Updates in Prevention of Surgical Site Infection: Comment

To the Editor:

Long *et al.*[1] provided a well-written and accessible review of new ideas in the field of surgical site infection prevention. Within their discussion of the patient's microbiome, the authors touch on the potential for interactions between the patient microbiome and anesthetic agents administered perioperatively. Although they accurately identify the immunosuppressive potential of volatile anesthetics and intravenous opioids, we think that it is important to note that there exist other agents capable of producing and maintaining general anesthesia. Medications like ketamine and propofol are immunomodulatory in different ways, and thus their use may also impact the development of surgical site infections.

Long *et al.*[1] cite two mouse model articles where exposure to volatile anesthetics was associated with a decrease in intestinal microbiome diversity.[2,3] In contrast, Guo *et al.*,[4] using a rat model, looked at the effect of a continuous infusion of propofol during a 3-h period on the intestinal microbiome and found little change in the diversity of the intestinal microbiome after exposure to propofol. Similarly, Gerb *et al.*[5] looked at the effects on the intestinal microbiome of mice after 10 daily exposures to a bolus dose of ketamine that rendered the mice unconscious for approximately 15 to 30 min per ketamine exposure and also found little change in the diversity of the intestinal microbiome.

No definitive evidence exists to recommend one type of anesthetic over another. Given the minimal impact on the intestinal microbiome, it might be tempting to conclude that replacing volatile anesthetics with agents such as propofol and ketamine might decrease the incidence of surgical site infection. But there is also evidence to the contrary. For example, Visvabharathy *et al.*[6] looked at susceptibility to infection due to exogenous bacteremia using *Listeria* and *Staphylococcus aureus* in mice receiving intravenous propofol compared to mice receiving intravenous ketamine with xylazine and found that propofol increased susceptibility to infection. In a research letter, Liu *et al.*[7] looked at the intestinal microbiome in 21 patients undergoing nephrectomy with propofol alone compared to sevoflurane alone compared to propofol and sevoflurane combined and found that the mixed anesthetic[7] was associated with the fewest perturbations.

Clearly it remains premature to advocate for a total intravenous technique in the absence of more clinically robust data. Further research in animal models and in humans is needed to try and elucidate not only if there is an optimal anesthetic agent for prevention of surgical site infection, but also what the combined effects of multiple anesthetics, as routinely administered when patients present for surgery, have on the patient's susceptibility to infection after surgery.

Surgical site infections are a multidisciplinary problem. Once more data are available, it may turn out that the effects of anesthetic agents are small and of minor importance in patients with normal immune systems. But the selection of anesthetic agents is one aspect we have almost complete control over; we should be making every effort to maximize the ability of the patient's immune system to combat infection.

Competing Interests

The authors declare no competing interests.

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Updates in Prevention of Surgical Site Infection: Reply

In Reply:

We thank Drs. Mundangepfupfu and Nadler for their letter[1] regarding our review, "Emerging Paradigms in the Prevention of Surgical Site Infection,"[2] in which they comment that other common anesthetic medications, beyond those highlighted in the article (volatile agents and opioids), may influence the microbiome or host immunologic response—specifically propofol and ketamine. We agree and thank them for raising this point. In addition, local anesthetics,[3] dexmedetomidine[4] and cisatracurium,[5] have also been shown to have immunomodulatory properties.

The authors further caution that evidence to date (primarily from animal models) is conflicted regarding the potential detrimental or protective effects of these agents on infection and that it is premature to advocate for the use of total intravenous anesthesia on such grounds. We agree with this statement and would like to emphasize that our review similarly does not advocate for use of total intravenous or any other anesthetic technique on this basis. Rather, our intent is to highlight the plausible influence of common anesthetics exposures on postoperative infection and the need for clinical research in this area.

The persistence of infection as a leading postoperative complication contrasts with historic improvements in other aspects of perioperative care and requires us to examine new avenues by which our practice may contribute to patient safety in this domain. We appreciate the insights and enthusiasm of Drs. Mundangepfupfu and Nadler and, particularly, their call for a multidisciplinary approach to studying the role of anesthetic factors in microbiome-mediated outcomes of surgery.

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Competing Interests

Dr. Alverdy is the founder of Covira Surgical (North Chicago, Illinois) and has received Royalties from ReShape Medical (San Clemente, California).

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Selection Bias in the Hypotension Prediction Index: Comment

To the Editor:

We read with interest the article by Enevoldsen and Vistisen about the predictive model of intraoperative