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

Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Benson J, Newmark RL, Maher CE. Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: a randomized controlled trial of the effect on neuromuscular and clinical recovery. *Anesthesiology*. 2018;128:27–37.

When muscle relaxants are used to facilitate intubation, a significant amount of residual neuromuscular blockade remains when reversal drugs are not administered; however, routine reversal is not a universal practice. While most anesthesiologists routinely reverse neuromuscular blockade if muscular weakness is suspected at the time of extubation, others caution against the routine use of anticholinesterase reversal agents, which have been associated with impaired upper airway and breathing function with increased risk of adverse postoperative respiratory events. Neostigmine has neuromuscular blocking properties when given in the absence of neuromuscular blockade and can induce paradoxical reduction in the train-of-four ratio (TOF ratio). This study tested the hypothesis that TOF ratios in patients receiving neostigmine at the time of postanesthesia care unit admission would not be less than TOF ratios in patients randomly assigned to receive a saline placebo. The authors also tested the hypothesis that the incidence of postextubation adverse respiratory symptoms and muscle weakness would not be increased in the neostigmine group. One hundred twenty patients undergoing general anesthesia received a small dose of rocuronium to facilitate intubation. Ninety patients achieved a TOF ratio of 0.9 to 1.0 and received either neostigmine or saline. Patients were subsequently monitored for muscle strength and postextubation respiratory adverse events. No significant difference in these parameters was noted between the 2 groups, leading the authors to conclude that administration of neostigmine at neuromuscular recovery was not associated with clinical evidence of anticholinesterase-induced muscle weakness.

Comment: This study is accompanied by an editorial (Brull SJ, Naguib M. How to catch unicorns (and other fairytales). *Anesthesiology*. 2018;128:1–3) that discusses long-standing beliefs and misconceptions about the relative risk and benefits of administering muscle relaxants. The editors praise the study by Murphy et al for debunking 4 common myths. First, the study shows no evidence that neostigmine, at a dose of 40 μg/kg, induces signs or symptoms of neuromuscular weakness, contradicting previous reports. Second, it challenges the belief that clinical assessment alone (eg, 5-second head lift) is sufficient to assess adequate muscle recovery and underscores the need for quantitative neuromuscular assessment (TOF ratio). The study also challenged the widely held belief that neuromuscular recovery can be subjectively assessed by watching or feeling the response to TOF stimulation. Finally, the "time elapsed" principle of reversal is debunked. This principle stated that reversal was not necessary if the duration since the last dose of neuromuscular blocking agent was greater than 1 or 2 elimination half-lives, noting that 21% of patients failed to recover to a TOF ratio of 0.9 in 163 minutes after a single dose of 0.3 mg/kg rocuronium. The editorial provides an extensive discussion of the foundation of these myths and adequately shows how the strength of this well-designed, randomized controlled study adequately challenges reports based on weaker observational reports and studies. (M. A. Saxen)

Kim HJ, Shin WJ, Park S, Ahn HS, Oh JH. The sedative effects of the intranasal administration of dexmedetomidine in children undergoing surgeries compared to other sedation methods: a systematic review and meta-analysis. *J Clin Anesth*. 2017;38:33–39.

Dexmedetomidine, a highly selective alpha 2 adrenergic receptor antagonist, has been used effectively as an intravenous and intramuscular sedative with little respiratory depression. This meta-analysis reviewed 11 randomized controlled trials (RCTs) published between January 1, 1987, and December 31, 2014. Dexmedetomidine was administered by the intranasal route, comparing the sedative effect (primary outcome) with that produced by other sedatives (fentanyl, midazolam, ketamine) administered by a variety of routes (nasal, buccal, oral) as well as controls (saline). Although moderate to severe degrees of heterogeneity were found, intranasal dexmedetomidine showed a similar sedative efficacy to intranasal ketamine and intranasal midazolam.

