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Preoperative CHG Bathing: The Evidence and the Issues

Numerous studies have demonstrated that surgical site infections (SSIs), considered to be the most frequently reported healthcare-associated infection (HAI), are associated with significant patient morbidity and mortality as well as escalating healthcare expenditures annually. Any intervention(s) that can mitigate risk associated with SSIs is another weapon in the arsenal against HAIs. Patient skin cleansing with chlorhexidine gluconate (CHG) is becoming a widely accepted and viable intervention, and has been the focus of researchers' efforts to determine its role in infection rate reduction.

By Kelly M. Pyrek

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Table of Contents

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One of the most talked-about issues at last year's IDWeek conference was patient bathing with CHG. The topic was included in a session called "Thorny Issues in Infection Prevention" in which panelists described practical solutions to real-world problems in infection prevention, compared the strengths and weaknesses of the solutions discussed, and debated strategies to assist in the implementation of the solutions presented. Moderated by Charles Huskins, MD, MSc, FIDSA, FSHEA, FPIDS, of Mayo Clinic and Thomas Talbot, MD, MPH, of Vanderbilt University, the panel included Loreen Herwaldt, MD, FIDSA, FSHEA; Susan Ray, MD, FIDSA; Stephen Parodi, MD, FIDSA; Edward Septimus, MD, FIDSA, FSHEA; and Danielle Zerr, MD, MPH, FPIDS.

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In an informal audience-participation survey conducted during the session, attendees were asked if their healthcare institution engaged in CHG bathing. Thirty-four percent said their facility did not participate in CHG bathing; 27 percent said CHG bathing was administered to all ICU patients; 24 percent reported that it was used for ICU patients and select non-ICU patients; and 12 percent said CHG bathing was administered to select ICU patients.

Septimus pointed out that CHG bathing of patients has seen renewed interest in the wake of publication of several recent studies indicating it as a successful intervention against HAIs. "In our study we saw a 44 percent reduction in all-cause bacteremias," Septimus said. "We implemented it in all adult ICUs and saw a 23 percent reduction in CLABSIs."

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In this cluster-randomized trial, Septimus, et al. (2014) sought to determine rates of blood culture contamination comparing three strategies to prevent intensive care unit (ICU) infections: screening and isolation, targeted decolonization, and universal decolonization. The trial involved 43 hospitals with 74 ICUs and was conducted from July 1, 2009 to Sept. 30, 2011. After a six-month baseline period, hospitals were randomly assigned to one of the three aforementioned strategies, with all participating adult ICUs in a given hospital assigned to the same strategy. Arm 1 implemented methicillin-resistant Staphylococcus aureus (MRSA) nares screening and isolation, arm 2 targeted decolonization (screening, isolation, and decolonization of MRSA carriers), and arm 3 conducted no screening but universal decolonization of all patients with mupirocin and chlorhexidine (CHG) bathing. Blood culture contamination rates in the intervention period were compared to the baseline period across all 3 arms.

During the baseline period, 7,926 blood cultures were collected from 3,399 unique patients: 1,099 sets in arm 1, 928 in arm 2, and 1,372 in arm 3. During the 18-month intervention period, 22,761 blood cultures were collected from 9,878 unique patients: 3,055 sets in arm 1, 3,213 in arm 2, and 3,610 in arm 3. The researchers reported that among all individual draws, for arms 1, 2 and 3, the contamination rates were 4.1 percent, 3.9 percent, and 3.8 percent for the baseline period and 3.3 percent, 3.2 percent, and 2.4 percent for the intervention period, respectively.

When the researchers evaluated sets of blood cultures rather than individual draws, the contamination rate in arm 1 (screening and isolation) was 9.8 percent (N = 108 sets) in the baseline period and 7.5 percent (N = 228) in the intervention period. For arm 2 (targeted decolonization), the baseline rate was 8.4 percent (N = 78) compared to 7.5 percent (N = 241) in the intervention period. Arm 3 (universal decolonization) had the greatest decrease in contamination rate, with a decrease from 8.7 percent (N = 119) contaminated blood cultures during the baseline period to 5.1 percent (N = 184) during the intervention period. Arm 3 resulted in the greatest reduction in blood culture contamination rates, with an unadjusted odds ratio (OR) of 0.56 and an adjusted OR of 0.55. The authors say their study demonstrated that universal decolonization with CHG bathing resulted in a significant reduction in blood culture contamination.

The panelists addressed their experiences with their facilities' CHG bathing policies, reporting varying degrees of success and detailing the inherent challenges, such as the need for establishing the business case for CHG bathing. As several panelists pointed out, in some hospitals there has been pushback from nurses and administrators regarding cost and the need for the C-suite to provide the resources necessary for these types of interventions that show demonstrable impact on infection rates.

Panelists also addressed clinician concerns about patients' skin sensitivities and their reactions to CHG's tendency toward stickiness until it dries. As Parodi observed, "You definitely need

to achieve consensus on the use of CHG, get nursing's buy-in and address competencies in terms of providing education and training about its use. For example, if you have a patient needing an occlusive dressing, it needs to be put on after the CHG has been applied and the CHG absolutely has to have dried first or you will get skin reactions. It requires education and checking competencies regularly. Because unfortunately, just one reaction tends to derail things quickly."

