ORIGINAL ARTICLE

Chlorhexidine Bathing in a Tertiary Care Neonatal Intensive Care Unit: Impact on Central Line–Associated Bloodstream Infections

Caroline Quach, MD, MSc;[1,2,3] Aaron M. Milstone, MD, MHS;[4,5] Chantal Perpête, RN, LSH, LSHH;[1] Mario Bonenfant, RN;[6] Dorothy L. Moore, MD, PhD;[1,2] Therese Perreault, MD[6]

BACKGROUND. Despite implementation of recommended best practices, our central line–associated bloodstream infection (CLABSI) rates remained high. Our objective was to describe the impact of chlorhexidine gluconate (CHG) bathing on CLABSI rates in neonates.

METHODS. Infants with a central venous catheter (CVC) admitted to the neonatal intensive care unit from April 2009 to March 2013 were included. Neonates with a birth weight of 1,000 g or less, aged less than 28 days, and those with a birth weight greater than 1,000 g were bathed with mild soap until March 31, 2012 (baseline), and with a 2% CHG-impregnated cloth starting on April 1, 2012 (intervention). Infants with a birth weight of 1,000 g or less, aged 28 days or more, were bathed with mild soap during the entire period. Neonatal intensive care unit nurses reported adverse events. Adjusted incidence rate ratios (aIRRs), using Poisson regression, were calculated to compare CLABSIs/1,000 CVC-days during the baseline and intervention periods.

RESULTS. Overall, 790 neonates with CVCs were included in the study. CLABSI rates decreased during the intervention period for CHG-bathed neonates (6.00 vs 1.92/1,000 CVC-days; aIRR, 0.33 [95% confidence interval (CI), 0.15–0.73]) but remained unchanged for neonates with a birth rate of 1,000 g or less and aged less than 28 days who were not eligible for CHG bathing (8.57 vs 8.62/1,000 CVC-days; aIRR, 0.86 [95% CI, 0.17–4.44]). Overall, 195 infants with a birth weight greater than 1,000 g and 24 infants with a birth weight of 1,000 g or less, aged 28 days or more, were bathed with CHG. There was no reported adverse event.

CONCLUSIONS. We observed a decrease in CLABSI rates in CHG-bathed neonates in the absence of observed adverse events. CHG bathing should be considered if CLABSI rates remain high, despite the implementation of other recommended measures.

Infect Control Hosp Epidemiol 2014;35(2):158-163

Neonates in neonatal intensive care units (NICUs) are especially susceptible to healthcare-associated infections (HAIs), given their immature immune system, the acuity of care needed, and the frequency of invasive procedures performed.[1,2] Moreover, HAIs have documented major impacts on premature infants outcomes. They have been associated with a 2-fold increase in the risk of death.[3] Postnatal sepsis occurring in infants born before 30 weeks of gestation has been associated with a 2-fold increase in the risk of cerebral palsy at 2 years of age.[4] Finally, coagulase-negative staphylococcus bloodstream infections have been associated with a 5.6-fold increase in the risk of cerebral palsy at 18–24 months of age (95% confidence interval [CI], 1.9–16.7).[5]

Central line–associated bloodstream infections (CLABSIs) are an important cause of morbidity and mortality in neonates.[1] Consensus guidelines have recommended measures and bundled practices.[6] However, when infection rates remain high despite compliance with standard measures, additional interventions can be considered.

Chlorhexidine gluconate (CHG) is a broad-spectrum topical antiseptic that is used in many different clinical settings to prevent infections.[7,8] Daily bathing with 2% CHG can prevent CLABSI and other HAIs in adult settings[9-13] and in pediatric intensive care units (ICUs).[14] However, given the paucity of safety data in infants less than 2 months of age, CHG use in NICUs has not been fully endorsed in HAI prevention guidelines.[6] A recent survey in US NICUs revealed that most units use CHG and, in most cases, without birth weight or age restrictions.[15] Given these data and because of high CLABSI incidence rates in our NICU, our CLABSI prevention team implemented CHG bathing for a subgroup of infants with central venous catheters (CVCs) as part of routine care. Because there are currently no data on the use of CHG bathing for the prevention of CLABSI in the NICU setting, our

