

and mental examinations of the central nervous system.²⁻⁴ Patient self-report of interval medical history and physical status provides unreliable data in the differential diagnosis of conditions that weaken memory. Thorough review of medical records after surgery is clearly necessary (albeit often unreported) in perioperative neurocognitive disorder research but is not a sufficient substitute for neurologic and psychiatric examination at the time of neuropsychologic testing. Surgery and anesthesia may hasten expression of known conditions, and detection of subtle changes may point to modifiable steps in the perioperative care of an undetermined proportion of patients. Only by exclusion of known conditions may neurocognitive signs and symptoms that arise from anesthetic and surgical harms of unknown origin be identified. In supplement 1 to their article, Evered *et al.* observe, “Remarkably research into POCD [perioperative neurocognitive disorder] (anesthesia and surgery) and AD [Alzheimer disease] has occurred independently of each other.”⁴ In an accompanying editorial, Cole and Kharasch underscore the value of working collaboratively to achieve the aims of the Perioperative Brain Health Initiative.⁵ Participation of neurologists, psychiatrists, and geriatricians able to distinguish neurocognitive conditions of known and unknown origin one from the other at the time of psychometric testing remedies a flaw in published perioperative neurocognitive disorder experimental designs.

Competing Interests

The author declares no competing interests.

Kirk J. Hogan, M.D., J.D. School of Medicine, University of Wisconsin, Madison, Wisconsin. khogan@wisc.edu

DOI: 10.1097/ALN.0000000000002832

References

1. Fred HL: The diagnosis of exclusion: An ongoing uncertainty. *Tex Heart Inst J* 2013; 40:379–81
2. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG; Nomenclature Consensus Working Group: Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery–2018. *ANESTHESIOLOGY* 2018; 129:872–9
3. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG, and The Nomenclature Consensus Working Group: Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery–2018. *ANESTHESIOLOGY* 2018; 129(suppl 2):3–4
4. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG, and The Nomenclature Consensus Working Group: Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery–2018. *ANESTHESIOLOGY* 2018; 129(suppl 1):10
5. Cole DA, Kharasch ED: Postoperative brain function. *ANESTHESIOLOGY* 2018; 129:861–3

(Accepted for publication May 9, 2019.)

Nomenclature for Perioperative Cognitive Disorders: Reply

In Reply:

We thank Mathew *et al.* and Dr. Hogan for their comments in response to our recent nomenclature recommendations for perioperative neurocognitive disorders.¹ We deeply appreciate the acknowledgment of the importance of this effort and are gratified to see both clinicians and investigators beginning to use it. We should stress again that this is a *clinical* nomenclature, each category of which requires symptoms or a complaint from the patient, caregiver, or family. The considerably more difficult, and likely contentious, effort to define perioperative neurocognitive disorder research criteria is underway and hopefully will reach consensus and publication in the next year or so. It is hoped that those using the research criteria will still make the attempt to map their results onto this clinical nomenclature to better enable translation into the community.

Despite our general agreement, we are familiar with the unease of Mathew *et al.* with the category “delayed neurocognitive recovery.” We readily acknowledge that it is in fact a new term, much like “mild cognitive impairment” was when introduced by the Alzheimer Association (Chicago, Illinois) and National Institutes of Aging (Bethesda, Maryland) several years ago. We do not understand why the novelty of a term should be grounds for eliminating it, as long as it fits the situation well. And we believe it fits quite well. The majority of our patients, even those who are older, recover their cognitive abilities in the first hours or days after anesthesia and surgery—the literature is unequivocal on this. Thus, the presence of symptomatic cognitive dysfunction weeks after surgery can only be considered as “delayed” relative to expectations. The term is not meant to be predictive, as it is never clear in any given individual whether their symptoms will go on to resolve, or to grow. Thus, an

individual may be diagnosed with delayed neurocognitive recovery at 30 days, and then mild (or major) neurocognitive disorder (postoperative) at 6 weeks or more. We acknowledge that 30 days was a somewhat arbitrary compromise—it could have just as easily been 6 weeks or 3 months—but the consensus view was that most surgical patients should have recovered their cognitive abilities by this point. We did, however, suggest that individual clinicians should exercise their judgment in adhering to these time points.

