The idea of partial MAC values has become part of the clinical jargon, and it is—more or less—an accurate reflection of partial potency because the slopes of the relationships for sevoflurane and isoflurane are quite similar. Moreover, it is common practice for patients as well as animals to use MAC multiples to compare the effects of various inhalational anesthetics on a wide variety of physiologic endpoints—for example, brain acetylcholine level,[5] cerebral blood flow,[6] vasoconstriction,[7] cardiac function,[8] and hemodynamics.[9] In fact, many reviewers insist on the use of MAC multiples.

As Dr. Cross suggests, in terms of equal points on two separate dose-response curves for our study, a more precise comparison would have been 1 MAC isoflurane *versus* 1 MAC sevoflurane. Unfortunately, neonatal mice do not tolerate prolonged exposure to isoflurane at 1 MAC without developing confounding physiologic derangements.[10] Thus, we used a lower concentration, that, by design, is commonly used clinically. This clinical applicability was an essential goal of our study, to compare the neurotoxicity of two agents at concentrations used clinically. We certainly agree with Dr. Cross that a more thorough method of comparing anesthetic neurotoxic potency would involve constructing full dose–response curves for apoptosis (or other endpoints) for each agent. Nevertheless, our results speak to common clinical practice as the immediate goal. We recognize that further work is necessary to establish the comparative mechanistic basis for these findings.

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Complications of C1-C2 Facet Injection

To the Editor:

The case report by Edlow *et al.*[1] is a valuable example of the vascular nature of the C1-C2 facet injection. However, the most valuable picture that would have shown whether the complication that occurred was truly because of an unusual complication of the procedure or whether it was because of simple misplacement of the needle was not included. The anterioposterior view would show how lateral the needle was placed; instead, only the lateral view is provided. The picture of dye spread from the lateral view shows significant spread, much more than what would be expected if the injection occurred purely intraarticular. The classic needle location in an anterioposterior view should show the needle placed in the lateral two-thirds of the joint. Any other picture would explain why this complication occurred. Live fluoroscopy was not used and may have spared this patient from a complication.

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It Is Time to Abandon Atlanto-Axial Joint Injections: Do No Harm!

To the Editor:

We applaud Edlow *et al.*[1] for publishing the case report of posterior circulation stroke after C1-C2 intraarticular facet steroid injection with evidence of diffuse microvascular injury. The same mechanism involved with cervical transforaminal epidural injections may be implicated in this case with vertebral artery penetration and embolic phenomenon, as the authors described. Complications at this level are not only related to vertebral artery penetration and similar to

transforaminal epidural injections, but they also encompass additional complications related to facet joint injections with penetration into the subarachnoid space, nerve roots, and spinal cord.

Considering the devastating nature of the complication presented, we would like to highlight a few more aspects pertinent to C1-C2 intraarticular injections, based on some anatomic observations and also related to the procedure performed, as described in the case report.

Anatomic Perspectives

We would like to comment first on the nomenclature of the joint as described in the article (C1-C2 intraarticular injection). Although the joint is between C1 and C2, most of the literature describes it as the lateral atlanto-axial (AA) joint rather than C1-C2 zygapophysial or facet joint. Zygapophysial joints are described from C2-C3 and below. Anatomic variations in morphology of C2 and the course of the vertebral artery are well recognized in the literature. Madawi *et al.*[2] found that the course of vertebral artery at C2 lateral mass was asymmetric in 52% of specimens. In a study of 98 dry C2 vertebra, Igarashi *et al.*[3] reported that 41% of specimens had asymmetric pedicles and approximately 20% of specimens were not suitable for screw fixation because the pedicle size was smaller than the diameter of a 3.5-mm screw. Computed tomography studies done by Noguiera-Barbosa and Defino[4] in 2005 demonstrated vertebral artery grooves in 30%. Approximately 12% of patients were considered at risk with unilateral anatomic variation, and another 6% were not suitable for screw fixation because of bilateral variation. In 2010, a three-dimensional CISS magnetic resonance imaging study[5] demonstrated that 40% of patients had significant anatomic variations on at least one side, prohibiting the insertion of transarticular screws. In another recent report, comprehensive computed tomography evaluation showed that the AA joint demonstrated larger variability in general, particularly in the sagittal plane.[6] There were several contributing sources to this variability. First, these joints were inherently less conforming because of their biconcave anatomy. There were also more deviations from the neutral position (because the head was turned or tilted to the left or the right), which influenced their resting relationships. Most noteworthy is that the understanding of variations of the vertebral artery and its branches is essential before performing any intervention in the AA joint area. As the artery exits the foramen transverserium of C2, it is no longer dorsally covered by bone, as it is in the subaxial plane. It first takes a lateral course, enters the foramen transverserium of the atlas, and then bends posteromedially dorsal to the lateral mass of the atlas. The posterior ponticulus may appear falsely as a widened C1 arch. Another important variation is a persistent first intersegmental artery where the vertebral artery travels between the atlas and the axis in the space normally occupied only by the C2 nerve root. This may be seen in up to 4%. A fenestrated segment of the vertebral artery is a rare but described entity, and a takeoff of the posteroinferior cerebellar artery in the region of the atlas or the axis may also occur.[7]

