Editorial

Preventing Surgical-Site Infections: The Importance of Timing and Glucose Control

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Our understanding of the physiology of wound healing and wound infection and the most effective strategies to reduce the risk of wound infection have progressed over a very long time. Perhaps the earliest significant advance in this field was the recognition of the role of bacteria in wound infection and the subsequent development first of antisepsis and then of asepsis. Important milestones in this progression included the development of the steam sterilizer, the introduction of rubber gloves for the surgical team, and effective techniques for skin preparation at the operative site. These developments occurred so long ago that no one currently practicing either surgery or infection control was present for their introduction. Nevertheless, occasional failures in their application, with resulting clusters of surgical-site infections (SSIs), serve to remind us of their continued importance.

The introduction of antibiotics in the 1950s did not bring the promise of reduced SSIs, as many had hoped, until laboratory studies by John Burke in the 1960s[1] and subsequent prospective clinical trials[2,3] demonstrated the elements required to achieve reduced infection rates through the use of prophylactic antibiotics. Hundreds of clinical trials since that time have refined our understanding of the most effective and appropriate methods of employing these useful drugs to prevent SSIs.[4,5] Although appropriate use of prophylactic antibiotics can reduce infection rates by 40% to 80%,[3-7] there is abundant evidence that unacceptable infection rates can result despite antibiotic administration in settings where wound management and antisepsis break down.[3,8]

In the 1970s and before, extensive hair removal with a razor at and around the operative site was common, in the belief that it improved local antisepsis, and the shaving often occurred the night before the operation. Several publications in the 1980s clearly demonstrated that this practice increased the risk of infection by promoting the growth of bacteria in microscopic (or macroscopic) cuts induced by the razor and populated by bacteria from hair follicles.[9-11] Current practice encourages no hair removal or limited hair removal occurring immediately prior to the operative procedure using clippers or depilatories rather than a razor. The effect of hair removal is most obvious in clean operative procedures, where exposure to endogenous bacterial is limited to skin flora. Despite this, one still can find razors stocked routinely in operating room supply carts in many modern hospitals and medical centers.

A number of investigators have demonstrated a strong association between the colonization of the nares with *Staphylococcus aureus* and subsequent staphylococcal SSIs following clean operative procedures.[12,13] Despite the promise suggested by the strategy of eliminating or suppressing carriage prior to scheduled clean operative procedures and several papers with historical controls that show a reduction in SSIs, we do not have any definitive, prospective publication demonstrating efficacy in a clinical setting to date. Finding and targeting the high-risk population in an efficient and cost- effective manner may be part of the problems. In addition, it may be that strategies aimed primarily at the nares fail to deal with simultaneous colonization of the axillae, groin, or rectum.

Temperature control in the operating room did not receive much attention in the past, but a recent study has demonstrated the value of preventing hypothermia during major operative procedures. When patients undergoing colectomy were randomized to have their temperature actively managed to maintain it as close as possible to 37°C, the SSI rate was approximately one third that of patients whose temperature was allowed to fall during the opera-

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tion.[14] Active warming of patients is now common in operating rooms throughout the United States. The exact reason for the reduction in wound infection rates with active warming of patients is not known, but it is known that subcutaneous blood flow and oxygen tension levels are higher in normothermic patients compared with hypothermic patients.

The relation between tissue oxygen levels and the risk of wound infection has been extensively investigated by Thomas Hunt and a number of colleagues since the late 1970s.[15,16] Among the interesting observations of these workers was the fact that, in animal models, higher tissue oxygen levels resulted in lower infection rates than normal oxygen levels and that reduced oxygen levels resulted in higher infection rates and more severe infections. They also observed that this effect, like that of prophylactic antibiotics, was maximum during the time of operation and for a short time afterward, and did not affect the incidence of SSI if instituted after an interval following the operative procedure. This is consistent with the concept of the decisive period of wound healing and infection risk proposed by Miles and Burke many years ago.[17,18] A subsequent study, again in patients having colectomy, demonstrated that the provision of high levels of inspired oxygen (80%) in the operating room and for 2 hours following the operation resulted in an SSI rate less than one half that of patients treated in the same manner but with 30% inspired oxygen.[19] Again, the effective period of treatment was demonstrated to be the immediate perioperative period.

