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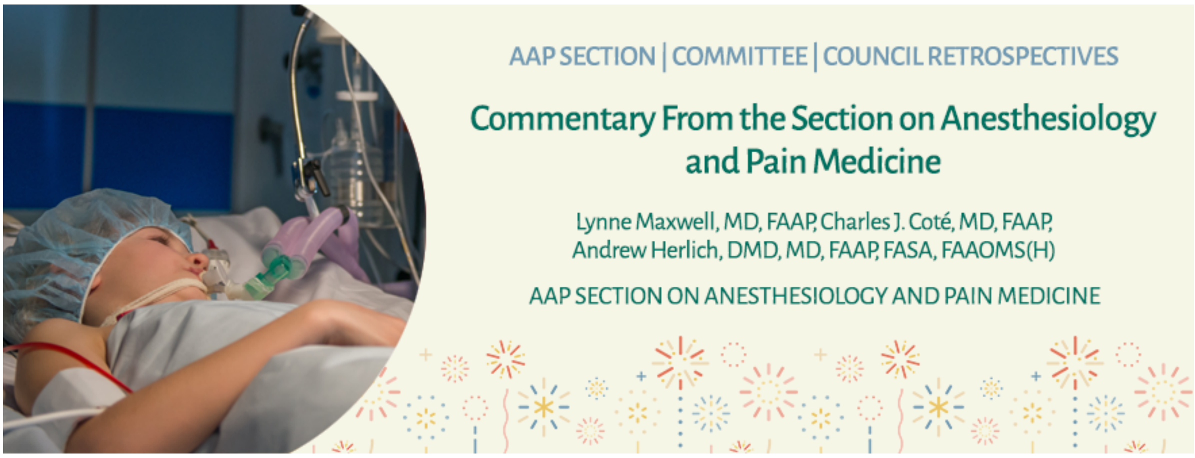

Commentary From the Section on Anesthesiology and Pain Medicine

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Founded in 1965, the American Academy of Pediatrics (AAP) Section on Anesthesiology and Pain Medicine (SOA) and its members are responsible for many of the landmark contributions to the perioperative care of children. The mission of the section is to improve the quality of health care for children and to be the voice of pediatric anesthesia for the pediatric community. The SOA educates pediatricians and other medical and surgical specialists in anesthesia and pain management–related issues as they apply to infants and children. We chose 3 landmark articles that have altered the practice of pediatric anesthesiology. Understanding respiratory distress syndrome shaped our knowledge of developmental pulmonary physiology and mechanics in infants and children. Establishing guidelines for the use of sedation and general anesthesia in pediatric patients represents a monumental achievement in patient safety but also demonstrates collaboration, cooperation, and advocacy between multiple specialties and societies. Advancements in surgery, imaging, and procedures would not be possible without safe sedation and anesthesia, but we owe it to our patients to continue to study ways to improve its safety and “First, do no harm.”

The Relative Effects of Prematurity and Asphyxia on the Development of Neonatal Respiratory Distress Syndrome

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Highlighted Article From *Pediatrics*

- Reynolds EO, Jacobson HN, Motoyama EK, et al. The effect of immaturity and prenatal asphyxia on the lungs and pulmonary function of newborn lambs: the experimental production of respiratory distress. *Pediatrics.* 1965;35(3):382-392

This 1965 paper published in *Pediatrics* was based on one of a remarkable series of animal studies performed in lambs by this group of investigators from Children's Hospital Medical Center (now Boston Children's Hospital), Albert Einstein Hospital (pathology), and Yale (pediatrics). In the same issue, the authors described "the development of the lungs of lambs." [1] These investigations were stimulated by the description of the role of abnormalities in surface tension properties in the lungs of premature infants with hyaline membrane disease described by Avery and Mead in 1959.[2]