Affiliations: 1. Division of Infection Control, Department of Pediatrics, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada; 2. Division of Infectious Diseases, Department of Pediatrics, McGill University, Montreal, Quebec, Canada; 3. Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Quebec, Canada; 4. Division of Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland; 5. Department of Hospital Epidemiology and Infection Control, Johns Hopkins Hospital, Baltimore, Maryland; 6. Division of Neonatology, Department of Pediatrics, McGill University, Montreal, Quebec, Canada.

Received August 12, 2013; accepted October 31, 2013; electronically published December 24, 2013.

 0899-823X/2014/3502-0008$15.00. DOI: 10.1086/674862

objective was to describe the impact of CHG on CLABSI rates in our NICU population.

METHODS

Study Setting and Population

The Montreal Children's Hospital (MCH) of the McGill University Health Centre is a tertiary care pediatric hospital with no in-hospital deliveries. Its 24-bed level III NICU is mainly a reference center with expertise in neonatal surgery (cardiac and gastrointestinal) that serves the Greater Montreal Area. It has on average 393 admissions per year, totaling an average of 7,229 annual patient-days. We performed a secondary data analysis of our HAI surveillance database, using a retrospective cohort design that included all infants with a CVC admitted to the MCH NICU between April 1, 2009, and March 31, 2013.

Infection Control Program

During the study period and regardless of birth weight and chronological and gestational age, CHG was used for skin antisepsis prior to CVC insertion and for dressing change. Table 1 summarizes our CHG and bathing protocol in the baseline period (before April 1, 2012). After April 1, 2012, with the support of the NICU leadership and clinical nurse practitioners, infants with a CVC and a birth weight greater than 1,000 g were bathed with a 2% CHG-impregnated cloth (Sage Products), following the same bathing schedule as described in Table 1. Use of CHG for CVC insertion and dressing change remained unchanged. Infants with a birth weight of 1,000 g or less were bathed with a mild soap until day of life 28, after which time a 2% CHG-impregnated cloth was used. Nurses used 2 CHG wipes per infant per bath. Clinical care protocols were similar for all infants in the NICU. Adverse events reporting was done by NICU nurses and reported to the program manager.

Study Design and Outcome

We used a quasi-experimental design to compare neonates eligible for CHG bathing (infants with a CVC and a birth weight greater than 1,000 g and those with a birth weight of 1,000 g or less after day of life 28) before and after the change in policy. As an additional control group to account for temporal trends, we compared a subgroup of infants with a birth weight of 1,000 g or less aged less than 28 days who were not eligible for CHG bathing and received the same bathing practice during both periods (mild soap). Our primary outcome was the incidence of CLABSI per 1,000 CVC-days in the baseline and intervention periods in infants bathed and not bathed with CHG.

HAI Surveillance, Definitions, and Outcomes

Surveillance for HAI has been done prospectively and routinely at the MCH since 1985. Our surveillance year starts on April 1 and ends on March 31 of the following year. Definitions for primary bloodstream infections and CLABSI cases have not changed since 2009. HAI surveillance nurses review laboratory data and medical records to determine CLABSI occurrence and fill a standardized case report form. The infection control practitioner and the infection control physician adjudicate cases, on the basis of information provided. Although technically not blinded to CHG exposure, CLABSI cases were adjudicated prospectively, without knowing the infant's birth weight and chronological age—key elements to determine CHG bathing exposure. These variables were analyzed retrospectively. We used the American National Healthcare Safety Network definition[16-19] for primary bloodstream infection and CLABSI, with the only difference that it was only on April 1, 2013, that our CLABSI definition required the need for the CVC to have been in place for at least 48 hours before CLABSI onset.[20] Central lines were defined as intravenous catheters that ended at or near the heart or in a great vessel.

