- Hogan QH, Prost R, Kulier A, Taylor ML, Liu S, Mark L: Magnetic resonance imaging of cerebrospinal fluid volume and the influence of body habitus and abdominal pressure. Anesthesiology 1996; 84:1341-9
- Palmer CM: Let's just call it "evidence-based practice." ANESTHESIOLOGY 2011; 114:481-2
- 4. Ginosar Y, Mirikatani E, Drover DR, Cohen SE, Riley ET:  $\rm ED_{50}$  and  $\rm ED_{95}$  of intrathecal hyperbaric bupivacaine coadministered with opioids for cesarean delivery. Anesthesiology 2004; 100:676-82
- Carvalho B, Collins J, Drover DR, Atkinson Ralls L, Riley ET: ED<sub>50</sub> and ED<sub>95</sub> of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. Anesthesiology 2011; 114:529-35
- DeLean A, Munson PJ, Rodbard D: Simultaneous analysis of families of sigmoidal curves: Application to bioassay, radioligand assay, and physiological dose-response curves. Am J Physiol 1978; 235:E97-102
- Ritz C, Streibig JC: Bioassay analysis using R. J Stat Software 2005; 12:5
- 8. Morgan BJT: Analysis of Quantal Response Data. New York, Chapman & Hall, 1992

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## In Reply:

We would like to thank Dr. Nathan L. Pace for his commentary and additional analysis of our study. We agree that entire dose-response curve analysis does permit a more robust statistical comparison than  $ED_{50}$  and  $ED_{95}$  single-point comparisons. Dr. Pace's reanalysis found  $ED_{50}$  and  $ED_{95}$  values similar to our original calculations. We concur with the differences Dr. Pace found in the dose-response curves, noting higher dose requirements in this morbidly obese population compared with a nonobese population studied previously. Despite evidence of different dose-responses and higher  $ED_{50}$  values in morbidly obese patients, we are hesitant to firmly conclude that obese patients require larger intrathecal doses of local anesthetics compared with nonobese patients for a number of reasons:

The primary objective of our study was to determine the ED<sub>50</sub> and ED<sub>95</sub> in our morbidly obese population. Comparisons of ED<sub>50</sub> and ED<sub>95</sub> values of these morbidly obese patients with those of a nonobese population previously studied by our group were only a secondary analysis and study endpoint. In addition, using historical controls from a number of years ago presents important limitations, as we mentioned in our manuscript. Historical controls are associated with many confounders and biases that may affect group comparisons. Both studies contained small study populations (42 morbidly obese and 42 nonobese patients); therefore, a few individuals can have a greater influence on the overall population dose-response curve than preferable. In addition, although we followed a methodology similar to that of the previous study, it was not identical (e.g., 5–11 mg doses administered in the obese population were compared with 6-12 mg doses in nonobese patients).

While we acknowledge Dr. Pace's analysis of a rightward shift in the dose-response curves of the morbidly obese pop-

ulation compared with a nonobese population, the limitations noted above remain. We therefore do not want to go as far as recommending increasing the intrathecal local anesthetic dose in the morbidly obese patients undergoing cesarean delivery. It is worth noting that no patient in our study received the calculated ED<sub>95</sub> of 14.3  $\pm$  0.9 mg, and we can therefore not comment on its safety. In contrast to expert advice, our study does suggest that the intrathecal bupivacaine dose should not be reduced for obese patients. Our findings also imply that morbidly obese patients are not wellsuited to a single-shot spinal technique. More variable responses to intrathecal dosing and longer surgical times indicate that catheter-based techniques are more appropriate. Our study also highlights that initial satisfactory sensory block to pinprick following small intrathecal doses does not ensure adequate intraoperative anesthesia for the duration of the surgical procedure.

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## Reference

 Carvalho B, Collins J, Drover DR, Atkinson Ralls L, Riley ET: ED<sub>50</sub> and ED<sub>95</sub> of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. Anesthesiology 2011; 114:529-35

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## Observations on the Study of Second Gas Effects

To the Editor:

This recent excellent study on the second gas effect was extremely interesting.1 I would like to ask several questions to further appreciation of the findings presented. Which ventilator type, mode, inspiratory/expiratory time settings, and fresh gas flows intraoperatively (vs. 9 l/m during emergence) were used? Some ventilator models self-correct to end expiratory volumes, whereas others (i.e., volume-controlled Narcomed II [Draeger Medical Inc., Telford, PA]) deliver fixed inspiratory volumes, which further affect expired volumes by changes in fresh gas flow as well as the additional significant N2O egress volumes. Increasing fresh gas flow from 3 l/m to 9 l/m to fixed ventilator inspiratory volumes using 1:2 inspiratory/ expiratory ratios can affect up to 200 versus 2,000 ml tidal versus minute volume changes, respectively. Although reported minute volumes are described as nonsignificantly different in N<sub>2</sub>O versus air/oxygen control group via ml × min × kg (ml/Kg/min???) in your table 1, the calculated respective 6,605 versus 5,749 absolute ml/min is 15% difference (was this significant statistically?), which would be even