Procedural Considerations

Based on the autopsy report, it appears that the needle never entered the joint space, as demonstrated by the hemorrhage overlying the AA joint and intact cervical dura. Second, it is not clear from the case report whether an anterolateral, lateral, or posterior approach was employed while performing the AA intraarticular injection. Based on our interpretation of the provided images, we assume that a nonstandard anterolateral or lateral approach was used for the injection. Unpredictable anatomic variance between the vertebral artery and the bony structures suggests that no reliable placement of a needle may be expected to be completely safe, and transarterial or intraarterial injections are always a potential disastrous complication. Even without any anatomic variations, as described in the previous section, the vertebral artery runs on the lateral third of the AA joint dorsally, although its precise location is variable, and passes superiorly into the foramen magnum medially at the level of the atlas. The technique of injection of the AA joint is approaching the AA from the medial aspect because the artery is located laterally. The lateral entry directly targets the vertebral artery along with the lack of live fluoroscopy. We also question the use of 2 ml triamcinolone solution (40 mg/ml). Triamcinolone is a particulate steroid, and such a high dose of steroid has no proven effectiveness. The literature is very sparse on facet joint injections and almost nonexistent in the case of AA injections. With the added risk of intraarticular injection with potential entry into the spinal canal, the indications for these injections are minimal, and medical necessity weighing risk-benefit ratio is highly in favor of not performing the procedure. If an AA intraarticular injection is to be performed, it should only be performed in a prone position with the midline or a medial placement of the needle with injection of preservative-free lidocaine and nonparticulate betamethasone. Disastrous complications, as highlighted by the case, specifically above C2-C3, may not be prevented with live fluoroscopy, digital subtraction, blunt needles, and injection of nonparticulate steroid.

In summary, the danger lies not only in transforaminal cervical epidural injections but also in intraarticular injections and poorly performed ligament or trigger point injections of the AA joint or the C2-C3 area. No such complications have been reported with medial branch blocks with local anesthetic with or without nonparticulate betamethasone and radiofrequency neurotomy. However, penetration into the spinal canal and damage to the nerve roots and spinal cord is always a possibility with medial branch blocks, and radiofrequency neurotomy in the cervical spine and care is advocated when using any technique in the region. Finally, the effectiveness of radiofrequency neurotomy and medial branch blocks has been illustrated in the cervical spine.[8,9] No such evidence exists for intraarticular AA joint injections, and the best course of action may be to abandon the practice.

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In Reply:

We thank Dr. Tang for his comments on our article[1] and agree that an anteroposterior view of the C1–C2 intraarticular facet injection would have provided valuable information regarding the trajectory of the needle in the medial-lateral plane. As Dr. Tang points out, an anteroposterior view would have confirmed whether needle misplacement occurred, as suggested by the significant extraarticular spread of radiographic contrast visualized on the lateral image. Indeed, there was no anteroposterior image stored during the conduct of this procedure at the outside institution, thus we have no way of verifying the final needle position. Likely, this image would have demonstrated that the needle tip had deviated dangerously too lateral toward the course of the vertebral artery.

We much appreciate the thoughtful response from Drs. Datta and Manchikanti, and we agree with the recommendation to abandon the practice of intraarticular cervical injections, because the risk seems far out of balance from the scant demonstrated benefit from this procedure. The nonvascular complications of cervical injections that Drs. Datta and Manchikanti describe, including penetration into the subarachnoid space, nerve roots, and spinal cord, further reinforce our position regarding the risk–benefit ratio of this procedure. Even when nonparticulate steroids are used to prevent microvascular injury in the event of an inadvertent vertebral injection, nonvascular complications can still lead to devastating neurologic injury.

Drs. Datta and Manchikanti raise several important points regarding the nomenclature that is used to describe neuroanatomic landmarks in cervical injections. We chose the term "C1–C2 intraarticular injection," as opposed to "lateral atlantoaxial joint injection" based on the documentation used in the procedure note and because both are frequently used in the published literature, but we do agree that the latter term is more common, particularly in recent publications.[2]

Perhaps most important among their comments, Drs. Datta and Manchikanti raise procedural considerations that affect the interpretation of our report and the very safety of performing injection of the lateral atlantoaxial joint. They state, "… It is not clear from the case report if an anterolateral, lateral or posterior approach was employed …" As shown in figure 1 of our report, the needle enters from a posterior approach.[1] The posterior approach is well described and potentially the safest approach to the injection of the lateral atlantoaxial joint.[3] Nonetheless, even if all appropriate safety measures are implemented, the risks of cervical injections of the lateral atlantoaxial joint are so devastating that they seem to outweigh the unproven benefits. Indeed, as Drs. Datta and Manchikanti suggest, "the best course of action may be to abandon the practice."

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Why No Casopitant-only Arm?

To the Editor:

In regard to the recent article by Singla *et al.*[1] concerning the neurokinin-1 receptor antagonist casopitant, I have a num-