The number of patient-days was defined as the total number of days that patients spent in the NICU. The number of CVC-days was defined as the total number of days of exposure to at least 1 CVC and was collected daily.[21,22]

Statistical Analysis

We calculated CLABSI rates per 1,000 CVC-days (CLABSI episodes divided by number of central line–days × 1,000) by year. The device utilization ratio was calculated by dividing the total number of CVC-days by the total number of patient-days. Incidence rate ratios (IRRs) were calculated to compare CLABSIs/1,000 CVC-days during the baseline (2009–2012)

TABLE 1. Chlorhexidine Use and Bathing Protocol at the Montreal Children's Hospital Neonatal Intensive Care Unit during the Baseline Period

Birth weight, g	Gestational age, weeks	Chronological age, days	CHG for CVC insertion and dressing change	Bathing frequency (mild soap)
≤1,000	≤28	<28	2% aqueous CHG	Twice a week
≤1,000	≤28	≥28	0.5% CHG in 70% alcohol	Twice a week
≤1,000	29–35	≥28	0.5% CHG in 70% alcohol	Every other day
>1,000	29–35	All ages	0.5% CHG in 70% alcohol	Every other day
>1,000	>35	All ages	0.5% CHG in 70% alcohol	Daily

NOTE. CHG, chlorhexidine gluconate; CVC, central venous catheter.

https://doi.org/10.1086/674862 Published online by Cambridge University Press

and intervention (2012–2013) periods. We first looked at the IRR in the baseline period to determine if there were a significant time trend before pooling all the baseline data together. We used Poisson regression (PROC GENMOD) to adjust for confounding variables: distribution of birth weight categories and year. To control for temporal trends, we compared patients that were eligible for CHG between the baseline and intervention periods and patients that were not eligible for CHG between the same 2 periods. Statistical significance was determined using 2-sided P values ($P < .05$). All statistical analyses were done using SAS 9.2 (SAS Institute).

RESULTS

During the study period, 1,571 infants were admitted to the NICU, of which 790 had a CVC. Table 2 describes the study population stratified by year. During the intervention period, 195 infants with a birth weight greater than 1,000 g (mean ± standard deviation [SD], 2,836 ± 938 g) were bathed with CHG-impregnated cloths. Of those, 144 (74%) were greater than 35 weeks of gestation and were bathed daily with CHG, 38 were 29–35 weeks and washed every other day, and 13 were less than 29 weeks and bathed twice a week. These infants were bathed for a median of 8 days (range, 1–212). There were also 24 infants with a birth weight of 1,000 g or less, aged 28 days or greater (mean birth weight ± SD, 785 ± 122 g), who were bathed with CHG; their mean gestational age was 26.1 ± 1.8 weeks, with a median chronological age of 39 days. These infants were bathed for a median of 19 days (range, 2–44), twice a week.

Description of CLABSI Rates

During the study period, a total of 75 CLABSIs occurred: 20 in 2009–2010, 25 in 2010–2011, 21 in 2011–2012, and 9 in 2012–2013. CLABSI rates varied from 2.32 (95% CI, 1.06–4.40) to 7.21 (95% CI, 4.41–11.14) per 1,000 CVC days (Table 3). The device utilization ratio varied from 0.43 to 0.58. During the baseline period, there was a non–statistically significant reduction in CLABSI rates, with an adjusted incidence rate ratio (aIRR) of 0.86 (95% CI, 0.63–1.16) when all patients were analyzed together. When looking only at the CHG group and the non-CHG group separately during the baseline period, CLABSI rates did not show a significant time trend ($P = .58$ and 0.13, respectively).

Impact on CLABSI Rates

Table 3 summarizes CLABSI rates per year and per CHG group. In the CHG group, CLABSI rates decreased from 4.92 to 1.28/1,000 CVC-days for infants with a birth weight greater than 1,000 g (crude incidence rate ratio [cIRR], 0.26 [95% CI, 0.07–0.72]). For infants with a birth weight of 1,000 g or less, aged at least 28 days, CLABSI rates decreased from 8.97 to 5.73/1,000 CVC-days (cIRR, 0.79 [95% CI, 0.15–2.60]). Pooling the results from all CHG-bathed infants, CLABSI rates decreased from 6.0 to 1.92/1,000 CVC-days (cIRR, 0.30 [95% CI, 0.12–0.70]). Once adjusted for the distribution of birth weight categories, the aIRR was 0.33 (95% CI, 0.15–0.73).