Addressing challenges to implementation, Septimus noted, "It's important to look at compliance and make sure the CHG bathing is performed correctly regardless of the preparation used. We found a lot of variation when we first implemented this across our organization. Another barrier is convincing your frontline healthcare workers that this is a smart intervention. The updated Compendium says it is a good practice." Septimus also addressed many of the common mistakes observed, including using the right amount of wipes or solution per the manufacturer's directions; looking at other products such as soaps and lotions currently used on units that can interfere with CHG's activity or inactivate it; and ensuring that the CHG dries thoroughly.

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Septimus noted that the Agency for Healthcare Quality and Research (AHRQ) offers a toolkit, Universal ICU Decolonization: An Enhanced Protocol, which offers step-by-step instructions for proper decolonization using mupirocin and CHG.

In the *Strategies to Prevent Central Line-Associated Bloodstream Infections in Acute Care Hospitals: 2014 Update* (Marschall, et al. 2014), CHG bathing is highlighted in the recommended practice of "Bathe ICU patients over 2 months of age with a chlorhexidine preparation on a daily basis. In long-term acute care hospitals, daily chlorhexidine bathing may also be considered as a preventive measure. The role of chlorhexidine bathing in non-ICU patients remains to be determined. The optimal choice of antiseptic agents is unresolved for children under 2 months of age. However, chlorhexidine is widely used in children under 2 months of age."

According to the Marschall, et al. (2014), "For chlorhexidine gluconate (CHG)–based topical antiseptic products, the Food and Drug Administration recommends 'use with care in premature infants or infants under 2 months of age; these products may cause irritation or chemical burns.' The American Pediatric Surgical Association recommends CHG use but states that 'care should be taken in using chlorhexidine in neonates and premature infants because of increased risk of skin irritation and risk of systemic absorption.' Concerns in children under 2 months have been noted elsewhere. Cutaneous reactions to CHG have also been reported in extremely-low-birth-weight neonates under 48 hours of age; however, in a small pilot trial of neonates under 1,000 grams and at least 7 days of age, severe contact dermatitis did not occur, although CHG was cutaneously absorbed. These findings have not been replicated in a recent trial in neonates weighing more than or equal to 1,500 grams. Some institutions

have used chlorhexidine-containing sponge dressings for CVCs and chlorhexidine for cleaning CVC insertion sites in children in this age group with minimal risk of such reactions. Providers must carefully weigh the potential benefit in preventing CLABSI in children under 2 months and the risks of CHG, recognizing that term and preterm infants may have different risks. Alternative agents, such as povidone-iodine or alcohol, can be used in this age group."

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Using a Standardized Regimen for Pre-Admission Patient Skin Cleansing

Charles Edmiston, PhD, professor of surgery and hospital epidemiologist in the Department of Surgery at the Medical College of Wisconsin, advocates using a standardized regimen for pre-admission skin cleansing using chlorhexidine gluconate. Edmiston has documented through his various research studies components of an effective, risk-reduction showering regimen, which suggests that the CHG shower/cleansing should be a component of every surgical care bundle and used for all elective surgeries, not just orthopedic or cardiothoracic procedures.

Forthcoming updated guidelines from the Association of periOperative Registered Nurses (AORN) and the Centers for Disease Control and Prevention (CDC)/HICPAC are evolving to indicate just one shower with a soap or antiseptic, and they do not recommend the use of CHG.

Existing guidance from the CDC (1999) says, "Require patients to shower or bathe with an antiseptic agent on at least the night before the operative day." Revised guidance (CDC, 2014) which is expected to be released this year indicates, "Advise patients to shower or bathe (full body) with either soap (antimicrobial or non-antimicrobial) or an antiseptic agent on at least the night before the operative day."

Existing guidance from AORN (2012) states, "Patients undergoing open Class I surgical procedures below the chin should have two preoperative showers with chlorhexidine gluconate (CHG) before surgery, when appropriate." Revised guidance (2015) indicates, "Patients should bathe or shower before surgery with either soap or a skin antiseptic on at least the night before or the day of surgery."

Edmiston says he isn't being swayed from his belief in the preponderance of evidence indicating multiple showers with CHG are appropriate and effective.

"The revised AORN guideline is very much in line with the HICPAC/CDC surgical site infection prevention guideline — they recommend just one shower," Edmiston says. "The CDC consulted the University of Pennsylvania Evidence Based Medicine Institute for its review and vetting of the evidence-based literature. A much lower emphasis was placed on retrospective, observational trials and prospective interventional cohort trials. While these studies are not considered as randomized controlled trials (RCT), they were however conducted in a thoughtful and organized manner by many well-respected investigators. I feel that they represent valid contributions to the preadmission shower/cleansing literature. The issue I have with the CDC guideline is that the document provides insufficient guidance. So infection preventionists are asking, 'what should we do?' Institutions will look at these guidelines and

say, 'They are not recommending CHG so why should we invest in it?' I am hoping that those of us who disagree with this guidance can — through our various publications and presentations — counteract some of the negative influence those future guidelines will have on our risk-reduction efforts. As an example, I recently received an email from an infection preventionist who wants our institution's evidence-based guidelines and justification for the use of CHG showers for patients under-going elective surgery, not just orthopedic procedures, but for every inpatient. I think IPs get it — it's the other ancillary healthcare professionals who don't have experience with CHG or exposure to the breath of medical/surgical literature supporting this endeavor. We must be diligent in emphasizing why hospitals should have a standardized patient skin-cleansing protocol and why two showers should be considered the gold standard for preadmission cleansing."

