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*In Reply:*—I do not wait until the Sodasorb is completely exhausted before I change it. I personally change it at the first sign of the indicator showing a change of color. I do this for two reasons. Since we are a small department and have no anesthesia technician, I do not want to need to change the Sodasorb in the middle of a long case. In addition, it has been reported<sup>1</sup> that ethyl violet in Sodasorb can be photodeactivated by the fluorescent lighting in the operating room. Therefore, this indicator of Sodasorb exhaustion may not be 100% reliable.

When the problem of premature exhaustion first arose, I believed it was due to the possible poor quality of the Sodasorb, but since the employee in question was discharged, our present stock of Sodasorb is performing as it had in the past. In lieu of this, I have no other explanation for the premature exhaustion of our Sodasorb except for the nitrous oxide abuse by the employee.

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### If Ventricular Conduction and Rhythm Disorders Are Caused by Bupivacaine, It Is Doubtful That Intraoperative Hyponatremia and Hyperkalemia Enhance Them

*To the Editor:*—Timour *et al.*, after maintaining constant arterial plasma concentrations of bupivacaine of 2.2–3.7 µg/ml concluded: "To the extent that animal data can be extrapolated to humans, we believe that if significant intraoperative hyponatremia or hyperkalemia are present (or are likely to occur), anesthetic techniques that might lead to high blood concentrations of bupivacaine, *e.g.*, epidural or brachial plexus block, should be used with caution. Hyponatremia or hyperkalemia could add to or even potentiate bupivacaine-induced inhibition of intraventricular conduction and result in serious rhythm disorders."

Their investigation is markedly dissimilar to the clinical situation. Sustained arterial plasma concentrations of 2.2–3.7 µg/ml do not occur in patients after administration of 125–225 mg bupivacaine 0.5–0.75% for epidural block (lumbar n = 20, caudal n = 6) or from 300 mg 0.5% for brachial plexus block (n = 10). Concentrations as great as 2.4 µg/ml may occur with these blocks in 15–30 min. However, in another 15–30 min, they are less than 1.9 mg/ml,<sup>2–4</sup> and they decrease with each elapsed minute.<sup>2–4</sup>

Therefore, allowing time from injection to establishment of operating anesthesia (15 min), draping of the patient (15 min), and the occurrence of hyponatremia or hyperkalemia intraoperatively, it is highly unlikely that the bupivacaine concentrations maintained in dogs could ever occur clinically. Even if they did, and even if hyponatremia or hyperkalemia or both occurred intraoperatively or existed prior to a regional block, our published data do not support the thesis of Timour *et al.*<sup>5–8</sup> Do they have clinical data? If so, citing them would be appreciated.

To conclude, anesthesiologists should be aware of the following: Animal data cannot be extrapolated to humans. They are only a rough guide line to the situation in humans.<sup>6,9–11</sup> Furthermore, as stated some years previously, "Believing in medicine is not enough, one must know."<sup>12</sup> "Extrapolating" or "believing" is extremely dangerous and only leads anesthesiologists eventually to state that animal data are facts pertinent to humans, when no clinical proof exists. As a result, techniques and drugs that may be the anesthesia of choice are not used. Perhaps most important is that such extrapolating has in the past,

and likely will in the future, result in the twisting of facts in a medicolegal case to serve a purpose for which they may not be intended.

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*In Reply:*—The letter by Dr. Moore criticizes the conclusion of our study,<sup>1</sup> namely, that "to the extent that animal data can be extrapolated to humans, we believe that if significant hyponatremia or hyperkalemia are present (or are likely to occur), anesthetic techniques that might lead to high blood concentrations of bupivacaine, e.g., epidural or brachial plexus block, should be used with caution. Hyponatremia or hyperkalemia could add to or even potentiate bupivacaine-induced inhibition of intraventricular conduction and result in serious rhythm disorders."<sup>1</sup>

Dr. Moore finds fault with our conclusions on two accounts. First, he states that animal data cannot be extrapolated to humans. Of course, one should not quantitatively extrapolate the results of an animal study to clinical practice. However, there is a history of cardiac arrest in patients<sup>2,3</sup> following the use of bupivacaine, and previous animal studies<sup>4-8</sup> have offered sound physiologic explanations for this phenomenon. We agree that the association of high plasma concentrations of bupivacaine (2.2-3.7 µg/ml) with severe hyponatremia (114 M) or hyperkalemia (7.7 M), as occurred in our study,<sup>1</sup> is rare. However, accidental intravascular injections during epidural anesthesia may occur relatively frequently (2-10%), particularly with multiorifice catheters.<sup>9</sup> Furthermore, continuously increasing plasma bupivacaine concentrations up to 4 µg/ml have been observed after 2 days following epidural infusions for postoperative pain relief.<sup>10</sup> Thus, to ignore results from an animal study<sup>1</sup> that suggests conditions under which cardiac arrest may occur is not sensible. In fact, if regional anesthesia is indicated in a patient with significant hyponatremia or hyperkalemia, the clinician might consider selecting a technique that is not associated with high blood anesthetic concentrations (*i.e.*, spinal rather than epidural anesthesia) or using an agent other than bupivacaine, or both. Another point regarding the use of animal studies to investigate clinical toxicity problems: What are the alternatives? Animal studies are used because patients cannot be put at risk while investigating the mechanisms, exacerbating factors, and treatments of drug toxicity; it then is reasonable to cautiously extrapolate the results of these studies to clinical practice.

Dr. Moore had a second criticism of our work that he emphasized by quoting from one of his own publications<sup>11</sup>: "Believing in medicine is not enough, one must know." The danger with this type of reasoning is obvious. Who really *knows* the truth? And what is to be made of a statement that one person fervently holds to be true, and yet another person with equal conviction holds to be false? We reject this criticism because we cannot accept the dogmatic approach proffered by Dr. Moore.

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