The low incidence of significant adverse neurologic outcomes prevents definitive conclusions regarding these complications after regional anesthesia. The difficulties involved in investigating these low frequency, zero tolerance, events can be appreciated by the fact that the relative safety of using nerve stimulation versus a paresthetic technique has never been adequately resolved, despite decades of debate. Although the relatively high incidence of transient postoperative neurologic symptoms after regional block can be used to assess the relative risk, the validity of these symptoms as a surrogate marker of significant injury is speculative. Although substantive data concerning significant injury are lacking, a large retrospective study recently reported five seizures and three nerve injuries in 3,290 patients undergoing peripheral nerve blocks guided by nerve stimulation, but no such events in 2,146 patients undergoing similar blocks guided by both nerve stimulation and ultrasound.10 There are obviously substantial limitations to such retrospective reviews. Nonetheless, these data, and the published and unpublished experience with ultrasound in this setting, fail to raise alarm and instead imply greater safety by the addition of ultrasound imaging. Whether this is indeed true is obviously of great interest.

Dr. Cory’s letter raises important questions regarding the potential impact of beam intensity on neurologic outcomes after regional anesthesia. Beam intensity is only one of the numerous differences between ultrasound guidance and other approaches to regional blockade that could impact safety, all of which mandate rigorous investigation.

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References

In Reply:
I would like to thank Dr. Shankar for his response regarding my concerns about ultrasound-guided regional anesthesia and for clarifying some of the ultrasound parameters. However, my main reason for writing was that we do not understand the interaction of ultrasound and local anesthetics. No literature exists, that I could locate, addressing the combination effects that have the potential to be significant. The literature also does not support a reduced nerve injury rate when ultrasound guidance is used. In the cases of nerve injury unrelated to positioning, especially pan-plexopathies, when the needle tip was visualized away from the nerve during injection, something other than direct trauma must be playing a role, and assumptions that direct trauma, nerve ischemia, or injection trauma were primarily responsible may be too simplistic.

As I pointed out in my original letter, ultrasound is demonstratively cytotoxic in vitro at intensities used for regional anesthesia, and comparison dosimetry with ionizing radiation has been performed.1,2 Also, local anesthetics have long been known to be neurotoxic above critical concentrations. Furthermore, the mechanisms of toxicity are different for the two agents. Although both ultrasound and ionizing radiation work primarily by free radical formation, activation of the mitogen-induced protein kinase system is likely responsible for local anesthetic neurotoxicity.3 The mechanism for an ultrasound-related nerve injury may be the formation of hydrogen peroxide from hydroxyl ion and subsequent membrane lipid peroxidation.4 This may be offset by the observation that local anesthetics have been shown capable of free radical scavenging, especially hydroxyl ions.5 The observations suggest that the combination may actually protect from any ultrasound-related toxicity. If another ultrasound neurotoxic effect is at play, the combination of the two agents may have additive or even synergistic effects. We simply do not know. When a chemotherapeutic agent, that is, cisplatin or methotrexate, is added to the mix, the effects on neurotoxicity may be dramatic.6,7

Regarding the references given by Dr. Shankar and myself to other neurologic effects in animals and humans, I do not read the literature as showing decades of animal research demonstrating clear safety. Rather, there seems to be a fair amount of noise in the literature with some compelling data showing adverse effects on fetal neuronal migration, opening of the blood brain barrier, and adult locomotor abnormalities in mice exposed in utero to diagnostic ultrasound levels.8–10 The study he quotes in...
humans has a problem in that the control group also received antenatal ultrasound. The mouse locomotor study indicates that any exposure in utero may be significant, suggesting that only a control group with no history of ultrasound exposure would be suitable—a very difficult study to arrange today.

I appreciate the observations of Drs. Gray and Draiser regarding the bioeffects of ultrasound, including the ability of high-intensity ultrasound to promote nerve regeneration. I remain unsure how to relate the Food and Drug Administration imposed limit of 720 mW/cm² for diagnostic imaging to the Psa@M_max ratings listed in the M-Turbo manual that are well into the hundreds of Watts per square centimeters range.

I am pleased that Drs. Gray and Draiser agree that more work is needed to address the interactions between ultrasound and local anesthetics. In referencing Orebaugh et al., regarding complication rates, I am reminded of the question of who was performing the block. I suspect these data come from resident-performed regional anesthesia, and if so, likely reflect the steep learning curve for safely performing blocks with anatomic landmarks and nerve stimulation as the only guide. It is very clear that ultrasound shortens the steep learning curve substantially but at the steep price of making practitioners ultrasound dependent.

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Transpulmonary Determination of Extravascular Lung Water: What You See Is What You Get and It’s Useful

To the Editor:

We read with interest the study by Easley et al. comparing changes in the extravascular lung water (EVLW), as measured by transpulmonary thermodilution (TPT), with changes in the lung tissue density by computed tomography (CT) in an acute lung injury model before and after endotoxin (lipopolysaccharide) administration and the accompanying editorial by Costa and Vidal Melo. Although the authors used a reasonable animal model in a well-conducted study, we find significant limitations in data interpretation and a major fault with their conclusions. The study suffers from a small sample size (n = 5), making comparisons between CT-tissue quantification of lung edema and EVLW by TPT (EVLW_TPT) difficult. A single EVLW_TPT outlier(fig. 3b, page 1070) seems responsible for most of the differences between the two techniques. However, even when including the outlier, there does not seem to be significant differences in EVLW values as measured by the two methods either after lung lavage or after intravenous lipopolysaccharide. After lung lavage, EVLW by CT was approximately 24 ml/kg versus 23 ml/kg for EVLW_TPT (P = 0.1), and after lipopolysaccharide, EVLW by CT was 26 ml/kg versus 29 ml/kg for EVLW_TPT (P = 0.2). Furthermore, CT methods for determining EVLW in acute lung injury are very complex and have not been substantiated enough to be considered an accepted standard, as has been pointed out in the editorial. Moreover, the authors have obtained perfusion images at a single location in the lung base, excluding the upper lung regions where increased perfusion may have resulted in an increase in the microvascular surface area for fluid exchange and could have increased EVLW significantly. Clearly, the study would have been strengthened hadgravimetric determination of EVLW been done instead of relying on the CT.

It is well established that lipopolysaccharide causes a rapid increase in capillary permeability and pulmonary recruitment of inflammatory cells, and its administration has been shown to increase

Drs. Phillips and Perel have served on the Medical Advisory Board for Pulsion Medical Systems, Munich, Germany, makers of the PICCO device. Neither has any further direct financial interests in the subject matter, materials, or equipment discussed or in competing materials.