This access also implied a blind needle advancing behind clavicular bone.

There are no statistically reliable data on the real rate of displacement of catheters in the supraclavicular brachial plexus. The 40% rate mentioned (Hauritz et al.7) exclusively referred to sciatic nerve approach, but our report speaks of ultrasound-guided access to the brachial plexus. On the other hand, Heil et al.8 reported a study in 10 healthy volunteers in whom access was different from the one we propose (supravacular tip, supravacular access), rendering it difficult to make comparisons. In addition, a large part of the literature analyzes displacement rates based on degrees of pain in high VAS, according to the authors, and only during the first 24 h: when indicated, a catheter for continuous block is usually necessary for a longer time. In any case, the lowest published rate of displacement is not less than 10%. In our center, after more than 8 yr of experience and a large sample of cases with the described technique (infraclavicular bone).

We do not propose this new technique with the intention of changing regional anesthesia practice, but we believe that the accumulated experience and the good results obtained make it at least advisable to share this knowledge with our colleagues.

**Competing Interests**
The authors declare no competing interests.

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**References**

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Nitrous Oxide and Decreased White Matter Integrity and Volume during Childhood

*To the Editor:* The article by Block et al.1 reports that 94% of teenagers with broadly distributed, decreased white matter integrity and volume on magnetic resonance imaging of their brains inhaled nitrous oxide for over an hour during surgery and anesthesia in their first year of life. A manuscript cited by Block et al. reports that 88% of children between the ages of 5 and 18 yr with lower gray matter density in the occipital cortex and cerebellum inhaled nitrous oxide during surgery and anesthesia before their fourth birthday.2 Nitrous oxide is the only inhalational anesthetic that causes demyelination, cerebral atrophy, and loss of developmental milestones in a susceptible child after use in clinical concentrations and durations.3 One hour of nitrous oxide administration is sufficient to inactivate methionine synthase by oxidation of cobalt in its vitamin B12 cofactor.4 Up to 20% of infants and children in North America express one or more alleles that impair the activity of enzymes in single carbon pathways in which methionine synthase is the pivotal participant.4 Up to 25% of infants and children before the age of 10 yr are deficient in vitamin B12 with levels less than 148 pmol/L.5 Accordingly, up to 5% of infants have both an inborn and an acquired deficiency of vitamin B12 at the time they are anesthetized with nitrous oxide. The incidence of both inborn and acquired deficiencies of vitamin B12 are far greater in children living in Latin America, Africa, and Asia.6 In children with all but extreme phenotypes, vitamin B12 deficiency may be asymptomatic and undiagnosed before surgery. Not surprisingly, use of nitrous oxide for anesthetic maintenance has declined markedly in the United States and Europe in recent years.7

In view of their findings and the facts above, do Block et al. presently recommend use of nitrous oxide for anesthetic maintenance in infants having procedures lasting an hour or longer? If not, what is the relevance of the author’s findings to contemporary pediatric anesthesia practice in which anesthetic maintenance with nitrous oxide is diminished? Is it not timely to reassure parents that at least one inhaled anesthetic associated with white and gray matter damage in susceptible children is no longer in widespread use?

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neurotoxic effects in neonatal animals and pertinent human evidence is limited. Therefore, we sought to probe the long-term effects of anesthetic agents in a structural neuroimaging study. We emphasized that, although our findings may be related to anesthesia and surgery during infancy, other explanations are possible. Our study sought to examine brain structure years after anesthetic exposure. Although this approach provides important information, one limitation is that anesthetic practices change over the years, so that, for maximal value, this approach needs to be combined with other approaches, including shorter-term follow-up as well as longitudinal studies. Our findings provide no basis to recommend for or against use of nitrous oxide when providing anesthesia for infants undergoing surgery, nor to reassure parents about contemporary anesthesia safety based on changes in anesthetics used in clinical practice. At present, we believe that individual pediatric anesthesiologists should decide whether to use nitrous oxide based on current evidence and their own clinical judgment of risks and benefits. Finally, we think that Hogan’s belief that nitrous oxide use is associated with neurotoxicity in young children merits further evaluation.

Competing Interests
The authors declare no competing interests.

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References

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