A Review of Current Literature of Interest to the Office-Based Anesthesiologist

Mitra VK, Einav S, Thies K-C, Nunnally ME, Gabrielli A, Maccioli GA, Weinberg G, Banerjee A, Ruetzler K, Dobson G, McEvoy M, O'Conner MF. Cardiac arrest in the operating room: resuscitation and management for the anesthesiologist: part 1. *Anesth Analg*. 2018;126:876–888.

and

McEvoy MD, Thies K-C, Einav S, Ruetzler K, Moitra VK, Nunnally ME, Banerjee A, Weinberg G, Gabrielli A, Maccioli GA, Dobson G, O'Conner MF. Cardiac arrest in the operating room: part 2—special situations in the perioperative period. *Anesth Analg*. 2018;126:889–903.

Cardiac arrest in the operating room and procedural areas has a spectrum of causes (eg, hypovolemia, gas embolism, and hyperkalemia) that are not directly reflected in the standard advanced cardiac life support (ACLS) recommendations. Rapid, appropriate evaluation and management of these causes require modification of the traditional algorithms. These events are almost always witnessed, are frequently known, and involve rescuer providers with knowledge of the patient and the procedure. In such a setting, there can be formulation of a differential diagnosis and a direct intervention that treats the likely underlying cause, resulting in concurrent resolution of the crisis. Similarly, periprocedural cardiac arrest (PPCA) can arise from other causes not addressed in the ACLS algorithms (eg, malignant hyperthermia, massive trauma, and local anesthetic toxicity). Formulation of an appropriate differential diagnosis and rapid, targeted interventions are critical for good patient outcomes. There is a growing body of literature describing the incidence, causes, treatment, and outcomes of PPCA. These narrative review articles provide expanded algorithms that incorporate both published evidence and expert opinion to aid the practicing anesthesiologist in addressing these crises.

Comment: These narrative reviews were written to bridge the gap between traditional ACLS, which is targeted toward managing cardiac arrest in the community, and cardiac arrest in the operating room. The spectrum of causes of circulatory crisis and cardiac arrest in surgery may be different than anywhere else inside or outside of the hospital. For example, vagal responses to surgical manipulation, vagotonic anesthetics, anesthesia-induced sympatholysis, and neuraxial

anesthesia are common causes of bradycardia. Hypoxia associated with difficult airway management and pulseless electrical activity from hemorrhagic hypovolemia are common causes of cardiac arrest in the operating room. Part 1 of this 2-part series culminates in a restatement of the ACLS algorithms, augmented with expert anesthesia commentary to account for these and other perioperative scenarios. Part 2 reviews the assessment and management of 8 special, anesthesia-related crises that every anesthesiologist should know: severe anaphylaxis, tension pneumothorax, local anesthetic toxicity, malignant hyperthermia, severe hyperkalemia, hypertensive crisis, trauma-related cardiac arrest, and pulmonary embolism. The information presented represents a combination of recommendations found in the Stanford Emergency Manual, the Harvard Checklist, and other sources. (Summary MA Saxen†)

Jevtovic-Todorovic V. Exposure of developing brain to general anesthesia: what is the animal evidence? *Anesthesiology*. 2018;128:832–839.

and

Davidson AJ, Sun LS. Clinical evidences for any effect of anesthesia on the developing brain. *Anesthesiology*. 2018;128:840–853.

This pair of review articles in the April 2018 issue of *Anesthesiology* are the result of the US Food and Drug Administration (FDA) safety communication concerning the use of general anesthesia in children (available at <https://www.fda.gov/Drugs/DrugSafety/ucm532356.htm>; accessed March 15, 2018). The warning, based upon a wealth of preclinical animal studies and relatively few human studies, stated that “repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women may affect the development of children’s brains.” This pair of review articles provides a current, comprehensive review and update on both the preclinical and clinical evidence underlying this concern. The review by Jevtovic-Todorovic summarizes a large body of preclinical scientific evidence gathered from several mammalian species that demonstrates a potential foundation for concern. The review focuses on nonhuman primates because their brain development is the closest to that of humans in timing of development and complexity. After comparing research in nonhuman