Although delayed neurocognitive recovery is not a predictive diagnosis, the literature suggests that many and perhaps most older patients with delayed neurocognitive recovery do in fact go on to have symptomatic recovery. Nevertheless, we readily acknowledge that symptomatic recovery may not always reflect full objective recovery or that a central nervous system injury has not occurred. The nature and natural history of a hypothetical central nervous system injury during anesthesia and surgery remain a major unanswered question, and we do not believe that a diagnosis of delayed neurocognitive recovery in any way impedes our ability to investigate it—quite the contrary. Why was symptomatic recovery delayed? Do biomarkers or careful psychometric testing indicate that there is full objective recovery, or was the recruitment of compensatory mechanisms responsible for symptom resolution? What does this predict for the future? The research questions related to delayed neurocognitive recovery are plentiful.

Finally, with respect to false hope and labeling, we strongly disagree. A diagnosis of mild neurocognitive disorder (postoperative) immediately after discharge maps directly onto the Alzheimer Association and National Institutes of Aging term, mild cognitive impairment, which many now know, or can quickly discover, may be a precursor diagnosis to Alzheimer disease. It is both inaccurate and emotionally charged to label the 30 to 40% of older patients who have cognitive symptoms a week after surgery as headed toward Alzheimer disease—a diagnosis that many fear more than death.

Thus, in summary, we believe the term “delayed neurocognitive recovery” is in fact a reasonable fit for the patients having both symptoms and objective evidence of cognitive dysfunction in the early weeks after surgical hospitalization discharge, and this terminology includes both the notion of persisting deficits and hope for recovery. However, it should not be construed as predicting ultimate recovery, or as a trivial occurrence. Rather, it provides a reasonable postoperative time frame for the clinician to evaluate the patient’s cognitive status and for the researcher to explore the biologic mechanisms and relationship between early and persistent cognitive dysfunction after anesthesia and surgery.

We thank Dr. Hogan for his comments regarding our nomenclature recommendations, and we acknowledge his concerns but are unsure how well they apply in this case. A diagnosis of exclusion is a diagnosis with “no means

of objective proof,”² and where the major element is the exclusion of other diagnoses. This is not the case for attribution of neurocognitive disorder, in which the major element consists of history, testing, and examination. Nevertheless, the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, criteria for neurocognitive disorder³ state that cognitive deficits must not be primarily attributable to another disorder, so like all medical diagnoses, the differential diagnosis list needs to be narrowed. This does not make perioperative neurocognitive disorder a diagnosis of exclusion.

Dr. Hogan suggests we are applying causation to the attribution of a diagnosis of perioperative neurocognitive disorder. The attribution of perioperative neurocognitive disorder described in the nomenclature document¹ is a syndromic diagnosis, not an etiologic diagnosis, and certainly not a biologic diagnosis. Indeed, we have yet to elucidate the likely multifactorial contributions which result in perioperative neurocognitive disorder. We do not suggest that anesthesia and surgery are necessarily the cause, but rather that the symptoms and observed deficits have occurred in a temporal association with anesthesia and surgery. It is hoped that by defining cognitive disorders associated with the perioperative period, to be consistent with those occurring in the same demographic of people in the community, we can begin to unravel the mechanisms that may be contributing to this unique decline. Indeed, a clinical diagnosis should facilitate an understanding of whether postoperative deficits are a continuing trajectory of already present decline, or if, in fact, the postoperative decline is a new disorder.

Finally, we concur and acknowledge that the appropriate specialists for diagnosis of perioperative neurocognitive disorder lie beyond anesthesiologists, hence our inclusion of a multidisciplinary team of geriatricians, neurologists, psychiatrists, neuropsychologists, researchers, and anesthesiologists (including Dr. Hogan) on the authorship of the nomenclature article. Our hope is that ultimately this work will result in improved pathways and referral systems for clinical care of these vulnerable patients, and a framework for the design of future clinical studies.

Acknowledgments

The Nomenclature Consensus Working Group participants are listed in appendix B of the original article. See Evered *et al.*¹

Competing Interests

The authors declare no competing interests.