In the non-CHG group—that is, infants with a birth weight of 1,000 g or less, aged less than 28 days—CLABSI rates remained stable, from 8.57 in the reference period to 8.62/1,000 CVC-days during the intervention period (cIRR, 1.01 [95% CI, 0.10–5.62]). Once adjusted for the distribution of birth weight categories, the aIRR was 0.86 (95% CI, 0.17–4.44).

Adverse Events

There was no dermatitis or adverse event reported during the 2012–2013 period.

DISCUSSION

The implementation of CHG bathing for select infants in the NICU with CVCs significantly reduced CLABSI rates and was well tolerated without reported adverse events. The group of infants not CHG bathed did not see any change in their CLABSI rate between the baseline and intervention periods, while the CHG-bathed group saw a decrease of more than 65% in their rates, even when adjusted for the distribution of birth weight categories. These elements support the fact that in our NICU, CHG bathing was effective in decreasing CLABSI rates while other measures put into place to decrease CLABSI rates remained unchanged.

Our results are in keeping with previous reports of CHG bathing effectiveness in other ICU populations. In adult ICUs, CHG bathing was associated with a 50% reduction in CLABSI rates (IRRs varying from 0.47 [95% CI, 0.25–0.88] to 0.50 [95% CI, 0.27–0.84]).[10-12] In the pediatric population, a recent

TABLE 2. Characteristics of the Study Population

Study year	No. of infants with CVC	No. of males (%)	Birth weight, mean ± SD (median), g	CVC-days (DUR)
2009–2010	171	107 (62.5)	2,471 ± 1,239 (2,670)	2,773 (0.43)
2010–2011	195	106 (54.4)	2,436 ± 1,160 (2,610)	3,848 (0.58)
2011–2012	195	104 (53.3)	2,560 ± 1,220 (2,864)	4,084 (0.53)
2012–2013	229	124 (54.1)	2,531 ± 1,134 (2,760)	3,882 (0.47)

NOTE. Study year was from April 1 to March 31 of subsequent year. CVC, central venous catheter; DUR, device utilization ratio; SD, standard deviation.

TABLE 3. Central Line–Associated Bloodstream Infection (CLABSI) Rates per Chlorhexidine Gluconate (CHG) Group and Year

			CLABSIs/1,000 CVC-days (no. of CLABSIs/annual CVC-days)				
			Reference period			Pooled reference	Intervention period
Birth weight, g	Age, days	CHG eligible	2009–2010	2010–2011	2011–2012	2009–2012	2012–2013
>1,000		Yes	4.36 (8/1836)	5.10 (13/2548)	5.10 (15/2939)	4.92 (36/7323)	1.28 (4/3126)
≤1,000	≥28	Yes	11.36 (8/704)	10.28 (11/1070)	5.54 (5/903)	8.97 (24/2677)	5.73 (3/524)
≤1,000	<28	No	17.17 (4/233)	4.44 (1/225)	4.13 (1/242)	8.57 (6/700)	8.62 (2/232)
Pooled CLABSI rate (95% CI)			7.21 (4.41–11.14)	6.51 (4.20–9.60)	5.14 (3.18–7.86)	6.17 (4.77–7.85)	2.32 (1.06–4.40)

NOTE. CI, confidence interval; CVC, central venous catheter.

randomized controlled trial found a decrease in primary bloodstream infections in pediatric ICUs and a 48% reduction in CLABSI rates (IRR, 0.52 [95% CI, 0.25–1.08]).[14] Our study is, to our knowledge, the first study to report the use of CHG bathing to decrease CLABSI rates in the NICU population.

