior to its entry and continuing sterility during its manipulation. Garland and colleagues\(^43\) performed molecular subtyping of organisms harvested from the skin surrounding neonatal peripherally inserted central catheter (PICC) insertion sites, their hubs, the catheter tips, and blood cultures, finding, as did the earlier observation by Salzman and colleagues,\(^44\) that hub colonization was often present and the organism was concordant with simultaneously drawn blood cultures (80% and 71%, respectively). Garland and colleagues concluded that at least 67% of the CLABSIs were intraluminally acquired. These studies form the scientific basis for using techniques and equipment that address each of these vulnerabilities, for example, insertion site decontamination, closed vascular access systems, needleless connectors, and scrupulous hub decontamination prior to entry.

**How is CLABSI Defined?**

Different definitions of bloodstream infections (BSI) or CLABSI have evolved as the subject has been increasingly studied. Regarding the actual definition of a bloodstream infection, the gold standard is a positive blood culture. The term nosocomial infection often includes hospital acquired pneumonia and urinary tract infections, and the term sepsis usually describes a clinical presentation not requiring a positive blood culture. A central line associated bloodstream infection is a bloodstream infection that occurs with a central line in place or within 48 hours of a central line being removed when no other source of infection is identified.\(^45\)

The other essential factor to be addressed in defining BSI is how to distinguish between a true infection and a contaminated specimen when a blood culture is positive with the growth of a common contaminant, eg, Coagulase-negative *Staphylococcus* (CONS). Various strategies are suggested to make this distinction, either
based on multiple cultures or the time to detection as a proxy for the quantity of organisms in the original sample. Studies in neonates suggest that as many as 33% to 50% of positive blood cultures with CONS are contaminants.\textsuperscript{2,46}

**MICROBIOLOGY**

The distribution of organisms associated with neonatal BSIs has been reported by the NICHD (15 United States neonatal ICUs) and by the Israel Neonatal Network, representing 28 Israeli neonatal ICUs\textsuperscript{10,47} (Table 1). Both large networks report a similar pattern of pathogens, with gram-positive organisms predominating. In both series the most common single organism associated with BSI was CONS (47% and 55% for Israel and the NICHD, respectively). This finding underscores the importance of incorporating specific criteria in the definition of laboratory confirmed bloodstream infection to account for the prevalence of this skin contaminant as a frequent source of infection. Both networks use the same composite definition of sepsis with CONS, requiring a positive blood culture and the presence of specific clinical symptoms.

Beyond the impact of CONS, gram-negative organisms, coagulase-positive *Staphylococcus*, and *Candida* species are the remaining pathogens commonly associated with neonatal bloodstream infection. Gram-negative organisms play an important role due to their obvious source coming from the maternal genitourinary tract with colonization at or shortly after birth. The gram-positive organisms, especially coagulase-positive and coagulase-negative staphylococci, are most often acquired from skin colonization, on the skin of both the patient and the health care workers’ hands.\textsuperscript{19,20} The gram-negative organisms and *Candida* species are also introduced into the patient’s bloodstream via the patient’s or health care worker’s skin as the primary source of colonization.

**Successful Programs Address a Mix of Technical and Contextual Factors**

Care “bundles” describe multiple interventions that are disseminated nearly simultaneously to address one or more interrelated clinical or administrative problems. The concept was popularized by the Institute for Healthcare Improvement (IHI)\textsuperscript{48} and has served as an important means to further innovation, especially with regard to preventing HAI.\textsuperscript{49} Their potential efficacy derives from 3 streams of evolving understandings about the challenges in preventing and controlling HAI: (1) the appreciation that consensus statements of “provisional best practices,” also termed guidelines, are an effective way to translate complex knowledge into effective practices; (2) the epidemiologic perspective that there are many contributing factors to HAI; and (3) the demonstrated utility of “bundled” interventions in the NICU to promote multiple, simultaneous, and effective changes in practices.\textsuperscript{2,50–56}

Guidelines have been a means to define medical and nursing practice consensus for decades.\textsuperscript{57} Reviews of their evolution, in particular with regard to their scientific quality, efficacy, and effectiveness, have been commented on by Sinuff and colleagues\textsuperscript{58} in general, by Boluyt and colleagues\textsuperscript{59} with regard to pediatrics, and by Merritt and colleagues\textsuperscript{60,61} with regard to neonatal examples. Guideline noncompliance studies have noted factors that impede implementation such as ambiguous evidence, perception of irrelevance to individual patient or contextual situations, and so forth.\textsuperscript{62,63} Nonetheless, on balance, systematic evaluations suggest that they are effective, especially when addressing multidimensional problem-solving tasks such as preventing CLABSI.