"We discovered during the study that if you simply gave an individual a bottle of 4% CHG and told them to shower without any instructions at all, the concentrations on the skin were barely sufficient to address the minimal concentration required to inhibit or kill staphylococci, including MRSA.

Edmiston and his colleagues have conducted a significant amount of research on exogenous skin flora levels and CHG bathing. "We published a study in the Journal of the American College of Surgeons in 2008 in which we looked at the skin-surface concentrations of CHG. We conducted that study because my group had published a paper in 2007 which was part of the FDA analysis of the 2 percent CHG cloth versus the 4 percent CHG soap. We wanted to see if there is any real difference in skin-surface CHG concentrations between 4 percent aqueous products and the 2 percent cloth. We discovered during the study that if you simply gave an individual a bottle of 4 percent CHG and told them to shower without any instructions at all, the concentrations on the skin were barely sufficient to address the minimal concentration required to inhibit or kill staphylococci, including MRSA. However, if you provided instructions that included taking two showers and a one-minute time-out prior to rinsing then we saw much higher skin-surface concentrations of CHG, approaching 120 ppm."

In this aforementioned study, Edmiston and Krepel, et al. (2008) randomized subjects into one of three shower (4 percent soap)/skin cleansing (2 percent cloth) groups (20 per group): (group 1 A/B) evening, (group 2 A/B) morning, or (group 3 A/B) evening and morning. After showering or skin cleansing, volunteers returned to the investigator's laboratory where CHG skin surface concentrations were determined at five separate skin sites. CHG concentrations were compared with CHG minimal inhibitory concentration that inhibits 90 percent (MIC90) of staphylococcal skin isolates. CHG MIC90 for 61 skin isolates was 4.8 parts per million (ppm). In group 1A, 4 percent CHG skin concentrations ranged from 17.2 to 31.6 ppm, and CHG concentrations were 361.5 to 589.5 ppm ($p < 0.0001$) in group 1B (2 percent). In group 2A (4 percent), CHG levels ranged from 51.6 to 119.6 ppm and 848.1 to 1,049.6 ppm in group 2B (2 percent), respectively ($p < 0.0001$). CHG levels ranged from 101.4 to 149.4 ppm in the 4 percent CHG group (group 3A) compared with 1,484.6 to 2,031.3 ppm in 2 percent

CHG cloth (group 3B) group ($p < 0.0001$). Effective CHG levels were not detected in the 4 percent CHG group in selected sites in seven (35 percent) subjects in group 1A, three (15 percent) in group 2A, and five (25 percent) in group 3A.

Edmiston then became interested in compliance-related issues. "I discovered that not all of our elective-surgery patients were using the 2 percent cloth, which is what we used in our institution," he says. "We found about 29 percent of the patients were not using it, and the reasons were varied — they didn't realize how important CHG cleansing was, while others said they simply forgot. Some patients said they thought one cleansing was sufficient. We realized that we had to think about some kind of technology through which we could use to remind the patients to take their showers. Again, we decided to measure compliance by looking at surface concentrations. We published our results this past year in the Journal of the American College of Surgeons, showing there was a significant difference (increase in skin-surface concentrations of CHG) between those individuals who were texted or received emails or voicemails as opposed to individuals who did not receive that kind of prompting. I came to the conclusion that reminders and prompting do works. Other studies have shown in the field of medicine that SMS-texting or emails can significantly increase a patient's medication compliance. There was however one flaw to that study though — we didn't recommend a time-out for those individuals who were showering — we just presented directions for showering and we prompted the individuals at a specific time to shower. What we discovered was that even though there was a significantly higher concentration of CHG on the skin of those who were texted compared to those who were not texted, we did not achieve the concentrations we saw in the 2008 paper, simply because we didn't have a time-out."

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In this aforementioned study, Edmiston and Krepel, et al. (2014) randomized 80 volunteers to four CHG showering groups. Groups A1 and A2 showered twice. Group A1 was prompted to shower via EAS. Groups B1 and B2 showered three times. Group B1 was prompted via EAS. Subjects in groups A2 and B2 were not prompted (non-EAS groups). Skin-surface concentrations of CHG (µg/mL) were analyzed using colorimetric assay at 5 separate anatomic sites. Study personnel were blinded to the randomization code; after final volunteer processing, the code was broken and individual groups were analyzed. Mean composite CHG skin-surface concentrations were significantly higher ($p < 0.007$) in EAS groups A1 (30.9 ± 8.8 µg/mL) and B1 (29.0 ± 8.3 µg/mL) compared with non-EAS groups A2 (10.5 ± 3.9 µg/mL) and B2 (9.5 ± 3.1 µg/mL). Overall, 66 percent and 67 percent reductions in CHG skin-surface concentrations were observed in non-EAS groups A2 and B2 compared with EAS study groups. Analysis of returned (unused) CHG (mL) suggests that a wide variation in volume of biocide was used per shower in all groups.