Lisbeth A. Evered, M.Biostat., Ph.D., Brendan Silbert, M.B., B.S., David Scott, M.B., B.S., Ph.D., Roderic Eckenhoff, M.D., on behalf of the Nomenclature Consensus Working Group.

St. Vincent's Hospital Melbourne and University of Melbourne,
Melbourne, Australia (L.A.E.). lis.evered@svha.org.au

DOI: 10.1097/ALN.0000000000002833

References

1. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG; Nomenclature Consensus Working Group: Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery—2018. *ANESTHESIOLOGY* 2018; 129:872–9
2. Fred HL: The diagnosis of exclusion: An ongoing uncertainty. *Tex Heart Inst J* 2013; 40:379–81
3. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Arlington, Virginia, American Psychiatric Association, 2013

(Accepted for publication May 9, 2019.)

Individualizing Intraoperative Ventilation: Comment

To the Editor:

We read with great interest the article by Pereira *et al.*¹ in a recent issue of *ANESTHESIOLOGY*. The authors explore electrical impedance tomography–based determination of an individualized positive end-expiratory pressure level to simultaneously limit both atelectasis and overdistension in mechanically ventilated patients during general anesthesia. While atelectasis is a well-recognized consequence of mechanical ventilation during general anesthesia, some authors previously considered overdistension as a non-clinically significant problem in the operating room.² We congratulate the authors for presenting data that challenge this assumption.

However, we feel that the authors omitted proper discussion of the discrepancy between their study and two other recent studies that failed to show a difference in postoperative atelectasis when assessed shortly after extubation.^{3,4} While Pereira *et al.* are to be commended for using computed tomography, the reference imaging technique, to

assess the amount of atelectasis postextubation, we wonder why the authors have chosen a –200 to +100 Hounsfield units interval to define nonaerated lung. In the reference quoted to explain their methodology,⁵ atelectasis was defined as –100 to +100 Hounsfield units, as in numerous other publications.^{6–8} To rule out the possibility of a classification bias, the authors should have analyzed their results using the generally accepted reference values for both poorly aerated (–500 to –100 Hounsfield units) and nonaerated (–100 to +100 Hounsfield units) lung. Moreover, they should have reported the degree of atelectasis in square centimeters, as used in their sample size calculation, to eliminate the presumption of a reporting bias. We write to request that the authors report results both in square centimeters, as well as according to the generally accepted Hounsfield units reference values to address these potential biases.

Finally, provided the aforementioned concerns are properly addressed, Pereira *et al.*'s work is a crucial piece of information, as the primary mechanism by which lung protective ventilation is thought to decrease postoperative pulmonary complication is through the successful decrease in postoperative atelectasis.⁹ The authors weaned their patients using the pressure-support mode maintaining the same intraoperative positive end-expiratory pressure level contrary to the other studies. Interestingly, weaning using assisted ventilatory modes is seldomly performed in the operating room while it is a commonly performed procedure in the intensive care unit. This cointervention might explain this trial's observed difference in postoperative atelectasis. We would also welcome comments from the authors about their choice of weaning method.

Competing Interests

The authors declare no competing interests.

Martin Girard, M.D., François Martin Carrier, M.D., M.Sc.,
Montreal University Hospital Center, Quebec, Canada
(M.G.). martin.girard@umontreal.ca

DOI: 10.1097/ALN.0000000000002834

References

1. Pereira SM, Tucci MR, Morais CCA, Simões CM, Tonelotto BFF, Pompeo MS, Kay FU, Pelosi P, Vieira JE, Amato MBP: Individual positive end-expiratory pressure settings optimize intraoperative mechanical ventilation and reduce postoperative atelectasis. *ANESTHESIOLOGY* 2018; 129:1070–81
2. Hedenstierna G, Edmark L: Protective ventilation during anesthesia: Is it meaningful? *ANESTHESIOLOGY* 2016; 125:1079–82
3. Nestler C, Simon P, Petroff D, Hammermüller S, Kamrath D, Wolf S, Dietrich A, Camilo LM, Beda A,