Heavy skin colonization, line placement with limited use of sterile barriers, site of line placement, line replacement over a guide wire, contamination of the catheter hub, line
placement greater than 7 days, inexperienced marginally skilled operators, and host susceptibility are among the many significant factors identified with the risk of a CLABSI in general.64 Neonatal reviews have identified additional factors: poor skin integrity and prolonged line necessity.53,65 Interventions that focus on only one challenge, even critically important ones such as hand hygiene, may not be associated with sustained gains; hence the need to implement changes simultaneously.48

Table 2 compares major dimensions of reported “bundle” implementations in NICUs during the last decade. Their assessment is problematic for several reasons. The NICUs do not all share the same metrics: some report all BSI regardless of deduced cause and then have varied the denominator by total admissions or by total patient days. Also, the CLABSI definition has been refined and then made more stringent66 over the last decade, making it impossible to compare rates from before 2008 to those reported subsequently. The latest changes have caused rates to decrease, based solely on definitional changes, by at least one-third.67 Because the reports span eras of rapidly falling baseline rates, processes associated with initial gains are no longer considered innovative changes that merit reporting, as NICUs implement additional changes in the quest to achieve “zero” infection levels.68

Table 1
Distribution of Pathogens Associated with Bloodstream Infections in Very Low Birthweight Infants

<table>
<thead>
<tr>
<th>Organism</th>
<th>Israel Neonatal Network</th>
<th>NICHD Network</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>(%)</td>
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<tr>
<td>Gram-positive organisms</td>
<td>1043</td>
<td>55.4</td>
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<tr>
<td>Coagulase-negative Staph</td>
<td>899</td>
<td>47.3</td>
</tr>
<tr>
<td>Coagulase-positive Staph</td>
<td>74</td>
<td>3.9</td>
</tr>
<tr>
<td>Enterococcus/group D Strep</td>
<td>54</td>
<td>2.9</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>6</td>
<td>0.3</td>
</tr>
<tr>
<td>Other</td>
<td>20</td>
<td>1.1</td>
</tr>
<tr>
<td>Gram-negative organisms</td>
<td>593</td>
<td>31.2</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>277</td>
<td>14.7</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>80</td>
<td>4.2</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>72</td>
<td>3.8</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>53</td>
<td>2.8</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>44</td>
<td>2.3</td>
</tr>
<tr>
<td>Other</td>
<td>67</td>
<td>3.6</td>
</tr>
<tr>
<td>Mixed organisms</td>
<td>34</td>
<td>1.8</td>
</tr>
<tr>
<td>Gram-negative and Gram-negative</td>
<td>18</td>
<td>0.9</td>
</tr>
<tr>
<td>Gram-negative and Gram-positive</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>Bacteria and fungi</td>
<td>6</td>
<td>0.3</td>
</tr>
<tr>
<td>Candida</td>
<td>210</td>
<td>11.1</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>49</td>
<td>2.6</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>36</td>
<td>1.9</td>
</tr>
<tr>
<td>Unspecified Candida/Fungal sp.</td>
<td>125</td>
<td>6.6</td>
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<tr>
<td>Total</td>
<td>1880</td>
<td>100</td>
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### Table 2
Bundle implementation in NICUs

<table>
<thead>
<tr>
<th>Processes specifically addressed</th>
<th>Kil03,167</th>
<th>Gol02</th>
<th>And05</th>
<th>Aly05</th>
<th>Sch06</th>
<th>Wir09</th>
<th>Lee09</th>
<th>Cur09</th>
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<tbody>
<tr>
<td>Diagnostic processes</td>
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<tr>
<td>Hand hygiene optimization</td>
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<td>Chlorhexidine use</td>
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<td>Skin breaks management</td>
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<td>Vascular access</td>
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<tr>
<td>Maximal barrier precautions</td>
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<td></td>
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<tr>
<td>PICC team inserts lines</td>
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<tr>
<td>PICC team manages lines</td>
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<tr>
<td>Dressing change management</td>
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<td>Line necessity review</td>
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<td>Closed vascular systems</td>
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<td>Line entry management</td>
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<td>Unit Culture: audit &amp; feedback</td>
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<tr>
<td>Unit Culture: multi-disciplinary</td>
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</table>
Other related process