Following recent studies, Edmiston says he started thinking about preoperative bathing in a new way. "One day I was in my office, talking to a surgical colleague about antibiotic prophylaxis, and the importance of the right dose at the right time, and especially a weight-based dose for some of our heavier patients," he says. "It hit me that we have always thought about the preadmission showering as a kind of a mundane activity — we really don't think about it as a medicinal process — so I decided that we needed to think about showering from a pharmacokinetic prospective. In essence we needed to think of the preadmission shower in the same manner in which we viewed delivery of an anti-infective for treatment or prophylaxis, to achieve maximal blood or tissue concentrations appropriate for any anticipated pathogen. We decided that for our next study that we would have three groups; one group where no timeout was taken, a one-minute timeout, and a two-minute timeout. We also wanted to determine if there is a difference between two or three showers, and we wanted to see if by using a whole bottle of 4 percent CHG as opposed to a half or some portion thereof, could we achieve a maximal skin-surface concentration. So now we are controlling for dose (the amount of CHG), controlling for time (the timeout) and also controlling for repetition (looking at the difference in skin-surface concentrations of CHG between two or three showers). The reason I included that third shower is that I was curious about the IHI Joint Project study which really didn't provide substantial documentation for why you need to take three versus two showers. We completed our study and we discovered that if you don't take a timeout, the concentrations you find on the skin are substantially lower compared to a one- or two-minute time out (p value equal to 0.001). We also discovered there was actually no difference in skin-surface concentrations of CHG between a one-minute timeout and a two-minute timeout. By using a whole bottle of CHG, you essentially saturated the skin, so you maximize the skin surface concentrations; taking that third shower did not provide any benefit whatsoever. So we have answered a few basic questions; one, that the timeout is extremely important for achieving maximal concentrations on the skin; that two or three showers are equivalent; and you need to use all four ounces of CHG, again to effect a maximal skin-surface concentration."

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What the Literature Says About CHG Bathing

Milstone, et al. (2008) summarizes recent inquiries into this subject matter: "Whether chlorhexidine baths alone can reduce MRSA infection remains unknown. However, recent evidence suggests that decontaminating ICU patients with daily chlorhexidine baths may reduce transmission of other multidrug-resistant organisms and prevent HAI. Daily bathing of ICU patients with chlorhexidine decreased skin and environmental contamination with VRE and reduced the incidence of VRE acquisition in a comparison of the intervention period with two periods of bathing involving baths that did not contain chlorhexidine. Not only did the intervention lead to

decreased colonization of VRE on the skin of patients, but also fewer healthcare workers' hands were contaminated with VRE. Evidence is mounting that daily bathing of ICU patients with chlorhexidine may also reduce HAI. A recent multicenter study evaluated daily bathing of adult ICU patients with chlorhexidine and found a 32 percent decrease in the acquisition of MRSA colonization, a surrogate for health care-associated transmission of MRSA. VRE acquisition decreased by 30 percent, and the incidence of all bloodstream infections (BSIs) decreased by 21 percent. This study evaluated a before-and-after intervention, and additional studies will be needed to confirm these promising results. Although there is growing literature evaluating the use of chlorhexidine baths for patients with recurrent MRSA abscesses and other infections with community-associated MRSA strains, further research is needed in this important area."

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Milstone (2008) adds, "Early studies demonstrated the utility of chlorhexidine-based soaps and hand scrubs; a natural extension of use of this agent lies in the field of preoperative baths and skin preparation for surgical patients. Postoperative surgical site infections are frequently caused by a patient's own skin flora, including those microorganisms that colonize body sites other than the surgical site. Similar to handwashing with chlorhexidine, chlorhexidine whole-body bathing significantly reduces microbial burden on the skin, and repeated baths lead to a progressive reduction of organisms over time. Preoperative bathing and scrubbing with chlorhexidine is superior to preoperative bathing and scrubbing with povidone-iodine in reducing skin colonization at the site of surgical incision. Preoperative baths are widely encouraged in clinical practice. Although we expect that decreasing general skin contamination in preoperative patients will decrease the number of SSIs, a clear cause-and-effect relationship has not been established to date."

Let's take a look at various studies.

Lin, et al. (2014) evaluated the effectiveness of daily chlorhexidine gluconate bathing in decreasing skin carriage of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae (KPC) among long-term acute care hospital patients. CHG bathing reduced KPC skin colonization, particularly when CHG skin concentrations greater than or equal to 128 µg/mL were achieved.

In their review, Chlebicki, et al. (2013) sought to identify prospective controlled trials evaluating whole-body preoperative bathing with chlorhexidine versus placebo or no bath for prevention of SSI. Sixteen trials met inclusion criteria with a total of 17,932 patients: 7,952 patients received a chlorhexidine bath, and 9,980 patients were allocated to various comparator groups. Overall, 6.8 percent of patients developed SSI in the chlorhexidine group compared with 7.2 percent of patients in the comparator groups. According to the researchers, chlorhexidine bathing did not significantly reduce overall incidence of SSI when compared with soap, placebo, or no shower or bath. The researchers noted, "Meta-analysis of available

clinical trials suggests no appreciable benefit of preoperative whole-body chlorhexidine bathing for prevention of SSI. However, most studies omitted details of chlorhexidine application. Better designed trials with a specified duration and frequency of exposure to chlorhexidine are needed to determine whether preoperative whole-body chlorhexidine bathing reduces SSI."

Edmiston and Bruden, et al. (2013) addressed the evidence-based literature and preliminary findings suggesting that CHG has a broad and safe range of applications when used as an adjunctive interventional strategy for reducing the risk of postoperative surgical site infections, and explain, "Renewed interest has emerged for use of the antiseptic bath/shower to reduce the microbial skin burden prior to hospital admission. Recent clinical studies have documented that multiple applications of 2 percent or 4 percent CHG using a standardized protocol results in high skin surface concentrations sufficient to inhibit/kill skin colonizing flora, including methicillin-resistant Staphylococcus aureus. A new focus for the use of CHG in surgical patients involves irrigation of the wound prior to closure with 0.05 percent CHG followed by saline rinse. Recent laboratory studies suggest that, following a one-minute exposure, 0.05 percent CHG produces a >5-log reduction against selective healthcare-associated pathogens and reduces microbial adherence to the surface of implantable biomedical devices. General, orthopedic, cardiothoracic, and obstetrical surgical studies have documented the safety of selective CHG formulations in elective surgical procedures."

