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Commentary

Chlorhexidine gluconate skin levels and organism decolonization: what we know and what we don't know

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Effective infection prevention measures have become increasingly important not only in the wake of the COVID-19 pandemic but also due to the growing complexity of patient care and the continued emergence of antibiotic- and antifungal-resistant pathogens. One of the most effective strategies for reducing microbial colonization and risk of subsequent infection, both among colonized patients and through reduced transmission to other patients, is routine bathing. Bathing with the antiseptic chlorhexidine gluconate (CHG) is increasingly being used to reduce bioburden on patient skin to help lower the risk of colonization and subsequent infection. Daily CHG bathing is an established tool to combat healthcare-associated infections in acute care settings, particularly in intensive care units (ICUs), where invasive medical devices, such as central venous catheters and urinary catheters, are frequently required but can increase infection risks.[1] Daily or routine CHG bathing has also been successfully implemented in post-discharge settings, where studies have shown a 30% reduction in risk of Methicillin-resistant *Staphylococcus aureus* infections through CHG decolonization protocols.[2]

Variability in practices across healthcare settings and a lack of clear consensus on frequency and CHG dose for bathing can translate to excessive or ineffective use.[3] Such gaps muddy the accepted benefits of CHG bathing on certain healthcare-associated infection outcomes, highlighting the critical knowledge deficits that remain. The relationship between frequency of CHG bathing and skin CHG levels and the resulting impact on skin microbial colonization remains poorly understood. These knowledge gaps directly hinder the development and implementation of optimal, evidence-based CHG bathing protocols. A new study by Rhee *et al.* and the Centers for Disease Control and Prevention's Prevention Epicenters Program in this month's issue of *Infection Control and Hospital Epidemiology* presents data that helps fill some of these important evidence gaps, helping to guide more effective recommendations regarding CHG bathing and improve process outcomes.[4] Their research, a serial cross-sectional study assessing adult ICU patients receiving daily CHG bathing across seven hospitals, aimed to examine the association between CHG skin concentrations and skin microbial detection. Patient samples were collected via six one-day point prevalence surveys in which all ICU patients had unilateral skin swabs collected from the anterior neck, inguinal region, and axilla. From each sample, CHG skin concentration was assessed, and bacterial and yeast cultures were performed (and in one hospital, a rectal or stool swab was cultured to detect carbapenemase-producing Enterobacterales (CPE) colonization). Linear mixed-effects multilevel modeling was performed to analyze the relationship between CHG skin concentration and microorganism recovery.

Across 2,176 samples and 736 eligible patients, the investigators found that for every 2-fold increase in CHG skin concentration, the adjusted odds of microbial recovery decreased by 16% for gram-positive organisms (aOR = .84, 95% confidence interval (CI), .80–.87; $P < .001$), by 7% for Candida species (aOR = .93. 95% CI, .89–.98; $P = .008$), by 4% for gram-negative organisms (aOR = .96, 95% CI, .91–1.02; $P = .17$), and by 6% for CPE (aOR = .94, 95% CI, .84–1.06; $P = .33$) We interpret these findings as demonstrating a strong association and larger effect size between higher CHG levels and reduced odds of gram-positive bacterial recovery, and as demonstrating much smaller effect sizes between CHG concentration and recovery of *Candida* species and gram-negative bacteria. The authors should be praised for the high quality of their work and study strengths that include the large number of sampled patients and the multi-site setting.

Rhee et al.'s findings point to several key lessons. First, and not particularly surprising, higher concentrations of CHG can inhibit microbial growth/colonization on patients, especially for gram-positive bacteria and, to a much lesser extent, *Candida* species and gram-negative bacteria. As the researchers noted, a common question and overall knowledge deficit rests in an exact threshold or "adequate" level for CHG skin concentrations that would translate to efficacy against microorganisms. Limited studies have noted potential thresholds of 18.75 μg/ml for gram-positive bacteria and 128 μg/ml for CPE, but these were assessed prior to and after CHG bathing in patients, whereas this study was performed independent of time from last CHG bath.[5] Ultimately there is a considerable need for more work to understand the true capacity of CHG to reduce the skin burden of gram-negative bacteria and *Candida* species, especially the emerging pathogen *Candida auris*. For example, is more frequent CHG bathing needed for *Candida* and gram-negative bacteria, or is a different decolonization bathing product needed? Second, this study, in particular, focuses solely on colonization, but further assessment is needed to identify CHG skin concentration levels (eg thresholds) that correlate with reduction in microbial growth, as well as the impact on subsequent microbial transmission within healthcare settings. Colonization contributes to infection, especially in the presence of invasive medical devices, but further assessment is

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necessary to understand the role of consistent CHG bathing to achieve certain concentrations to inhibit patient-to-patient transmission. In short, this study prompts a need for further research regarding CHG thresholds for decolonization, the relationship between CHG levels and microbial colonization, and how this relationship may impact transmission in healthcare settings to potentially reduce healthcare-associated infections.

There are further implications for this research, as well as additional questions it inspires. Identifying maximum time between CHG baths, in addition to specific thresholds for skin concentrations, to maintain efficacy is necessary to drive more precise policies and process outcomes. The success of CHG bathing in day-to-day infection control practices relies on consistency, which can be varied and is often bundled with other interventions.[6] More precise recommendations and protocols can help increase standardization and consistency. In terms of health preparedness and enhancing healthcare resilience to novel and emerging infectious diseases, precise guidance for CHG skin concentration levels and frequency of bathing can establish a strong infection prevention foundation that has translational capacity in emergent circumstances. More work is also needed in the important area of microbiome alteration and impact to antibiotic-resistant bacteria and fungi, and necessary levels to lower risk of patient infections and patient-to-patient transmission. A more precise understanding and quantification of organism burden levels translating to infection rather than just bioburden would be beneficial, especially in relation to decolonization protocols. CHG bathing is an important component of infection prevention, but the time for imprecise and blanket recommendations is past, underscoring a need for investing in further research and more precise implementation protocols.

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