<table>
<thead>
<tr>
<th>Earlier enteral feeds</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>rct</th>
<th>p/p</th>
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<tbody>
<tr>
<td>Ventilator circuit management</td>
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<td>Antibiotic use</td>
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<td>Visit restrictions</td>
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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Design</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>p/p</th>
<th>rct</th>
<th>p/p</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Reduction</td>
<td>34.0%</td>
<td>62%</td>
<td>57%</td>
<td>87%</td>
<td>55%</td>
<td>25%</td>
<td>32%</td>
<td>93%</td>
</tr>
<tr>
<td>Level at end of process</td>
<td>16.5%</td>
<td>5.8*</td>
<td>9%</td>
<td>2.0^a</td>
<td>3.8^b</td>
<td>3.2^a</td>
<td>17.4^c</td>
<td>0.2^d</td>
</tr>
</tbody>
</table>

The black squares indicate that NICUs emphasized additional efforts to ensure compliance with existing standard CDC definition. The gray squares indicate use of existing standard definition without mention of additional efforts to ensure compliance.

*Abbreviations: p/p, pre-/post-study design; rct, randomized controlled trial.

^a BSI/1000 line days pre 08 CDC definition.
^b BSI/1000 patient days pre 08 CDC definition.
^c all BSI per 100 patients pre 08 CDC definition.
^d CLABSIs per 1000 line days 08 CDC definition.
Finally, the thematic presentation of an intervention begs the question of “context” and “the devil in the details” surrounding each described intervention. Aboelela and colleagues completed a systematic review of bundle implementations and noted the scarcity of data about component compliance or, when reported, the wide variance of compliance rates making evaluation of any particular intervention’s efficacy problematic. Even simple extrapolation from a list of interventions described by the collaborative’s leadership may only indicate an idealization of what may have been implemented. For instance, in the Canadian NICU dissemination trial, there were 34 recommended processes to be implemented by the 5 study NICUs, making a total of 170 possible practices to be implemented. Of these, 36% were already in place before the study, 38% were implemented during the study, and 25% of them were ignored. Notwithstanding these caveats, as well as recognizing that many items included in “bundles” have not, or cannot, be evaluated using conventional randomized controlled trial methodology, the authors propose that the following processes contribute to prevention and control of CLABSI in NICUs based on the compilation shown in Table 2, the additional evidence noted in this discussion, and their personal experiences with 3 prevention networks.

**Improve Your Unit’s “Safe Culture” Measures**

The landmark reports from the Institute of Medicine, *To Err is Human* and *Crossing the Quality Chasm*, brought together the foundations of and galvanized the future agenda for efforts to improve patient safety. Although safety efforts affect all patient processes, the discussion here is limited to summarizing the relevance of these efforts to decreasing CLABSI as demonstrated by the successful efforts of Pronovost and colleagues in the Michigan Keystone ICU Project. Their efforts started with reflecting on how we would know that patients are safer. Pronovost and colleagues proposed a balance of “immature” measures: 2 rate-based measures (CLABSI rate and percentage compliance with a ventilator-associated pneumonia prevention bundle) and 2 qualitative measures (how often the authors learn from defects and whether a unit has a safe culture). These investigators used the measure of safety culture tool validated by their colleague Sexton. As noted in its communication, the 5-point Likert scaled question: “In this ICU, it is difficult to speak up if I perceive a problem with patient care” has the strongest correlation with the complete questionnaire’s scoring of teamwork climate. More dramatically, the CLABSI decreases noted in the 108 participating ICUs were highly correlated with improvements in the “Teamwork Climate” scale of the simultaneously administered safety attitude questionnaire associated with a targeted program to improve the units’ safety climate. Thus, the authors recommend that units make this issue an integral part of their initial effort. Possibly their hospital will have implemented a house-wide effort that can satisfy this need. Alternatively, the authors have found that NICUs can implement program metrics as simple as periodically distributing the single question shown above on the staff’s sense of safely voicing concerns, akin to the famous Toyota “Stop the Line” mantra, and use it to monitor their efforts to improve the culture of safety in their units.

**Implementation of Evidence-Based Practices**

**Hand hygiene**

**Perform hand hygiene before contact with central lines** Hand antisepsis must be performed before and after contact with the patient and any equipment that comes in contact with the patient, or touching contaminated objects in the environment. If gloves have been used, hand antisepsis should be performed on their removal.
Hand antisepsis refers to the use of either a waterless alcohol product or an antiseptic detergent containing chlorhexidine gluconate (CHG) or triclosan.

Alcohol-based waterless agents have been shown to be at least as effective as or in some studies more effective than CHG and triclosan, against gram-positive and gram-negative bacteria and most viruses. Soaps containing CHG or triclosan are necessary when hands are visibly soiled to remove the organic material, and they have a theoretical advantage in that both agents have a residual effect after rinsing. Alcohol is nevertheless a very effective antiseptic agent, despite the lack of residual effect. Alcohol has been shown in numerous clinical studies to be more effective than antiseptic washes due to its ease of use, ready availability, and reduced skin irritation. It is the recommended agent of choice in the hospital setting, including the NICU. Effective alcohol products contain either isopropyl alcohol (IPA) or ethyl alcohol (EA) at 60% to 95%. These products also have emollients that substantially improve their tolerance by health care workers.

