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Intracarotid Etomidate

To the Editor:—We read with great interest the review by Dr. Joshi *et al.* on intracarotid delivery of drugs.[1] In spite of recent advances in functional magnetic resonance imaging, the Wada test is still an important test for presurgical evaluation of patients with epilepsy.[2] The intracarotid sodium amytal test (Wada test) has been used to lateralize cerebral dominance for speech and to evaluate memory in each hemisphere.[3] Anesthesiologists are generally not involved in this procedure. In some centers, an anesthesiologist is on stand-by during the procedure to manage potential complications, namely stroke.

In the article by Dr. Joshi *et al.,* there is mention that baseline sedation provided by the anesthesiologist in attendance would further complicate the interpretation of the Wada test and also suggests use of a judicious amount of sedation during the procedure. We disagree with the suggestion by the authors for the use of sedation during the procedure. These tests are done for evaluation of memory and language with unilateral intracarotid injection of drugs. Any sedation during the procedure will interfere with the memory testing.[4]

As a result of the recurrent shortages in the availability of sodium amytal, other agents are being used for Wada testing. As mentioned in the article, propofol or methohexitone have been used with limited success.[5] Jones-Gotman *et al.* have published their work in the use of etomidate for the Wada test.[6] They have shown that etomidate is a viable alternative to sodium amytal, and its administration by bolus followed by infusion offers an improvement over the traditional Wada test. It is given as a 2-mg initial bolus (0.03-0.04 mg/kg) over 30 to 60 s, then an infusion of 0.003 to 0.004 mg/kg/min (approximately 6 ml/h neat etomidate 2 mg/ml) until the speech assessment and memory objects have been introduced. Many centers in the world are now switching to this etomidate speech and memory test. Manufacturer's recommendations mandate an anesthesiologist to administer etomidate, so many anesthesiologists are now involved.[7] In our institution, we have been using etomidate for the Wada test for the past year with great success. In addition, bilateral injection is our standard practice. The second injection is made only after the confirmation of complete clearance of the drug effects (both clinically and electroencephalographically).

Lashmi Venkatraghavan, M.D., F.R.C.A., F.R.C.P.C.,* Anna Perks, F.R.C.A. *Toronto Western Hospital, Toronto, Ontario, Canada. lashmi.venkatraghavan@uhn.on.ca

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In Reply:—We thank Dr. Venkatraghavan for raising two specific comments on our review: The first is the use of sedation during Wada testing; the second is the use of intraarterial etomidate for the same procedure.[1] Both comments reinforce our general theme that there are significant variations in handling of anesthesia and interventional drugs, selection, and doses during endovascular procedures.

With regard to the "judicious use of sedation during Wada testing," Dr. Venkatraghavan correctly point out that Wada testing often is done without an anesthesiologist's supervision with minimal or no sedation. However, the anesthesiologists are routinely involved when any intervention is contemplated, such as during superselective Wada testing. For these longer procedures we use small doses of midazolam (1–2 mg), propofol (10–25 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and fentanyl 0.5–1.5 μg/kg). These drugs are withheld at least 20 min before memory or psychomotor testing. Dundee and Wilson tested for anterograde amnesic action of midazolam (5 mg) and found the onset to be within 3 to 5 min, with the effect lasting 20 min.[2] Bulach *et al.* looked at midazolam pretreatment in a dose range of 2 to 10 mg and found a dose-dependent impairment of anterograde memory, but no effect on retrograde amnesia.[3] To our best knowledge there is no hard evidence to suggest that 1 to 2 mg of midazolam given 20 to 60 min before testing impairs conventional memory tests.

The question arises whether studies in healthy subjects apply to those with preexisting neurologic deficits. Low doses of residual sedative/hypnotics are known to unmask neurologic deficits and could in theory impair memory tests.[4] Hence, even if data from healthy volunteers might suggest a lack of amnesic effect with low doses of midazolam, caution needs to be exercised in prescribing sedatives or hypnotics to those with suspected neurologic deficits. What helped in framing the policies at our institution was a quality improvement review of patient data to assess the use of midazolam during Wada testing that found no impairment of memory.

We are thankful to Dr. Venkatraghavan for elaborating on the use of etomidate for Wada testing that is also supported by our experimental data.[5] These comments illustrate the diversity in the selection and dose of drugs used intraarterially or systemically during endovascular procedures. We emphasize that the surgeons and anesthesiologists should formulate a coherent management strategy based on the specific needs of the patient and endovascular procedure.