Comment: The authors have indeed assembled and reviewed the existing data; however, the weakness of this review is inherent to all meta-analyses, and the authors have clearly outlined the limitations. Importantly, although these studies were all RCTs, the dosing of dexmedetomidine differed, the duration of time from

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administration to sedation assessment surely differed and is not identified, and importantly, the method of intranasal administration (tuberculin syringe versus atomizer) is not stated. The method of nasal administration, as well as the dosage, could play a large role in sedation outcomes achieved. The atomizer has been shown to produce a better effect. The tuberculin method risks that the patient has uneven distribution in the nares and that the patient coughs or swallows the medication. As dexmedetomidine has negligible bioavailability by the oral route, swallowing the drug would likely cause a minimal effect. Furthermore, comparing the intranasal dexmedetomidine to other sedatives via other routes is not of great value, particularly as there are very few studies using different drugs and routes. Albeit the meta-analysis seems to indicate that dexmedetomidine can be effective when administered intranasally, it is not possible to draw definitive conclusions regarding its comparative efficacy to the other sedatives and routes. This meta-analysis, like all of them, emphasizes the importance of designing and carrying out a well-designed randomized (double blind if possible) controlled study with a large patient sample (single or multi-institution) and well-defined outcomes in as homogenous population as possible. (K. P. Mason)

Litman RS, Griggs SM, Dowling JJ, Riazi S. Malignant hyperthermia susceptibility and related diseases. *Anesthesiology*. 2018;128:159–167.

This commentary summarizes recent advances in understanding the genetics and molecular biology underlying malignant hyperthermia (MH) for the purpose of distinguishing patients who can safely receive volatile agents and succinylcholine from those who should receive a trigger-free anesthetic. Mutations in 3 specific genes account for MH susceptibility in approximately 70% of patients. Three main groups of patients are discussed: those with a family history of genetic predisposition to MH, those with diseases associated with MH susceptibility, and patients with myotonic disorders that are associated with non-MH anesthetic-induced rhabdomyolysis. Phenotypes associated with MH susceptibility are presented as well as a list of diseases associated with non-MH anesthetic-induced rhabdomyolysis. Recommendations are summarized in a table at the end of the article.

Comment: Significant morbidity arising from MH ranges from 25% to 35%, while mortality may be as high as 9.5%. The identification of MH-susceptible individuals remains the mainstay of preventing an MH event. Some long-standing guideposts remain to help clinicians in this effort. For example, MH contracture testing is still considered the gold standard for diagnosing MH and ruling out MH susceptibility. Also, patients with degenerative primary muscle disorders, such as Duchenne syndrome or muscular dystrophy, should not receive succinylcholine or inhaled agents unless indicated for unavoidable clinical reasons. However, clinical practice often presents situations that are less clear, such as the healthy patient who presents with a vague history of a relative who developed hyperthermia in the distant past, for which medical records are not available. Dr Litman's article, along with the accompanying editorial (Larach MG. A primer for diagnosing and managing malignant hyperthermia susceptibility. *Anesthesiology*. 2018;128;8–10) provide a wealth of very practical information, including a description of what type of patient should be managed as MH susceptible, when and where susceptible patients be anesthetized, and a description of the type of anesthesia recommended for MH-susceptible patients. Taken together, these articles provide the anesthesiologist with a comprehensive, evidence-based resource for current understanding and addressing MH susceptibility. (M. A. Saxen)

Gentry KR, Lepere K, Opel DJ. Informed consent in pediatric anesthesiology. *Pediatr Anesth*. 2017;27:1253–1260.