Ensure compliance with hand hygiene expectations  Despite the strong recommendations and educational campaigns urging health care workers to perform appropriate hand hygiene before and after patient contact, studies have repeatedly documented that compliance is well below expectations. Health care workers are aware of the science of pathogen transmission, but are often overwhelmed in their minute-to-minute tasks of routine patient care and responding to bedside emergencies related to patient instability. It has been shown that there are up to 20 opportunities for hand hygiene per hour and that hand hygiene compliance approximates 40%. Barriers to hand hygiene compliance are related to lack of ready access to hand hygiene products, skin irritation of health care workers’ hands, understaffing, overcrowding, and lack of any direct consequence for noncompliance.

Hand hygiene interventions are most effective in reducing CLABSI if they focus on the processes related to central line manipulation, ie, insertion, maintenance, and access to these lines. This approach has been demonstrated in examples of successful central line bundle implementation, where the hand hygiene survey processes are specifically aimed at these interventions. Targeting the central line manipulations provides a more concentrated effort in the area where consequences of nonadherence to hand hygiene regimens are the greatest.

Insertion of central lines

Use maximal barrier precautions for insertion of central catheters Maximal barrier precautions require the use of sterile cap, mask, gown, gloves, and drape. The rationale for this practice is the reduction of contamination during insertion of an indwelling catheter. The benefits of this approach have been demonstrated in prospective randomized trials with adult critical care patients. In a randomized controlled trial, Mer- mel studied maximal barrier precautions during the insertion of pulmonary artery catheters and showed a significant effect of this practice on the reduction of CLABSI.

Perform skin antisepsis at the catheter entry site Use of a CHG solution is recommended in this situation. The residual effect of CHG-containing preparations gives them preference for prolonged antimicrobial action to inhibit extraluminal migration of organisms colonizing the skin surface once the catheter is placed. In numerous studies with adult patients, CHG-containing solutions have been shown to be superior to povidone-iodine in reducing the incidence of bloodstream infection. Garland and colleagues also showed a similar advantage of CHG over povidone-iodine in neonates. Concerns over sensitivity reactions with CHG have been raised, but these should be weighed against the relative benefits of this agent over those without
residual effect and the fact that all skin antiseptics have relative adverse effects, for example, systemic absorption with iodine causing thyroid suppression and local skin reactions along with systemic absorption of alcohol in neonates. CHG is the recommended skin antisepsis agent in the Association of Women’s Health, Obstetric and Neonatal Nurses/National Association of Neonatal Nurses skin guideline and is specified in the Central Line Bundle adapted from the IHI used in the Michigan Keystone ICU Project. Local skin reactions can be mitigated by rinsing with sterile water after a 30-second application, as the residual effect will still remain. Due to ongoing concerns over local reactions, many centers limit the use of CHG preparations in the most premature infants, at least in the immediate perinatal period, choosing povidone instead.

**Use a dedicated team** Use a dedicated team of individuals who have received special training for insertion, maintenance, and monitoring of central lines. Numerous studies have demonstrated the advantages of this approach. By assuring that proper technique is used by those with the most expertise in the technical aspects as well as clinical decision-making regarding management of line complications, lines are placed with fewer attempts and CLABSI rates have been decreased.

**Select the appropriate site** Catheter insertion site is emphasized by the Centers for Disease Control and Prevention (CDC) in the 2002 Guideline and is a prominent component of the IHI Central Line Bundle. Factors influencing these recommendations are the association of phlebitis with CLABSIs along with the known association of phlebitis with lines placed in the lower extremities compared with the upper extremities. The density of skin flora is another factor behind this recommendation, with the subclavian site preferable over the internal jugular or femoral sites, due to the lower density of skin colonization. These factors are less relevant in neonates as lower extremity catheters have actually been shown to have fewer infectious complications than those in upper extremities. Intuitively, the density of colonization at the insertion site should be a factor in umbilical lines, but Butler-O’Hara and colleagues have shown that umbilical lines left in for 28 days have the same infection rate compared with the practice of removal at 7 days followed by placement of a PICC line for 21 days.