Although at the time of this publication, respiratory distress syndrome (RDS) of the newborn had been correlated with prematurity and an associated reduction in surface tension properties of lung extracts, it remained unclear whether and to what extent prenatal asphyxia contributed to the pathogenesis of RDS. To address this question, the investigators designed and meticulously executed an elegant study. They delivered lambs by cesarean section over a range of gestational ages from very premature to full term. Thirteen pregnant ewes from 125 to 154 days of gestation (6 in group A between 125 and 129 days and 7 in group B between 130 to 154 days) were delivered by cesarean section, and the newborn lambs were supported with oxygen and ventilation in an effort to avoid hypoxia, hypercarbia, and acidosis. Twelve pregnant ewes from 131 to 143 days of gestation (6 in group C between 130 and 136 days and 6 in group D between 138 to 143 days) were exposed to 1.5 to 4 hours of hypoxia (by ventilating with reduced FiO_2 gas at low tidal volumes) and then underwent cesarean section delivery. Acidosis of the ewe, fetus, and newborn lamb was ascertained by measurement of carotid artery blood gases. The investigators measured surface tension of lung extracts in all lambs, examined lung histology, and quantitated osmiophilic inclusion bodies, thought at the time to be the source of the substance responsible for the decrease in surface tension.

All 6 of the most premature group A of non-asphyxiated newborn lambs demonstrated the typical findings associated with RDS (histopathology characterized by severe atelectasis, alveolar necrosis, and hyaline membranes; elevated surface tension of lung extracts; and clinical respiratory distress). Four of the 6 lambs in group C subjected to prenatal asphyxia had similar pathology and clinical appearance as the more premature lambs compared to 1 of 4 lambs in group B of similar gestational age. However, only 1 of 6 lambs in group D exhibited these characteristics. From these results, the investigators concluded that asphyxia could increase the likelihood and severity of RDS but that the influence of prematurity on the likelihood of RDS was of greater importance than that of asphyxia.

We chose this article from the first quarter century of *Pediatrics* because (1) it is a seminal publication in the early evolution of knowledge about the pathophysiology of RDS of the newborn, including the role of surfactant; (2) these investigators doggedly pursued these studies to inform advances in pediatrics, neonatology, and anesthesiology; and (3) one of the authors (Etsuro K. Motoyama) went on to contribute greatly to the body of knowledge on pulmonary pathophysiology, modes of ventilation, and lung mechanics in anesthetized and non-anesthetized children. Much of what we know about developmental pulmonary physiology and mechanics in infants and children (both healthy and with co-existing disease, with and without anesthesia), is due to Dr. Motoyama's meticulous and voluminous research, which continues to the present day. [3]

Note: Etsuro K. Motoyama is currently professor emeritus at Children's Hospital Pittsburgh. He was the 2003 recipient of the Robert M. Smith award from the AAP Section on Anesthesia and Pain Medicine.

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Pediatric Anesthesiology 58 Years' Old

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Highlighted Articles From *Pediatrics*

- Committee on Drugs, Section on anesthesiology. Guidelines for the elective use of conscious sedation, deep sedation, and general anesthesia in pediatric patients. *Pediatrics*. 1985;76(2):317-321
- Coté CJ, Karl HW, Notterman DA, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: analysis of medications used for sedation. *Pediatrics*. 2000;106(4):633-644
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- Cravero JP, Blike GT, Beach M, et al. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium. *Pediatrics*. 2006;118(3):1087-1096
- Coté CJ, Wilson S, American Academy of Pediatrics, American Academy of Pediatric Dentistry. Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures. *Pediatrics*. 2019;143(6):e20191000
- Kamat PP, McCracken CE, Simon HK, et al. Trends in outpatient procedural sedation: 2007-2018. *Pediatrics*. 2020;145(5):e20193559

The Section on Anesthesiology and Pain Medicine (SOA; established 1965),[1] has published numerous guidelines regarding perioperative care,[2] pain management,[3] opioid addiction,[4] procedural sedation,[5] etc.[6-8] This commentary focuses on the development of procedural sedation safety guidelines that were requested by AAP leadership after several pediatric deaths occurred during sedation for dental procedures; this request was prescient because this safety issue continues despite AAP initiatives.[9]

The early sedation guidelines (1985[10] and 1992[11]) by SOA recommended practices similar to those for anesthesiology: health evaluation, appropriate fasting, informed consent (at that time it was uncommon to obtain consent for sedation), pulse oximetry,[12,13] a time-based record (vital signs, medications), the need for age- and size-appropriate equipment, no out-of-facility prescriptions (then common for dental and radiologic procedures), and an appropriately staffed recovery area with strict discharge criteria.