Informed consent for pediatric anesthesia is unique because it is obtained from surrogates (ie, parents) rather than from the patient and sought after parents have authorized the surgical intervention. There are limited data on how pediatric anesthesia informed and consent discussions are conducted. This study examined 97 preanesthesia discussions between 41 different anesthesia providers and parents of children undergoing elective surgery in a tertiary pediatric hospital. Transcripts of the discussions were analyzed to identify 7 elements of informed consent: description of the plan, alternatives, risks, benefits, discussion of uncertainties, assessment of comprehension, and solicitation of decision. This analysis shows most pediatric preanesthesia discussions included $\geq$5 informed consent elements and described the plan, mention risks, and mention benefits. While most providers covered most informed consent elements, the solicitation of agreement to proceed occurred in only 18% of the conversations. Inclusion of the latter 3 consent elements (discussion of uncertainties, assessment of comprehension, and solicitation of agreement) was associated with parental recall of these elements but not understanding.

Comment: To a practicing trial lawyer, the startling information in this article is that in only 18% of the case studies did the conversation regarding "informed

consent" ever proceed to the solicitation of, or an agreement by, the parent regarding the treatment. Stated otherwise, in 82% of the cases, the parents were never asked nor ever gave consent to proceed. And that is the purpose of the communication. Informed consent is a legal doctrine that in the United States can be traced to early 20th-century legal precedence, whereby physicians are held liable for a battery (impermissible touching) if they violate an "individual's fundamental right to decide what is being done with his or her body." The American Medical Association's Code of Ethics has long defined informed consent as communication that results in the patient's authorization or agreement to undergo a specific medical intervention. All 50 states have legislation that requires some level of informed consent. Failure to obtain informed consent can lead to legitimate claims by patients against providers for medical negligence and battery. The conclusions regarding client satisfaction are interesting but irrelevant in the context of meeting the legal obligation to obtain consent. What does it matter that the client appreciated the conversation, was satisfied, and believed he or she received appropriate information if the child is injured during treatment? The finding that most pediatric preanesthesia discussions "include $\geq$5 informed consent elements" is not surprising. There have been studies in other medical disciplines that support the same conclusion. This article is strong support for the argument that these providers fail to obtain permission to perform treatment in most cases and underlines the critical need to develop other methods and tools to get the job done. (S. L. Cohen)

Applebaum JL, Agarkar M, Connis RT, Nickinovich DG, Warner MA. Practice advisory for the prevention of postoperative peripheral neuropathies 2018. *Anesthesiology*. 2018;128:11–26.

This updated report by the American Society of Anesthesiologists Task Force on Prevention of Perioperative Peripheral Neuropathies applies to adult patients undergoing sedation or anesthesia in operating rooms, recovery rooms, intensive care units, outpatient procedural units, and office-based practices. Seven hundred ninety-five citations covering the period between January 1, 1999, through July 31, 2009, were reviewed, resulting in 31 new studies being included in this update. The new literature consisted entirely of observational reports or case reports that found neuropathies occurring in the brachial plexus, ulnar, radial, sciatic, femoral, and peroneal nerves. The new evidence continues to support existing recommendations.

Comment: This report focuses on perioperative positioning of the adult patient, use of protective padding, and avoidance of contact with hard surfaces that may apply direct pressure on susceptible peripheral nerves. It does not address neuropathies that may result from the administration of local anesthetics. While several of the recommendations address patient positions not used in dental office-based anesthesia, many others are relevant, particularly when considering the aging demographic of patients who may present for dental office-based anesthesia. Examples include avoiding flexion of the elbow to decrease the risk of ulnar neuropathy, avoiding extension of the elbow beyond the range that is comfortable during preoperative assessment to avoid median nerve injury, and avoiding the use of automated blood pressure cuffs below the antecubital fossa, when possible. (M. A. Saxen)

Stewart L. Cohen
Trial Lawyer and Senior Partner
Cohen, Placitella & Roth, P.C.
2001 Market Street, Suite 2900
Philadelphia, PA 19103

Keira P. Mason, MD
Associate Professor of Anesthesia
Harvard Medical School
Boston Children's Hospital
Boston, MA

Mark A. Saxen, DDS, PhD
Indiana Office-Based Anesthesia
Indianapolis, IN