**Maintenance of central lines**

**Minimize access ports** Line setups should be designed to minimize the number of ports/connections. Each port of entry and connector must be viewed as an independent opportunity for line contamination. The intuitive notion that minimizing entry points will reduce opportunities for violating technique is strengthened by a prospective randomized clinical trial in which a significantly higher rate of CLABSI events was associated with the use of triple-lumen catheters than with single-lumen catheters. Needleless ports are recommended because they do not require opening to provide access, and they can be cleaned thoroughly before entry. Closed medication systems decrease opportunities for contamination, especially when connecting ports are placed far from areas contaminated by diapers.

**Change line setups and access ports in a timely fashion** Intravenous administration sets should be changed at recommended intervals: parenteral solutions containing dextrose or amino acids every 72 hours; lipid-containing solutions and sets used for administration of blood products every 24 hours. Needleless access ports should be changed at least as often as administration sets. Some manufacturers may recommend a longer interval for changing, but in vivo clinical studies point to
contamination of these ports as a source of CLABSI\textsuperscript{102–104} and demonstrate the presen-
tce of bacterial biofilm on the connectors by 72 hours in a majority of patients
studied.\textsuperscript{105}

**Manage the insertion site**  Dressings covering the catheter insertion site are important
in securing the line, which prevents migration, dislodgement, or breakage, and aids in
preventing the entry of microorganisms at the insertion site. Sterile gauze or sterile
transparent dressings have been studied and neither material has been shown to
be superior in preventing CLABSIs.\textsuperscript{106,107} Transparent occlusive dressings are used
more commonly as they allow one the ability to inspect the insertion site for local
complications and potential line dislodgement, but they are more difficult to manage
if blood is oozing from the insertion site. The CDC recommends changing the dressing
if it becomes damp, loosened, or visibly soiled.\textsuperscript{19} It is also recommended to be
changed every 48 hours if it is a gauze or tape dressing, if there is a gauze beneath
an occlusive dressing, or if a transparent dressing is no longer adherent to the
skin.\textsuperscript{108–110} Surgical cap, mask, and sterile gloves should be worn by the personnel
making the dressing change. In addition to these CDC minimum recommendations,
a sterile gown is suggested by others, primarily based on expert opinion.\textsuperscript{108} The
same method of skin antisepsis recommended for initial insertion, that is, CHG solu-
tion, is recommended for the dressing change, due to the residual effect.

**Sterilize access ports before entry**  The original studies showed efficacy with disinfec-
tion of needless access devices with IPA, but recent guidelines suggest that CHG/IPA
combinations may be better.\textsuperscript{98,102,103,111} Menyhay and Maki\textsuperscript{112} evaluated 3 needleless
valve connectors by exposing each to a known load of contaminating bacteria. Of the
30 connectors accessed after conventional disinfection (3–5 second swabbing using
a sterile swab of 70% IPA), 67\% were found to have significant growth of colony-form-
ing units in the broth recovered from subsequent flushing. Donlan and colleagues\textsuperscript{105}
showed a 63\% incidence of biofilm contamination composed primarily of CONS in
a series of needleless connectors collected from patients on a bone marrow transplant
unit. Kaler\textsuperscript{113} compared disinfection of 3 different needleless devices using 15-second
hub scrubs with either 3\% CHG/70\% IPA or 70\% IPA, and found them to be equally
effective. These data motivate current recommendations to scrub connectors for 15
seconds before and after entry. CHG or IPA are both recommended as noted here,
but CHG is increasingly being described as the preferred disinfecting agent, perhaps
because of its demonstrated persistence. The UK National Health Service Hospitals
Guideline advises that an alcoholic chlorhexidine gluconate solution (preferably 2\%
CHG in 70\% IPA) should be used and allowed to dry when decontaminating the injec-
tion port or catheter hub before and after it has been used to access the system.\textsuperscript{114}
Soothill and colleagues\textsuperscript{115} describe a pediatric transplant service’s 75% decrease in
CLABSI after switching connection disinfectants to 2\% CHG/70\% IPA from 70\%
IPA in accord with this recommendation. Recently, manufacturers have introduced
new self-swabbing disinfecting caps, although further evaluations of how these
various products can be effectively implemented are needed.\textsuperscript{116}

Bacteria, following entry into a device, can develop biofilm within the device that
extends throughout the catheter. Scanning electron microscopy of needleless connec-
tors shows the typical features of both bacterial cells and apparent extracellular poly-
meric substances within the device\textsuperscript{36,105,117} (**Figs. 1–3**). Bacteria gain adherence to
the smooth catheter surfaces through a process termed conditioning, whereby organic
molecules such as proteins are absorbed by the polymer and then alter its mechanical
characteristics. Murga and colleagues\textsuperscript{118} demonstrated how blood, when drawn back
and forth through a catheter, can serve as an adequate source of conditioning materials to promote biofilm formation by gram-negative bacteria. Donlan and colleagues have reviewed alternative means to eradicate biofilm: antibiotic lock protocols are presently available and effective for sensitive bacteria, but less so for fungi; other means, such as ultrasound, bacteriophages, quorum-sensing inhibitors, or enzymes are currently being developed and evaluated.