NICU teams have been reticent to use CHG in their patient population because of concerns with adverse events, mainly skin irritation. Some studies have noted potential CHG absorption in very premature infants, given their immature skin, and reflections on hexachlorophene, a topical antiseptic that was used to control staphylococcal colonization in newborn infants. Previous reports had shown an association between the use of 3% hexachlorophene soap, a chlorinated phenol, as a topical antiseptic detergent in premature infants and the development of vacuolar encephalopathy of the brain stem reticular formation.[23,24] Absorption of hexachlorophene has been documented, with blood levels ranging from 148 to 4,350 μg/L and a significant correlation between blood concentration and infants' weight, skin condition, and gestational age.[25]

Chlorhexidine, a chlorinated cationic biguanide, is not related to hexachlorophene and is commonly used in North American NICUs; 61% of 90 NICUs in the United States reported using CHG, most commonly for CVC skin preparation, without age or birth restrictions.[7] A recent survey of Canadian tertiary care pediatric hospitals and US freestanding children's hospitals also showed that 5 of 50 NICUs (10%) used CHG for bathing.[26] CHG has been detected in the blood of some preterm and term infants after whole body washing: in 95% of 10 infants when the sample was a capillary blood and in 5% of 17 infants when the sample was a venous blood taken 12 hours after bathing, with levels ranging from 91 to 460 μg/L. According to the authors, CHG concentrations found in capillary blood samples were likely due to topical contamination.[27] In another study, CHG—when used for skin antisepsis prior to CVC placement in neonates weighing 1,500 g or more who were 7 days or older—was not associated with dermatitis. Of the 48 enrolled infants, 7 (14.6%) had detectable CHG concentrations ranging from 13 to 100 μg/L.[28] A study of 20 preterm neonates, with a median gestational age of 28 2/7 weeks, who had 1 limb washed with a 2% CHG-impregnated cloth before peripherally inserted central catheter placement showed that 10 had detectable CHG concentrations with levels ranging from 1.6 to 206 μg/L; no infant developed a dermatitis.[29] In children aged greater than 3 months, CHG blood level was detected after CHG bathing in 1 of 12 (8.3%) children enrolled, at a concentration of 57 μg/L, with no evidence of CHG accumulation.[30] A study of neonatal rhesus monkeys washed daily with CHG did not show any absorption through the skin, even after repeated washing with an 8% CHG solution for 90 days.[31]

Despite extensive use and evidence that some absorption occurs, CHG has not been associated thus far with any documented neurological adverse event, except when instilled directly in the middle ear.[27] In the context of a NICU with high CLABSI rates, where bloodstream infections and sepsis in preterm infants have documented adverse outcomes in terms of neurological development and mortality,[4,5,32] benefits of decreasing the incidence of CLABSI outweigh the theoretical risk that could be associated, although not proven, with CHG use. Finally, repeated use of CHG for bathing has not been associated with increasing minimum inhibitory concentrations or development of resistance in exposed bacterial strains.[33-36]

Our study has some limitations. First, because CHG bathing was part of a clinical care protocol, we cannot speculate on compliance to guidelines; we therefore analyzed our data using an intent-to-treat analysis. Comparing groups of infants who were CHG bathed and not bathed, regardless of the compliance to CHG bathing, would tend to decrease the magnitude of the association found because of dilution of the exposure in the CHG bathed group. Moreover, we noted a decrease in our device utilization ratio in the fourth year of study. We were not able to say whether this decrease was due to faster removal of unnecessary CVCs or secondary to decreased need for intravenous access for antimicrobials as a consequence of lower CLABSI rates. Our policy always included early removal of unnecessary CVCs, which did not change during the study period. In terms of CHG safety, we monitored only for dermatitis. Finally, because our NICU does not have in-hospital deliveries, our NICU does not tend to admit very small and young premature babies. In fact, an

important proportion of our patient population are either admitted for surgical reasons—yet born at 35 weeks or greater—or are premature infants that are older when transferred to our unit. Therefore, our results and findings may not be generalized to all NICUs.