primates to earlier studies in rodents, Jevtovic-Todorovic supports the concern expressed by the FDA warning while noting the relevance of the animal findings remains to be confirmed in humans. The second review, by Davidson and Sun, shows that most, but not all, large population-based studies find evidence for associations between surgery in early childhood and slightly worse subsequent academic achievement or increased risk for a later diagnosis of behavioral disability. In several studies the amount of added risk is very small; however, there is some evidence for greater association with multiple exposures. These results may be consistent with preclinical data; however, the possibility of confounding effects limits these findings as associations, with only weak evidence for causation. There is also strong evidence that brief exposure is not associated with any long-term risk in humans.

Comment: Three separate editorials accompany these 2 important reviews and all offer additional, poignant insights. “The Challenges of Translation” by Karasch¹ discusses the difficulty of translating animal research into clinical medicine, and provides examples where preclinical animal studies yielded sound results, but failed to translate into clinical medicine because the models did not adequately reflect human experience. For example, shortly after the introduction of isoflurane in 1981, studies in animal models predicted isoflurane would cause myocardial ischemia because of its ability to produce coronary vasodilation with accompanying coronary steal. Subsequent widespread use of isoflurane in clinical practice showed no evidence of ischemic toxicity in humans. Likewise, the concern about the potential nephrotoxicity of sevoflurane was based upon studies in rats and weak evidence from one human volunteer study. Controversy ensued and an FDA-mandated label was placed on the product; however, numerous subsequent studies in humans failed to show evidence of renal toxicity. Karasch notes that although concerns about sevoflurane nephrotoxicity have been reduced to a historical footnote, the warnings and restrictions on the mandated label remain.

Contrasting observations are provided by Warner et al (“Anesthesia and Neurodevelopment in Children”)² who note that multiple examples exist in which concerns about the toxicity of a chemical arose from laboratory observations and were later confirmed in children despite the absence of an obvious clinical problem. A well-known example is the toxicity of polycyclic aromatic hydrocarbons, a class of environ-

mental hydrocarbons generated by incomplete combustion. After further development, these authors point out that (a) causal inferences can be made from animal and observational studies in the absence of randomized clinical trials; (b) because of the inherent power, longitudinal cohort studies should be considered to clarify the current ambiguity about anesthetic neurotoxicity in children; and (c) whether initial observations are made in the laboratory or in clinical practice is not germane to the validity and significance of the finding.

The editorial by Culley and Avram (“Young Brain and Anesthesia: Refusal of Anesthesia is Not an Option!”)³ provides considerations for the anesthesiologist who must discuss the risks and benefits of anesthetic procedures with parents of young children and assist them in making informed decisions about the use of general anesthesia. The authors recall anesthesia practice 25 years ago, when surgery was performed on awake or paralyzed infants and children without the benefit of analgesics, sedatives, or anesthetics. This practice was driven by fear that such drugs would increase the risk of adverse surgical outcomes and the belief that infants did not experience pain. These beliefs were subsequently overturned, leading to the current paradigm that recognizes routine use of general anesthetics and analgesics is integral to the humane practice of pediatric anesthesiology. Although there may be risk associated with exposure to general anesthesia, not having surgery or a procedure that requires general anesthesia without adequate anesthesia and analgesia is simply not an option. (Summary MA Saxen†)

Bergese SD, Mestek ML, Kelley SD, McIntyre R, Uribe AA, Sethi R, Watson JN, Addison PS. Multicenter study validating accuracy of a continuous respiratory rate measurement derived from pulse oximetry: a comparison with capnography. *Anesth Analg*. 2017;124:1153–1159.