Soon thereafter, the Joint Commission (JCAHO) adopted the AAP safety concepts and recommended that anesthesiologists oversee all pediatric and adult sedation. These recommendations were addressed in several American Society of Anesthesiologist's (ASA) guidelines.[14,15] In 2002, an updated AAP guideline unified sedation definitions across the AAP, ASA, and JCAHO.[16] Safety recommendations were based in part on pediatric data (60 deaths) from the FDA adverse drug reporting system (*Pediatrics,* 2000).[17,18] These papers addressed systems issues that had resulted in adverse outcomes from procedural sedation administered by non-anesthesiologists and identified deficiencies in training, inadequate knowledge of sedating medications, and lack of rescue skills as contributory factors (29/60 deaths were dental).

The guideline, in conjunction with the 2006 updated guideline from the American Academy of Pediatric Dentistry (AAPD),[19] strongly recommended that sedation providers maintain advanced pediatric airway skills, measure expired carbon dioxide to assess respirations continuously, be familiar with airway adjuncts (supraglottic devices), participate in continuous quality processes, and use simulation training. The guideline added an acronym for preparing a safe sedation environment (Table 1) and decision algorithms. Near the time of this guideline update, the Pediatric Sedation Research Consortium was formed by Dr. Joseph Cravero, an anesthesiologist, and others (now numbering over 40 institutions). This consortium developed highly efficient sedation services primarily staffed by non-anesthesiologists (hospital medicine, emergency medicine, and critical care physicians). They prospectively collected outcome and safety data based on practices defined in the AAP sedation guideline.[20] In 2020, they published their experience with 432,842 sedation encounters (2007-2018).[21] This report and others confirmed that adhering to the roadmap and safety principles provided by AAP guidelines refined over time provides a safe sedation environment and may obviate the need for an anesthesiologist.[22,23]

In 2016, the AAPD requested guidance regarding expired carbon dioxide measurement during sedation; this additional monitor was *now required for deep sedation*. [20] Shortly before this revision, another tragic event in California had resulted in the death of a 6-year-old due to dental sedation without adequate staff or training for successful rescue. This resulted in an attempt to pass legislation (Caleb's Law).[9] AAP leadership in California, as well as members of our section, testified in support, but failed. Dental providers use assistants who have passed the Dental Anesthesia Assistant Certification Examination (DAANCE)[24] as independent observers. However, DAANCE consists of just 36 hours of internet study and circumvents the AAP guideline recommendations.[25] A joint statement from 4 national organizations condemns this practice: *"The model that the AAOMS continues to embrace does not ensure an appropriately qualified, dedicated monitor who is prepared to meaningfully help in the event of a patient emergency."*[25]

However, looking at the cup as half-full rather than half-empty, AAP leadership encouraged a revised joint AAP/AAPD sedation guideline with new requirements for dental procedures.[5] This new wording completely reversed the single-provider model whereby the operating dentist provides sedation/anesthesia and simultaneously performs the procedure!: "*The independent observer in the dental facility,…must be 1 of the following: a physician anesthesiologist, a certified registered nurse anesthetist, a second oral surgeon, or a dentist anesthesiologist. The second individual, who is the practitioner in the dental facility performing the procedure, must be trained in PALS (or APLS) and capable of providing skilled assistance to the independent observer with the rescue of a child experiencing any…adverse event."*[5]

This long-term AAP safety advocacy goal has been staged on the pages of *Pediatrics* since 1985 and continues into the present. Unfortunately, our safety mission is still incomplete. Even in 2023, SOA and AAP leadership must advocate on a state-by-state basis to change dental practice regulations. We encourage pediatricians to educate families to ask specific questions about the qualifications of the professionals responsible for procedural sedation and whether the monitoring equipment adheres to AAP recommendations.