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A Cochrane review noted that "Preoperative bathing or showering with an antiseptic skin wash product is a well-accepted procedure for reducing skin bacteria (microflora). It is less clear whether reducing skin microflora leads to a lower incidence of surgical site infection." In the review, Webster and Osborne (2012) examined randomized controlled trials comparing any antiseptic preparation used for preoperative full-body bathing or showering with non-antiseptic preparations in people undergoing surgery. For this fourth update, no new studies were identified. Seven trials involving a total of 10,157 participants were included. Four of the included trials had three comparison groups. The antiseptic used in all trials was 4 percent chlorhexidine gluconate. Three trials involving 7,791 participants compared chlorhexidine with a placebo. Bathing with chlorhexidine compared with placebo did not result in a statistically significant reduction in SSIs; the relative risk of SSI (RR) was 0.91. When only trials of high quality were included in this comparison, the RR of SSI was 0.95. Three trials of 1443 participants compared bar soap with chlorhexidine; when combined there was no difference in the risk of SSIs (RR 1.02, 95% CI 0.57 to 1.84). Three trials of 1,192 patients compared bathing with chlorhexidine with no washing, one large study found a statistically significant difference in favor of bathing with chlorhexidine (RR 0.36, 95%CI 0.17 to 0.79). The smaller studies found no difference between patients who washed with chlorhexidine and those who did not wash preoperatively.

Popovich, et al. (2012) used a colorimetric, semi-quantitative indicator to measure CHG concentration on skin (neck, antecubital fossae, and inguinal areas) of patients bathed daily with CHG during their MICU stay and after discharge from the MICU, when CHG bathing stopped. CHG concentration on skin was measured and skin sites were cultured quantitatively. The relationship between CHG concentration and microbial density on skin was explored in a mixed-effects model using gram-positive colony-forming unit (CFU) counts. For 20 MICU patients studied (240 measurements), the lowest CHG concentrations (0-18.75 µg/mL) and the highest gram-positive CFU counts were on the neck (median, 1.07 log(10) CFUs. CHG concentration increased post-bath and decreased over 24 hours. In parallel, median log(10) CFUs decreased pre- to post-bath (0.78 to 0) and then increased over 24 hours to the baseline of 0.78. A CHG concentration above 18.75 µg/mL was associated with decreased gram-positive CFUs. In all but two instances, CHG was detected on patient skin during the entire interbath (approximately 24-hour) period (18 of 20 patients). In 11 patients studied after MICU discharge (80 measurements), CHG skin concentrations fell below effective levels after one to three days. In MICU patients bathed daily with CHG, CHG concentration was inversely associated with microbial density on skin; residual antimicrobial activity on skin persisted up to 24 hours. Determination of CHG concentration on the skin of patients may be useful in monitoring the adequacy of skin cleansing by healthcare workers.

In their review, Kamel, et al. (2012) sought to evaluate the clinical effectiveness of preoperative skin antiseptic preparations and application techniques for the prevention of surgical site infections (SSIs). Twenty studies (9,520 patients) were included in the review. The results indicated that pre-surgical antiseptic showering is effective for reducing skin flora and may reduce SSI rates. As the researchers note, "The evidence suggests that preoperative antiseptic showers reduce bacterial colonization and may be effective at preventing SSIs. The antiseptic application method is inconsequential, and data are lacking to suggest which antiseptic solution is the most effective. Disinfectant products are often mixed with alcohol or water, which makes it difficult to form overall conclusions regarding an active ingredient. Large, well-conducted randomized controlled trials with consistent protocols comparing agents in the same bases are needed to provide unequivocal evidence on the effectiveness of one antiseptic preparation over another for the prevention of SSIs."

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Tanner, et al. (2012) describe a randomized trial with 60 participants to compare the effect of soap and two antiseptic washing products on colony forming units (CFUs) for up to six hours. The researchers found that chlorhexidine gluconate and octenidine were significantly more effective than soap in reducing CFUs in the underarm, and chlorhexidine was significantly more effective than soap in reducing CFUs in the groin.

National recommendations on pre-operative management of infection risks were issued in France in 2004; Borgey, et al. (2012) sought to assess compliance with the French national guidelines for pre-operative skin preparation in 2007. A prospective audit was undertaken in French hospitals through interviews with patients and staff, and observation of professional practice. Compliance with five major criteria selected from the guidelines was studied: patient information, pre-operative showering, pre-operative hair removal, surgical site disinfection and documentation of these procedures. Data for 41,188 patients from all specialties at 609 facilities were analyzed. Patients were issued with information about pre-operative showering in 88.2 percent of cases. The recommended procedure for pre-operative showering, including hair washing, with an antiseptic skin wash solution was followed by 70.3 percent of patients; this percentage was higher when patients had received appropriate information. Compliance with hair removal procedures was observed in 91.5 percent of cases, and compliance with surgical site disinfection recommendations was observed in 25,529 cases. The researchers found that information was given to the patient in 35.6 percent of cases; pre-operative surgical hygiene in 82.3 percent of cases; and pre-operative site disinfection in 71.7 percent of cases.

