

## EDITORIAL



## Minimizing Surgical-Site Infections

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Primitive ancestors of *Homo sapiens* and their colonizing bacteria have coevolved for approximately 500,000 years; some experts estimate that the total number of human cells is  $10^{13}$  and the total number of colonizing microbes is  $10^{14}$ . Despite this 10-to-1 inequity, the balance of power is influenced by an intact human immune system and the integrity of the skin and mucous membranes. Operative procedures disrupt this balance, resulting in a risk of surgical-site infections from endogenous flora, including colonizing strains of *Staphylococcus aureus*.

Each year in the United States, more than 30 million operative procedures are performed. The risk of infection depends on the skill of the surgeon, the degree of contamination defined by the type of surgery (i.e., clean, clean-contaminated, or contaminated), and the patient's status with respect to underlying coexisting conditions and carriage of *S. aureus*. Approximately 20 to 30% of surgical-site infections are caused by *S. aureus*, and over half of these arise from the endogenous flora.

In an attempt to reduce surgical morbidity, the Surgical Infection Prevention Project and the Surgical Care Improvement Project have outlined evidence-based recommendations, bundling several strategies into a comprehensive approach. They include the initial administration of perioperative antibiotics within 1 hour before surgery, the preoperative use of hair clippers or no hair removal (as opposed to shaving of hair), and the maintenance of normothermia during colorectal surgery.<sup>1</sup>

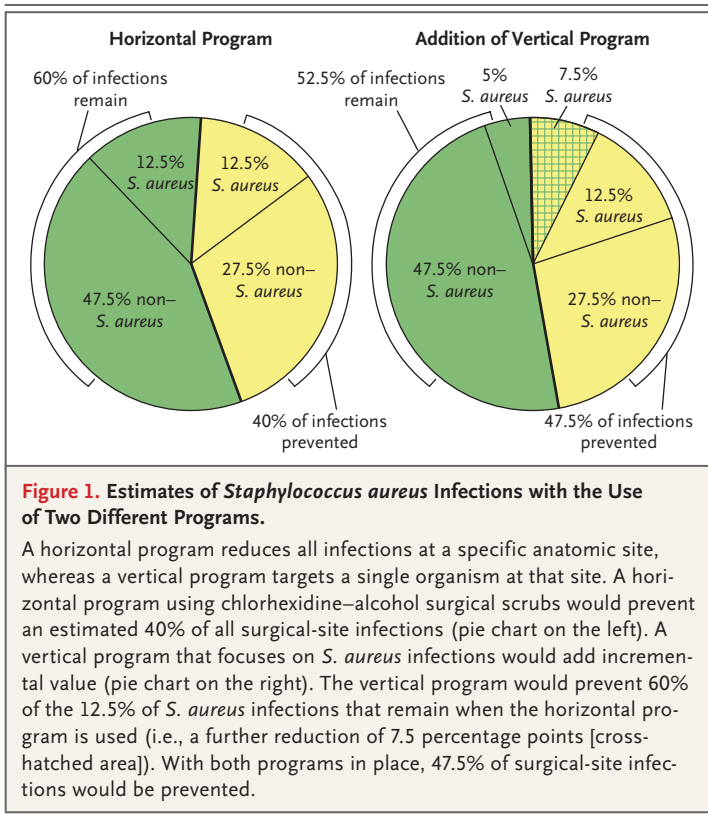
Because *S. aureus* is a virulent pathogen that can cause surgical-site infections, some studies have focused on eliminating nasal carriage of this organism preoperatively. Results of a recent meta-analysis suggested that topical mupirocin applied

intranasally would reduce the rate of surgical-site infections due to *S. aureus* by 45% in the subgroup of patients who are carriers.<sup>2</sup> It is also known that the skin is an important extranasal reservoir not only for *S. aureus* but also for other organisms implicated in postoperative infections.

Two well-controlled, multicenter, randomized studies reported in this issue of the *Journal* offer valuable insights for controlling surgical-site infections. Bode and colleagues demonstrated the efficacy of rapid, preoperative screening for nasal carriage of *S. aureus* along with the prophylactic treatment of patients who had positive results with the use of intranasal mupirocin twice a day for 5 days and daily baths with chlorhexidine soap.<sup>3</sup> Patients scheduled to undergo simple operative procedures were excluded, and only those who were expected to remain in the hospital for at least 4 days were randomly assigned to either active treatment or placebo. The subgroup of surgical-site infections caused by *S. aureus* was reduced by 60% among those in the active treatment group as compared with those treated with the placebo nasal ointment plus placebo soap.