In conclusion, while all other preventive measures for the prevention of CLABSI remained unchanged in our NICU, as supported by the stable CLABSI rates in our control population of non-CHG-bathed infants, the use of 2% CHG-impregnated cloths for bathing was effective in decreasing CLABSI rates. Its use should thus be considered, under specific circumstances, when other preventive measures have failed.

ACKNOWLEDGMENTS

We would like to thank the Montreal Children's Hospital neonatal intensive care unit team for their support and participation on improving patient safety; Ms. Milagros Gonzales, MSc, for her help in data cleaning and validation; Ms. Martine Claveau, RN, NNP, and Martine Chagnon, RN, for their help and support in the implementation of the bathing protocols; and the healthcare-associated infection (HAI) surveillance team: Ms. Lina Moisan and Evelyn Sarmiento, HAI surveillance nurses, and Ms. Claudine McDuff and Stephanie Lacharite, data entry.

Potential conflicts of interest. A.M.M. has received grant support from Sage Products. Sage, however, played no role in the current study; Sage did not provide CHG–impregnated clothes, did not provide grant support, was not involved in the study design, and did not have any input on the manuscript. All other authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Caroline Quach, MD, MSc, Montreal Children's Hospital, C1242-2300 Tupper Street, Montreal, Quebec H3H 1P3, Canada (caroline.quach@mcgill.ca).

REFERENCES

1. Brodie SB, Sands KE, Gray JE, et al. Occurrence of nosocomial bloodstream infections in six neonatal intensive care units. *Pediatr Infect Dis J* 2000;19(1):56–65.
2. Schulman J, Stricof R, Stevens TP, et al. Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. *Pediatrics* 2011;127(3):436–444.
3. Goldmann DA, Freeman J, Durbin WA Jr. Nosocomial infection and death in a neonatal intensive care unit. *J Infect Dis* 1983; 147(4):635–641.
4. Shah DK, Doyle LW, Anderson PJ, et al. Adverse neurodevelopment in preterm infants with postnatal sepsis or necrotizing enterocolitis is mediated by white matter abnormalities on magnetic resonance imaging at term. *J Pediatr* 2008;153(2):170–175.e1.
5. Schlapbach LJ, Aebischer M, Adams M, et al. Impact of sepsis on neurodevelopmental outcome in a Swiss National Cohort of extremely premature infants. *Pediatrics* 2011;128(2):e348–e357.
6. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52(9):e162–e193.
7. Chapman AK, Aucott SW, Milstone AM. Safety of chlorhexidine gluconate used for skin antisepsis in the preterm infant. *J Perinatol* 2012;32(1):4–9.
8. Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. *Clin Infect Dis* 2008;46(2):274–281.
9. Karki S, Cheng AC. Impact of non-rinse skin cleansing with chlorhexidine gluconate on prevention of healthcare-associated infections and colonization with multi-resistant organisms: a systematic review. *J Hosp Infect* 2012;82(2):71–84.
10. Exline MC, Ali NA, Zikri N, et al. Beyond the bundle: journey of a tertiary care medical intensive care unit to zero central line–associated bloodstream infections. *Crit Care* 2013;17(2):R41.
11. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med* 2013;368(6):533–542.
12. Montecalvo MA, McKenna D, Yarrish R, et al. Chlorhexidine bathing to reduce central venous catheter–associated bloodstream infection: impact and sustainability. *Am J Med* 2012; 125(5):505–511.
13. Rupp ME, Cavalieri RJ, Lyden E, et al. Effect of hospital-wide chlorhexidine patient bathing on healthcare-associated infections. *Infect Control Hosp Epidemiol* 2012;33(11):1094–1100.
14. Milstone AM, Elward A, Song X, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. *Lancet* 2013;381(9872): 1099–1106.
15. Tamma PD, Aucott SW, Milstone AM. Chlorhexidine use in the neonatal intensive care unit: results from a national survey. *Infect Control Hosp Epidemiol* 2010;31(8):846–849.
16. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36(5):309–332.
17. Horan TC, Arnold KE, Rebmann CA, Fridkin SK. Network approach for prevention of healthcare-associated infections. *Infect Control Hosp Epidemiol* 2011;32(11):1143–1144.
18. Horan TC, Emori TG. Definitions of key terms used in the NNIS System. *Am J Infect Control* 1997;25(2):112–116.
19. Horan TC, Lee TB. Surveillance: into the next millennium. *Am J Infect Control* 1997;25(2):73–76.
20. National Healthcare Safety Network. *Device-Associated Module CLABSI.* Atlanta: Centers for Disease Control and Prevention, 2013. http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf. Accessed July 29, 2013.
21. Centers for Disease Control and Prevention (CDC). *Device-Associated (DA) Module.* Atlanta: CDC, 2009. http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf. Accessed December 16, 2013.
22. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32(8):470–485.
23. Shuman RM, Leech RW, Alvord EC Jr. Neurotoxicity of hexachlorophene in humans. II. A clinicopathological study of 46 premature infants. *Arch Neurol* 1975;32(5):320–325.
24. Kimbrough RD. Review of recent evidence of toxic effects of hexachlorophene. *Pediatrics* 1973;51(2):391–394.
25. Tyrala EE, Hillman LS, Hillman RE, Dodson WE. Clinical phar-