Lastly, needleless connector design has gone through several phases and it is still not clear if, and how, the design features affect the likelihood of these connectors becoming contaminated. Investigation of outbreaks associated with needleless connectors suggest that particular design characteristics may be associated with more frequent contamination when used in actual clinical environments as distinguished from evaluations under laboratory conditions. The previously mentioned Society for Healthcare Epidemiology of America/Infectious Diseases Society of America strategies statement cautions users of positive-pressure needleless connectors to weigh their risks and benefits, which has in turn generated controversy. The unsettled state of these technologies obliges clinicians to

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**Fig. 1.** Scanning electron microscopy images show the rim (arrow 1) and a small part of the access port (arrow 2) of a connector that has been used on an intensive care patient. (From Ryder M. Improve CRBSI prevention: target intraluminal risks. Executive Healthcare Management 2009; Issue 8; with permission. Available at: http://www.executivehm.com/article/Improve-CRBSI-Prevention-Target-Intraluminal-Risks/.)

**Fig. 2.** Higher magnifications reveal that large areas of the rim are covered with a dense biofilm. (From Ryder M, Schaudinn C, Gorur A, et al. Microscopic evaluation of microbial colonization on needleless connectors. Publication Number 5-36, APIC Annual Education Conference, Denver, CO 2008; with permission.)
maintain a constant vigilance for emerging technologies and their evaluations under both laboratory and clinical conditions.

**Monitor the necessity of central lines** The longer a central line is in place, the greater is the risk of infection. This observation has been confirmed in several studies in newborns.\(^{10,124–126}\) In the largest of these studies, Stoll and colleagues\(^{10}\) showed that use beyond 22 days was a critical threshold for all types of central lines, after which the risk of infection increased substantially. Chathas and colleagues\(^{124}\) showed the same increased risk at 21 days. The primary purpose and ongoing need for the central catheter should be assessed on a daily basis to facilitate its removal in a timely manner.

**Ensure compliance with line management expectations** Compliance-enhancing measures include continuing efforts to ensure adequate initial training to perform the procedures, provision of adequate supplies for their execution, and ongoing programs to encourage and monitor their implementation. Kilbride and colleagues\(^2\) reported that institutional NICU cohesion around these practices was observed to be very high, and epitomized implementation of the concept of “unit culture” as a necessary ingredient for successful practice of a care process, especially when that process requires frequent daily repetitions, often for weeks to months, by many different personnel.

**Evaluate and Incorporate Quality Improvement Methods into your Unit’s Operation**

Sustained quality improvement is highly dependent on successful administration of both the adoption and application of technical processes within the NICUs. Medical and nursing professionals may underestimate the necessity of addressing this factor because of the difficulty in addressing it or, worse, denigrate it because of the lack of randomized controlled trials to validate it. A recent critical review of Six Sigma, Lean, and Studer Group transformational strategies in health care found no studies using randomized controlled trial evaluation designs and only a few studies using pre-/post-interventional evaluative designs.\(^{127}\) Despite the weakness of the published reports, the market acceptance and adoption of these transformational strategies...
suggests a large body of experiential evidence driving their acceptance as fulfilling this administrative need.

Griffiths and colleagues evaluated studies of organizational factors affecting successful infection control programs and reached similar conclusions: lack of high-quality studies but prerequisites to achieving infection control must include processes that address senior and ward leadership, staff morale, and stability. Specific implemented techniques include the use of the “Toyota Production System” ideas in the successful CLABSI prevention work described at the Allegheny General Hospital and at the University of Washington Children’s Hospital. Studer Group ideas were used in the HAI prevention work described by Murphy. Nelson and colleagues, who have developed the concept of the “clinical microsystem” as the building block for understanding the management and transformation of clinical practice and have provided excellent tools for addressing these tasks. Edwards, as Director of Dartmouth-Hitchcock NICU, has collaborated with them in adapting and demonstrating the utility of these concepts to the NICU environment and HAI prevention.

