Dear Editor,

We read with interest the article of Bouvy et al.1 in which they used a rodent model to assess the impact of CO₂ and gasless laparoscopy as well as laparotomy on peritoneal tumor growth and abdominal wall metastases. The study demonstrates that laparotomy is associated with the greatest degree of postoperative tumor growth. Although laparoscopy results in less postoperative tumor burden, a difference is also noted depending on whether the laparoscopy is gasless or CO₂-based. In their discussion, the authors reference a study of ours2 relating to the effects of laparotomy, CO₂ laparoscopy, and air laparoscopy on peritoneal immune response. In that study, we demonstrated that exposure of the peritoneal cavity to air regulates early inflammatory responses to surgery in a murine model and found that the most profound perturbations in postoperative proinflammatory responses occurred in the air laparoscopy and laparotomy study groups. Bouvy et al. have misinterpreted our data when they state that we found intraperitoneal macrophage activity to be compromised after CO₂ insufflation. In fact, the presence of CO₂ in the peritoneal cavity was associated with preservation of macrophage function and CD11b receptor status. More importantly, this study demonstrated, for the first time, that disregulated peritoneal macrophage function in the air laparoscopy and laparotomy groups could be attributed to factors in circulating air that appeared to induce endotoxin translocation into both the peritoneal cavity and the systemic circulation. The study also implicated endotoxin as the factor responsible, as identical alterations in peritoneal immune function occurred in each of these groups. There is precedent for this: Rylander et al.3 previously reported that air contains small amounts of endotoxin (approximately 1 mg/m³).

We are interested in their findings in relation to intraperitoneal tumor growth. Studies in our laboratory have similarly demonstrated that breach of the peritoneal cavity through a laparotomy wound results in a significant increase in extraperitoneal primary tumor growth, as well as increases in the number of hepatic and pulmonary metastases compared with CO₂ laparoscopy and anesthesia only. Increased tumor growth correlated with decreases in natural killer cell and lymphokine activated killer cell function in the laparotomy and, to a lesser extent, CO₂ laparoscopy study groups.4 More recent studies have gone on to demonstrate that air laparoscopy and direct injection of endotoxin into the peritoneal cavity result in increases in tumor growth similar to that seen with laparotomy.5

Moreover, work in progress in our laboratory has shown that near-laparotomy (abdominal wound with no peritoneal membrane breach), with no peritoneal cavity exposure, results in a negligible change in intraperitoneal immune function and postoperative extraperitoneal tumor growth. Of even greater interest is the finding that C3H-HeJ endotoxin hyporesponsive mice do not exhibit the early increase in postoperative tumor growth seen in their C3H-HeN counterparts, once again implicating endotoxin as a critical mediator of not only the postoperative inflammatory response but also tumor growth. We believe that confirmation of these findings in humans will have significant implications for patients undergoing cancer surgery, specifically in terms of modulating micrometastatic tumor growth in the early postoperative period.

Several studies have now suggested that the concept of the lesser trauma of minimal access surgery being responsible for lesser magnitudes of proinflammatory and immunologic perturbations is unduly simplistic. The brilliant intuition of Joseph Lister that disease dust (i.e., germs) within the atmosphere was responsible for wound infection heralded the modern era of surgery. We would propose that these organisms and their products are responsible for phenomena previously attributed to surgical trauma. Laparoscopic surgery has clearly demonstrated that beneficial modulation of the proinflammatory and immunologic responses can occur. The total exclusion of air or the elimination of endotoxin from the open surgical field may bring similar benefits. The confirmation or refutation of this hypothesis in the clinical arena is clearly important.

References


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Authors’ Reply

We thank Drs. Redmond and Bouchier-Hayes for their interesting commentary on our paper.1

It is obvious that the consequences of the interaction between CO₂ and macrophages on tumor defense mechanisms remain unsettled. In the study by Watson et al.,2 the release of cytokines by macrophages was less after CO₂ insufflation than after air insufflation or laparotomy. Cytokines are essential mediators in the activation of lymphocytes that may play a role in killing tumor cells. However, phagocy-