The Perioperative Neurocognitive Disorders

Remarkable progress in perioperative care over the past decades has led to more complex surgery now being offered to the frail and elderly. One of the unresolved challenges has been dealing with the associated risk of both short- and long-term postoperative cognitive impairment. This wonderful book condenses all of the latest information from many clinical disciplines and diverse fields of research, with overviews of key topics, practical advice for clinicians, and crucial insights for researchers. The breadth and depth of coverage, and expert evidence-based critique, are impressive. This is an essential reference text for perioperative clinicians, researchers and students.

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In the age of maintaining brain health, the preservation of cognitive well-being, and the increasing awareness of the burden and role of delirium, *The Perioperative Neurocognitive Disorders* presents a clear roadmap to help navigate this complex clinical landscape. Organized in four sections, the book successfully melds four differing, yet interrelated, perspectives. The editors, Roderic Eckenhoff and Niccolò Terrando, have amassed important contributions that span the conceptual basis of cognitive function, the pathophysiology, the symptomatology/diagnosis, and the clinical recommendations for perioperative neurocognitive disorders. As international public health efforts continue to expand and develop ever more effective multi-modal strategies to preserve and maintain personal independence, *The Perioperative Neurocognitive Disorders* provides a key resource for multiple audiences spanning from health care providers to health care policy formulators.

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Contents

Section 4 Clinical Recommendations and Prevention

The plate section (Chapter 13 figures only) is found between pages 148 and 149

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Preface

Introduction, Definitions, and Nomenclature

The occurrence of personality, sensory, and cognitive disturbances after anesthesia and surgery has been recognized for many decades, although the magnitude, duration, and causes have remained a matter of debate. Certainly the transient occurrence of delirium after surgery is well known, and the various forms are reviewed here by Drs. Proekt (Chapter 1) and by Drs. Gabbard, Sieber, and Oh (Chapter 2). The more durable forms of cognitive impairment after surgery have been more enigmatic. In the past two decades, the application of strict neurocognitive testing by research groups has definitively documented impairments lasting from weeks to months, and thus a term was coined: *postoperative cognitive dysfunction* (POCD), a "syndrome" reviewed in depth here by Drs. Nelli, Culley, and Crosby (Chapter 3). Complicating the analysis of POCD has been the fact that a large number of patients may actually have cognitive improvement as a result of enhanced mobility after orthopedic surgery or reduced pain perhaps following cancer resection. Thus, postoperative cognitive improvement (POCI) is reviewed here by Drs. Arias, Sibille, and Price (Chapter 4). Completing Section 1 of this book is the more contentious, but critically important, topic of whether anesthesia and surgery result in a persistent cognitive disorder, such as mild cognitive impairment or dementia, an area discussed in detail by Drs. Schenning and Hogan (Chapter 5).

An interesting aspect of these early "definitive" clinical studies is the strict research definitions for impairment, often reflecting change from preoperative values, a topic reviewed expertly by Dr. Evered (Chapter 11) in the beginning of Section 3. Interestingly, these definitions and criteria were used without any requirement for a subjective complaint. Furthermore, even the research definitions varied, as did the timing of evaluation, and there existed no metric for magnitude. Finally, despite similarity of the cognitive impairments and risk factors (age, education, etc.) to cognitive disorders in the general geriatric community, the terminology was different and not recognized outside of the discipline of anesthesiology. Thus, an interdisciplinary group of international physicians, scientists, and neuropsychologists met several times over a three-year period, with the goal of producing a new clinical nomenclature for the perioperative neurocognitive disorders (PND). This is now released as of October 2018, and meets the goal of aligning the terminology with that of the general geriatric community by starting with the DSM-5 terminology and definitions. Delirium already exists in the DSM-5, but the adoption of the modifier, "postoperative" was encouraged to recognize the very common occurrence of postoperative delirium (POD). Similarly, both mild and major neurocognitive disorder (NCD) (roughly, mild cognitive impairment [MCI] and dementia, respectively) are suggested to include the same modifier if first detected within 12 months of operation. If first detected more than 12 months after surgery, the modifier is dropped as any association with the surgery is difficult to make. Since this nomenclature is intended to be used clinically, it is critical to note that both forms of NCD require a subjective complaint, a large departure from previous studies of POCD. Because surgery represents a distinct point in time, and since it is occasionally associated with prolonged recovery, the period of time between discharge and full apparent physical and physiological recovery could be associated with cognitive

