in our study had some restrictive pulmonary disease and impaired carbon monoxide diffusion capacity secondary to bleomycin treatment. The authors compared "available" (again no numbers given) alveolar–arterial oxygen differences [$P(A-a)_{O_2}$ preoperatively and postoperatively within Group 1 and found no statistical differences. Were these values within normal range both preoperatively and postoperatively? Again, we are not told. In our series the mean preoperative $P(A-a)_{O_2}$ was higher than the normal range in both survivors and nonsurvivors and, although unchanged in the survivors after operation, was greatly increased in the nonsurvivors in the immediate postoperative period even when the patients had no signs or symptoms of respiratory distress. We believe this to be of prime importance.

Hypoxemia is not a problem with these patients, for their disease and treatment necessitates careful monitoring throughout a surgical procedure, which includes frequent blood gas analysis.

The authors did have two postoperative pulmonary complications that they chose to view as routine. Such exclusion of complications must be suspected especially in a retrospective study.

The authors have ignored clinical reports which support our findings. Douglas and Coppin report a retrospective study of 20 surgical procedures in 14 patients with one pulmonary complication.[3] A patient who died of respiratory failure 17 days postoperatively was described recently by Hulbert *et al.*[4] A retroperitoneal exploration was performed with the use of an $F_{I_{O_2}}$ of 0.4 after preoperative bleomycin therapy. Postmortem examination and microscopic findings were similar to our patients and support our hypothesis.

The authors also have ignored a laboratory study by Toledo *et al.*,[5] which examined the interactions of O_2 and bleomycin using a murine model. They concluded that exposure to a nontoxic but elevated O_2 concentration can potentiate the toxic effects of bleomycin. This study was designed similarly to our own unpublished study, which suggested pulmonary damage as evidenced by increased collagen in the lungs of the bleomycin oxygen mice. It was inconclusive, for we were forced to terminate the study after 14 days because of a lack of laboratory facilities. Toledo *et al.* carried the study to 10 weeks with most impressive results.

In view of our clinical experience and the continuing reports in the literature a more definitive study is needed before we would recommend altering a most effective method to deal with a potentially catastrophic situation.

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In reply:—We believe that the data presented in our article[1] support the conclusion that in the bleomycin-treated surgical patients that we studied, O_2-enriched anesthetic gas mixtures did not result in clinically demonstrable pulmonary toxicity.

Goldiner and Rooney[2] stated in their letter that our patient population of 13 undergoing 15 procedures is small. It should be remembered that Goldiner *et al.* reported on five patients who consecutively succumbed to pulmonary failure. The experimental group contained

only 12 patients studied prospectively. Goldiner *et al.* studied the first retrospectively and the second prospectively. This obviously introduces bias into the analysis that cannot be controlled. Our retrospective study has the advantage that bias in patient management should not have occurred.

On the question of pulmonary function tests our article as originally submitted contained the data in table form. In brief, prospective vital capacity (V_c) and carbon dioxide diffusion capacity was reported for 8 of 13 patients in the high oxygen group (Group 1) with only three abnormal diffusion capacities. Data were available for all three patients in the low oxygen group (Group 2). One had a V_c of 68% predicted and one other had a low diffusion capacity. The greater number of patients with abnormal PFTs in Goldiner's study clearly was stated in our conclusion. This is one of the differences between the patients in the two studies.

The data for $P(A-a)_{O_2}$ submitted in our original draft revealed three Group 1 patients and no Group 2 patients with increased $P(A-a)_{O_2}$ preoperatively. Results were reported for 9 of 13 Group 1 patients and all of the Group 2 patients. As stated in our article, the Group 1 ($P(A-a)_{O_2}$ differences did not increase postoperatively in contrast to the Goldiner *et al.* series.

The postoperative pulmonary complications observed in our series, atelectasis and bacterial pneumonia, are common after long abdominal operations. It is important to remember that common problems still are the major source of morbidity in patients with uncommon diseases. In one large study of postoperative pulmonary complications, there was an incidence of atelectasis exceeding 10% after laparotomy.[3] At present, these problems hardly can be related to oxygen toxicity and the adult respiratory distress syndrome (ARDS). ARDS is difficult to miss clinically, as is death, the complications reported by Goldiner *et al.* The fact that they had five consecutive deaths is indeed disturbing but does not necessarily implicate oxygen as the culprit. Goldiner *et al.* changed other aspects of their care, including the application of invasive monitoring with pulmonary artery catheters.

Goldiner and Rooney cite several studies to support the hypothesis that oxygen is toxic to patients after bleomycin therapy. The study by Douglas and Coppin describes 14 bleomycin-treated patients undergoing 20 operations.[4] In the entire group, one case of pulmonary failure was noted. This patient after undergoing bronchoscopy and mediastinoscopy with oxygen-enriched gas mixtures developed dyspnea and hypoxemia on room air 2 days postoperatively, which resolved with time. A second procedure with low oxygen did not precipitate a recurrence. Goldiner and Rooney cite this transient pulmonary dysfunction as supporting their viewpoint. Indeed this series seems to support our view that oxygen can be administered safely to patients after bleomycin therapy.

The study by Toledo *et al.* involves a murine model of increased oxygen toxicity during concurrent bleomycin administration.[5] The investigators state in their discussion that, although increased mortality was observed in the animals treated with 40% oxygen and bleomycin concurrently, they could not be certain that the lung was the site of the interaction or that the animals died of respiratory failure. The authors further state that their data do not allow them to comment on the importance of concurrent *versus* sequential O_2 and bleomycin administration in producing potentiation of toxicity. This study, while interesting, does not test Goldiner's hypothesis.

All the studies reported thus far, including our own, have problems of experimental design. The hypothesis advanced by Goldiner *et al.* remains interesting but unproven. We would welcome a prospective, preferably multiinstitutional, study to examine this question but until that time dogmatic insistence on restriction of oxygen during anesthesia may be associated with more risk than benefit in these patients.

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