In the second study, Darouiche and colleagues found a greater than 40% reduction in total surgical-site infections among patients undergoing clean-contaminated surgery who had received a single chlorhexidine–alcohol scrub as compared with a povidone–iodine scrub.<sup>4</sup> No patients received intranasal mupirocin in this study, yet the rate of *S. aureus* surgical-site infections was reduced by approximately 50% in the chlorhexidine–alcohol group (see the Supplementary Appendix to the article by Darouiche et al., available at NEJM.org).

Chlorhexidine–alcohol has been recommended by the Centers for Disease Control and Preven-



tion as the antiseptic of choice to reduce vascular catheter-associated bloodstream infections.<sup>5</sup> As compared with povidone–iodine, the chlorhexidine–alcohol solution has been found to reduce catheter-associated infections by approximately 50%.<sup>6</sup> Recently, researchers in six intensive care units (ICUs) at four institutions examined the rates of colonization of and bloodstream infections due to methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE) during a 6-month period during which patients were bathed daily with nonmedicated soap followed by a 6-month period of daily bathing with a chlorhexidine solution.<sup>7</sup> During the latter period, the MRSA acquisition rate decreased by 32%, VRE acquisition decreased by 50%, and the number of bloodstream infections due to VRE decreased by 73%. The same design was used in a study involving a single ICU, which showed an 87% reduction in all catheter-related bloodstream infections when patients were bathed with chlorhexidine.<sup>8</sup>

Such data add credibility to the findings of more favorable outcomes among patients treated with chlorhexidine products before undergoing

surgery. Nevertheless, researchers at a single institution tested three types of surgical-site scrubs, using a sequential-implementation study design. On primary analysis, the rate of surgical-site infections was lower with iodine povacrylex in alcohol than with either povidone–iodine or chlorhexidine–alcohol.<sup>9</sup>

From a population-based perspective, a program that substantially reduces all infections at a specific anatomical site (i.e., a horizontal program) is more valuable than one that targets a single organism at that site (i.e., a vertical program). Given a horizontal program (chlorhexidine–alcohol scrub) that reduces overall infection rates by 40% and eliminates 50% of *S. aureus* infections, one can estimate the incremental value of an additional vertical program that focuses on the remaining *S. aureus* infections. Assume that *S. aureus* infections represent 25% of all infections, that 50% of *S. aureus* infections remain, and that the number of these infections can be further reduced by 60%. The absolute improvement of 7.5 percentage points (i.e.,  $[25\% \times 50\%] \times 60\%$ ) would be the maximal incremental effect of the vertical program on the total infection rate (Fig. 1).

The Darouiche study supports the value of a relatively inexpensive horizontal program, which was remarkably effective: the number of patients who would need to be treated to prevent one surgical-site infection was found to be 17.

Although the reduction in *S. aureus* surgical-site infections in the study by Bode et al. was impressive, the relative contributions of the intervention components — that is, decolonization in the nares and the use of chlorhexidine soap — are unclear. A total of 250 patients would need to be screened and 23 carriers would need to be treated to prevent one *S. aureus* infection. This organism is responsible for an important subgroup, yet still a minority, of surgical-site infections. Unfortunately, the influence on total infection rates at surgical sites was not recorded but could be estimated to be 15% (a 25% prevalence of *S. aureus*  $\times$  60% reduction). The value of this well-conducted study is that it suggests a prophylactic approach for carriers of *S. aureus* who are candidates for surgical procedures associated with a high risk of deleterious outcomes should *S. aureus* infection develop at the surgical site. In this category, I would include all cases of open-heart surgery as well as any procedure in which a foreign body is placed (e.g., orthopedic and neurosurgical

implant procedures) as especially high-risk operations, and I would also include any surgical procedure in patients whose immune systems are severely impaired.

In summary, the weight of evidence suggests that chlorhexidine–alcohol should replace povidone–iodine as the standard for preoperative surgical scrubs. The use of intranasal mupirocin and chlorhexidine baths for carriers of *S. aureus* who have been identified preoperatively by means of a real-time polymerase-chain-reaction assay could be reserved primarily for patients who are undergoing cardiac surgery, all patients receiving an implant, and all immunosuppressed surgical candidates. Currently, the incremental value of preoperative baths with chlorhexidine alone for all surgical patients is unclear, but this relatively straightforward procedure could be examined critically in future studies. In the meantime, the data reported in these two studies offer remarkably safer strategies for all patients who require surgery.

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