The association of diabetes mellitus with an increased risk for SSI has been recognized for many years. More recently, as reviewed in the article by Latham et al in this issue, granulocyte functions, including adherence, chemotaxis, phagocytosis, and bactericidal activity, have been shown to be affected by hyperglycemia.[20] Others have shown that improved glucose control achieved with an insulin infusion in the perioperative period can reduce SSI rates in diabetic cardiac surgery patients when compared with historic controls.[21] Latham and colleagues prospectively gathered hemoglobin A1c values on 1,000 diabetic and nondiabetic cardiac patients prior to planned coronary artery bypass or valve procedures. They confirmed the previously observed increase (almost threefold) in infection rates in diabetics. They also found that 4.2% of the patients had previously undiagnosed diabetes, and the infection rate in these patients was equal to the rate in diagnosed diabetics. More interestingly, they demonstrated that the greatest risk for SSI correlated with postoperative hyperglycemia (blood glucose levels greater than 200 mg/dL) rather than with the level of hemoglobin A1c or with preoperative hyperglycemia (they apparently did not have intraoperative glucose levels available). This appears to correlate with data regarding the time course of antibiotic efficacy and the effect of temperature and oxygen levels. The most important blood glucose measurements were the postoperative measurements rather than a measure of long-term control (hemoglobin A1c) or even of hyperglycemia in the preoperative period. These authors found a strong association in both diabetic and nondiabetic patients between hyperglycemia at least once during the 48 hours following operation and SSI. It would be very interesting to explore whether the critical period for glucose control extends to 48 hours or whether, like antibiotics, temperature, and oxygen, the effect is much stronger during and shortly after the operative procedure. One can imagine a future study in which frequent measurements of blood glucose are made in all patients (diabetic and nondiabetic) during the operative procedure and in the postanesthesia-care unit (recovery room) either as an observational study such as this one or with intensive intervention. This could shed further light on the decisive period during which tight glucose control has the greatest influence on the risk of SSI. An ideal intervention trial would compare two different algorithms with different goals for glucose management, comparing infection rates and complications or difficulties associated with tighter glucose control.

Latham and colleagues point out that many of the known risk factors for SSI are factors that cannot be changed by the physician such as gender, age, obesity, underlying diseases, and duration of surgery.[20] However, over the past century and particularly the last 40 years, we have learned how to limit the access of endogenous bacteria to the wound, discourage their proliferation when they do get there, and optimize host physiology through attention to nutrition in some highly selected cases and to temperature and oxygenation in all cases. Latham found that 159 (48%) of 328 diabetic patients and 139 (12%) of 654 nondiabetic patients experienced hyperglycemia in the first 48 postoperative hours. In other words, 47% of patients who experienced postoperative hyperglycemia were not diabetic, and 30% of all patients undergoing cardiac surgery experienced at least one postoperative hyperglycemic episode. Each group of hyperglycemic patients (diabetic and nondiabetic) experienced an approximately twofold higher SSI rate than the comparable group that did not experience hyperglycemia. Thirty percent of the excess infections attributable to hyperglycemia occurred in nondiabetic patients. If the 298 patients with postoperative hyperglycemia had been kept below 200 mg/dL by intensive perioperative glucose monitoring and control, and if that control had reduced their infection rate to the rate observed in this study for patients without postoperative hyperglycemia, there would have been a reduction of 19 infections out of 72, or 26%. That is a difference worth confirming and achieving.

Since this editorial was written, two highly relevant and supportive articles to the points made above have been published.[22,23]

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