Table 1 Safety acronym

SOAPME
S = suction
O = oxygen, adequate supply source
A = airway, size appropriate equipment to manage a non-breathing child (tracheal tubes, laryngoscope blades and handle, supraglottic airway adjuncts
P = pharmacy, all drugs needed to support life, reversal agents
M = monitors, pulse oximeter, size-appropriate probes, EKG, non-invasive blood pressure, capnograph
E = equipment, defibrillator, infusion pumps

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Anesthetics and Surgery Impact the Development of a Child: What Should Pediatricians Tell the Parents?

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Highlighted Article From *Pediatrics*

- Flick RP, Katusic SK, Colligan RC at al. Cognitive and behavior outcomes after early exposure to anesthesia and surgery. *Pediatrics.* 2011;128(5):e1053-e1061

Shortly after the turn of the millennium, several publications1[,2] implicated common anesthetic agents as causes of extensive neurodegeneration and apoptosis in both developing and adult rat brains. One specific article found "…widespread neurodegeneration in the developing rat brain and persistent learning deficits."[1] However, animal research does not always translate to findings in humans.

In a 2011 article in *Pediatrics*, Flick and colleagues at the Mayo Clinic proposed that there was a causal relationship between *multiple anesthetics/surgical procedures before age two* and a "…significant risk…" for future development of learning disabilities tracked through age 10. This relationship was independent of health status at the times of surgery. These investigators used 2 separate methods to establish the relationship; previous investigators had employed only a single method.

Leveraging the extensive resources of the Mayo Clinic and the Olmsted Medical Center, the authors revisited a previously established case cohort study of children who had anesthesia/surgery and those who did not have these interventions. The database was inclusive from January 1, 1976, through December 31, 1982. The authors excluded children who had emigrated, had died before age 5, or had demonstrated severe neurodevelopmental delay or cognitive impairment. The health status analyses used the American

Society of Anesthesiologist Physical Status as well as the Johns Hopkins ACG (adjusted clinical groups) System based on *International Classification of Diseases* version 9.

The study patients were entered through age 5 and were assigned by computer to morbidity clusters. After extensive analysis, the authors found that multiple anesthesias/surgical procedures were significantly associated with the later recognition of learning disabilities. They did not find an association with behavioral abnormalities. The authors were concerned that *more than one* exposure (anesthesia and surgery) could have a long-term adverse effect on "…human neurodevelopment…." The authors did detail that halothane was the main anesthetic, so whether the findings extrapolate to current anesthetics such as sevoflurane is unknown. The authors also did not address whether longer durations of anesthesia and surgery increased the risk of learning disabilities.

This was the first study that carefully investigated the effects of anesthetic/surgical exposure in children. This gateway article in *Pediatrics* alerted pediatricians about adverse effects of repetitive general anesthesia exposures in children on learning and behavior. Within 1 year of the landmark article, Ing and colleagues from multiple international centers published a follow-up study in *Pediatrics* that addressed language ability and cognitive function after exposure to anesthesia prior to age 3. The authors found that among their cohort, children exposed to general anesthesia were more likely to have a "…higher relative risk of language and abstract reasoning deficits at age 10 than unexposed children," [2] supporting the conclusions by Flick and colleagues.

This study also raised a number of unsettling questions. Should pediatricians not recommend repeat myringotomy and polyethylene tube insertions? Would their patients develop life-long problems because of the procedures and the associated anesthetics? What recommendations should be made for children who normally would be expected to need multiple procedures under anesthesia, for instance, children with myelomeningocele, osteogenesis imperfecta, or congenital cardiac anomalies? Is it possible to distinguish the effect of the anesthesias/procedures from the effect of the morbidity itself? But in the end, who would not recommend staged correction of a complex craniofacial malformation or a combined bilateral cleft lip and cleft palate?

Fortunately, we are likely to read future publications in *Pediatrics* that will provide greater insight into these issues. With their seminal report, Flick and colleagues charted an initial course for this challenging line of investigation, but it will require much more sophisticated work to bring it to fruition.

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