macology of hexachlorophene in newborn infants. *J Pediatr* 1977;91(3):481–486.
26. Klieger SB, Potter-Bynoe G, Quach C, Sandora TJ, Coffin SE. Beyond the bundle: a survey of central line–associated bloodstream infection prevention practices used in US and Canadian pediatric hospitals. *Infect Control Hosp Epidemiol* 2013;34:1208–1210.
27. Cowen J, Ellis SH, McAinsh J. Absorption of chlorhexidine from the intact skin of newborn infants. *Arch Dis Child* 1979;54(5):379–383.
28. Garland JS, Alex CP, Uhing MR, Peterside IE, Rentz A, Harris MC. Pilot trial to compare tolerance of chlorhexidine gluconate to povidone-iodine antisepsis for central venous catheter placement in neonates. *J Perinatol* 2009;29(12):808–813.
29. Chapman AK, Aucott SW, Gilmore MM, Advani S, Clarke W, Milstone AM. Absorption and tolerability of aqueous chlorhexidine gluconate used for skin antisepsis prior to catheter insertion in preterm neonates. *J Perinatol* 2013;33:768–771.
30. Lee A, Harlan R, Breaud AR, et al. Blood concentrations of chlorhexidine in hospitalized children undergoing daily chlorhexidine bathing. *Infect Control Hosp Epidemiol* 2011;32(4):395–397.
31. Gongwer LE, Hubben K, Lenkiewicz RS, Hart ER, Cockrell BY. The effects of daily bathing of neonatal rhesus monkeys with an antimicrobial skin cleanser containing chlorhexidine gluconate. *Toxicol Appl Pharmacol* 1980;52(2):255–261.
32. Adams-Chapman I, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant. *Curr Opin Infect Dis* 2006;19(3):290–297.
33. Fritz SA, Hogan PG, Camins BC, et al. Mupirocin and chlorhexidine resistance in *Staphylococcus aureus* in patients with community-onset skin and soft tissue infections. *Antimicrob Agents Chemother* 2013;57(1):559–568.
34. Sangal V, Girvan EK, Jadhav S, et al. Impacts of a long-term programme of active surveillance and chlorhexidine baths on the clinical and molecular epidemiology of meticillin-resistant *Staphylococcus aureus* (MRSA) in an intensive care unit in Scotland. *Int J Antimicrob Agents* 2012;40(4):323–331.
35. Soma VL, Qin X, Zhou C, Adler A, Berry JE, Zerr DM. The effects of daily chlorhexidine bathing on cutaneous bacterial isolates: a pilot study. *Infect Drug Resist* 2012;5:75–78.
36. Popovich KJ, Lyles R, Hayes R, et al. Relationship between chlorhexidine gluconate skin concentration and microbial density on the skin of critically ill patients bathed daily with chlorhexidine gluconate. *Infect Control Hosp Epidemiol* 2012;33(9):889–896.