Shailendra Joshi, M.D.,* Phillip M. Meyers, M.D., Eugene Ornstein, M.D., Ph.D. *College of Physicians and Surgeons of Columbia University, New York, New York. sj121@columbia.edu

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Electrical Nerve Stimulation and Subepineurial Staining: Not Only Mechanical Factors Count

To the Editor:—We read with interest the article published by Rigaud *et al.*[1] The authors addressed the very important and insufficiently explored relationship between the parameters of electrical nerve stimulation and the precise position of the stimulating needle tip. Unfortunately, little data exist defining this relationship in special clinical situations like neuromuscular and metabolic diseases, and we applaud the authors for their effort.

While acknowledging the factual results of this study, we disagree with the authors' interpretation of the findings regarding hyperglycemic dogs. Specifically, ink streaks under the epineurium were interpreted as needle penetration and intraneural injection. In our opinion, review of the photomicrographs (fig. 3 in the publication) does not necessarily support this conclusion. In these figures the amount of ink lodged under the epineurium appears negligible in comparison with that located outside the nerve, and the internal neural architecture remains intact.

It is possible that such marginal staining could have a biochemical rather than a mechanical explanation. In diabetes, an impairment in energy balance and tissue edema could result in a sufficient increase in epineurial permeability to allow some ink already in close contact to the nerve (as in fig. 2 in the publication) to penetrate the epineurium in the absence of any direct trauma. An alternative explanation could be migration of ink *via* dilated vasa nervorum. Eventually, performing the same experiment with ultrasound-guided injection would be very interesting.

In the absence of clinical data suggesting frequent nerve damage from performing electrical guided nerve blocks on diabetic patients, one of two possible conclusions of this study should be considered: penetration of local anesthetic inside the epineurium (with or without needle penetration) does not result in nerve damage, or that the results of this study are pertinent only to this specific experimental condition and do not warrant clinical extrapolation.

The answer to this question has particular importance in the context of the ongoing debate about the relative risk of electrical stimulation-guided blocks in comparison with ultrasound guidance.

Boris Yanovski, M.D.,* Bruce Ben-David, M.D., Jacques E. Chelly, M.D., Ph.D., M.B.A. *University of Pittsburgh Medical Centers, Pittsburgh, Pennsylvania. yanovskib@upmc.edu

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In Reply:—We thank Drs. Yanovski *et al.* for their interest in our paper.[1] They raise the point that there are alternative explanations for our observations of traces of ink within the sciatic nerves of hyperglycemic dogs other than our conclusion that the needle tip was positioned there during the ink injection. They argue that the accumulation of ink within the nerve is less than what was found outside the nerve, and ink penetration through the intact epineurium is a more likely explanation.

Publication necessarily degrades the images and limits their number, so not all of the relevant sections can be shown. The original high-resolution images (see figure 1, Supplemental Digital Content 1, http://links.lww.com/A1219; figure 2, Supplemental Digital Content 2, http://links.lww.com/A1220; figure 3, Supplemental Digital Content 3, http://links.lww.com/A1212) show clear dissection of ink among the fascicles of the nerves and travel of this ink as rivulets within the nerve to areas distant from the external accumulation in patterns not expected for direct diffusion. In other images, there is substantial destruction of the normal nerve anatomy at the injection site.

Finding the majority of the ink outside the nerve is compatible with our interpretation that injection was originally into the nerve, since the nerve is not capacious and the short path for retrograde flow along the outside of the needle shaft is not likely to be occluded by adjacent tissue pressure. Passage of the ink through membranous barriers is unlikely. The tissue was harvested immediately and frozen within 10 min, so limited time was available for such a process. Also, particulate ink such as was used for this study does not transit through membranes or vascular walls, and for this reason is routinely employed for vascular labeling.[2]

Bleeding seen within the nerves is clearly visible in the original photographs only in specimens showing intraneural ink (please see the supplemental digital content), which independent of ink distribution patterns conclusively indicates an intraneural needle placement. Overall, we believe the most likely explanation for these various observations is that needle insertion guided by electrical stimulation resulted in intraneural placement in the hyperglycemic dogs.

Geza Gemes, M.D., Marcel Rigaud, M.D., Quinn Hogan, M.D.* *Medical College of Wisconsin, Milwaukee, Wisconsin. qhogan@mcw.edu

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