Monitoring respiratory rate may alert caregivers to changes in clinical condition; however, current approaches to measuring and monitoring respiratory rate limit the ability to provide prompt clinical intervention. In this study, the authors compared photoplethysmogram to capnography to analyze the validity of respiratory rates as determined by an algorithm. The algorithm was incorporated into a commercially available software application that reports respiratory rate continuously from a standard pulse oximeter. This

¹ Karasch ED. The challenges of translation. *Anesthesiology*. 2018;28:693–696.

² Warner DO, Shi Y, Flick RP. Anesthesia and neurodevelopment in children. *Anesthesiology*. 2018;128:700–702.

³ Culley DJ, Avram MJ. Young brain and anesthesia: refusal of anesthesia is not an option! *Anesthesiology*. 2018;128:697–699.

comparison was studied in healthy subjects and patients hospitalized in a low-acuity care setting to obtain regulatory clearance. The authors hypothesized the Nellcor Respiration Rate Software algorithm incorporated into pulse oximetry plethysmogram (Medtronic, Boulder, Colo) would report respiratory rates within 3 breaths per minute of the capnography reference.

Data was collected from 26 volunteer subjects and 53 hospital patients, yielding 243 paired respiratory rate measurements. Overall, 94% of respiratory rate measurements reported were within 3 breaths per minute of the capnography respiration rate reference. Relative to baseline, the respiratory rate varied during the data collection period by 6.2 ± 2.8 breaths per minute, representing a variation of 62.7%. The Pearson product moment coefficient shows a linear correlation between the Medtronic Nellcor Respiration Rate Software and the reference respiratory rate, as $R = 0.92 \pm 0.02$ ($p < .001$).

Comment: The Anesthesia Patient Safety Foundation strongly recommends monitoring ventilation and oxygenation in postoperative patients. Pulse oximetry and capnography are standard methods for monitoring oxygenation and ventilation. Capnography, however, requires careful attention to ensure adequate sampling of the respiratory gases. This may not be possible in the postoperative period where close attention is lacking. Unrecognized hypoventilation during recovery has resulted in death of postoperative patients. Considerable research is being directed to develop a noninvasive monitor to reliably forewarn impending hypoventilation and hypoxia. One of the key requirement of these devices or technologies must be to minimize false-positive alarms, and this has been the major limitation of existing monitors. This study highlights a novel algorithm in pulse oximetry software to determine respiratory rates.

The data in this study demonstrate that Medtronic Nellcor Respiration Rate Software determines respiratory rate reliably when compared to the gold standard method, capnography. However, this study was performed in healthy subjects and patients hospitalized in a low-acuity care setting where the pulse oximeter worked reliably. Even in these carefully selected patients, 12% of the data from plethysmogram was omitted because of artifacts. Additional studies are needed to examine the reliability of this device in postoperative patients where the conditions differ compared to healthy adult patients, such as movement artifact, quality of pulse oximeter waveform in the postoperative period, fluid balance and blood volume status affecting plethysmograms, peripheral vasoconstriction, and other factors. (Summary BS Kodali†)

Matioc A. An anesthesiologist's perspective on the history of basic airway management, the "progressive" era, 1904 to 1960. *Anesthesiology*. 2018;128:254–271.

This paper is the third in a series on the history of basic airway management. The review is comprehensive and well referenced, and will likely be enlightening to even anesthesiology historians. Dentist anesthesiologists trained in the 1970s or earlier will recall being taught some of the ideas in this paper by their mentors who were trained in this era. Several dental innovators are acknowledged, including S.S. White, C.K. Teter, and J.A. Heidbrink.

At the beginning of the 20th century, surgeons perceived general anesthesia, administered by nonspecialized providers, as inadequate and in need of a paradigm shift secondary to long and agitated inhalation inductions, anesthetic agent or pollution, poor muscle relaxation and pain control, nausea, vomiting, anesthetic shock, pneumonia, nephritis, and death. This was especially true as surgery progressed from superficial procedures to more invasive operations and new surgical specialties emerged. A 1960 paper found that the mortality risk associated with anesthesia was 4/10,000 operations.

