

Thus, the best route to appropriate and fair compensation for services for both clinicians and medical facilities is to embrace education and adopt future processes (e.g., technology assist<sup>3</sup>) that optimize the accuracy and reproducibility of the ASA Physical Status classification by all providers, and efforts to optimize interrater reliability should continue or even be enhanced by the ASA and other leading organizations.

However, given the long-term design and intent of the ASA Physical Status system, it is not clear that any changes to this system that aim to directly impact economics—as distinct from the society's 80-yr-long (and continuing) efforts to improve accuracy and reproducibility and provide a valuable tool for its clinicians—are desirable. We should make changes based on a need for clinical improvement and let the economic process evolve in parallel. That effort is best led by the ASA with other key stakeholders as we consider any future refinements to our classic ASA Physical Status system.

### Competing Interests

Dr. Todd was the Editor-in-Chief of ANESTHESIOLOGY, the Official Journal of the American Society of Anesthesiologists (ASA; Schaumburg, Illinois), from 1997 to 2006. Dr. Todd was also awarded the 2016 Excellence in Research Award by the ASA. Dr. Cole is vice president of the Anesthesia Patient Safety Foundation (Rochester, Minnesota), a foundation of the ASA, and is a past president of the ASA. Dr. Prielipp is a former member of the Board of Directors of the Anesthesia Patient Safety Foundation and serves on the speakers' bureau for Merck Co., Inc. (Kenilworth, New Jersey) and as an opinion leader for 3M (Minneapolis, Minnesota). The other authors declare no competing interests.

Balazs Horvath, M.D., F.A.S.A., Benjamin Kloesel, M.D., M.S.B.S., Michael M. Todd, M.D., Daniel J. Cole, M.D., F.A.S.A., Richard C. Prielipp, M.D., M.B.A., F.C.C.M. University of Minnesota School of Medicine, Minneapolis, Minnesota (B.H.). bhorvath@umn.edu

DOI: 10.1097/ALN.0000000000004147

### References

1. Abouleish AE, Gal J, Troianos C, Merrick S, Cohen N, Stead S: Review of the ASA Physical Status Classification: Comment. ANESTHESIOLOGY 2022; 136:864–5
2. Flynn DN, Lund ET, Grant SA: Review of the ASA Physical Status Classification: Comment. ANESTHESIOLOGY 2022; 136:865–6
3. Horvath B, Kloesel B, Todd MM, Cole DJ, Prielipp RC: The evolution, current value, and future of the American Society of Anesthesiologists Physical Status Classification System. ANESTHESIOLOGY 2021; 135:904–19

(Accepted for publication January 14, 2022. Published online first on February 7, 2022.)

## Vasopressor Effects on Cerebral Microcirculation: Comment

### To the Editor:

We read with great interest the study by Koch *et al.*,<sup>1</sup> which concluded that “ephedrine results in better brain microcirculation and oxygen delivery than phenylephrine” and raised “concerns regarding phenylephrine for blood pressure augmentation in patients with cerebral pathology.” The results of this prospective, randomized trial are similar to those of a network meta-analysis<sup>2</sup> of 399 patients from nine randomized trials comparing various inotropes/vasopressors used to treat intraoperative hypotension in patients mostly without cerebral pathology. That analysis found that dopamine, ephedrine, and norepinephrine had the lowest probability of adversely affecting cerebral oxygen saturation as measured by cerebral oximetry and that phenylephrine, compared with the other inotropes/vasopressors, decreased cerebral oxygen saturation. Koch *et al.*'s findings on the deterioration of microcirculation after phenylephrine administration on the side of the brain not affected by brain pathology highlight the importance of considering the cerebrovascular effect of vasopressors in every patient, not only the ones with cerebral pathologies. Phenylephrine is very effective in restoring systemic blood pressure to normal values. Clinicians tend to favor what has been described by Thiele *et al.*<sup>3</sup> as the “tangible bias,” which is our tendency to fix what we can see and understand, that is, systemic blood pressure, over what we cannot: macro- and microscopic cerebral perfusion. Koch *et al.*'s results should prompt clinicians to choose the appropriate vasopressor to maintain optimal cerebral microcirculation.

### Competing Interests

The authors declare no competing interests.