Bleasdale, et al. (2007) sought to determine whether patients bathed daily with chlorhexidine gluconate (CHG) have a lower incidence of primary bloodstream infections (BSIs) compared with patients bathed with soap and water. The study design was a 52-week, two-arm, crossover (i.e., concurrent control group) clinical trial with intention-to-treat analysis. The study setting was the 22-bed medical intensive care unit (MICU), which comprises two geographically separate, similar 11-bed units, of a 464-bed public teaching hospital in Chicago. The study population comprised 836 MICU patients. During the first of two study periods (28 weeks), one hospital unit was randomly selected to serve as the intervention unit in which patients were bathed daily with 2 percent CHG-impregnated washcloths; patients in the concurrent control unit were bathed daily with soap and water. After a two-week wash-out period at the end of the first period, cleansing methods were crossed over for 24 more weeks. Main outcome measures included incidences of primary BSIs and clinical (culture-negative) sepsis (primary outcomes) and incidences of other infections (secondary outcomes). Patients in the CHG intervention arm were significantly less likely to acquire a primary BSI (4.1 vs 10.4 infections per 1,000 patient days. The incidences of other infections, including clinical sepsis, were similar between the units. Protection against primary BSI by CHG cleansing was apparent after five or more days in the MICU.

Byrne, et al. (1990) reports that as part of the preparation for a large prospective trial investigating the effect of preoperative whole body disinfection on the postoperative wound infection rate, a preliminary volunteer study was carried out to establish the optimum number of preoperative washes required to achieve a maximum level of skin disinfection and if showering or bathing is a more efficient method of skin disinfection. Ten healthy volunteers were recruited. The results showed a significant decrease in the skin flora after the first and second showers (a decrease of 93.55 percent and 77.49 percent respectively), but no further significant fall with subsequent showers. There was a significant fall (p less than 0.005) in skin flora after a single bath (a decrease of 70.98 percent) with subsequent baths producing

no further significant reduction in skin flora. From these results it is recommended that three preoperative showers with 4 percent chlorhexidine detergent be used as an optimum preoperative whole body disinfection regimen. Three showers ensures against less thorough washing by the patients compared to the healthy volunteers in the study and fits easily into a preoperative regimen.

Garibaldi, et al. (1988) evaluated the efficacy of total body showering and incision site scrub with disinfectant agents in a randomized, prospective study of 575 patients undergoing selected surgical procedures. Patients who showered twice with 4 percent chlorhexidine gluconate had lower mean colony counts of skin bacteria at the surgical incision site in the operating room prior to the final scrub than patients who showered twice with povidone-iodine solution or medicated bar soap. Patients in the chlorhexidine group had no growth on 43 percent of the incision site skin cultures compared with 16 percent in the povidone-iodine group and 6 percent in the soap and water group. Patients who showered and who were scrubbed with chlorhexidine also had lower rates of intraoperative wound contamination. Bacteria were recovered from the wounds of 4 percent of patients using this regimen compared with 9 percent for patients who used povidone-iodine and 15 percent for patients who showered with medicated soap and water and were scrubbed with povidone-iodine. The researchers noted no difference in surgery-specific infection rates among patients in the three treatment groups; however, they say the sample sizes were too small to evaluate this outcome parameter adequately. These data suggest that preoperative showering and scrubbing with chlorhexidine is an effective regimen to reduce extrinsic intraoperative contamination of the surgical wound from skin bacteria. The efficacy of this regimen to prevent postoperative wound infection needs to be evaluated in a well-designed, carefully controlled prospective trial with adequate numbers of patients to achieve statistically valid conclusions.

Patients who showered twice with 4% chlorhexidine gluconate had lower mean colony counts of skin bacteria at the surgical incision site in the operating room prior to the final scrub than patients who showered twice with povidone-iodine solution or medicated bar soap.

Kaiser, et al. (1988) undertook a prospective randomized observer-blinded study comparing the ability of preoperative showers with chlorhexidine gluconate, povidone-iodine, and a lotion soap to diminish the staphylococcal skin flora of patients. By block randomization, patients scheduled for an elective cardiac operation or coronary artery angioplasty were assigned to shower with one of the study skin cleansers either once (evening only) or twice (both evening and morning) before the procedure. Semiquantitative samples for culture were obtained from the subclavian and inguinal sites on the evening before the procedure (baseline culture) and again the next morning before the operation. The chlorhexidine skin cleanser consistently reduced staphylococcal colony counts at both the subclavian and inguinal sites before the procedure. This reduction was significant for patients showering both evening and morning ($p < 0.05$). The use of the povidone-iodine skin cleanser inconsistently affected skin flora.

Patients using lotion soap either experienced no change or had an increase in colony counts. The researchers say chlorhexidine is more effective than povidone-iodine in diminishing skin colonization with staphylococci in patients before operation, and that repeated applications of chlorhexidine are superior to a single shower with this agent.

A multidisciplinary program (bundle) that spanned the phases of perioperative care helped reduce SSIs in patients undergoing colorectal surgery (CRS) at an academic medical center.

CHG as Part of Care Bundles and Risk Reduction

CHG bathing is being included in a number of care bundles and comprehensive SSI-reduction strategies. A multidisciplinary program (bundle) that spanned the phases of perioperative care helped reduce SSIs in patients undergoing colorectal surgery (CRS) at an academic medical center. The research was conducted by Jeffrey E. Keenan, MD, of Duke University Medical Center in Durham, N.C., and colleagues.