The most common delivery technique was open drop of an inhalational agent onto a gauze-covered wire frame mask. For a time, endotracheal intubation faced firm opposition from experienced anesthetists and the technique was not expected to become routine. The same was said of positive-pressure inhalation. In 1961 routine intubation was discouraged as just a convenience for the practitioner "too lazy or too unskilled to hold the mask properly."

For many years N_2O was administered without O_2 , a technique that was perceived to be more beneficial than combining the agents, for instance because the limitation of O_2 increased the potency of the anesthetic, hypercapnia stimulated respiration, and lower metabolism during anesthesia required less O_2 . Dentists are mentioned as being the proponents of this technique and were successful because they, like most physicians, were not particularly concerned with cyanosis. Instruction manuals of early gas-oxygen delivery systems endorsed a hypoxic technique (5–10% O_2) and recommended disregarding cyanosis, disseminating the concept of the necessity and safety of cyanosis.

The introduction of intravenous agents (thiopental 1936, curare 1942, succinylcholine 1950) resulted in the transition of anesthesiologists from passive ether administrators to active controllers of vital functions. A 1955 study reported that succinylcholine generated a rapid and deep paralysis and face mask ventilation was "easier than under any other circumstances, except

possibly in the fresh cadaver.” Early studies in muscle relaxation often involved paralyzed volunteers who may or may not have been intubated. Multiple late-1950s papers utilizing such volunteers confirmed that mouth-to-mouth ventilation was superior to mouth-to-nose ventilation and any manual technique. (Summary DA Orr*)

Taenzer AH, Perreard IM, MacKenzie T, McGrath SP. Characteristics of desaturation and respiratory rate in postoperative patients breathing room air versus supplemental oxygen: are they different? *Anesth Analg*. 2018;126:826–832.

Routine monitoring of postoperative patients with pulse oximetry–based surveillance monitoring has been shown to reduce adverse events. However, there is some concern that pulse oximetry is limited in its ability to detect deterioration quickly enough to allow for intervention in patients receiving supplemental oxygen. This study expands on the current limited knowledge of differences in desaturation and respiratory rate characteristics between patients breathing room air and those receiving supplemental oxygen. Sixty-seven patients undergoing overnight recovery from surgery were examined. Thirty-four of the patients received supplemental oxygen and 33 of the patients were maintained on room air. The number of desaturation events, along with the speed and magnitude of desaturation, was compared between the 2 groups. Additionally, nighttime pulse rate, oxygen saturation, respiratory rate, and the transition times from normal oxygen saturation levels to desaturated states were also compared. Desaturation characteristics did not differ between patients receiving supplemental oxygen and breathing room air with regard to speed, depth, or duration of desaturation. Transition time for desaturations to reach low oxygen saturation alarms was not different, and respiratory rate remained in the normal range during these events. These findings suggest that pulse oximetry–based surveillance monitoring for deterioration detection can be used equally effectively for patients on supplemental oxygen and those on room air.

Comment: The authors suggest the desaturation events in these patients was due to pulmonary shunting secondary to atelectasis, explaining why the administration of oxygen did not affect characteristics of desaturation between the groups. The authors also acknowledge the limitations of this study. The sample sizes are small, confounding variables are not controlled, and it would be unethical to allow more prolonged or severe desaturations to be studied. One cannot conclude from this study that supplemental

oxygen in the postop period is a safe or unsafe practice. The study simply demonstrates that pulse oximetry can be used equally effectively to detect deterioration in patients with or without supplemental oxygen. (Summary MA Saxon†)

Daniel L. Orr DDS, MS (Anesth), PhD, JD, MD,
The University of Nevada Las Vegas School of Dental
Medicine,
Las Vegas, Nevada

Mark A Saxon, DDS, PhD,
Indiana Office-Based Anesthesia,
Indiana University School of Dentistry,
Indianapolis, Indiana

Bhavani Shankar Kodali, MD,
Department of Anesthesia,
Brigham and Women’s Hospital,
Harvard Medical School,
Boston, Massachusetts