impairment that is transient in nature. The DSM-5 is silent in such cases. Thus a new term was introduced to label cognitive impairment in this period (discharge to 30 days post-operative); delayed neurocognitive recovery (dNCR), with the same requirement for a subjective complaint. A review of the literature suggests that this is the most common form of PND, although it is not clear at the time of this writing whether the occurrence of dNCR is an independent risk factor for the subsequent development of NCD.

Although clues to the underlying causes of cognitive impairment were sought in these early clinical studies (e.g., incidence of intraoperative hypotension, and hypoxemia), little was apparent, and thus the mechanisms awaited discovery through preclinical studies, and area we deal with in Section 2. Initial preclinical work into mechanisms implicated the anesthetic drugs themselves. This made intuitive sense because the target organ of these drugs is the brain, and it seemed plausible that not all effects might be reversible. And indeed, the anesthetic drugs, especially the volatile ones, appeared to interact with neuro-degeneration pathways in a way that should accelerate pathology and presumably the associated cognitive decline. This area is expertly considered in the chapters by Drs. Vlisides and Xie (Chapter 7) and Drs. Powlovich and Zuo (Chapter 8). However, when taken from test-tube and cell culture to intact, wild-type animals, it became less clear that the anesthetic alone was causing significant harm. The models and behavioral paradigms that investigators use to test these hypotheses are varied, results often subtle, and variable, and open to alternate interpretations. Thus Drs. Eckenhoff and Cunningham provide Chapter 6 in Section 2, which deals with the subject of animal studies, their proper conduct, and outcomes to inform the reader of these important issues.

Since our elderly patients clearly have a large incidence of cognitive problems after anesthesia and surgery, and since the animals did not after anesthesia alone, perhaps the surgery itself had the larger cognitive impact. This was plausible as it was already known that activation of the peripheral innate immune response can either be directly transferred to the brain across a leaky blood-brain barrier, or telegraphed to the brain via vagal afferents. Substantial evidence has accrued to support this notion, and is detailed in a chapter by Drs. Alam and Ma (Chapter 9). Finally, since it is clear that comorbidities like diabetes and cardiovascular disease are risk factors for cognitive impairments, we include a chapter in Section 2 by Drs. Maze and Feng (Chapter 10) on the contributions of these conditions, as well as general metabolic condition, to PND.

Are there biomarkers that can help risk-stratify and monitor our older patients? These would be extremely important, not only in individuals to help establish risk, but also in research to enrich study populations for those most at risk, as well as to provide clues for underlying mechanisms. The use of both blood and cerebrospinal fluid (CSF) biomarkers is discussed by Drs. Berger, Smith, and Khan in Chapter 12 of Section 3, and the use of imaging biomarkers is presented by Dr. Ibinson (Chapter 13).

To close this book, we ask what should practitioners of perioperative medicine do about perioperative brain health? First and foremost, the brain remains the one organ system that is not subjected to preoperative testing, despite being the target organ of general anesthetics. Furthermore, it is now clear that preexisting cognitive impairment is the most robust risk factor for postoperative delirium and other forms of PND. In Section 4, Drs. Fahey, Crosby, and Culley (Chapter 14) provide a description of how cognition might be routinely evaluated in an efficient manner, and how this might identify patients at risk, and for subsequent focused care. Second, what should we be telling patients and their families about cognitive changes postoperatively? The topic of informed consent with what is arguably the

most common perioperative complication is dealt with by Mr. Silbert and Dr. Scott in Chapter 15 of Section 4 as well. Finally, are there best practices with respect to the anesthetic approach, drugs, monitoring, and postoperative care to optimize brain health? Drs. Eckenhoff and Terrando (Chapter 16) summarize what "best practices" there are at this point to achieve this goal. It is our sincere hope that this particular chapter will grow substantially in the near future.