Efforts that have used systematic approaches, called bundles, that aim to incorporate best practices across the phases of perioperative care have had varied success. The authors evaluated an SSI bundle implemented at an academic medical center in 2011 and examined during a study period that stretched from 2008 through 2012 so before and after outcomes could be assessed. Elements of the bundle included evidence-based and commonsense measures, including educational materials, disinfecting showers before surgery, antibiotics and wound care. The study included 559 CRS cases (346 cases before the bundle and 213 after the bundle was implemented). Matched pre-bundle and post-bundle groups each had 212 patients. The bundle was associated with reduced superficial SSIs (19.3 percent vs. 5.7 percent) and postoperative sepsis (8.5 percent vs. 2.4 percent). No significant differences were seen in deep SSIs, organ-space SSIs, wound disruption, length of stay, 30-day readmission or variable direct costs. During the post-bundle period, superficial SSIs were associated with a 35.5 percent increase in variable direct costs ($13,253 vs. $9,779) and a nearly 72 percent increase in length of stay (7.9 days vs. 4.6 days).

"Further study is needed to assess whether the bundle can be effective with wider application and what level of compliance with bundle measures is needed to achieve good results," the authors write. In a related commentary, "Bundling for High-Reliability Health Care," Ira L. Leeds, MD, MBA, and Elizabeth C. Wick, MD, of Johns Hopkins University, Baltimore, write: "For colorectal surgery, the leading harm is surgical site infections, but strong initiatives to reduce these have stalled because of a lack of clear evidence to support that improvement is possible." They add, "A series of recent studies, including the study by Keenan, et al. in this issue of *JAMA Surgery*, support that colorectal surgical site infection is a preventable harm with adherence to published evidence, best practice guidelines and culture change. These studies demonstrate ways in which the field is naturally placed to develop high-reliability organizational models that build up from patient-care units rather than conventional efforts that

typically come down from administrative institutional mandates," they conclude.

Edmiston is a proponent of the bundle concept. "We published a paper in 2011 which talked about the shortcomings of the SCIP initiative, and what we need to do is come at it from a more comprehensive strategy," he says. "You must look at risk-reduction strategies that have an impact, not only in the wound but in other areas of the body that may initiate risk in that patient. Glycemic control is important, as is the use and timing of appropriate antimicrobial prophylaxis, but there are other interventions you can use that will protect the integrity of the wound. So we have been looking at this bundle concept closely and we just submitted a paper for publication that is a meta-analysis examining all of the surgical papers out there that incorporate some kind of bundle. I think that bundles are a holistic response to the problem and a significant risk-reduction strategy. A paper by Keenan in *JAMA Surgery* several months ago recommended a pre-admission shower strategy using CHG. So, I think the bundle is extremely important, especially those bundles that recognize the value of CHG pre-admission showers as a risk reduction strategy. There is no magic bullet, but if we can incorporate some core evidence-based strategies — and I believe CHG is one of them — we can bundle these processes and have a significant impact on risk reduction."

"There is no magic bullet, but if we can incorporate some core evidence-based strategies — and I believe CHG is one of them — we can bundle these processes and have a significant impact on risk reduction."

Edmiston adds, "We have always felt that the majority of infections is associated with patients' own endogenous flora. But here we have an intervention that if applied correctly, can significantly reduce the surface skin burden of those organisms that are most often associated with surgical site infections, in a relatively simplistic manner. If you apply the principles we have worked out in all of our papers, then we can get very good results in terms of lowering that burden. That lowered burden — which may not be achievable for all patients — is going to have an impact on reducing risk overall. What I like about the pre-admission shower is that before the patient even gets into the OR we have loaded CHG onto the surface so we have a barrier of protection which is well above the minimal inhibitory concentration for most surgical pathogens. Whatever they then do in the OR will be additive, but it's not going to take away from what's already on the surface."

In terms of risk reduction, Edmiston, et al. (2010) note, "A suggested risk reduction strategy has been the preadmission shower or skin cleansing with chlorhexidine gluconate (CHG). Although older clinical trials question the clinical efficacy of cleansing with CHG, recent evidence-based scientific and clinical studies support two types of CHG application (i.e., a 2 percent CHG-coated cloth or 4 percent CHG soap) using a standardized, timed process before hospital admission as an effective strategy for reducing the risk of postoperative surgical site infection.

The Issue of Reduced Susceptibility

Regarding the impact of the use of chlorhexidine-based products on bacteria's reduced susceptibility to chlorhexidine, the *Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals: 2014 Update* states, "Widespread use of chlorhexidine-based products (e.g., use of chlorhexidine bathing, antisepsis, and dressings) may promote reduced chlorhexidine susceptibility in bacterial strains. However, testing for chlorhexidine susceptibility is not standardized. The clinical impact of reduced chlorhexidine susceptibility in gram-negative bacteria is unknown."

Bacteria responsible for dangerous bloodstream infections may be growing less susceptible to this common antiseptic, according to a recent study led by investigators at Johns Hopkins and published in the September 2014 issue of *Infection Control and Hospital Epidemiology*. As we have seen, CHG has been increasingly used in hospitals in light of recent evidence that daily antiseptic baths for patients in ICUs may prevent infections and stop the spread of healthcare-associated infections. The impact of this expanded use on the effectiveness of the disinfectant is not yet known.