Manage your project leadership using the “Plan-Do-Study-Act” methodology
Alternatively, variations of the “Plan-Do-Study-Act” (PDSA) methodology have been promoted as effective means for managing practice adoption. PDSA is the methodology advocated principally by the influential IHI (see IHI Improvement Methods at http://www.ihi.org/ihi/topics/improvement/improvementmethods/). Caldwell, in Mentoring Strategic Change in Health Care, provides very practical advice on how to manage change using the Plan-Do-Check-Act model. For instance, the California Perinatal Quality Care Collaborative (CPQCC) Toolkit incorporates and models these recommended steps in its guide for NICU CLABSI prevention project management. Other neonatal CLABSI prevention projects have used the PDSA model to guide their efforts. The authors recommend PDSA methods, especially in the context of NICUs whose quality improvement methodology is not tied to other methods adopted hospital-wide in their medical centers.

Build internal and external levels of collaboration as a means to participate in learning communities
Collaboration is at the heart of team learning. Bohmer and Edmondson have highlighted differences between individual and team learning: whereas the former describes the individual’s learning as a one-way knowledge transfer, learning as “keeping up,” and repetition as the path to best practice, team learning occurs at multiple levels involving all those who participate in the process, is an ongoing process that develops and refines knowledge-in-use, and is one in which reflection rather than repetition is the critical process.

At the tactical level, team learning should be an integral part of each NICU’s daily processes. Effectively applied learning processes, such as the aforementioned PDSA cycles or clinical microsystem development, exemplify some of the ways that this can be realized, and they should become the norm for unit learning. The authors recommend that each NICU seek to involve increasing numbers of their staff in these team-learning processes and, in consideration of this structural quality improvement goal, that units include a metric to reflect their progress toward this goal.

At the operational level, CLABSI prevention requires successful collaboration with many individuals and departments based outside of the NICU hierarchy. Each of these entities needs to be tactfully and respectfully approached to ensure appropriate...
understanding as to how each functionary can best work to serve the patient’s interests. Practical points, such as how lines can be arranged prior to off-NICU procedures so as to anticipate the anesthesiologist’s, surgeon’s, or radiologist’s needs, can avoid unintended breaks in line care during these procedures. Likewise, all visiting consultants, house staff, and technicians need to understand how they can comply with the unit’s policies for protecting lines and maintaining the patient’s environment. The magnitude and the challenges of these learning processes cannot be overestimated, nor their overemphasized.

At the strategic level, collaboration among like-minded colleagues from other institutions, both near and far, is increasingly being seen as a more effective way of spreading useful ideas between centers. Successful collaboratives cultivate mutual trust, support nonlinear development of problem-solving strategies, and focus on process and outcome measurement to drive change. There are now many productive neonatal collaboratives, whether based on voluntary relationships, for example, VON, or structural affiliations, CPQCC and Pediatrix Medical Group, which exemplify the utility and feasibility for each NICU to participate in one or more collaborative relationships.

Ensure audit and feedback

Audit and feedback are time-honored methods to define objectives and measure their achievement, which build on the notion that standardization is the foundation of excellence. Audits can address care processes, outcomes, or both. Process audits can be viewed as retrospective mirrors of prospectively deployed checklists. For instance, auditing hand hygiene practice has been a mainstay of HAI prevention. Audit results drove the adoption of alcohol-based hand rubs to improve hand hygiene compliance in busy ICUs. However, further consideration has led to understanding how poorly global hand hygiene audits reflect actual performance. “Secret shoppers” have been used to obtain unobtrusive observations, but their utility is mitigated by difficulties in assuring the observer’s continuing anonymity and staff expense proxy measures, such as the volume of consumed disinfectants have been used with some effect. Of greater concern is recent evidence that compliance falls off during multi-step complex tasks, suggesting that observation schedules should be weighted more toward complex events.

These experiences form the basis for the authors’ recommendation that NICU managers take a broader view to identifying the process steps critical to achieving lowered CLABSI rates. At a minimum, periodic audits of line set-up and line entry should be incorporated into the NICU routine in a manner similar to the accepted norms for hand hygiene compliance, as was recently demonstrated in a California collaborative. This collaborative demonstrated how to periodically audit for a range of essential HAI prevention processes and noted prompt compliance improvement.