Anna Maria Bombardieri, M.D., Ph.D., Ban C. H. Tsui, M.D., M.Sc. Stanford University School of Medicine, Stanford, California (A.M.B.). abomba@stanford.edu

DOI: 10.1097/ALN.0000000000004149

### References

1. Koch KU, Mikkelsen IK, Espelund US, Angley H, Tietze A, Oettingen GV, Juul N, Østergaard L, Rasmussen M: Cerebral macro- and microcirculation during ephedrine *versus* phenylephrine treatment in anesthetized brain tumor patients: A randomized

clinical trial using magnetic resonance imaging. *ANESTHESIOLOGY* 2021; 135:788–803

- Bombardieri AM, Singh NP, Yaeger L, Athiraman U, Tsui BCH, Singh PM: The regional cerebral oxygen saturation effect of inotropes/vasopressors administered to treat intraoperative hypotension: A Bayesian network meta-analysis. *J Neurosurg Anesthesiol* 2021 [Epub ahead of print]
- Thiele RH, Nemergut EC, Lynch C III: The physiologic implications of isolated alpha(1) adrenergic stimulation. *Anesth Analg* 2011; 113:284–96

(Accepted for publication January 20, 2022. Published online first on February 14, 2022.)

## Vasopressor Effects on Cerebral Microcirculation: Reply

### In Reply:

We thank Bombardieri and Tsui<sup>1</sup> for their excellent comments and interest in our study.<sup>2</sup> We agree with Bombardieri and Tsui that the deterioration of microperfusion and possibly tissue oxygenation after phenylephrine administration in the “healthy” brain hemisphere<sup>2</sup> indicates that different vasopressors may also have a different influence on microperfusion and tissue oxygenation in the healthy anesthetized brain and should be further explored.<sup>3</sup> In our opinion, future studies on the effects of different vasopressors on the cerebral macro- and microcirculation should be considered in the context of their different effects on the systemic circulation to provide a fully integrated picture of their influence on organ perfusion and oxygenation.<sup>4</sup> Due to current difficulties in monitoring brain microcirculation and cerebral tissue oxygenation, we tend to rely on systemic parameters such as heart rate and blood pressure when treating patients with inotropes/vasopressors. However, a recent publication suggests that brain tissue oxygen saturation, as measured by near-infrared spectroscopy, may reflect cerebral metabolic supply–demand balance during vasopressor therapy.<sup>4</sup> Although the use of near-infrared spectroscopy is associated with limitations, such as extracranial signal contamination, it may currently be the only way to provide a continuous indication of brain microperfusion and tissue oxygenation.

### Competing Interests

Dr. Rasmussen declares a financial relationship with the Health Research Foundation of the Central Denmark Region (Aarhus, Denmark). Dr. Koch declares no competing interests.

Klaus Ulrik Koch, M.D., Ph.D., Mads Rasmussen, M.D., Ph.D.  
Aarhus University Hospital, Aarhus, Denmark (K.U.K.).  
klaukoch@rm.dk

DOI: 10.1097/ALN.0000000000004150

### References

- Bombardieri AM, Tsui BCH: Vasopressor effects on cerebral microcirculation: Comment. *ANESTHESIOLOGY* 2022; 136:867–8
- Koch KU, Mikkelsen IK, Espelund US, Angleys H, Tietze A, Oettingen GV, Juul N, Østergaard L, Rasmussen M: Cerebral macro- and microcirculation during ephedrine versus phenylephrine treatment in anesthetized brain tumor patients: A randomized clinical trial using magnetic resonance imaging. *ANESTHESIOLOGY* 2021; 135:788–803
- Bombardieri AM, Singh NP, Yaeger L, Athiraman U, Tsui BCH, Singh PM: The regional cerebral oxygen saturation effect of inotropes/vasopressors administered to treat intraoperative hypotension: A Bayesian network meta-analysis. *J Neurosurg Anesthesiol* 2021 [Epub ahead of print]
- Koch KU, Zhao X, Mikkelsen IK, Espelund US, Aanerud J, Rasmussen M, Meng L: Correlation between cerebral tissue oxygen saturation and oxygen extraction fraction during anesthesia: Monitoring cerebral metabolic demand–supply balance during vasopressor administration. *J Neurosurg Anesthesiol* 2021 [Epub ahead of print]

(Accepted for publication January 20, 2022. Published online first on February 14, 2022.)

## Recent U.S. Food and Drug Administration Labeling Changes for Hydroxyethyl Starch Products Due to Concerns about Mortality, Kidney Injury, and Excess Bleeding

### To the Editor:

The U.S. Food and Drug Administration (Silver Spring, Maryland) is requiring safety labeling changes to the