"Hospitals are appropriately using chlorhexidine to reduce infections and control the spread of antibiotic-resistant organisms," says study lead author Nuntra Suwantarat, MD. "However, our findings are a clear signal that we must continue to monitor bacteria for emerging antiseptic resistance as these antibacterial washes become more widely used in hospitals."

In the study, investigators compared bacterial resistance between cultures from patients in eight ICUs receiving daily antiseptic washes to patients in 30 non-ICUs who did not bathe daily with CHG. Bacterial cultures obtained from patients with regular antiseptic baths showed reduced susceptibility to CHG when compared with those from patients who did not have antiseptic baths. Regardless of unit protocol, 69 percent of all bacteria showed reduced CHG susceptibility, a trend that requires vigilant monitoring.

> Bacterial cultures obtained from patients with regular antiseptic baths showed reduced susceptibility to CHG when compared with those from patients who did not have antiseptic baths.

"The good news is that most bacteria remain vulnerable to CHG, despite the reduced susceptibility. Daily baths with a CHG solution remain effective against life-threatening bloodstream infections," says Suwantarat.

The investigators caution that the clinical implications of their findings remain unclear. For example, antibiotic susceptibility tests are commonly used to determine whether patients will respond to antibiotic treatment. A similar correlation between antiseptic susceptibility and response to an antiseptic are not as well defined. Identifying particular bacteria and settings in which these bacteria will not respond to antiseptic agents used in hospitals is an important next step.

"CHG has been around since 1954," says Edmiston, "so imagine the number of anti-infectives that have come and gone since then. And then look at the antibiotics when as soon as they are released, we see papers published that discuss the resistance that has already developed.

One of the beauties of a biocide or antiseptic is that they don't have a single mechanism of action. Antibiotics often have a single mechanism of action — there is some mutation in the bacteria that has altered that binding site, then the organism will express resistance. But this is not the case for CHG and other biocides."

Edmiston continues, "When you look at the literature critically, you can't really define CHG in terms of resistance. You have to define it in terms of reduced susceptibility. Because antibiotics have what's called a break point, determined based on the maximum serum concentration, which is then correlated to the MIC90 for the most common surgical pathogens. You can't do that with CHG. So what we have seen over the years with the Gram-positives such as MRSA, go anywhere from 4 micrograms to maybe as high as 10 or 12. The Gram-negatives have always been intrinsically resistant to CHG — especially Acinetobacter — not so much in SSIs but especially in the ICU. We have seen levels of decreased susceptibility in the range of 125 to 168 micrograms per mL. The vast majority of Gram-negatives are still well over 100 micrograms per mL. It is also very important to remember that when you look at the data, there has never been a published study documenting high levels of reduced susceptibility to CHG. You can never say never, of course, but CHG has been around a very long time and has withstood the test of time. I do not have the same level of concern others have expressed, primarily because what I know about CHG's mechanisms of action — especially if we are using it efficaciously, with the maximal skin surface concentrations, then we are not going to be applying suboptimal concentrations to patients' skin. 'Resistance' is an easy term to use, but we can't compare biocides like we compare antibiotics."

"Although decreased susceptibility to chlorhexidine has been reported, it has not been convincingly shown to be associated with repeated exposure to chlorhexidine.

Adding to the topic, Milstone, et al. (2008) observes, "Although decreased susceptibility to chlorhexidine has been reported, it has not been convincingly shown to be associated with repeated exposure to chlorhexidine. Proposed mechanisms include drug inactivation, efflux, and decreased uptake. Vancomycin-resistant enterococci (VRE) and vancomycin-susceptible enterococci, for example, have equivalent susceptibilities to chlorhexidine. Some Pseudomonas species and other non-fermenting Gram-negative organisms have high-level resistance to chlorhexidine. Plasmid-mediated resistance mechanisms to antiseptics are documented for staphylococci, as are increased MICs; however, the clinical significance of these increased MICs has not been determined, because they are usually far less than the commonly used chlorhexidine concentrations. Decreased susceptibility and the potential for emergence of resistance exist. Several laboratory studies have raised concerns that emergence of biocide non-susceptibility may result in cross-resistance to antibiotics, but data are limited. As antiseptics become used more broadly, surveillance of clinical isolates should be considered to identify an epidemiologically significant trend toward decreasing antiseptic and antibiotic susceptibility."

Conclusion

As Milstone, et al. (2008) summarize, "Historically, most infection prevention and control measures have focused on asepsis of healthcare providers and the environment. Emerging evidence for the role of host decontamination in preventing HAI is changing the paradigm and paving a new path for novel infection prevention interventions. Chlorhexidine has a long-standing track record of being a safe and effective product with broad antiseptic activity and little evidence of emerging resistance. As the limelight is directed toward control and prevention of HAIs, chlorhexidine-containing products may provide a vast tool kit for infection control practitioners. Increasing rates of multidrug-resistant bacteria, including MRSA and VRE, demand evidence-based research of novel interventions to prevent transmission of multidrug-resistant organisms and HAI. A delicate balance must be achieved between the rigorous regulatory oversight inherent in the traditional research model and the necessity for innovative quality-improvement initiatives, such that novel products can be tested in high-risk populations, including children. Given the promising preliminary studies discussed above, further research is essential to support evidence-based recommendations for the use of many chlorhexidine products in infection control and prevention."

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