Feedback needs to be both objective and subjective but, more importantly, on time and frequent. Objective displays of progress as manifested by various process and outcome metrics serve to enable everyone in the NICU to “know the score.” Leaders can model their concern by including simple inquiries during their rounds about “what’s the score,” for example, how many days has it been since our last CLABSI? Annotated “run charts,” that is, statistical process control charts that include pointers describing the dates of key initiatives, serve to reinforce the staff’s understanding that positive change does occur. There can never be enough recognition of achievements, whether individual or by the group, especially when delivered by higher management levels. And celebrations, accompanied by “healthy” foods, are always welcomed by NICU staff members!
Implement a real-time positive blood culture review process
Reflecting on adverse events is a key characteristic of high reliability organizations (HRO).\textsuperscript{147–150} CLABSI events deservedly rate this type of attention, starting with the first receipt in the NICU of a positive blood culture report.\textsuperscript{129} The authors have used an investigatory technique that seeks to gather circumstantial evidence surrounding each event, based on published and personal experiences of implicated associations with CLAB-SIs.\textsuperscript{137} Anecdotal reports indicate that users found these focused reviews well worth their time. Perhaps the most important user observation has been that investigations beginning at the first report of a positive culture enable far richer verbal recollection of antecedent events than when inquiries are limited solely to chart reviews. These observations then need to be followed by critical thinking as to what system changes could have prevented the sequence of events leading to the infection. Their value is enhanced when the experiences and learning are shared anonymously with peers in a collaborative, as each description can often generate new hypotheses or productive solutions.

Monitor Emerging Practices
The aforementioned interventions are discussed in the context of the central line bundle, reflecting the common strategies that have proven to be effective when introduced simultaneously. As such, these practices are focused and short term, chosen in many cases for their more rapid effect. There still are potentially useful interventions that should be considered in designing a unit-specific strategy to reduce CLABSI, even though they may not yield gains in the relatively short term of bundle interventions.

Intravenous immunoglobulin
Nineteen randomized controlled trials of prophylactic intravenous immunoglobulin (IVIG) including approximately 5000 infants were reviewed in a meta-analysis by Ohlsson and Lacy,\textsuperscript{151} showing a significant decrease in incidence of infection with an overall reduction of 3%. However, because of the potential morbidity of this treatment and its high cost relative to a small treatment effect, IVIG is not generally recommended.

Vancomycin prophylaxis
Strategies incorporating prophylactic systemic vancomycin have shown efficacy in reducing overall sepsis and CONS sepsis rates.\textsuperscript{152} Garland and colleagues\textsuperscript{153} reported a randomized trial demonstrating the efficacy of a vancomycin-heparin lock solution in reducing the incidence of CLABSI. Due to concern over selection of vancomycin-resistant organisms, these strategies are not widely recommended, although in certain situations where staphylococcal sepsis is prevalent they may be justified.

Human milk feedings
Three small randomized controlled trials and several observational studies have been reported in which human milk feedings were compared with formula for protection against neonatal sepsis.\textsuperscript{154} Human milk was shown to have a protective effect, but the overall quality of the studies is poor. Human milk feeding has numerous other nutritional benefits along with any shown in these studies, and is recommended even in the absence of quality data proving its benefit in reducing sepsis. Early introduction of human milk may also promote earlier establishment of full enteral nutrition, thus contributing to shorter duration of central line use.\textsuperscript{155,156}

Reduced intravenous lipid duration
Lipids have been shown in 2 observational studies to be associated with increased CONS bacteremia.\textsuperscript{157,158} The association is thought to be due to an
immunosuppressive effect of intravenous lipids as well as the propensity to support microbial growth.\textsuperscript{159} The nutritional value of the extra energy provided by lipids should be balanced by their potential risk for CLABSI.

**Technical innovation**

Important technological developments are constantly underway. These include antibiotic impregnated catheters,\textsuperscript{160–164} antibiotic dressings for central lines with either CHG or silver,\textsuperscript{165–167} new designs of needleless connectors with features to minimize the opportunity for biofilm development, antibiotic releasing caps, and specialized scrubbers for needleless connectors.\textsuperscript{114,119,120} These developments are often first reported in trade journals before publication in the medical literature, illustrating the importance of monitoring development in these areas as well as traditional sources. However, caution should be exercised with adoption of new technologies, as there may be harmful side effects more prevalent in vulnerable premature infants or incompatibilities of materials leading to their dysfunction.

**SUMMARY**

CLABSI results in increased mortality and adverse outcomes related to multiple systems with lifelong consequences. CLABSIs have come to be recognized as preventable adverse events that result from lapses in technique at multiple levels of care. This recognition is essential to instill the appropriate sense of personal accountability for individual health care workers necessary to motivate change. Strategies to reduce CLABSI have been described in the literature over the past decades. Successful changes have incorporated these strategies into bundles of practice that are more effective when introduced simultaneously. New clinical and technological studies demonstrate that the science of CLABSI reduction is dynamic, with ongoing modifications in technique and innovations in hardware elements. Equally important in efforts at CLABSI reduction is a thoughtful and systematic approach tailored to the unique elements that comprise an individual NICU, addressing the social as well as the scientific elements of change.

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